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## Original Article

# Association between house renovation during pregnancy and wheezing in the first year of life: The Japan environment and children's study

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VOCs, volatile organic compounds;

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interval; RS virus, respiratory syncytial

virus; SES, socioeconomic status; Th, T-

helper; IL, interleukin

## ABSTRACT

**Background:** Wheezing is a common symptom in infants, which may occasionally develop into asthma. There are many factors related to infant wheezing, including anatomical features, viral infections, and passive smoking. There are only a few reports on the association between renovation and pregnancy worldwide, and reports on this association are inadequate in Japan. This study aimed to examine the association between house renovation and new construction during pregnancy and wheezing in infants during the first year of life using data from the Japan Environment and Children's Study (JECS).

**Methods:** Data of pregnant women registered in JECS were collected using self-administered questionnaires during the second/third trimester and 1 month after delivery. Childbirth records were completed by the doctors. Similarly, wheezing in infants was evaluated using self-administered questionnaires 1 year after birth. Logistic regression analysis was used to determine the primary outcome.

**Results:** In total, 75,731 infants, excluding those with unknown gender, who were not singleton infants, and who relocated during pregnancy and the first month of life, were examined in this study. Renovation during pregnancy increased the prevalence of wheezing (odds ratio [OR]: 1.33, 95% confidence interval [CI]: 1.20–1.48) and recurrent wheezing (OR: 1.22, 95% CI: 1.00–1.48) in the first year of life. The relationship between new construction during pregnancy and wheezing in infants was insignificant (OR: 0.98, 95% CI: 0.90–1.06).

**Conclusions:** Renovation during pregnancy may be a risk factor for wheezing in infants, and should be avoided.

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## Introduction

The airway of infants has a narrower inner diameter, less elasticity, and less muscle smoothness than that of adults. In addition, infants usually secrete significant amounts of mucus, and their ciliated epithelium is not well developed. These anatomical and physiological features predispose infants to wheezing. Other

factors, such as viral infections and passive smoking, are also known risk factors for infant wheezing.<sup>1</sup> Furthermore, in some infants, wheezing may develop into asthma.<sup>2</sup> Several environmental factors and chemical substance exposures during pregnancy have been reported to increase the risk of wheezing during infancy and asthma later in life. These include exposure to smoking,<sup>3,4</sup> agricultural chemicals,<sup>5</sup> and air pollution.<sup>6</sup> However, the factors influencing infant wheezing during pregnancy remain unclear.

Recently, house renovation has been reported to be related to wheezing or asthma in childhood<sup>7–9</sup> and obstructive bronchitis in infants with atopy risk.<sup>10</sup> Although the chemicals released from building materials have been suspected to be the causative agent, there are only a few reports on the association between house renovation during pregnancy and wheezing in infants, and they

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suggested that renovation during pregnancy may become a risk factor for wheezing in infants.<sup>11,12</sup> Moreover, studies assessing the relationship of new construction during pregnancy and infant wheezing are lacking. In addition, there are regional differences in construction methods, materials, and laws; however, there are no studies on the relationship between renovation and new construction during pregnancy and infant wheezing in Japan.

The Japan Environment and Children's Study (JECS) is a large-scale nationwide, multicenter, prospective birth cohort study that commenced in January 2011. The JECS has been implemented as a national project funded by the "Ministry of Environment, Japan". Its main objective is to elucidate the environmental factors affecting children's health and development.

Therefore, this study, the largest of its kind, aimed to examine the association between renovation or new construction during pregnancy and wheezing in infants using data from JECS.

## Methods

### Study design and participants

The JECS has 15 Regional Centers in Japan.<sup>13</sup> Pregnant women, in their first trimester, who visited a maternity hospital in the Regional Centers of and related to the centers of JECS, or the reception counter of a municipality office, to get a Maternal and Child Health Handbook provided by local public organizations were recruited in this cohort study between January 2011 and March 2014. After registration, the data of pregnant women were collected using self-administered questionnaires during the first and second/third trimester and 1 month after delivery.<sup>14,15</sup> Delivery information, such as the delivery method, gestational age, and sex, was completed by doctors, midwives, nurses, and/or research coordinators. The data for children were collected 1 month, 6 months, and 1 year after delivery using self-administered questionnaires.

