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1 **Exposure to house dust phthalates in relation to asthma and allergies in both children and**
2 **adults**

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1 **Abstract**

2 Although an association between exposure to phthalates in house dust and childhood asthma
3 or allergies has been reported in recent years, there have been no reports of these associations
4 focusing on both adults and children. We aimed to investigate the relationships between phthalate
5 levels in Japanese dwellings and the prevalence of asthma and allergies in both children and adult
6 inhabitants in a cross-sectional study. The levels of seven phthalates in floor dust and multi-
7 surface dust in 156 single-family homes were measured. According to a self-reported
8 questionnaire, the prevalence of bronchial asthma, allergic rhinitis, allergic conjunctivitis, and
9 atopic dermatitis in the 2 years preceding the study was 4.7%, 18.6%, 7.6%, and 10.3%,
10 respectively. After evaluating the interaction effects of age and exposure categories with
11 generalized liner mixed models, interaction effects were obtained for DiNP and bronchial asthma
12 in adults ($P_{\text{interaction}}=0.028$) and for DMP and allergic rhinitis in children ($P_{\text{interaction}}=0.015$).
13 Although not statistically significant, children had higher ORs of allergic rhinitis for DiNP,
14 allergic conjunctivitis for DEHP, and atopic dermatitis for DiBP and BBzP than adults, and liner
15 associations were observed ($P_{\text{trend}} < 0.05$). On the other hand, adults had a higher OR for atopic
16 dermatitis and DEHP compared to children. No significant associations were found in phthalates
17 levels collected from multi-surfaces. This study suggests that the levels of DMP, DEHP, DiBP,
18 and BBzP in floor dust were associated with the prevalence of allergic rhinitis, conjunctivitis, and
19 atopic dermatitis in children, and children are more vulnerable to phthalate exposure via
20 household floor dust than are adults. The results from this study were shown by cross-sectional
21 nature of the analyses and elaborate assessments for metabolism of phthalates were not considered.
22 Further studies are needed to advance our understanding of phthalate toxicity.

- 1 **Abbreviations:**
- 2 BBzP, benzyl butyl phthalate
- 3 DBP, dibutyl phthalate
- 4 DEHA, di-2-ethylhexyl adipate
- 5 DEHP, di-2-ethylhexyl phthalate
- 6 DEP, diethyl phthalate
- 7 DiBP, di-iso-butyl phthalate
- 8 DiNP, di-iso-nonyl phthalate
- 9 DMP, dimethyl phthalate
- 10 DnBP, di-n-butyl phthalate
- 11 ETS, environmental tobacco smoke
- 12 GC/MS, gas chromatography/mass spectrometry
- 13 LOD, limit of detection
- 14 MBzP, mono benzyl phthalate
- 15 MDL, method detection limits
- 16 PVC, polyvinyl chloride
- 17 SVOC, semi-volatile organic compounds

1 **Highlights**

- 2 • We investigated the relationships between house dust phthalate levels in Japanese
3 dwellings and the recent prevalence of asthma and allergies in both children and adult
4 inhabitants.
- 5 • Phthalates levels in house dust were more strongly associated with children's rhinitis and
6 atopic dermatitis compared to adults.
- 7 • Statistically significant association between phthalate levels and allergies were only found
8 in floor dust.
- 9 • Children are more vulnerable to phthalate exposure via floor dust than adults.

- 1 **Key words**
- 2 Phthalates
- 3 House dust
- 4 Children
- 5 Bronchial asthma
- 6 Allergic conjunctivitis
- 7 Atopic dermatitis

1 **1. Introduction**

2 Through the 1980s, the prevalence of asthma and allergies among children increased in
3 developed countries (Asher et al., 2006). In fact, the increase in the prevalence of asthma and
4 allergies in adults as well as in children has gained attention during recent years (WHO, 2005).
5 Various reviews have focused on the associations between increasing asthma and allergies and
6 indoor environmental factors such as house dust mite allergens, environmental tobacco smoke,
7 mould, pets, and nitrogen dioxide. Thus, the indoor environment may have contributed to the
8 increase in asthma and allergies. One of the reasons for increasing asthma and allergies are
9 phthalates. Phthalates have been used as plasticisers for various plastic products, such as toys,
10 food containers, furniture, personal care products, medical devices, and paints. And humans are
11 exposed to phthalates throughout their lifetime, beginning in foetal stages. Due to their hand-to-
12 mouth behaviour and eating without hand washing after playing, assessing the exposure of
13 children to dust contaminated with SVOCs is regarded as an important issue (Wormuth et al.,
14 2006; U.S. EPA, 2002).

15 Dust ingestion contributes to most to the ingestion of high-molecular-weight phthalates such
16 as DEHP and BBzP in children (Beko et al., 2013). Because phthalates are not chemically bound
17 to products, they can easily diffuse within materials, leach out, and then disperse into the air or
18 adhere to airborne particles and settled dust (Fujii et al., 2003). Therefore, phthalates easily
19 penetrate into house dust that settles on phthalate-containing products (Seto and Saito, 2002). We
20 previously reported that high levels of DEHP in dust were detected in dwellings with polyvinyl
21 chloride (PVC) flooring (Ait Bamai et al., 2013). The same findings were reported in previous
22 epidemiological studies (Bornehag et al., 2005; Kolarik et al., 2008a). However, compared to
23 other previous studies, the levels of DEHP in house dust in Japan were higher than in studies from
24 Sweden (Bornehag et al., 2005), Bulgaria (Kolarik et al., 2008), Germany (Abb et al., 2009;
25 Fromme et al., 2004), Denmark (Langer et al., 2010) (Clausen et al., 2003), Taiwan (Hsu et al.,

1 2012), China (Guo and Kannan 2011), and the USA (Guo and Kannan 2011; Rudel et al., 2003),
2 and thus, DEHP exposure is of particular concern for Japan (Ait Bamai et al., 2013).

3 Since the 2000s, various experimental studies have reported that several phthalates have
4 adjuvant effects on Th2 differentiation and Th2-promoted antigen-specific production of IgG1 and
5 IgE in mice (Hansen et al., 2007; Larsen et al., 2007). Epidemiological studies have reported
6 positive relationships between phthalates in dust or phthalate-related products, such as PVC
7 flooring and asthma or allergic symptoms, since the late 1990s (Jaakkola et al., 2004; Jaakkola et
8 al., 2000; Jaakkola et al., 1999; Larsson et al., 2010; Oie et al., 1997; Bornehag et al., 2004;
9 Kolarik et al., 2008b; Callesen et al., 2013). Recently, the relationship between urinary phthalate
10 metabolites and allergic symptoms has been investigated in epidemiological studies (Bertelsen et
11 al., 2013; Callesen et al., 2013; Hoppin et al., 2013; Hsu et al., 2012; Just et al., 2012; Wang et al.,
12 2014).

13 However, only four epidemiological studies regarding the relationship between phthalates in
14 house dust and inhabitants' asthma or allergies have been reported (Kolarik et al., 2008; Callesen
15 et al., 2013; Hsu et al., 2012; Bornehag et al., 2004). Previous studies evaluated only children aged
16 2-9 years old and did not consider allergic symptoms in teenagers and adults. To our knowledge,
17 there have been no studies that have focused on the differences of allergic impacts on the exposure
18 to house dust phthalates between children and adults. Therefore, the specific aim of the current
19 study was to investigate the relationship between phthalate levels in Japanese dwellings and the 2-
20 year prevalence of bronchial asthma and allergies among the inhabitants of such dwellings, both
21 children and adults.

22

23 **2. Materials and methods**

24 Details of the study design and methods used for the environmental measurements have
25 been reported previously (Araki et al., 2010; Kanazawa et al., 2010; Kishi et al., 2009; Takigawa

1 et al., 2010); therefore, only a brief description is provided here.

2 2.1. *Study population*

3 This study is a second follow-up cross-sectional study that was conducted from September to
4 December 2006; 156 detached dwellings and their 516 inhabitants were evaluated. The details of
5 the methods have been described elsewhere (Araki et al., 2010; Araki et al., 2013; Kishi et al.,
6 2009; Takigawa et al., 2010). Briefly, in 2003, questionnaires on baseline indoor-air quality were
7 sent to 6080 randomly selected single-family homes from six regions of Japan, Sapporo,
8 Fukushima, Nagoya, Osaka, Okayama, and Fukuoka, that had been constructed within the
9 previous 7 years. Ultimately, 2297 households responded (a response rate of 41.1%) (Kishi et al.,
10 2009). Of the responding households, 425 agreed to home visits for environmental measurements
11 in 2004 (Saijo et al., 2011; Takigawa et al., 2010), and the first follow-up of 270 households was
12 conducted in 2005. From September to December 2006, the second follow-up of 624 inhabitants
13 in 182 single-family homes was conducted. Out of the 182 houses, 26 houses were excluded
14 because the amount of both floor and multi-surface dust were less than 25 mg and we could not
15 measure phthalate levels. Therefore, 516 inhabitants in 156 single-family homes where more than
16 25 mg of house dust from either floor or multi-surfaces and other environmental measurements
17 could be obtained, were included in this study. Although the original study protocol was
18 prospective, and the inhabitants agreed to allow environmental measurements over a period of 3
19 years, we only included the results from the second follow-up study because measurements of
20 phthalates in house dust were only conducted in 2006. The resulting potential selection bias was
21 addressed by comparing the participants who continued with the study to those who did not, using
22 the data from 2003 and 2004. No significant differences were found (Araki et al., 2010).

23

24 2.2. *Questionnaire*

1 The investigators who visited each dwelling, distributed and collected questionnaires for the
2 inhabitants to complete. All inhabitants were asked to complete the personal questionnaire which
3 consisted of two sections: personal characteristics and symptoms of bronchial asthma and allergies.
4 Parents completed the personal questionnaires for inhabitants younger than 6 years old. Personal
5 characteristics included questions on gender, age, ETS (environmental tobacco smoke) (current
6 smoker/ non-smoker, ETS/ non-smoker, non-ETS), time spent in the home (continuous), and self-
7 reported stress level (high/ medium/ low). History of bronchial asthma, allergic rhinitis, allergic
8 conjunctivitis, and atopic dermatitis was assessed by asking “Have you ever been seen at a
9 hospital because of bronchial asthma in the past 2-years?”; “Have you ever been seen at a hospital
10 because of allergic rhinitis in the past 2-years?”; “Have you ever been seen at a hospital because of
11 allergic conjunctivitis in the past 2-years?”; “Have you ever been seen at a hospital because of
12 atopic dermatitis in the past 2-years?” A reply of “Yes” was considered to be positive in this study
13 (Araki et al., 2012, 2013). The 2-year prevalence of bronchial asthma, allergic rhinitis, allergic
14 conjunctivitis, and atopic dermatitis are described as “asthma”, “allergic rhinitis”, “allergic
15 conjunctivitis”, and “atopic dermatitis” hereafter.

16 A dwelling questionnaire was distributed to each house and filled out by the head of the family.
17 The dwellings-focused questionnaire included questions about building structure (wood/ others),
18 age of housing (3-5/ 6-8 years), renovations within the preceding year (yes/ no), current smoker at
19 home (yes/ no), furry pets inside the home (yes/ no), wall-to-wall carpeting (yes/ no), floor
20 materials (wood/ others), wall materials (PVC/ others), and frequency of mechanical-ventilation
21 usage (always/ often/ occasionally/ never/ no ventilation), signs of dampness (yes/ no): visible
22 mould, mouldy odours, condensation on windowpanes, water leakage within the preceding 5 years,
23 and high humidity in the bathroom.