Data for this study were extracted from the dataset released in March 2018 (dataset jecs-an-20180131).

### Questionnaires

Data on the method of delivery (vaginal or cesarean), term of delivery status (preterm was considered <37 weeks), birth status (live or stillborn), singleton/multiple birth status, and sex (boy, girl, unknown gender) were obtained from personal medical record transcripts at the time of delivery.

Smoking habits during pregnancy of mother and father, allergy, and medical history of pregnant women were obtained from the questionnaires during registration. Information on their educational background, whether renovation was being conducted, and the number of years they lived in the present house, presence of mold in the room was collected via questionnaires administered during the second/third trimester. Information about passive smoking of infant was collected from a questionnaire provided after 1 months of infant's birth. Information on the presence of siblings and/or pets was collected from a questionnaire provided after 6 months of infant's birth. Information about the infants' allergic diseases (food allergy and atopic dermatitis), wheezing, history of infectious diseases (respiratory syncytial [RS] virus infection, lower respiratory inflammation, upper respiratory inflammation, otitis media), nursery admission, and lactation status was obtained from questionnaires completed 1 year after birth. Complete breastfeeding was defined only as breastfeeding until 6 months of age without using bottle-feeding, in the questionnaire completed 1 year after birth.

Detailed questions for pregnant women were as follows: active smoking and passive smoking from husband during pregnancy

were measured on a 4-point scale: 1 = never; 2 = previously did but quit before finding out about the current pregnancy; 3 = previously did but quit after finding out about the current pregnancy; 4 = Yes, I still smoke. In this study, only "4 = Yes, I still smoke" was defined as smoking during pregnancy. For allergic diseases, the presence of bronchial asthma, allergic rhinitis/pollinosis, atopic dermatitis, food allergy, and allergic conjunctivitis was checked. Similarly, sick building syndrome and multiple chemical sensitivity syndrome were examined. The mothers' medical histories were confirmed via self-report for diseases that were diagnosed by the doctor. The socioeconomic status (SES) was evaluated based on the maternal educational background (Low SES: Final education was junior or senior high school; High SES: An educational level higher than low SES). The age of the house/apartment (building) was recorded using the following categories: 1 = less than 1 year; 2 = 1 year or more and less than 3 years; 3 = 3 years or more and less than 5 years; 4 = 5 years or more and less than 10 years; 5 = 10 years or more and less than 20 years; 6 = 20 years or more; 7 = unknown. New construction was defined as a project aged less than 1 year. Similarly, the questionnaire noted whether the house renovation/interior finishing was completed after getting pregnant, with the response dichotomized as 1 = yes or 2 = no. Ask the following questions about the presence of mold in the house: Mold growing somewhere in the house 1 = Yes, 2 = No. Additionally, a questionnaire about relocation from residence during pregnancy and passive smoke in newborns provided after 1 months of infant's birth as follows. Moving after filling the questionnaire of second/third trimester, recorded as: 1 = yes, 2 = no. Family members' smoking after the baby was born 1 = No one smoked, 2 = Somebody smoked but not in the presence of the baby, 3 = Somebody smoked in the presence of the baby. We defined only "1 = No one smoked" as no passive smoking.

The child's medical histories were confirmed doctor's diagnosis with mother.

### Evaluation of wheezing in infants

The questionnaire included questions on the occurrence of wheezing in the first year of life. If this was the case, mothers were equally asked about the number of wheezing attacks with the following responses to choose from: 0, 1–3, and  $\geq 4$ . This questionnaire was a modified International Study of Asthma and Allergies in Childhood questionnaire for children aged 6–7 years with translation validation in Japanese.<sup>16–18</sup> In this study, if wheezing was indicated, regardless of the number of times, the case was classified as an infant with wheezing. Four or more episodes of wheezing were defined as recurrent wheezing.

### Statistical analysis

All statistical analyses were performed using SAS ver.9.4 (SAS Institute, Cary, NC, USA). The characteristics and presence of renovation were compared between participants with and without wheezing. A logistic regression model was used to calculate adjusted odds ratios (OR) and their 95% confidence intervals (CI) for the association between augmentation and infant wheezing during pregnancy. The covariates in the model were pre-selected based on previously published literature and biological validity. In the logistic regression analysis, the mother's history of allergic disease was defined as at least one of the following: atopic dermatitis, allergic conjunctivitis, food allergy, allergic rhinitis/pollinosis, and asthma. The medical history of respiratory infection of children was defined using at least one of the following conditions: upper respiratory inflammation, lower respiratory tract inflammation, RS virus infection, and otitis media. A history of the mother's allergy,

sick building syndrome, chemical hypersensitivity, SES, active smoking during pregnancy, passive smoking during pregnancy housing a pet, presence of mold in the house, presence of siblings, admission to nursery at 1-year, exclusive breastfeeding, preterm birth, cesarean section, children's history of respiratory infection, children's food allergy, passive smoking in children, and history of atopic dermatitis were treated as covariates.

Similarly, we stratified the history of respiratory infections in infants and their mothers' allergic diseases and examined the relationship between renovation or new construction and wheezing.

### Ethics

The JECS protocol was approved by the Institutional Review Board on the epidemiological study of the Ministry of the Environmental Health and Ethics Committees of all participating

institutions. Written informed consent was obtained from all participants.

### Results

The JECS collected data of 103,062 pregnancies, 104,065 fetuses, and 100,144 live births. In total, 1889 multiple births and 11 unknown gender were excluded. Furthermore, 6043 participants who relocated during the second/third trimester and 1 month of delivery were excluded from this study. The exclusion criteria were applied because it was unclear how long the subjects lived in the renovated or newly built house during pregnancy. Infants and mothers who relocated after one year old were included in this study.

In total, 16,830 records were excluded owing to unsuccessful follow-ups or insufficient answers. Finally, 75,731 were included in this study (Fig. 1).