24

25 *2.3. Measurement of phthalate concentrations in settled dust*

1 Dust collection, gas chromatography/mass spectrometry (GC/MS) analytical methods, and
2 quality assurance measures have been previously reported (Araki et al., 2013; Kanazawa et al.,
3 2010; Saito et al., 2007). Briefly, dust samples were categorised as one of two types: floor dust or
4 multi-surface dust. Floor dust samples were collected from all surfaces of the living room floor for
5 1 min/m². Samples of multi-surface dust were collected from the surface of objects that were more
6 than 35 cm above the living room floor, such as shelves, cupboards, doorframes, window frames,
7 TV sets, audio sets, and personal computers. The same type of hand-held vacuum cleaner
8 (National HC-V15, 38W, Matsushita Electric Works, Ltd., Osaka, Japan) equipped with a paper
9 dust bag (Nichinichi Pharmaceutical Co., Ltd., Mie, Japan) was used in all dwellings. To avoid
10 cross-contamination between samples, vacuum nozzles were washed in an ultrasound bath, and
11 vacuum cleaners were wiped with ethanol after each sample was collected. The collected dust was
12 stored in stoppered glass test tubes that had been cleaned with acetone. The tubes were sealed with
13 fluoroc-tape, wrapped with aluminium foil, and kept at -20 °C until the day of analysis. Using
14 tweezers, unwanted substances, such as human and animal hair, insects, food scraps, and scrap
15 paper, were removed from the dust samples. One millilitre of acetone per 25 mg dust was added to
16 each sample (25-50 mg dust/sample). The dust collected in the test tubes was subjected to
17 ultrasonic extraction with residue analysis-grade acetone (Wako Pure Chemical Industries, Ltd.,
18 Osaka, Japan) for 20 minutes and allowed to stand overnight. An internal standard (IS), 0.1 lg/ml
19 DnBP-d4 was added to each sample for monitoring and quantification. After centrifugation at
20 2500 g for 10 min, the supernatants were injected onto a Ultra-1 column (Agilent J&W Scientific
21 Inc., Folsom, CA, USA) for GC/MS (Agilent Technologies Inc., Palo Alto, CA, USA) at the
22 Tokyo Metropolitan Institute of Public Health in Tokyo, Japan. The operating conditions for
23 GC/MS are shown in Table S1. Seven phthalates and DEHA were analysed using GC/MS in SIM
24 mode at a temperature of 280°C. The quantification ion of DnBP-d4 was 153, and the
25 quantification and confirmation ions of target compounds were as follows: DMP, 163, 194; DEP,

1 149, 177; DiBP, 149, 223; DnBP, 149, 223; BBzP, 149, 206; DEHP, 149, 167; DiNP, 149, 167;
2 DEHA, 129, 147.

3

4 2.4. *Quality assurance and quality control*

5 A calibration curve was constructed using six different concentrations (0.05, 0.1, 0.5, 1.0,
6 2.0, or 5.0 lg/ml for each of the 8 compounds) together with IS (0.1 lg/ ml) in acetone for GC/MS
7 analysis. Good linear correlations between the concentration of target compounds and the ratio of
8 the peak area of each compound with respect to the IS were obtained. Recovery tests were
9 performed using dust samples. After 50 ng of each phthalate was individually added to each 50
10 mg dust sample, the air-dried samples were extracted with 1 ml of acetone and analysed by
11 GC/MS (n =3). The recovery rate \pm standard deviation ranged from 80.5 ± 1.6 for DMP to $99.9 \pm$
12 4.5 for DINP (Table S2). The instrumental limit of detection (LOD) was defined as the absolute
13 amount of an analyte that yielded a signal-to-noise ratio of 3 (S/N =3). As for DnBP and DEHP,
14 which were detected in methods blanks, LOD was calculated from 10-fold of the standard
15 deviation (10SD), which was calculated from the blank tests (n=6). The method detection limits
16 (MDLs) were calculated based on the LODs, the sample weight, and the volume of the extract.
17 The calculated MDL for each of the phthalates in dust is shown in Table 1; phthalates with
18 concentrations below the MDL were assigned a value of half the MDL. A phthalate was identified
19 when its peak was within ± 5 seconds of the retention time of a specific phthalate in the calibration
20 standard and the relative noise intensity was within $\pm 20\%$ of that from the standard phthalate.
21 Quantification of each phthalate was first determined based on the peak area ratio of the standard
22 curve, and then the concentrations of individual phthalates in the dust samples (C_{dust}) ($\mu\text{ g/g}$) were
23 calculated based on Equation 1:

$$24 \quad C_{\text{dust}} = [(A_{\text{sample weight}} - A_{\text{travel blank}}) \times E] \div (v \times W) \quad (1)$$

1 where $A_{\text{sample weight}}$ is the sample weight injected for GC/MS (ng), $A_{\text{travel blank}}$ is the weight of the
2 travel blank injected for GC/MS (ng), E is the extract volume (ml), v is the injected volume ($\mu\text{ l}$),
3 and W is the weight (g) of the dust sample that was used for extraction. To avoid phthalate
4 contamination, all glass tubes and stainless steel equipment used in sample collection and analysis
5 were ultrasonicated for 10 min in acetone, rinsed with acetone, and then air dried. To examine the
6 background levels of phthalates from materials used for sampling, the vacuum dust bag and the
7 ethanol-soaked cotton used to wipe the vacuum nozzle were extracted with acetone and analysed
8 by GC/MS to confirm that there were no phthalate peaks (Kanazawa et al., 2010; Saito et al, 2007).

9

10 2.5. *Other environmental measurements*

11 House dust mite allergen, house dust phosphorus flame retardants (PFRs), airborne fungi,
12 formaldehyde, and volatile organic compounds (VOCs) in the air were also measured. The
13 methods and results for the analysis of these environmental factors have been described elsewhere
14 (Araki et al., 2010, 2013). Briefly, house dust for mite allergens was collected using the same
15 procedure for floor dust sampling. Samples were stored at $-20\text{ }^{\circ}\text{C}$ in a plastic bag and sent to
16 Nichinichi Pharmaceutical Co., Ltd. (Mie, Japan) where 5 mg of fine house dust was sieved with a
17 $300\text{ }\mu\text{m}$ mesh and measured. *Dermatophagoides pteronyssinus* 1 allergen (Der p1) and
18 *Dermatophagoides farinae* 1 allergen (Der f1) levels were determined using commercially
19 available monoclonal antibody-based colorimetric enzyme-linked immunosorbent assays (ELISA)
20 (Der p1 and Der f1 ELISA kits; Nichinichi Pharmaceutical Co., Ltd, Mie, Japan). Dust treatment
21 and measurement of dust mite allergens were carried out using the method described by Ogino et
22 al. (2002). If allergen levels were lower than the detection limit ($0.1\text{ }\mu\text{g/g}$ fine dust), they were
23 considered to be $0.05\text{ }\mu\text{g/g}$ of fine dust. The sum of the determined Der p1 and Der f1 is described
24 as “mite allergen Der1” hereafter.

25

1 2.6. Data analysis

2 To ensure validity of the analysis of the phthalates, we only included the dust samples that
3 were greater than 25 mg in the analysis (Araki et al., 2013; Kanazawa et al., 2010). Therefore,
4 among the 182 homes in the second follow-up study, 156 were included. Furthermore, among
5 these 156 homes, 8 and 36 homes had missing data for floor dust and multi-surface dust,
6 respectively. Thus, 112 homes had complete data for both floor dust and multi-surface dust, and
7 yielded samples that were above 25 mg (used for the correlation analysis). As for outcomes, 516
8 subjects had complete data on personal factors, and home environmental factors used as
9 confounders in the linear models. Therefore, in the present study, the results of the analyses on
10 floor dust and multi-surface dust include 148 homes with 496 inhabitants and 120 homes with 389
11 inhabitants, respectively. The correlation coefficient values between floor and multi-surface dust
12 were calculated using the Spearman's rank correlation test for the samples both floor and multi-
13 surface dust collected (Table S3). Participants aged between 0 and 14 years old were considered to
14 be "children" and those 15 years or older were considered to be "adults" because in the field of
15 Japanese pediatrics, children are defined as being under 15 years old. Tertile phthalate levels were
16 created according to the observed distribution of phthalate concentration in dust (lowest
17 concentration category as the reference). Linear associations based on of phthalate level tertiles are
18 shown as ORs of each outcome, 95% CI, (confidence intervals) and P for trend (P_{trend}). A DEHA
19 level was created using a low/ high variable according to median concentrations of DEHA because
20 the number of cases for DEHA distribution was insufficient to create tertiles. DMP and DEP
21 levels were assessed using a 0/1 variable (absent/ present) due to the low detection rate. To take
22 into account the relatedness of household members, associations between the prevalence of asthma
23 and allergies and the levels of phthalates in house dust were evaluated using a generalized linear
24 mixed effect model. The results are presented as crude and adjusted odds ratios (ORs) with 95%
25 CIs. Potential confounders were selected from previous studies and included gender (male/

1 female), age strata ($\leq 14/ +15$ years old), ETS (current smoker/ non-smoker, ETS/ non-smoker,
2 non-ETS), furry pets inside the house (yes/ no), and signs of dampness (yes/ no). Signs of
3 dampness are represented using a “dampness index (0-5)” calculated by summing the number of
4 observations in each dwelling based on five signs (Kishi et al., 2009; Saijo et al., 2012). Other
5 potential confounders [Der 1 (continuous), other phthalates (continuous), airborne fungi
6 (continuous), formaldehyde (continuous), total VOC (continuous), and building characteristics
7 such as structure (wood/ others), age of house (3-5/ 6-8 years), and floor materials (wood/ others)]
8 were selected if the estimate of the association between the health outcome and exposure were
9 changed by $>10\%$. Der 1 and other phthalates with a change of $>10\%$ in the estimate were
10 included in the model. Each phthalate was adjusted for the sum of other phthalate concentrations
11 except its own; DEHP was adjusted for the sum of DMP, DEP, DiBP, DnBP, BBzP, DiNP, and
12 DEHA. We created two models: the variables of gender, age strata, ETS, furry pets inside the
13 house, dampness index, and Der 1 were used as confounders in Model 1; the variable of other
14 phthalates was fitted in the final model (Model 2) to evaluate a mutually adjusted model. To test
15 the interaction effect between children and adults, we tested for the interaction effects of age strata
16 (child/ adult) and exposure (phthalates) categories using generalized liner mixed effect models.
17 Each of the ORs for exposure in children and adults was estimated using simultaneous estimations.
18 Interaction effects are shown as P for interaction ($P_{\text{interaction}}$). The association of each of the
19 phthalates was modelled separately. For statistical analyses, a two-tailed test and a 5% level of
20 significance were used. All analyses were performed using SPSS 19 for Macintosh (SPSS Inc.,
21 Chicago, IL, USA) and SAS 9.3 (SAS Institute Inc., Cary, NC).

22

23 2.7. *Ethical considerations*

24 The study protocol was approved by the ethics board for epidemiological studies at the
25 Hokkaido University Graduate School of Medicine and by the ethics boards at all of the regional

- 1 universities involved in the study. All participants and their parents, when relevant, provided
- 2 written informed consent to participate in the study.

1 3. Results

2 Table 1 shows the phthalate distribution in dust. DEHP was found at the highest median
3 concentration and was detected in 100% of both floor and multi-surface dust. DINP had the
4 second highest concentration in both floor and multi-surface dust, followed by DnBP, DEHA, and
5 DEP. DMP was not detected in more than half of the samples of both floor and multi-surface dust.
6 For all phthalates, floor and multi-level dust concentrations were positively correlated ($P < 0.01$)
7 (Table S3). The level of DiBP was significantly higher in floor dust than in multi-surface dust ($P <$
8 0.001) (Table S3).

9 Table 2 shows the personal characteristics and prevalence of bronchial asthma and allergies.
10 The number of participants/household (Mean [range]) was 3.8 (2-7). The allergy with the highest
11 prevalence was allergic rhinitis in both children and adults.