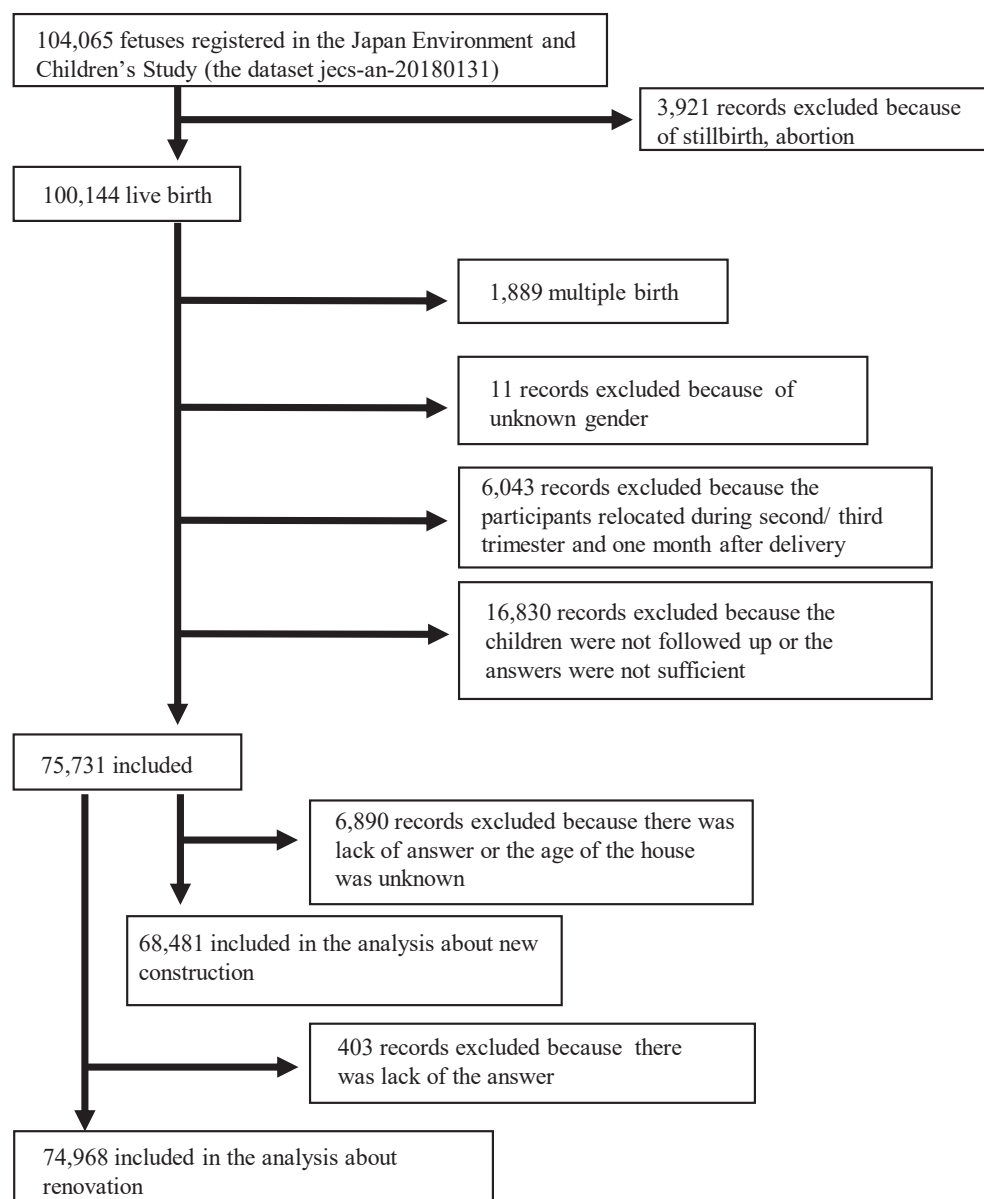


Fig. 1. Flowchart of participants.

The clinical characteristics of the study population and the proportion of wheezing infants during the first year of life are shown in Table 1. Of the 74,968 participants, 2341 had their houses renovated during pregnancy (infants without wheezing, 1796; with wheezing, 545), and 72,627 did not have their houses renovated during pregnancy (infants without wheezing, 58,631; with wheezing, 13,996).

**Table 1**  
Characteristics of participants with or without wheezing.

| N = 75,371                                  |       | Without wheezing (%)<br>N = 60,753 | With wheezing (%)<br>N = 14,618 | P value |
|---------------------------------------------|-------|------------------------------------|---------------------------------|---------|
| Sex                                         |       |                                    |                                 |         |
|                                             | Boys  | 29,989 (77.7)                      | 8615 (22.3)                     | <0.001  |
|                                             | Girls | 30,764 (83.7)                      | 6003 (16.3)                     |         |
| Mothers' medical history                    |       |                                    |                                 |         |
| Atopic dermatitis                           | (-)   | 51,345 (81.0)                      | 12,081 (19.0)                   | <0.001  |
|                                             | (+)   | 9408 (78.8)                        | 2537 (21.2)                     |         |
| Allergic conjunctivitis                     | (-)   | 54,882 (81.1)                      | 12,791 (18.9)                   | <0.001  |
|                                             | (+)   | 5871 (76.3)                        | 1827 (23.7)                     |         |
| Food allergy                                | (-)   | 58,034 (80.8)                      | 13,766 (19.2)                   | <0.001  |
|                                             | (+)   | 2719 (76.1)                        | 852 (23.9)                      |         |
| Allergic rhinitis/pollinosis                | (-)   | 39,044 (81.7)                      | 8734 (18.3)                     | <0.001  |
|                                             | (+)   | 21,709 (78.7)                      | 5884 (21.3)                     |         |
| Asthma                                      | (-)   | 55,074 (81.8)                      | 12,234 (18.2)                   | <0.001  |
|                                             | (+)   | 5679 (70.4)                        | 2384 (29.6)                     |         |
| Mothers' characteristics                    |       |                                    |                                 |         |
| Sick building syndrome                      | (-)   | 60,568 (80.6)                      | 14,562 (19.4)                   | 0.131   |
|                                             | (+)   | 185 (76.8)                         | 56 (23.2)                       |         |
| Chemical hypersensitivity                   | (-)   | 60,670 (80.6)                      | 14,593 (19.4)                   | 0.324   |
|                                             | (+)   | 83 (76.9)                          | 25 (23.1)                       |         |
| Socioeconomic status                        | low   | 20,415 (79.3)                      | 5314 (20.7)                     | <0.001  |
|                                             | high  | 40,338 (81.3)                      | 9304 (18.7)                     |         |
| Mothers' chemical exposure during pregnancy |       |                                    |                                 |         |
| Active smoking                              | (-)   | 58,747 (81.0)                      | 13,775 (19.0)                   | <0.001  |
|                                             | (+)   | 2006 (70.4)                        | 843 (29.6)                      |         |
| Passive smoking from husband                | (-)   | 34,090 (82.4)                      | 7288 (17.6)                     | <0.001  |
|                                             | (+)   | 26,663 (78.4)                      | 7330 (21.6)                     |         |
| Renovation <sup>†</sup>                     | (-)   | 58,631 (80.7)                      | 13,996 (19.3)                   | <0.001  |
|                                             | (+)   | 1796 (76.7)                        | 545 (23.3)                      |         |
| New construction <sup>‡</sup>               | (-)   | 51,660 (80.6)                      | 12,430 (19.4)                   | 0.007   |
|                                             | (+)   | 3612 (82.3)                        | 779 (17.7)                      |         |
| Environment of the children                 |       |                                    |                                 |         |
| Housing a pet                               | (-)   | 46,121 (80.8)                      | 10,993 (19.2)                   | 0.071   |
|                                             | (+)   | 14,632 (80.1)                      | 3625 (19.9)                     |         |
| Siblings                                    | (-)   | 27,267 (86.0)                      | 4440 (14.0)                     | <0.001  |
|                                             | (+)   | 33,486 (76.7)                      | 10,178 (23.3)                   |         |
| Going to nursery at one year old            | (-)   | 47,235 (85.5)                      | 8001 (14.5)                     | <0.001  |
|                                             | (+)   | 13,518 (67.1)                      | 6617 (32.9)                     |         |
| Exclusive breast feeding                    | (-)   | 35,729 (79.4)                      | 9252 (20.6)                     | <0.001  |
|                                             | (+)   | 25,024 (82.3)                      | 5366 (17.7)                     |         |
| Passive smoking at home                     | (-)   | 30,748 (82.7)                      | 6438 (17.3)                     | <0.001  |
|                                             | (+)   | 30,005 (78.6)                      | 8180 (21.4)                     |         |
| Mold in the house                           | (-)   | 22,785 (82.7)                      | 4783 (17.3)                     | <0.001  |
|                                             | (+)   | 37,968 (79.4)                      | 9835 (20.6)                     |         |
| Birth history                               |       |                                    |                                 |         |
| Preterm birth                               | (-)   | 58,239 (80.8)                      | 13,875 (19.2)                   | <0.001  |
|                                             | (+)   | 2514 (77.2)                        | 743 (22.8)                      |         |
| Caesarean section                           | (-)   | 49,561 (80.7)                      | 11,849 (19.3)                   | 0.146   |
|                                             | (+)   | 11,192 (80.2)                      | 2769 (19.8)                     |         |
| Medical history of children                 |       |                                    |                                 |         |
| RSV infection                               | (-)   | 57,163 (84.1)                      | 10,805 (15.9)                   | <0.001  |
|                                             | (+)   | 3590 (48.5)                        | 3813 (51.5)                     |         |
| Lower respiratory inflammation              | (-)   | 59,152 (83.6)                      | 11,573 (16.4)                   | <0.001  |
|                                             | (+)   | 1601 (34.5)                        | 3045 (65.5)                     |         |
| Upper respiratory inflammation              | (-)   | 48,157 (83.3)                      | 9638 (16.7)                     | <0.001  |
|                                             | (+)   | 12,596 (71.7)                      | 4980 (28.3)                     |         |
| Otitis media                                | (-)   | 54,922 (82.3)                      | 11,783 (17.7)                   | <0.001  |
|                                             | (+)   | 5831 (67.3)                        | 2835 (32.7)                     |         |
| Atopic dermatitis                           | (-)   | 49,886 (81.3)                      | 11,460 (18.7)                   | <0.001  |
|                                             | (+)   | 10,867 (77.5)                      | 3158 (22.5)                     |         |
| Food allergy                                | (-)   | 57,015 (81.0)                      | 13,340 (19.0)                   | <0.001  |
|                                             | (+)   | 3738 (74.5)                        | 1278 (25.5)                     |         |

<sup>†</sup> 403 were excluded because of lack of the answers.