12 Table 3 shows the generalized liner mixed effects analysis and interaction effects of age
13 strata and phthalate categories of the association between phthalates in house dust and prevalence
14 of bronchial asthma and allergies. As for floor dust, we obtained significantly positive liner
15 associations between asthma and DiBP and DnBP, respectively. The prevalence of allergic rhinitis
16 was significantly associated with DMP ($P = 0.002$), and a slightly positive liner association was
17 observed for BBzP, however, it was not statistically significant ($P_{\text{trend}} = 0.058$). A significantly
18 positive liner association was obtained between the prevalence of allergic conjunctivitis and
19 DEHP. Significantly positive liner associations were also obtained between the prevalence of
20 atopic dermatitis and DiBP, BBzP, and DEHP, respectively. Significant interaction effects were
21 obtained between bronchial asthma and DiNP, and between allergic rhinitis and DMP. No
22 significant associations were obtained in multi-surface dust.

23 Table 4 shows simultaneous estimation of age strata with generalized liner mixed effect
24 model of the associations of phthalates in floor dust and prevalence of bronchial asthma and
25 allergies (n=496 participants; 148 homes). In the case of bronchial asthma and allergic rhinitis

1 obtained from the interaction effects in Table 3, the ORs of bronchial asthma were higher in adults
2 compared to children for DiNP. However, no significant liner associations were obtained. The
3 ORs for allergic rhinitis were higher in children compared to adults for DMP. Moreover, for
4 participants, where DMP from floor dust was detected, higher ORs for allergic rhinitis were
5 obtained compared to participants who lived in dwellings where it was not. Although there was no
6 statistical significance for interaction effect ($P_{\text{interaction}} = 0.427$), we observed positive liner
7 associations between allergic conjunctivitis and DEHP in both children and adults, and the ORs
8 obtained were higher for children than adults. In the same way, although there were no statistically
9 significant interaction effects between atopic dermatitis and DiBP, BBzP, and DEHP, respectively
10 ($P_{\text{interaction}} > 0.05$), we observed significantly positive liner associations between atopic dermatitis
11 and DiBP and BBzP in children, and between atopic dermatitis and DEHP in adults. The ORs
12 obtained for atopic dermatitis were higher in children than in adults for DiBP and BBzP, but lower
13 for DEHP. Before mutually adjusting the model, we observed significantly positive liner
14 associations between allergic rhinitis and DiBP in children ($P_{\text{trend}} = 0.016$) and BBzP in both
15 children ($P_{\text{trend}} = 0.007$), and adults ($P_{\text{trend}} = 0.044$) (Table S4). Moreover, these ORs for allergic
16 rhinitis were higher in children than in adults. However, there was no statistical significance
17 regarding the interaction effect for both DiBP and BBzP ($P_{\text{interaction}} > 0.05$ in Table S4).

18 Table 5 shows simultaneous estimation of age strata with generalized liner mixed effect
19 model of the associations of phthalates in multi-surface dust and prevalence of bronchial asthma
20 and allergies (n= 389 participants; 120 homes). There were no significant associations between
21 the prevalence of asthma and allergies and any phthalates in multi-surface dust.

1 **4. Discussion**

2 Our results from the present study suggest that the associations between house dust
3 phthalates and the prevalence of allergic rhinitis, allergic conjunctivitis, and atopic dermatitis were
4 stronger for children than for adults, On the other hand, the prevalence of bronchial asthma was
5 higher in adults than in children after simultaneously estimating for the interaction effects of age
6 and exposure categories using generalized liner mixed models. Moreover, theses results were
7 obtained in dust collected from floor surfaces only. We suggest that children are more vulnerable
8 to phthalate exposure via floor dust than are adults. Environmental contaminants more severely
9 affect children than adults due to 1) a higher ratio of body surface area to volume than adults, and
10 2) behavioural and physiological differences (U.S.EPA, 2002). For example, children are more
11 highly exposed to house dust than are adults because of their hand-to-mouth behaviour and eating
12 food without hand washing after playing. Additionally, children frequently eat food that has been
13 dropped on the floor (U.S.EPA 2011). Finally, children generally spend more time at home
14 compared to adults. Our results are consistent with these behavioural and physiological theories.

15 In this study positive associations between levels of phthalates in dust and prevalence of
16 asthma and allergies were obtained only for the dust samples collected from floor surfaces. Floor
17 dust samples were collected from all surfaces of the living room floor. In Japan, people generally
18 sit on the floor when relaxing. Therefore, floor dust more highly affected inhabitants' prevalence
19 of bronchial asthma and allergies than multi-surface dust. In addition, children sit and play on the
20 floor more than adults do when spending time in the house. The main routes of exposure to house
21 dust for inhabitants are expected to be by inhalation, dermal contact, and, especially for children,
22 by ingestion (Beko and others 2013). Thus, when using house dust in an exposure assessment, it is
23 very important to note the collection site of the dust samples.

24 In the present study, high levels of DiBP were related to bronchial asthma and atopic
25 dermatitis. Hoppin et al. (2004) reported that urinary monobutyl phthalate (MBP), a metabolite of

1 di-butyl phthalate, was associated with decrements of pulmonary function. Our results on the
2 association between DnBP and bronchial asthma were consistent with this study. On the other
3 hand, as for atopic dermatitis, no epidemiological studies have reported any adverse dermal effects
4 of DBP. Only animal studies focusing on skin irritations and sensitisations have been conducted,
5 but no association was observed (European Chemicals Bureau, 2004). DBPs are used for
6 consumer product such as PVC-toys, personal care products, cosmetics, and perfume. Further
7 studies are needed to confirm our results. The levels of BBzP were related to atopic dermatitis.
8 Bornehag et al. (2004) reported that allergic dermatitis in children was related to the high levels of
9 BBzP in house dust (Bornehag et al., 2004). Just et al. (2012) reported that prenatal exposure of
10 BBzP was related to children's eczema at 60 months of age. Our results are consistent with these
11 previous studies. In this study, the high levels of DEHP were related to allergic conjunctivitis and
12 atopic dermatitis. We previously reported that DEHP levels in floor dust were associated with
13 mucosal symptoms in inhabitants (Kanazawa et al., 2010). DEHP may cause mucosal symptoms
14 such as eye and dermal irritation. However, data available for both humans and animals are
15 insufficient to show any irritation/ sensitisation effect on the eye or skin due to DEHP, further
16 studies are needed to confirm our results.

17 When simultaneously estimating for the allergic impacts on the exposure to house dust
18 phthalates for children and adults, children had higher ORs than adults for the associations
19 between allergic rhinitis and DiBP; between allergic conjunctivitis and DEHP; and between atopic
20 dermatitis and DiBP and BBzP. Before adjusting for other phthalates, levels of DiBP were
21 associated with allergic rhinitis in children (Table S4). This suggests that the impact of DiBP may
22 be reversed with other phthalate such as DEHP and DiNP. On the other hand, our data showed
23 that bronchial asthma was associated with DiNP in adults. Hoppin e al. (2013) reported that
24 urinary MBzP level was associated with current allergic symptoms (wheeze, asthma, hay fever,
25 and rhinitis) in adults, but inversely associated with current hay fever in child (6-17 years old)

1 (Hoppin et al., 2013). However, we did not have any results that were consistent with those found
2 in Hoppin's study in neither children nor adults. In this study, most ORs for interaction effects and
3 their *P* for interaction were not statistically significant. Because of our small sample size, it was
4 difficult to show any statistical significance using interaction models. While our sample size may
5 have been too small to evaluate interaction effects by age strata, our results suggest that stronger
6 associations between prevalence of allergies and levels of phthalate were found in children
7 compared to adults.

8 Furthermore, epidemiological evidence of associations between phthalates and allergic
9 symptoms are limited. Only four epidemiological studies have reported an association between
10 phthalates in house dust and asthma and allergies (Bornehag et al., 2004; Callesen et al., 2013;
11 Hsu et al., 2012; Kolarik et al., 2008b). Although house dust is not the primary means of exposure
12 to phthalates, it does represent an important source of phthalate exposure in both children and
13 adults. Therefore, further studies are needed to confirm our findings.

14 Phthalate levels in house dust have been measured in several previously reported studies
15 (Abb et al., 2009; Becker et al., 2004; Bornehag et al., 2005; Bornehag et al., 2004; Clausen et al.,
16 2003; Guo and Kannan, 2011; Hsu et al., 2012; Kanazawa et al., 2010; Kang et al., 2012; Kolarik
17 et al., 2008a; Kolarik et al., 2008b; Langer et al., 2010; Nagorka et al., 2005; Oie et al., 1997;
18 Rudel et al., 2003). Comparing the levels of phthalates in our study to those of the other studies
19 (Abb et al., 2009; Bornehag et al., 2004; Clausen et al., 2003; Fromme et al., 2004; Guo and
20 Kannan, 2011; Hsu et al., 2012; Kang et al., 2012; Kolarik et al., 2008b; Langer et al., 2010;
21 Nagorka et al., 2005), DEHP levels in our study were slightly higher than those reported in the
22 other studies in both floor and multi-surface dust. In contrast, BBzP, DnBP, and DINP levels were
23 lower in our study compared to the other studies. We previously reported that house dust levels of
24 DEHP were higher and that BBzP levels were lower in Japan than in other countries, especially in

1 comparison to the levels in Europe and the U.S. (Ait Bamai et al., 2013). Our results were
2 consistent with our previous report.

3 There are several limitations in this study. First, since the participants in this study were
4 those still remaining at the phase three follow-ups, selection bias may have occurred. Ultimately,
5 this study was a cross-sectional study, and any causal relationships between phthalate levels and
6 health outcomes were not discernible. Second, our study only included detached dwellings aged
7 less than 8 years, thus our results may not be applicable to other types of dwellings. Selection bias
8 of the population may be occurred. Moreover, since there are differences in the phthalate levels in
9 house dust between newly built houses and old houses, the phthalate levels in this study will be
10 generalizable only to relatively new dwellings. Third, environmental measurements were
11 conducted only once. Seasonal and environmental factors affect the quantity and composition of
12 house dust (Mercier et al., 2011). However, we consciously used the same sampling season
13 between six regions from October to December in 2006. Moreover, pore size of the dust bag filter
14 that we used for dust sampling was not measured. Therefore, it is possible that we missed those
15 phthalates attached to smaller particles of dust when we collected the dust. Fourth, we could only
16 measure a limited number of environmental factors related to allergies. Several environmental
17 factors known to influence allergies such as mite allergens and mould were measured; however,
18 other factors such as particle matter were not considered. Fifth, because many statistical analyses
19 on the relation between phthalates and allergies were carried out, statistical significance may have
20 occurred by chance. Thus, false positive associations are possible. Our sample size may also have
21 been too small to evaluate interaction effects by age strata. Moreover, socio-economic status such
22 as household income and educations were not assessed. However, because all participants lived in
23 their own newly built detached house, it was considered that their socio-economic statuses was
24 similar and belonged to the middle class (Saijo et al., 2004). Lastly, health outcomes were
25 assessed using questionnaires of 2-years prevalence of bronchial asthma and allergies. Any

1 biological markers to assess outcomes such as immunoglobulin E were not measured. On the other
2 hand, Callesen et al. (2013) recently reported that DEHP in dust was associated with children's
3 wheeze based on symptoms reported in a questionnaire, but not based on doctors' diagnoses
4 (Callesen et al., 2013). Moreover, bronchial asthma is not diagnosed in the case of acute bronchial
5 infections based on the 2012 Japan pediatric guidelines for the treatment and management of
6 asthma (Hamazaki et al., 2012). Therefore, misclassification of health outcomes may have
7 occurred. The cut-off point of the age categories used in this study was "below 15" for "children"
8 and "more than 15 years old" for "adults" thus the association between house dust and allergies in
9 toddlers could not be determined. The prevalence of bronchial asthma and allergies are different in
10 toddlers, teenagers, and adults. We could not carry out multivariate analyses in three age
11 categories (toddlers, teenagers, and adults) due to the small numbers of toddlers. Moreover,
12 "pediatrics" is commonly defined as those under 15 year of age in Japan. Therefore, we used this
13 definition in the present study and then adjusted for the influence of age using "age strata" in the
14 analyses.