<sup>‡</sup> 6890 were excluded because of lack of the answers.

The prevalence of wheezing was 23.3% (545/2341) and 19.3% (13,996/72,627) in the group who had and did not have their houses renovated during pregnancy, respectively. The logistic regression analysis revealed that renovation during pregnancy increased the prevalence of wheezing in the first year of life (OR: 1.33, 95% CI: 1.20–1.48) and similar tendency was seen with recurrent wheezing (OR: 1.22, 95% CI: 1.00–1.48) (Table 2). The relationship between new construction during pregnancy and wheezing in infants was not significant (OR: 0.98, 95% CI: 0.90–1.06) (Table 2). Stratified analysis based on the mothers' medical history of allergic diseases revealed that renovation during pregnancy was a risk factor for wheezing in both groups (OR: 1.25, 95% CI: 1.08–1.44, presence of mothers' allergy and OR: 1.44, 95% CI: 1.23–1.68, absence of mothers' allergy) and recurrent wheezing in the absence of mothers' allergy group (OR: 1.39, 95% CI: 1.03–1.86) (Table 3). Stratified analysis based on the medical history of respiratory infections at 1 year of age revealed that renovation during pregnancy was a risk factor for wheezing in infants of both groups (OR: 1.18, 95% CI: 1.02–1.36, presence of children's respiratory infection and OR: 1.51, 95% CI: 1.30–1.75, absence of children's respiratory infection) and recurrent wheezing in the absence of children's respiratory infection group (OR: 1.57, 95% CI: 1.16–2.12) (Table 4). The relationship between new construction and wheezing was not significant in any stratified analysis (Table 3, 4).

## Discussion

The prevalence of wheezing disorders and asthma in childhood has increased substantially over recent decades.<sup>19</sup> Wheezing is common in infancy and is influenced by various factors; it may develop into asthma in some infants.<sup>20</sup> Asthma is considered a heterogeneous disease,<sup>21</sup> and various factors, such as family history,<sup>22</sup> genetic influence,<sup>23</sup> perennial allergen sensitization,<sup>24</sup> viral infections,<sup>25</sup> and tobacco smoking,<sup>26</sup> are speculated to be involved in its onset. In addition, our study showed that various factors, such as sex, smoking during pregnancy, history of mothers' allergy, and viral infection in children, affected wheezing at 1 year of age (Table 1). However, the rapid increase in the incidence of asthma in recent years cannot be solely explained by individual factors, and lifestyle and environmental changes might have a considerable influence. This large-scale nationwide, multicenter, prospective birth cohort study showed that house renovation during pregnancy is a risk factor for wheezing.

Urban residents spend 87% of their day indoors.<sup>27</sup> In particular, pregnant women and infants in urban areas may tend to spend a considerable amount of time indoors. Some changes in the living

**Table 2**

Multivariate logistic regression analysis for wheezing and recurrent wheezing in renovation or new construction.

|                               | Wheezing <sup>†</sup> |         | Recurrent wheezing |         |
|-------------------------------|-----------------------|---------|--------------------|---------|
|                               | OR (95% CI)           | P value | OR (95% CI)        | P value |
| Renovation (n = 74,968)       | 1.33 (1.20–1.48)      | <0.001  | 1.22 (1.00–1.48)   | 0.051   |
| New construction (n = 68,481) | 0.98 (0.90–1.06)      | 0.577   | 1.04 (0.88–1.23)   | 0.643   |

OR, odds ratio; CI, confidence interval.

Model was adjusted for allergic medical history, sick building syndrome, chemical hypersensitivity, active smoking during pregnancy, passive smoking from husband and during pregnancy, mold in the house, housing a pet and socioeconomic status on mothers and sex, presence of siblings, admission to nursery at 1 year, exclusive breast feeding, preterm birth, caesarean section, respiratory infection, passive smoking at home, atopic dermatitis and food allergy on children.

<sup>†</sup> Including recurrent wheezing.