15 In this study, we suggest that the levels of DMP, DEHP, DiBP, and BBzP in floor dust were
16 associated with the prevalence of allergic rhinitis, conjunctivitis, and atopic dermatitis in children,
17 and children are more vulnerable to phthalate exposure via household floor dust than are adults.

18

19 **5. Conclusion**

20 This cross-sectional study showed the associations between the prevalence of bronchial
21 asthma and allergies and levels of phthalates in house dust using interaction effects of age and
22 exposure categories in a generalized liner mixed effect model. Interaction effects were obtained
23 between DMP and allergic rhinitis in children and between DiNP and bronchial asthma in adults.
24 Levels of DMP, DiNP, DEHP, DiBP, and BBzP in floor dust had liner associations with the
25 prevalence of allergic rhinitis, conjunctivitis, and atopic dermatitis. Furthermore, a stronger

1 association was seen in children compared to adults. No significant associations were found in
2 phthalates levels collected from multi-surfaces. This may suggest that humans, especially children
3 are exposed to phthalates from lower place rather than higher place. Elaborate assessments for
4 metabolism of phthalates were not considered, and further studies are needed to advance our
5 understanding of phthalate toxicity.

6

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1 **References**

- 2 Abb, M.; Heinrich, T.; Sorkau, E.; Lorenz, W. Phthalates in house dust. *Environ Int.* 35:965-970; 2009
- 3 Ait Bamai Y, Araki A, Kawai T, Tsuboi T, Saito I, Yoshioka E, et al. Associations of phthalate
4 concentrations in floor dust and multi-surface dust with the interior materials in Japanese
5 dwellings. *Science of the Total Environment* 2013; 468-469C:147-157.
- 6 Araki, A.; Kawai, T.; Eitaki, Y.; Kanazawa, A.; Morimoto, K.; Nakayama, K., et al. Relationship
7 between selected indoor volatile organic compounds, so-called microbial VOC, and the
8 prevalence of mucous membrane symptoms in single family homes. *Sci Total Environ.*
9 408:2208-2215; 2010
- 10 Araki, A.; Kanazawa, A.; Kawai, T.; Eitaki, Y.; Morimoto, K.; Nakayama, K., et al. The relationship
11 between exposure to microbial volatile organic compound and allergy prevalence in single-
12 family homes. *Sci Total Environ.* 423:18-26; 2012
- 13 Araki, A.; Saito, I.; Kanazawa, A.; Morimoto, K.; Nakayama, K.; Shibata, E., et al. Phosphorus flame
14 retardants in indoor dust and their relation to asthma and allergies of inhabitants. *Indoor Air*;
15 2013
- 16 Asher, M.I.; Montefort, S.; Bjorksten, B.; Lai, C.K.W.; Strachan, D.P.; Weiland, S.K., et al. Worldwide
17 time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in
18 childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet.*
19 368:733-743; 2006
- 20 Becker, K.; Seiwert, M.; Angerer, J.; Heger, W.; Koch, H.M.; Nagorka, R., et al. DEHP metabolites in
21 urine of children and DEHP in house dust. *Int J Hyg Environ Health.* 207:409-417; 2004
- 22 Beko, G.; Weschler, C.J.; Langer, S.; Callesen, M.; Toftum, J.; Clausen, G. Children's Phthalate Intakes
23 and Resultant Cumulative Exposures Estimated from Urine Compared with Estimates from Dust
24 Ingestion, Inhalation and Dermal Absorption in Their Homes and Daycare Centers. *PLoS One.*
25 8:e62442; 2013
- 26 Bertelsen RJ, Carlsen KC, Calafat AM, Hoppin JA, Haland G, Mowinckel P, et al. Urinary biomarkers

1 for phthalates associated with asthma in Norwegian children. *Environ Health Perspect* 2013;
2 121: 251-6.

3 Bornehag, C.G.; Lundgren, B.; Weschler, C.J.; Sigsgaard, T.; Hagerhed-Engman, L.; Sundell, J.
4 Phthalates in indoor dust and their association with building characteristics. *Environ Health*
5 *Perspect.* 113:1399-1404; 2005

6 Bornehag, C.G.; Sundell, J.; Weschler, C.J.; Sigsgaard, T.; Lundgren, B.; Hasselgren, M., et al. The
7 association between asthma and allergic symptoms in children and phthalates in house dust: A
8 nested case-control study. *Environ Health Perspect.* 112:1393-1397; 2004

9 Callesen M, Beko G, Weschler CJ, Langer S, Brive L, Clausen G, et al. Phthalate metabolites in urine
10 and asthma, allergic rhinoconjunctivitis and atopic dermatitis in preschool children. *Int J Hyg*
11 *Environ Health* 2013.

12 Callesen M, Beko G, Weschler CJ, Sigsgaard T, Jensen TK, Clausen G, et al. Associations between
13 selected allergens, phthalates, nicotine, polycyclic aromatic hydrocarbons, and bedroom
14 ventilation and clinically confirmed asthma, rhinoconjunctivitis, and atopic dermatitis in
15 preschool children. *Indoor Air* 2013.

16 Clausen, P.A.; Bille, R.L.L.; Nilsson, T.; Hansen, V.; Svensmark, B.; Bowadt, S. Simultaneous
17 extraction of di(2-ethylhexyl) phthalate and nonionic surfactants from house dust -
18 Concentrations in floor dust from 15 Danish schools. *J Chromatogr A.* 986:179-190; 2003

19 Davis, B.J.; Maronpot, R.R.; Heindel, J.J. Di-(2-Ethylhexyl) Phthalate Suppresses Estradiol and
20 Ovulation in Cycling Rats. *Toxicol Appl Pharmacol.* 128:216-223; 1994

21 Doull, J.; Cattley, R.; Elcombe, C.; Lake, B.G.; Swenberg, J.; Wilkinson, C., et al. A cancer risk
22 assessment of di(2-ethylhexyl)phthalate: Application of the new US EPA risk assessment
23 guidelines. *Regul Toxicol Pharmacol.* 29:327-357; 1999

24 Eder, W.; Ege, M.J.; von Mutius, E. The asthma epidemic. *N Engl J Med.* 355:2226-2235; 2006

25 Etzel, R.A. How environmental exposures influence the development and exacerbation of asthma.
26 *Pediatrics.* 112:233-239; 2003

1 European Chemicals Bureau. European Union Risk Assessment Report. dibutyl phthalate (DBP). .
2 Institute for Health and Consumer Protection, EU, 2004.

3 European Chemicals Bureau.. European Union Risk Assessment Report. bis(2-ethylhexyl)phthalate
4 (DEHP). Institute for Health and Consumer Protection, EU, 2008.

5 Fromme, H.; Lahrz, T.; Piloty, M.; Gebhart, H.; Oddoy, A.; Ruden, H. Occurrence of phthalates and
6 musk fragrances in indoor air and dust from apartments and kindergartens in Berlin (Germany).
7 *Indoor Air*. 14:188-195; 2004

8 Fujii, M.; Shinohara, N.; Lim, A.; Otake, T.; Kumagai, K.; Yanagisawa, Y. A study on emission of
9 phthalate esters from plastic materials using a passive flux sampler. *Atmos Environ*. 37:5495-
10 5504; 2003

11 Guo, Y.; Kannan, K. Comparative Assessment of Human Exposure to Phthalate Esters from House Dust
12 in China and the United States. *Environmental Science & Technology*. 45:3788-3794; 2011

13 Hamazaki Y, Kawano Y, Ebisawa M, Kondo N. 2012 Japan pediatric guidelines for the treatment and
14 management of asthma: Kyowa planning 2012.

15 Hansen JS, Larsen ST, Poulsen LK, Nielsen GD. Adjuvant effects of inhaled mono-2-ethylhexyl
16 phthalate in BALB/cJ mice. *Toxicology* 2007; 232: 79-88.

17 Hoppin, J.A.; Ulmer, R.; London, S.J. Phthalate exposure and pulmonary function. *Environ Health*
18 *Perspect*. 112:571-574; 2004

19 Hoppin JA, Jaramillo R, London SJ, Bertelsen RJ, Salo PM, Sandler DP, et al. Phthalate exposure and
20 allergy in the U.S. population: results from NHANES 2005-2006. *Environ Health Perspect* 2013;
21 121: 1129-34.

22 Hsu, N.Y.; Lee, C.C.; Wang, J.Y.; Li, Y.C.; Chang, H.W.; Chen, C.Y., et al. Predicted risk of childhood
23 allergy, asthma, and reported symptoms using measured phthalate exposure in dust and urine.
24 *Indoor Air*. 22:186-199; 2012

25 Jaakkola, J.J.; Parise, H.; Kislitsin, V.; Lebedeva, N.I.; Spengler, J.D. Asthma, wheezing, and allergies
26 in Russian schoolchildren in relation to new surface materials in the home. *Am J Public Health*.

1 94:560-562; 2004

2 Jaakkola, J.J.; Verkasalo, P.K.; Jaakkola, N. Plastic wall materials in the home and respiratory health in
3 young children. *Am J Public Health*. 90:797-799; 2000

4 Jaakkola, J.J.K.; Oie, L.; Nafstad, P.; Botten, G.; Samuelsen, S.O.; Magnus, P. Interior surface materials
5 in the home and the development of bronchial obstruction in young children in Oslo, Norway.
6 *Am J Public Health*. 89:188-192; 1999

7 Just, A.C.; Whyatt, R.M.; Perzanowski, M.S.; Calafat, A.M.; Perera, F.P.; Goldstein, I.F., et al. Prenatal
8 Exposure to Butylbenzyl Phthalate and Early Eczema in an Urban Cohort. *Environ Health*
9 *Perspect*. 120:1475-1480; 2012

10 Kanazawa, A.; Saito, I.; Araki, A.; Takeda, M.; Ma, M.; Saijo, Y., et al. Association between indoor
11 exposure to semi-volatile organic compounds and building-related symptoms among the
12 occupants of residential dwellings. *Indoor Air*. 20:72-84; 2010

13 Kang, Y.; Man, Y.B.; Cheung, K.C.; Wong, M.H. Risk Assessment of Human Exposure to
14 Bioaccessible Phthalate Esters via Indoor Dust around the Pearl River Delta. *Environ Sci*
15 *Technol*. 46:8422-8430; 2012

16 Kishi, R.; Saijo, Y.; Kanazawa, A.; Tanaka, M.; Yoshimura, T.; Chikara, H., et al. Regional differences
17 in residential environments and the association of dwellings and residential factors with the sick
18 house syndrome: a nationwide cross-sectional questionnaire study in Japan. *Indoor Air*. 19:243-
19 254; 2009

20 Koch, H.M.; Gonzalez-Reche, L.M.; Angerer, J. On-line clean-up by multidimensional liquid
21 chromatography-electrospray ionization tandem mass spectrometry for high throughput
22 quantification of primary and secondary phthalate metabolites in human urine. *Journal of*
23 *Chromatography B-Analytical Technologies in the Biomedical and Life Sciences*. 784:169-182;
24 2003

25 Kolarik, B.; Bornehag, C.G.; Naydenov, K.; Sundell, J.; Stavova, P.; Nielsen, O.F. The concentrations
26 of phthalates in settled dust in Bulgarian homes in relation to building characteristic and cleaning

1 habits in the family. *Atmos Environ.* 42:8553-8559; 2008a

2 Kolarik, B.; Naydenov, K.; Larsson, M.; Bornehag, C.G.; Sundell, J. The association between phthalates
3 in dust and allergic diseases among Bulgarian children. *Environ Health Perspect.* 116:98-103;
4 2008b

5 Lake, B.G.; Price, R.J.; Cunninghame, M.E.; Walters, D.G. Comparison of the effects of di-(2-
6 ethylhexyl)adipate on hepatic peroxisome proliferation and cell replication in the rat and mouse.
7 *Toxicology.* 123:217-226; 1997

8 Langer, S.; Weschler, C.J.; Fischer, A.; Beko, G.; Toftum, J.; Clausen, G. Phthalate and PAH
9 concentrations in dust collected from Danish homes and daycare centers. *Atmos Environ.*
10 44:2294-2301; 2010

11 Larsen ST, Nielsen GD. The adjuvant effect of di-(2-ethylhexyl) phthalate is mediated through a
12 PPARalpha-independent mechanism. *Toxicol Lett* 2007; 170: 223-8.