**Table 3**

Multivariate logistic regression analysis for wheezing and recurrent wheezing by presence or absence of mothers' allergic diseases.

|                                   |                      | Wheezing <sup>†</sup> |         | Recurrent wheezing |         |
|-----------------------------------|----------------------|-----------------------|---------|--------------------|---------|
|                                   |                      | OR (95% CI)           | P value | OR (95% CI)        | P value |
| Renovation Mothers' allergy       | Present (n = 37,752) | 1.25 (1.08–1.44)      | 0.002   | 1.10 (0.85–1.44)   | 0.467   |
|                                   | Absent (n = 37,216)  | 1.44 (1.23–1.68)      | <0.001  | 1.39 (1.03–1.86)   | 0.03    |
| New construction Mothers' allergy | Present (n = 34,758) | 0.93 (0.83–1.05)      | 0.229   | 1.03 (0.83–1.28)   | 0.798   |
|                                   | Absent (n = 33,723)  | 1.03 (0.91–1.18)      | 0.608   | 1.05 (0.81–1.37)   | 0.701   |

OR, odds ratio; CI, confidence interval.

Model was adjusted for sick building syndrome, chemical hypersensitivity, active smoking during pregnancy, passive smoking from husband and during pregnancy, mold in the house, housing a pet, and socioeconomic status on mothers and sex, presence of siblings, admission to nursery at 1 year, exclusive breast feeding, preterm birth, caesarean section, respiratory infection, passive smoking at home, atopic dermatitis and food allergy on children.

<sup>†</sup> Including recurrent wheezing.

environment due to renovation works during pregnancy may affect wheezing in infancy.

In analyses of associations between renovation and asthma in children, most studies revealed positive associations for asthma or asthmatic symptoms.<sup>8,9</sup> A cross-sectional survey of 31,049 children aged 2–14 years performed in China showed that house renovation in the past 2 years was significantly associated with cough, phlegm, current wheeze, doctor-diagnosed asthma, and current asthma.<sup>7</sup> Renovation during the first two years of life had a significant influence on the appearance of obstructive bronchitis in the first (OR: 4.1 95% CI: 1.4–11.9) and second year of life.<sup>10</sup>

However, there are a few reports on the association between house renovation during pregnancy and wheezing in infants. In the "LINA birth cohort study" conducted in Leipzig on 622 expecting mothers, the data revealed that floor covering during pregnancy

contributed to an increased risk of physician-treated wheezing during the first 12 months after birth, particularly in infants with an atopic predisposition.<sup>11</sup> In China, a retrospective cohort study was performed, and 40,010 children aged 3–6 years were recruited to collect data on the health status, home renovation, and addition of new furniture within 1 year before pregnancy, during pregnancy, at the age of 0–1 year, and after the age of 1 year. Those authors confirmed that renovation and adding new furniture during early childhood and pregnancy could be risk factors for childhood asthma.<sup>12</sup>

Previous reports on the association between renovation and wheezing indicated the effects of volatile organic compounds (VOCs), which are volatile substances, such as formaldehyde, used in building materials such as paints and adhesives. Renovation can increase the emission of VOCs. According to a study using a self-administered questionnaire on symptoms and indoor exposure (including indoor painting during the last 12 months), exposure to chemical emissions from indoor paint in adults was related to asthma, and it indicated that some VOCs may cause airway inflammation.<sup>28</sup> Similarly, semi-volatile organic compounds (SVOCs), such as di-(2-ethylhexyl) phthalate and tributyl phosphate, are equally used in building materials and have been reported to be risk factors for wheezing and asthma.<sup>29,30</sup>

It is difficult to determine whether the association between renovation during pregnancy and wheezing results from the direct exposure of pregnant women or residual substance effects on the children after birth. It has been reported that VOCs remain for about 8 weeks after renovation.<sup>31</sup> Therefore, it is unlikely that renovation VOCs during pregnancy will affect postnatal children. Meanwhile, SVOCs are non-volatile, remain in the environment for a relatively long time, and may have an effect both during pregnancy and after birth.