13 Larsson, M.; Hagerhed-Engman, L.; Kolarik, B.; James, P.; Lundin, F.; Janson, S., et al. PVC--as
14 flooring material--and its association with incident asthma in a Swedish child cohort study.
15 *Indoor Air.* 20:494-501; 2010

16 Mercier, F.; Glorennec, P.; Thomas, O.; Le Bot, B. Organic Contamination of Settled House Dust, A
17 Review for Exposure Assessment Purposes. *Environmental Science & Technology.* 45:6716-
18 6727; 2011

19 Nagorka, R.; Scheller, C.; Ullrich, D. Plasticizer in house dust. *Gefahrst Reinhalt Luft.* 65:99-105; 2005

20 OECD. Bis(2-ethylhexyl)adipate (DEHA) CAS N°: 103-23-1. In: OECD, ed; 2010

21 Oie, L.; Hersoug, L.G.; Madsen, J.O. Residential exposure to plasticizers and its possible role in the
22 pathogenesis of asthma. *Environ Health Perspect.* 105:972-978; 1997

23 Rudel, R.A.; Camann, D.E.; Spengler, J.D.; Korn, L.R.; Brody, J.G. Phthalates, alkylphenols, pesticides,
24 polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and
25 dust. *Environmental Science & Technology.* 37:4543-4553; 2003

26 Saijo, Y.; Kishi, R.; Sata, F.; Katakura, Y.; Urashima, Y.; Hatakeyama, A., et al. Symptoms in relation

1 to chemicals and dampness in newly built dwellings. *Int Arch Occup Environ Health.* 77:461-
2 470; 2004

3 Saijo, Y.; Kanazawa, A.; Araki, A.; Morimoto, K.; Nakayama, K.; Takigawa, T., et al. Relationships
4 between mite allergen levels, mold concentrations, and sick building syndrome symptoms in
5 newly built dwellings in Japan. *Indoor Air.* 21:253-263; 2011

6 Saito, I.; Onuki, A.; Seto, H. Indoor organophosphate and polybrominated flame retardants in Tokyo.
7 *Indoor Air.* 17:28-36; 2007

8 Seto, H.; Saito, I. Survey and Health Effects Caused by Chemicals in Indoor Air. *Ann Rep Tokyo Metr*
9 *Res Lab PH:*179-190; 2002

10 Singh, A.R.; Lawrence, W.H.; Autian, J. Embryonic-Fetal Toxicity and Teratogenic Effects of Adipic
11 Acid Esters in Rats. *J Pharm Sci.* 62:1596-1600; 1973

12 Singh, A.R.; Lawrence, W.H.; Autian, J. Dominant Lethal Mutations and Antifertility Effects of Di-2-
13 Ethylhexyl Adipate and Diethyl Adipate in Male Mice. *Toxicol Appl Pharmacol.* 32:566-576;
14 1975

15 Stapleton, H.M., Klosterhaus, S., Eagle, S., Fuh, J., Meeker, J.D., Blum, A. and Webster, T.F. Detection
16 of organophosphate flame retardants in furniture foam and U.S. house dust, *Environ. Sci.*
17 *Technol.*, 43, 7490–7495; 2009

18 Takigawa, T.; Horike, T.; Ohashi, Y.; Kataoka, H.; Wang, D.H.; Kira, S.H. Were volatile organic
19 compounds the inducing factors for subjective symptoms of employees working in newly
20 constructed hospitals? *Environmental Toxicology.* 19:280-290; 2004

21 Takigawa, T.; Wang, B.L.; Saijo, Y.; Morimoto, K.; Nakayama, K.; Tanaka, M., et al. Relationship
22 between indoor chemical concentrations and subjective symptoms associated with sick building
23 syndrome in newly built houses in Japan. *Int Arch Occup Environ Health.* 83:225-235; 2010

24 U.S.EPA. IRIS Summary for Di(2-ethylhexyl)adipate (CASRN 103-23-1). 1994

25 U.S.EPA. Child-Specific Exposure Factors Handbook. 2002

26 U.S.EPA. Exposure Factors Handbook. 2011

- 1 van den Eede, N., Dirtu, A.C., Neels, H. and Covaci, A. Analytical develop-
2 ments and preliminary
3 assessment of human exposure to organophosphate flame retardants from indoor dust, *Environ.*
4 *Int.*, 37, 454–461; 2011
- 5 Wang IJ, Lin CC, Lin YJ, Hsieh WS, Chen PC. Early life phthalate exposure and atopic disorders in
6 children: a prospective birth cohort study. *Environ Int* 2014; 62: 48-54.
- 7 WHO. The public health implications of asthma-PUBLIC HEALTH REVIEWS. 2005
- 8 Wormuth, M.; Scheringer, M.; Vollenweider, M.; Hungerbuhler, K. What are the sources of exposure to
9 eight frequently used phthalic acid esters in Europeans? *Risk Anal.* 26:803-824; 2006

Table 1Distribution of phthalate in house dust ($\mu\text{g/g}$ dust).

| | | CAS No. | MDL | Floor (n=148) | | | | | | Multi-surface (n=120) | | | | | |
|------|---------------------------|------------|------|---------------|------|------|------|------|-------|-----------------------|------|------|------|------|-------|
| | | | | >MDL (%) | Min. | 25% | Med. | 75% | Max | >MDL (%) | Min. | 25% | Med. | 75% | Max |
| DMP | dimethyl phthalate | 131-11-3 | 0.2 | 18.9 | <MDL | <MDL | <MDL | <MDL | 61.3 | 23.3 | <MDL | <MDL | <MDL | <MDL | 5.2 |
| DEP | diethyl phthalate | 84-66-2 | 0.24 | 57.4 | <MDL | <MDL | 0.28 | 0.45 | 2.9 | 57.5 | <MDL | <MDL | 0.26 | 0.52 | 9000 |
| DiBP | di-iso-butyl phthalate | 84-69-5 | 0.08 | 100 | 0.21 | 1.2 | 2.4 | 5.5 | 262 | 99.2 | <MDL | 1 | 1.9 | 3.5 | 1360 |
| DnBP | di-n-butyl phthalate | 84-74-2 | 3.5 | 97.3 | <MDL | 10.5 | 19.3 | 51.2 | 2100 | 99.2 | <MDL | 10.3 | 20.6 | 40.8 | 3640 |
| BBzP | benzyl butyl phthalate | 85-68-7 | 0.2 | 98.6 | <MDL | 0.8 | 1.9 | 3.9 | 60.5 | 95.8 | <MDL | 0.9 | 1.7 | 3.9 | 431 |
| DEHP | di-2-ethylhexyl phthalate | 117-81-7 | 0.84 | 100 | 98.2 | 424 | 759 | 1410 | 12100 | 100 | 31.6 | 298 | 854 | 1863 | 10200 |
| DiNP | di-iso-nonyl phthalate | 28553-12-0 | 4 | 100 | 9.12 | 51.8 | 95 | 198 | 5820 | 98.3 | <MDL | 43 | 92.3 | 284 | 13100 |
| DEHA | di-2-ethylhexyl adipate | 103-23-1 | 0.33 | 100 | 0.39 | 2.7 | 4.6 | 8.5 | 692 | 98.3 | <MDL | 2.63 | 5.4 | 8.4 | 1360 |

MDL: method detection limit

Table 2

Personal characteristics and **prevalence of bronchial asthma and allergies** (n=516 participants; 156 houses).

| | | Total | | 0-14 years old | | ≥15 years old | |
|--|-------------------------|-------|------|----------------|------|---------------|------|
| | | n | % | n | % | n | % |
| Gender | Male | 251 | 48.6 | 64 | 50.8 | 187 | 48.0 |
| | Female | 265 | 51.4 | 62 | 49.2 | 203 | 52.1 |
| Age strata | ≤ 2 | 16 | 3.1 | 16 | 12.6 | | |
| | 3 - 5 | 35 | 6.8 | 35 | 27.6 | | |
| | 6 - 14 | 76 | 14.7 | 76 | 59.8 | | |
| | 15-29 | 64 | 12.4 | | | 64 | 16.5 |
| | 30-44 | 138 | 26.8 | | | 138 | 35.5 |
| | 45-59 | 105 | 20.3 | | | 105 | 27.0 |
| | 60 =< | 82 | 15.9 | | | 82 | 21.0 |
| Environmental Tobacco Smoke (ETS) | Current smokers | 49 | 9.5 | 0 | 0.0 | 49 | 12.6 |
| | Non smoker ETS | 74 | 14.3 | 25 | 19.8 | 49 | 12.6 |
| | Non smoker non-ETS | 393 | 76.2 | 101 | 80.2 | 292 | 74.8 |
| Prevalence of bronchial asthma and allergies past 2 years | Bronchial asthma | | | | | | |
| | Yes | 24 | 4.7 | 15 | 11.9 | 9 | 2.3 |
| | Allergic rhinitis | | | | | | |
| | Yes | 96 | 18.6 | 39 | 31.0 | 57 | 14.6 |
| | Allergic conjunctivitis | | | | | | |
| | Yes | 39 | 7.6 | 18 | 14.3 | 21 | 5.4 |
| Atopic dermatitis | | | | | | | |
| Yes | 53 | 10.3 | 28 | 22.2 | 25 | 6.4 | |

Table 3. The generalized liner mixed effect analysis and interaction effects of age strata and phthalate categories of the association between phthalates in house dust and prevalence of bronchial asthma and allergies.

| | Floor dust (N=496) | | | | | | | | Multi-surface dust (N=389) | | | | | | | | | |
|--------------------------------|--------------------|------------------|---------------|-------------------|---------------|-------------------------|----------------|-------------------|----------------------------|-------|------------------|--------------|-------------------|-------------|-------------------------|---------------|-------------------|-------------|
| | n | Bronchial asthma | | Allergic rhinitis | | Allergic conjunctivitis | | Atopic dermatitis | | n | Bronchial asthma | | Allergic rhinitis | | Allergic conjunctivitis | | Atopic dermatitis | |
| | | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | | aOR ^b | (95% CI) | aOR ^b | (95% CI) | aOR ^b | (95% CI) | aOR ^b | (95% CI) |
| DMP | | | | | | | | | | | | | | | | | | |
| 0 vs 1 ^c | 496 | 3.16 | (0.74,13.55) | 2.86 | (1.49,5.49)** | 1.83 | (0.59,5.70) | 2.56 | (1.00,6.55) | 389 | 2.07 | (0.45,9.49) | 0.55 | (0.24,1.29) | 0.17 | (0.02,1.31) | 0.36 | (0.08,1.52) |
| P for interaction ^d | | 0.334 | | 0.015 | | 0.512 | | 0.991 | | 0.617 | | 0.685 | | 0.072 | | 0.069 | | |
| DEP | | | | | | | | | | | | | | | | | | |
| 0 vs 1 ^c | 496 | 1.1 | (0.25,4.78) | 1.03 | (0.57,1.87) | 0.58 | (0.24,1.42) | 1.14 | (0.46,2.77) | 389 | 2.60 | (0.48,13.98) | 1.19 | (0.53,2.65) | 0.94 | (0.31,2.87) | 1.24 | (0.5,3.11) |
| P for interaction ^d | | 0.900 | | 0.370 | | 0.842 | | 0.401 | | 0.632 | | 0.312 | | 0.686 | | 0.705 | | |
| DiBP | | | | | | | | | | | | | | | | | | |
| Low | 169 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 165 | 2.25 | (0.48,10.57) | 1.87 | (0.83,4.22) | 1.07 | (0.38,3.01) | 5.52 | (1.68,18.14)** | 133 | 3.00 | (0.59,15.26) | 1.70 | (0.59,4.85) | 4.37 | (1.19,16.03)* | 1.79 | (0.77,4.15) |
| High | 162 | 5.09 | (1.17,22.15)* | 1.05 | (0.47,2.32) | 1.64 | (0.64,4.18) | 4.84 | (1.46,16.00)* | 125 | 1.57 | (0.34,7.34) | 1.65 | (0.57,4.73) | 1.62 | (0.41,6.33) | 1.29 | (0.57,2.95) |
| P for trend | | 0.030 | | 0.909 | | 0.304 | | 0.010 | | 0.567 | | 0.353 | | 0.490 | | 0.541 | | |
| P for interaction ^d | | 0.506 | | 0.071 | | 0.132 | | 0.123 | | 0.062 | | 0.602 | | 0.052 | | 0.904 | | |
| DnBP | | | | | | | | | | | | | | | | | | |
| Low | 168 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 130 | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 164 | 2.05 | (0.52,8.16) | 1.17 | (0.55,2.51) | 1.67 | (0.56,4.98) | 1.47 | (0.62,3.47) | 130 | 1.41 | (0.37,5.29) | 0.91 | (0.41,2.06) | 1.13 | (0.41,3.08) | 1.24 | (0.56,2.77) |
| High | 164 | 4.54 | (1.23,16.79)* | 1.00 | (0.44,2.26) | 1.13 | (0.37,3.44) | 1.19 | (0.46,3.07) | 129 | 3.49 | (0.89,13.69) | 1.24 | (0.51,3) | 0.76 | (0.21,2.69) | 1.02 | (0.38,2.76) |
| P for trend | | 0.024 | | 0.997 | | 0.836 | | 0.714 | | 0.073 | | 0.636 | | 0.664 | | 0.966 | | |
| P for interaction ^d | | 0.836 | | 0.677 | | 0.183 | | 0.915 | | 0.810 | | 0.858 | | 0.246 | | 0.809 | | |
| BBzP | | | | | | | | | | | | | | | | | | |
| Low | 166 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 130 | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 167 | 3.46 | (0.82,14.55) | 1.27 | (0.64,2.52) | 0.65 | (0.23,1.83) | 3.69 | (1.41,9.68)** | 130 | 1.19 | (0.31,4.55) | 1.28 | (0.54,3.05) | 2.87 | (0.80,10.28) | 1.16 | (0.48,2.78) |
| High | 163 | 2.97 | (0.78,11.35) | 1.98 | (0.98,4.03)† | 1.40 | (0.56,3.49) | 5.46 | (2.06,14.48)** | 129 | 1.60 | (0.42,6.09) | 0.93 | (0.41,2.13) | 2.48 | (0.67,9.19) | 1.06 | (0.43,2.62) |
| P for trend | | 0.111 | | 0.058 | | 0.464 | | 0.001 | | 0.485 | | 0.869 | | 0.174 | | 0.902 | | |
| P for interaction ^d | | 0.949 | | 0.250 | | 0.903 | | 0.641 | | 0.117 | | 0.432 | | 0.066 | | 0.450 | | |
| DEHP | | | | | | | | | | | | | | | | | | |
| Low | 167 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 164 | 1.50 | (0.43,5.23) | 1.61 | (0.74,3.47) | 1.41 | (0.47,4.23) | 2.03 | (0.81,5.12) | 130 | 1.07 | (0.33,3.46) | 1.15 | (0.51,2.58) | 0.54 | (0.17,1.75) | 2.01 | (0.84,4.84) |
| High | 165 | 1.69 | (0.52,5.48) | 1.70 | (0.77,3.76) | 6.11 | (2.26,16.53)** | 2.60 | (1.07,6.3)* | 128 | 1.13 | (0.34,3.72) | 1.80 | (0.84,3.86) | 1.21 | (0.42,3.51) | 1.93 | (0.74,5.02) |
| P for trend | | 0.381 | | 0.187 | | 0.000 | | 0.035 | | 0.840 | | 0.130 | | 0.727 | | 0.175 | | |
| P for interaction ^d | | 0.853 | | 0.102 | | 0.427 | | 0.341 | | 0.787 | | 0.573 | | 0.222 | | 0.282 | | |
| DiNP | | | | | | | | | | | | | | | | | | |
| Low | 170 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 163 | 1.35 | (0.25,7.33) | 1.24 | (0.62,2.45) | 1.19 | (0.48,2.96) | 1.39 | (0.65,3.00) | 130 | 0.96 | (0.24,3.83) | 1.35 | (0.64,2.83) | 1.39 | (0.56,3.46) | 0.78 | (0.36,1.68) |
| High | 163 | 2.13 | (0.47,9.55) | 1.85 | (0.93,3.67)† | 0.86 | (0.31,2.43) | 1.22 | (0.54,2.75) | 128 | 0.76 | (0.17,3.42) | 1.03 | (0.47,2.24) | 0.45 | (0.11,1.76) | 0.88 | (0.41,1.90) |
| P for trend | | 0.324 | | 0.080 | | 0.775 | | 0.633 | | 0.716 | | 0.946 | | 0.247 | | 0.740 | | |
| P for interaction ^d | | 0.028 | | 0.133 | | 0.615 | | 0.790 | | 0.090 | | 0.736 | | 0.967 | | 0.646 | | |
| DEHA | | | | | | | | | | | | | | | | | | |
| Low | 249 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 197 | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| High | 247 | 3.72 | (0.79,17.55) | 1.00 | (0.53,1.91) | 1.10 | (0.47,2.56) | 2.32 | (0.9,6.03) | 192 | 3.39 | (0.58,19.94) | 0.89 | (0.42,1.86) | 0.55 | (0.17,1.84) | 0.92 | (0.35,2.37) |
| P for interaction ^d | | 0.207 | | 0.648 | | 0.484 | | 0.900 | | 0.165 | | 0.642 | | 0.685 | | 0.984 | | |

^a: Adjusted for gender (male, female), age strata (≤ 14 , $+15$ years old), environmental tobacco smoke (current smoker/ non-smoking, ETS/ non-smoking, non-ETS), dampness index (0-5), furry pets inside the home (yes, no), and Der1 (continuous) plus the sum of other phthalates: DiBP in floor dust were adjusted for the sum of floor dust phthalate concentration except DiBP; DMP, DEP, DnBP, BBzP, DEHP, DiNP, and DEHA in floor dust.

^b: Adjusted for gender (male, female), age strata (≤ 14 , $+15$ years old), environmental tobacco smoke (current smoker/ non-smoking, ETS/ non-smoking, non-ETS), dampness index (0-5), furry pets inside the home (yes, no), and Der1 (continuous) plus the sum of other phthalates: DiBP in multi-surface dust were adjusted for the sum of multi-surface dust phthalate concentration except DiBP; DMP, DEP, DnBP, BBzP, DEHP, DiNP, and DEHA in multi-surface dust.

^c: a categorical variable of "absence / presence".

^d: P for interaction was separately estimated by adding an interaction term of age strata and phthalate categories into the model adjusted by the variables as above^a.

†: $P < 0.1$; *: $P < 0.05$; **: $P < 0.01$

Table 4. Simultaneous estimation of age strata with generalized liner mixed effect model of the associations of phthalates in floor dust and prevalence of bronchial asthma and allergies (n=496 participants; 148 homes).

| | n | Bronchial asthma | | | | Allergic rhinitis | | | | Allergic conjunctivitis | | | | Atopic dermatitis | | | |
|---------------------|-----|------------------|--------------|------------------|---------------|-------------------|---------------|------------------|-------------|-------------------------|---------------|------------------|--------------|-------------------|----------------|------------------|---------------|
| | | Child (n=122) | | Adult (n=374) | | Child (n=122) | | Adult (n=374) | | Child (n=122) | | Adult (n=374) | | Child (n=122) | | Adult (n=374) | |
| | | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) |
| DMP | | | | | | | | | | | | | | | | | |
| 0 vs 1 ^b | 496 | 3.16 | (0.74,13.55) | 1.28 | (0.37,4.42) | 2.86 | (1.49,5.49)** | 0.43 | (0.11,1.65) | 1.83 | (0.59,5.7) | 0.99 | (0.24,4.03) | 2.56 | (1.00,6.55) | 2.58 | (0.86,7.76) |
| DEP | | | | | | | | | | | | | | | | | |
| 0 vs 1 ^b | 496 | 1.25 | (0.41,3.82) | 1.10 | (0.25,4.78) | 1.68 | (0.67,4.22) | 1.03 | (0.57,1.87) | 0.58 | (0.24,1.42) | 0.50 | (0.16,1.63) | 2.15 | (0.76,6.05) | 1.14 | (0.46,2.77) |
| DiBP | | | | | | | | | | | | | | | | | |
| Low | 169 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 165 | 4.37 | (0.36,53.63) | 1.16 | (0.16,8.17) | 3.54 | (0.86,14.52) | 0.99 | (0.47,2.05) | 1.97 | (0.35,11.07) | 0.59 | (0.19,1.8) | 11.95 | (1.37,104.00)* | 2.55 | (0.89,7.31) |
| High | 162 | 8.94 | (0.86,92.99) | 2.90 | (0.52,16.16) | 2.30 | (0.60,8.89) | 0.48 | (0.22,1.02) | 3.27 | (0.68,15.67) | 0.82 | (0.31,2.2) | 15.03 | (1.91,117.99)* | 1.56 | (0.44,5.53) |
| P for trend | | 0.067 | | 0.224 | | 0.225 | | 0.056 | | 0.138 | | 0.690 | | 0.010 | | 0.49 | |
| DnBP | | | | | | | | | | | | | | | | | |
| Low | 168 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 164 | 1.29 | (0.28,5.85) | 3.27 | (0.35,30.26) | 1.34 | (0.39,4.61) | 1.02 | (0.5,2.11) | 1.77 | (0.33,9.46) | 1.58 | (0.53,4.65) | 1.64 | (0.43,6.34) | 1.32 | (0.47,3.71) |
| High | 164 | 3.50 | (0.68,18.07) | 5.88 | (0.61,56.74) | 1.16 | (0.34,3.93) | 0.87 | (0.38,1.99) | 2.09 | (0.45,9.64) | 0.61 | (0.16,2.35) | 1.27 | (0.33,4.82) | 1.12 | (0.35,3.61) |
| P for trend | | 0.134 | | 0.125 | | 0.813 | | 0.734 | | 0.344 | | 0.467 | | 0.72 | | 0.85 | |
| BBzP | | | | | | | | | | | | | | | | | |
| Low | 166 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 167 | 3.30 | (0.57,19.20) | 3.63 | (0.39,34.17) | 1.90 | (0.63,5.75) | 0.85 | (0.39,1.86) | 0.66 | (0.14,3.12) | 0.64 | (0.19,2.17) | 4.02 | (1.01,16.03)* | 3.40 | (0.78,14.75) |
| High | 163 | 2.98 | (0.51,17.38) | 2.96 | (0.29,30.21) | 3.04 | (0.92,10.04) | 1.29 | (0.60,2.80) | 1.48 | (0.33,6.56) | 1.34 | (0.47,3.79) | 6.55 | (1.70,25.29)** | 4.54 | (1.06,19.43)* |
| P for trend | | 0.225 | | 0.358 | | 0.068 | | 0.513 | | 0.608 | | 0.587 | | 0.007 | | 0.041 | |
| DEHP | | | | | | | | | | | | | | | | | |
| Low | 167 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 164 | 1.67 | (0.28,9.89) | 1.35 | (0.22,8.31) | 3.15 | (0.88,11.32) | 0.82 | (0.38,1.78) | 1.77 | (0.31,10.26) | 1.12 | (0.29,4.37) | 1.79 | (0.46,6.92) | 2.31 | (0.66,8.08) |
| High | 165 | 1.92 | (0.38,9.80) | 1.49 | (0.23,9.51) | 3.24 | (0.93,11.34) | 0.89 | (0.39,2.07) | 9.31 | (1.72,50.38)* | 4.01 | (1.28,12.6)* | 1.74 | (0.49,6.17) | 3.87 | (1.09,13.79)* |
| P for trend | | 0.431 | | 0.676 | | 0.066 | | 0.794 | | 0.010 | | 0.017 | | 0.389 | | 0.037 | |
| DiNP | | | | | | | | | | | | | | | | | |
| Low | 170 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 163 | 1.86 | (0.48,7.27) | 0.98 | (0.06,15.36) | 1.64 | (0.53,5.08) | 0.93 | (0.43,2.03) | 5.12 | (0.61,43.03) | 3.73 | (0.85,16.4) | 3.30 | (0.99,10.94) | 0.59 | (0.21,1.68) |
| High | 163 | 0.61 | (0.12,3.04) | 7.40 | (0.95,57.99)† | 3.04 | (1.01,9.18)* | 1.12 | (0.53,2.38) | 0.97 | (0.10,9.03) | 2.70 | (0.59,12.3) | 1.43 | (0.35,5.9) | 1.04 | (0.39,2.78) |
| P for trend | | 0.546 | | 0.057 | | 0.049 | | 0.765 | | 0.976 | | 0.200 | | 0.616 | | 0.944 | |
| DEHA | | | | | | | | | | | | | | | | | |
| Low | 249 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| High | 247 | 1.16 | (0.34,3.92) | 3.72 | (0.79,17.55) | 1.28 | (0.53,3.06) | 1.00 | (0.53,1.91) | 0.67 | (0.21,2.15) | 1.10 | (0.47,2.56) | 2.12 | (0.8,5.61) | 2.32 | (0.90,6.03) |