In the "LINA birth cohort study" mentioned earlier, blood samples of mothers during pregnancy and cord blood samples were analyzed for concentrations of T-helper (Th)1/Th2 cytokines, Interleukin (IL)-4, IL-5, IL-13.<sup>32</sup> The findings revealed that neonates affected by renovation activities during pregnancy had significantly higher concentrations of IL-4, IL-5, and IL-13 in their cord blood. This suggests a Th2 predominant response. Moreover, renovation during pregnancy may affect the immune status of the newborn and cause allergic diseases.<sup>32</sup> IL-4, IL-5, and IL-13 are known to be associated with asthma.<sup>33</sup> Furthermore, in animal models, elevation in IL-4 and IL-5 and airway inflammation were observed in mice exposed to VOCs released from flooring.<sup>34</sup>

In our study, new construction during pregnancy did not contribute to the OR in infant wheezing. However, the reason for this result is unclear. New construction may have confounding factors that reduce the risk of building materials, such as VOCs and SVOCs. For example, the ventilation status and building materials may contribute to the reduction of the risk factors.

Mothers' history of allergic diseases and children's respiratory infections are already known risk factors for wheezing and asthma.<sup>22,25</sup> The most important result of this study is that, even in cases wherein these risk factors were not present, renovation during pregnancy increased the frequency of wheezing in infants. Therefore, it is better to avoid renovation during pregnancy, regardless of the mother's allergic status.

The strength of this paper was the large sample size. Besides, the questionnaire used in this study was not exclusively designed for allergic diseases. Therefore, selection bias on allergic diseases at the time of enrollment was expected to be low.

One of the limitations of this study was that the diagnosis of wheezing was obtained via a self-administered questionnaire from mothers, 1 year after birth, and details of wheezing, including the severity, were unclear. In addition, we could not include in the

**Table 4**

Multivariate logistic regression analysis for wheezing and recurrent wheezing by presence or absence of children's respiratory infections.

|                                                   |                      | Wheezing <sup>†</sup> |         | Recurrent wheezing |         |
|---------------------------------------------------|----------------------|-----------------------|---------|--------------------|---------|
|                                                   |                      | OR (95% CI)           | P value | OR (95% CI)        | P value |
| Renovation Children's respiratory infection       | Present (n = 28,152) | 1.18 (1.02–1.36)      | 0.023   | 1.04 (0.80–1.34)   | 0.779   |
|                                                   | Absent (n = 46,816)  | 1.51 (1.30–1.75)      | <0.001  | 1.57 (1.16–2.12)   | 0.003   |
| New construction Children's respiratory infection | Present (n = 25,900) | 0.99 (0.89–1.11)      | 0.471   | 1.06 (0.86–1.30)   | 0.611   |
|                                                   | Absent (n = 42,581)  | 0.96 (0.84–1.09)      | 0.506   | 1.01 (0.76–1.34)   | 0.933   |

OR, odds ratio; CI, confidence interval.

Model was adjusted for allergic medical history, sick building syndrome, chemical hypersensitivity, active smoking during pregnancy, passive smoking from husband and during pregnancy, mold in the house, housing a pet and socioeconomic status on mothers and sex, presence of siblings, admission to nursery at 1 year, exclusive breast feeding, preterm birth, caesarean section, passive smoking at home, atopic dermatitis and food allergy on children.

<sup>†</sup> Including recurrent wheezing.

analysis, details of renovation such as materials, construction method, the scale and place, the actual period spent in their own home during pregnancy, the exact timing of the renovation, and data of chemical concentration for such as VOCs in indoor environments.

Future studies are needed to analyze whether renovation during pregnancy increases the risk of not only wheezing but also asthma, which should be more objectively assessed. Furthermore, we need to investigate in more detail what factor of renovation during pregnancy increases the frequency of wheezing.

In conclusion, renovation during pregnancy may be a risk factor for wheezing in infants. These findings are important not only for individuals who are already exposed to certain risk factors but also every pregnant woman. The relationship between new construction and wheezing in infancy has not been ascertained. Therefore, further research should be performed to investigate which environmental factors in renovation impact wheezing in infants. The findings of such research may lead to the discovery of one of the preventions of asthma.

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## Conflict of interest

The authors have no conflict of interest to declare.

## Authors' contributions

TF designed the study, collected the data, performed the statistical analysis, interpreted the data, and wrote the manuscript. HH performed the statistical analysis and interpreted the data. MO designed the study, interpreted the data, and wrote the manuscript. MSa, TU, YTan, NT, MSh, and YTak interpreted the data, and critically reviewed the manuscript. All authors approved the final version of the manuscript.

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