^a: Adjusted for gender (male, female), age strata (=<14, +15 years old), environmental tobacco smoke (current smoker/ non-smoking, ETS/ non-smoking, non-ETS), dampness index (0-5), furry pets inside the home (yes, no), and Der1 (continuous) plus the sum of other phthalates: DiBP in floor dust were adjusted for the sum of floor dust phthalate concentration except DiBP; DMP, DEP, DnBP, BBzP, DEHP, DiNP, and DEHA in floor dust.

^b: a categorical variable of "absence / presence".

†: P<0.1; *: P<0.05; **:P<0.01

Table 5.

Simultaneous estimation of age strata with generalized liner mixed effect model of the associations of phthalates in multi-surface dust and prevalence of bronchial asthma and allergies (n= 389 participants; 120 homes).

| | n | Bronchial asthma | | | | Allergic rhinitis | | | | Allergic conjunctivitis | | | | Atopic dermatitis | | | |
|---------------------|-----|------------------|--------------|------------------|--------------|-------------------|--------------|------------------|-------------|-------------------------|---------------|------------------|--------------|-------------------|--------------|------------------|-------------|
| | | Child (n=100) | | Adult (n=289) | | Child (n=100) | | Adult (n=289) | | Child (n=100) | | Adult (n=289) | | Child (n=100) | | Adult (n=289) | |
| | | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) |
| DMP | | | | | | | | | | | | | | | | | |
| 0 vs 1 ^b | 389 | 2.07 | (0.45,9.49) | 1.35 | (0.38,4.79) | 0.55 | (0.24,1.29) | 0.76 | (0.24,2.42) | 1.23 | (0.34,4.38) | 0.17 | (0.02,1.31) | 0.36 | (0.08,1.52) | 2.29 | (0.84,6.2) |
| DEP | | | | | | | | | | | | | | | | | |
| 0 vs 1 ^b | 389 | 2.60 | (0.48,13.98) | 1.54 | (0.42,5.62) | 0.62 | (0.22,1.71) | 1.19 | (0.53,2.65) | 1.31 | (0.34,5.02) | 0.94 | (0.31,2.87) | 0.93 | (0.31,2.79) | 1.24 | (0.50,3.11) |
| DiBP | | | | | | | | | | | | | | | | | |
| Low | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 133 | 4.76 | (0.46,49.40) | 1.89 | (0.67,21.02) | 2.16 | (0.34,13.52) | 1.34 | (0.55,3.25) | 5.12 | (0.61,43.03) | 3.73 | (0.85,16.44) | 1.63 | (0.42,6.38) | 1.96 | (0.67,5.76) |
| High | 125 | 5.83 | (0.49,68.59) | 0.42 | (0.37,4.80) | 1.55 | (0.25,9.54) | 1.74 | (0.64,4.73) | 0.97 | (0.10,9.03) | 2.70 | (0.59,12.34) | 1.51 | (0.38,6.03) | 1.10 | (0.37,3.28) |
| P for trend | | 0.485 | | 0.160 | | 0.632 | | 0.273 | | 0.976 | | 0.200 | | 0.555 | | 0.859 | |
| DnBP | | | | | | | | | | | | | | | | | |
| Low | 130 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 1.96 | (0.29,13.06) | 1.01 | (0.14,7.1) | 0.91 | (0.26,3.18) | 0.92 | (0.38,2.26) | 0.92 | (0.23,3.68) | 1.38 | (0.34,5.51) | 1.36 | (0.36,5.11) | 1.13 | (0.41,3.15) |
| High | 129 | 4.34 | (0.62,30.41) | 2.81 | (0.47,16.73) | 1.32 | (0.35,4.98) | 1.16 | (0.47,2.89) | 0.40 | (0.07,2.44) | 1.42 | (0.31,6.37) | 1.16 | (0.25,5.39) | 0.90 | (0.25,3.17) |
| P for trend | | 0.139 | | 0.256 | | 0.680 | | 0.750 | | 0.321 | | 0.650 | | 0.846 | | 0.866 | |
| BBzP | | | | | | | | | | | | | | | | | |
| Low | 130 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 2.40 | (0.42,13.54) | 0.59 | (0.09,3.69) | 2.87 | (0.75,11.03) | 0.57 | (0.22,1.51) | 9.81 | (1.06,91.23)* | 0.84 | (0.23,3.06) | 1.60 | (0.41,6.21) | 0.84 | (0.27,2.59) |
| High | 129 | 4.56 | (0.66,31.48) | 0.56 | (0.10,3.24) | 1.26 | (0.34,4.63) | 0.69 | (0.28,1.72) | 7.71 | (0.85,69.97)† | 0.80 | (0.22,2.91) | 1.47 | (0.39,5.57) | 0.76 | (0.24,2.47) |
| P for trend | | 0.123 | | 0.519 | | 0.722 | | 0.424 | | 0.070 | | 0.730 | | 0.570 | | 0.650 | |
| DEHP | | | | | | | | | | | | | | | | | |
| Low | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 0.47 | (0.08,2.68) | 2.42 | (0.46,12.8) | 1.29 | (0.34,4.87) | 1.03 | (0.42,2.55) | 0.19 | (0.04,0.98) | 1.56 | (0.41,5.93) | 1.69 | (0.37,7.77) | 2.40 | (0.81,7.09) |
| High | 128 | 1.18 | (0.23,6.10) | 1.08 | (0.14,8.08) | 2.20 | (0.60,8.05) | 1.48 | (0.64,3.39) | 0.59 | (0.14,2.54) | 2.49 | (0.65,9.63) | 3.02 | (0.69,13.34) | 1.24 | (0.35,4.4) |
| P for trend | | 0.842 | | 0.940 | | 0.234 | | 0.356 | | 0.474 | | 0.184 | | 0.143 | | 0.743 | |
| DiNP | | | | | | | | | | | | | | | | | |
| Low | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 0.90 | (0.17,4.87) | 1.02 | (0.14,7.45) | 2.49 | (0.79,7.85) | 0.73 | (0.29,1.84) | 1.18 | (0.34,4.17) | 1.63 | (0.53,5.04) | 1.63 | (0.53,5.04) | 1.18 | (0.34,4.17) |
| High | 128 | 0.25 | (0.03,2.38) | 2.30 | (0.42,12.56) | 1.19 | (0.35,4.12) | 0.88 | (0.38,2.07) | 0.52 | (0.08,3.54) | 0.38 | (0.07,2.20) | 0.38 | (0.07,2.20) | 0.52 | (0.08,3.54) |
| P for trend | | 0.226 | | 0.334 | | 0.779 | | 0.775 | | 0.506 | | 0.278 | | 0.576 | | 0.838 | |
| DEHA | | | | | | | | | | | | | | | | | |
| Low | 197 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| High | 192 | 0.81 | (0.23,2.83) | 3.39 | (0.58,19.94) | 0.68 | (0.25,1.82) | 0.89 | (0.43,1.86) | 0.39 | (0.11,1.43) | 0.55 | (0.17,1.84) | 0.90 | (0.3,2.69) | 0.92 | (0.35,2.37) |

^a: Adjusted for gender (male, female), age strata (≤14, +15 years old), environmental tobacco smoke (current smoker/ non-smoking, ETS/ non-smoking, non-ETS), dampness index (0-5), furry pets inside the home (yes, no), and Der1 (continuous) plus the sum of other phthalates: DiBP in multi-surface dust were adjusted for the sum of floor dust phthalate concentration except DiBP; DMP, DEP, DnBP, BBzP, DEHP, DiNP, and DEHA in multi-surface dust.

^b: a categorical variable of "absence / presence".

†: P< 0.1; *: P< 0.05; **:P< 0.01

Table S1

The operating conditions for GC/MS

| Component | Codition |
|------------------------|---|
| Gas Chromatograph | HP 5890 Series □ GC |
| Mass spectral detector | HP 5971A MSD |
| Column | Ultra-1 12 m×0.2 mm i.d.×0.33 μm |
| Oven temperature | 120°C(2 min)-20°C /min-200°C -10°C /min-270°C (5 min) |
| Carrier gas | Helium, 40 kPa(constant pressure mode) |
| Inlet temperature | 280°C |
| Injection volume | 2μL, splitless mode (purge on time 0.5 min) |
| Detector temperature | 280°C |
| Acquisition mode | SIM |

Table S2

| Compounds | Recovery rate (%) (n=3) | LOD ($\mu\text{g/g}$)* |
|-----------|-------------------------|--------------------------|
| DMP | 80.5 \pm 1.6 | 0.10 |
| DEP | 89.9 \pm 2.5 | 0.12 |
| DiBP | 97.9 \pm 5.4 | 0.04 |
| DnBP | 90.2 \pm 3.3 | 1.8 |
| BBzP | 95.3 \pm 5.8 | 0.10 |
| DEHP | 87.3 \pm 4.9 | 0.42 |
| DiNP | 99.9 \pm 4.5 | 2.0 |
| DEHA | 92.7 \pm 7.4 | 0.17 |

DMP, dimethyl phthalate; DEP, diethyl phthalate; DiBP, di-iso-butyl phthalate; DnBP, di-n-butyl phthalate; BBzP, benzyl butyl phthalate; DEHP, di-2-ethylhexyl phthalate; DEHA, di-2-ethylhexyl adipate

LOD, Limit of detection (based on a signal-to-noise ratio of 3)

Table S3Distribution of phthalate in house dust ($\mu\text{g/g}$ dust) (n=112).

| | Floor (n=112) | | | | | | Multi-surface (n=112) | | | | | ρ^a |
|------|---------------|------|------|------|-------|------|-----------------------|------|------|------|-------|----------|
| | MDL | Min. | 25% | Med. | 75% | Max | Min. | 25% | Med. | 75% | Max | |
| DMP | 0.20 | <MDL | <MDL | <MDL | <MDL | 61.3 | <MDL | <MDL | <MDL | 0.18 | 5.19 | |
| DEP | 0.24 | <MDL | <MDL | 0.26 | 0.43 | 2.86 | <MDL | <MDL | 0.26 | 0.52 | 9000 | 0.368** |
| DiBP | 0.08 | 0.49 | 1.43 | 2.52 | 5.49 | 262 | <MDL | 1.00 | 1.8 | 3.45 | 47.1 | 0.577** |
| DnBP | 3.50 | <MDL | 11.2 | 19.1 | 45.80 | 1476 | <MDL | 11.0 | 21.1 | 43.1 | 3640 | 0.268** |
| BBzP | 0.20 | <MDL | 0.80 | 2.20 | 4.7 | 60.5 | <MDL | 0.87 | 1.65 | 3.85 | 431 | 0.398** |
| DEHP | 0.84 | 98.2 | 445 | 795 | 1510 | 8780 | 40.9 | 298 | 908 | 2010 | 10200 | 0.376** |
| DiNP | 4.00 | 9.12 | 50.7 | 94.2 | 199 | 5820 | <MDL | 47.2 | 94.2 | 284 | 13100 | 0.464** |
| DEHA | 0.33 | <MDL | 2.72 | 4.81 | 7.73 | 692 | <MDL | 2.70 | 5.25 | 8.80 | 1360 | 0.423** |

^a: Spearman's correlations between floor and multi-surface dust; ** p<0.01

Table S4

The generalized liner mixed analysis of phthalates in floor dust and prevalence of asthma and allergies (n=496 participants; 148 homes).

| | n | Bronchial asthma | | | | Allergic rhinitis | | | | Allergic conjunctivitis | | | | Atopic dermatitis | | | |
|--------------------|-----|------------------|--------------|------------------|---------------|-------------------|----------------|------------------|---------------|-------------------------|---------------|------------------|-------------|-------------------|----------------|------------------|---------------|
| | | Child | | Adult | | Child | | Adult | | Child | | Adult | | Child | | Adult | |
| | | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) |
| DMP | | | | | | | | | | | | | | | | | |
| 0 v 1 ^b | 496 | 2.72 | (0.66,11.1) | 1.31 | (0.39,4.40) | 2.70 | (1.41,5.16)** | 0.44 | (0.11,1.69) | 1.10 | (0.28,4.37) | 2.05 | (0.73,5.75) | 2.45 | (0.82,7.3) | 2.33 | (0.92,5.89) |
| DEP | | | | | | | | | | | | | | | | | |
| 0 v 1 ^b | 496 | 1.08 | (0.25,4.66) | 1.23 | (0.40,3.74) | 1.66 | (0.67,4.10) | 1.02 | (0.56,1.86) | 0.67 | (0.21,2.13) | 0.74 | (0.32,1.72) | 2.03 | (0.72,5.72) | 1.10 | (0.45,2.69) |
| DiBP | | | | | | | | | | | | | | | | | |
| Low | 169 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 165 | 1.13 | (0.34,50.36) | 1.1 | (0.16,7.79) | 11.25 | (1.29,97.96)* | 2.45 | (0.86,7.01) | 2.14 | (0.37,12.38) | 0.64 | (0.20,1.99) | 11.25 | (1.29,97.96)* | 2.45 | (0.86,7.01) |
| High | 162 | 7.57 | (0.74,77.72) | 2.61 | (0.47,14.36) | 12.76 | (1.62,100.45)* | 1.42 | (0.40,5.10) | 4.15 | (0.88,19.63)† | 0.95 | (0.36,2.51) | 12.76 | (1.62,100.45)* | 1.42 | (0.40,5.1) |
| P for trend | | 0.088 | | 0.269 | | 0.016 | | 0.590 | | 0.073 | | 0.918 | | 0.016 | | 0.590 | |
| DnBP | | | | | | | | | | | | | | | | | |
| Low | 168 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 164 | 1.14 | (0.25,5.3) | 3.09 | (0.33,28.96) | 1.60 | (0.42,6.10) | 1.31 | (0.47,3.65) | 2.21 | (0.38,12.82) | 1.83 | (0.62,5.43) | 1.60 | (0.42,6.1) | 1.31 | (0.47,3.65) |
| High | 164 | 2.76 | (0.58,13.18) | 5.04 | (0.52,48.7) | 1.20 | (0.34,4.20) | 1.08 | (0.35,3.35) | 3.07 | (0.74,12.78) | 0.88 | (0.26,2.94) | 1.20 | (0.34,4.2) | 1.08 | (0.35,3.35) |
| P for trend | | 0.203 | | 0.1617 | | 0.777 | | 0.890 | | 0.123 | | 0.831 | | 0.777 | | 0.890 | |
| BBzP | | | | | | | | | | | | | | | | | |
| Low | 166 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 167 | 3.34 | (0.58,19.12) | 3.63 | (0.38,34.30) | 4.11 | (1.03,16.42)** | 3.37 | (0.78,14.63) | 0.61 | (0.13,2.79) | 0.64 | (0.20,2.09) | 4.11 | (1.03,16.42)* | 3.37 | (0.78,14.63) |
| High | 163 | 2.99 | (0.51,17.53) | 2.96 | (0.29,30.27) | 6.48 | (1.66,25.32)** | 4.47 | (1.04,19.18)* | 1.48 | (0.34,6.46) | 1.32 | (0.49,3.55) | 6.48 | (1.66,25.32)** | 4.47 | (1.04,19.18)* |
| P for trend | | 0.224 | | 0.359 | | 0.007 | | 0.044 | | 0.603 | | 0.582 | | 0.007 | | 0.044 | |
| DEHP | | | | | | | | | | | | | | | | | |
| Low | 167 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 164 | 1.68 | (0.28,10.06) | 1.35 | (0.22,8.34) | 1.68 | (0.44,6.39) | 2.25 | (0.65,7.84) | 1.55 | (0.27,8.79) | 1.04 | (0.26,4.13) | 1.68 | (0.44,6.39) | 2.25 | (0.65,7.84) |
| High | 165 | 1.93 | (0.40,9.32) | 1.48 | (0.23,9.46) | 1.44 | (0.42,4.95) | 3.38 | (0.96,11.85) | 6.76 | (1.33,34.21) | 3.12 | (1.02,9.58) | 1.44 | (0.42,4.95) | 3.38 | (0.96,11.85) |
| P for trend | | 0.414 | | 0.680 | | 0.561 | | 0.057 | | 0.021 | | 0.046 | | 0.561 | | 0.057 | |
| DiNP | | | | | | | | | | | | | | | | | |
| Low | 170 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 163 | 1.86 | (0.48,7.23) | 0.97 | (0.06,15.12) | 3.29 | (1,10.86) | 0.59 | (0.21,1.68) | 1.52 | (0.39,5.97) | 1.13 | (0.39,3.26) | 3.29 | (1.00,10.86)* | 0.59 | (0.21,1.68) |
| High | 163 | 0.59 | (0.12,2.9) | 7.15 | (0.95,53.65)† | 1.44 | (0.36,5.86) | 1.04 | (0.40,2.73) | 1.72 | (0.37,7.88) | 1.08 | (0.38,3.05) | 1.44 | (0.36,5.86) | 1.04 | (0.40,2.73) |
| P for trend | | 0.518 | | 0.056 | | 0.607 | | 0.935 | | 0.487 | | 0.881 | | 0.607 | | 0.935 | |
| DEHA | | | | | | | | | | | | | | | | | |
| Low | 249 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| High | 247 | 1.12 | (0.34,3.73) | 3.59 | (0.77,16.79) | 2.03 | (0.77,5.33) | 2.25 | (0.87,5.82) | 0.77 | (0.24,2.46) | 1.24 | (0.54,2.87) | 2.03 | (0.77,5.33) | 2.25 | (0.87,5.82) |

^a: Adjusted for gender (male, female), age strata (=<14, +15 years old), environmental tobacco smoke (current smoker/ non-smoking, ETS/ non-smoking, non-ETS), dampness index (0-5), furry pets inside the home (yes, no), and Der1 (continuous).^b: a categorical variable of “absence / presence”.

†: P<0.1; *: P<0.05; **:P<0.01

Table S5

The generalized liner mixed analysis of phthalates in multi-surface dust and prevalence of asthma and allergies (n=389 participants; 120 homes).

| | n | Bronchial asthma | | | | Allergic rhinitis | | | | Allergic conjunctivitis | | | | Atopic dermatitis | | | |
|--------------------|-----|------------------|--------------|------------------|--------------|-------------------|---------------------------|------------------|-------------|-------------------------|---------------|------------------|-------------|-------------------|---------------------------|------------------|-------------|
| | | Child | | Adult | | Child | | Adult | | Child | | Adult | | Child | | Adult | |
| | | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) | aOR ^a | (95% CI) |
| DMP | | | | | | | | | | | | | | | | | |
| 0 v 1 ^b | 389 | 2.55 | (0.59,11.00) | 1.53 | (0.47,4.97) | 1.01 | (0.32,3.20) | 0.66 | (0.30,1.49) | 1.41 | (0.39,5.11) | 0.20 | (0.03,1.47) | 0.45 | (0.11,1.8) | 2.22 | (0.82,6.03) |
| DEP | | | | | | | | | | | | | | | | | |
| 0 v 1 ^b | 389 | 2.62 | (0.52,13.26) | 1.55 | (0.43,5.59) | 0.61 | (0.22,1.70) | 1.17 | (0.54,2.51) | 1.28 | (0.35,4.66) | 0.90 | (0.33,2.47) | 0.97 | (0.32,3) | 1.47 | (0.58,3.72) |
| DiBP | | | | | | | | | | | | | | | | | |
| Low | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 133 | 1.88 | (0.17,20.35) | 4.78 | (0.46,50.22) | 1.41 | (0.36,5.57) | 2.13 | (0.73,6.24) | 5.24 | (0.63,43.58) | 3.53 | (0.8,15.49) | 1.41 | (0.36,5.57) | 2.13 | (0.73,6.24) |
| High | 125 | 0.43 | (0.04,4.87) | 5.92 | (0.52,67.44) | 1.46 | (0.36,5.90) | 1.43 | (0.47,4.41) | 0.95 | (0.10,8.86) | 2.46 | (0.58,10.5) | 1.46 | (0.36,5.9) | 1.43 | (0.47,4.41) |
| P for trend | | 0.491 | | 0.151 | | 0.598 | | 0.527 | | 0.963 | | 0.223 | | 0.598 | | | |
| DnBP | | | | | | | | | | | | | | | | | |
| Low | 130 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 2.01 | (0.30,13.4) | 0.98 | (0.14,6.74) | 1.27 | (0.32,5.05) | 1.34 | (0.45,3.95) | 0.94 | (0.23,3.83) | 1.34 | (0.36,5.05) | 1.27 | (0.32,5.05) | 1.34 | (0.45,3.95) |
| High | 129 | 4.12 | (0.64,26.74) | 2.65 | (0.47,14.96) | 1.40 | (0.31,6.32) | 1.19 | (0.37,3.81) | 0.39 | (0.07,2.17) | 1.34 | (0.36,5.01) | 1.40 | (0.31,6.32) | 1.19 | (0.37,3.81) |
| P for trend | | 0.137 | | 0.268 | | 0.664 | | 0.771 | | 0.282 | | 0.664 | | 0.664 | | 0.771 | |
| BBzP | | | | | | | | | | | | | | | | | |
| Low | 130 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 2.41 | (0.43,13.55) | 0.59 | (0.10,3.52) | 1.85 | (0.47,7.34) | 1.03 | (0.33,3.2) | 8.57 | (0.88,82.96) | 0.76 | (0.21,2.77) | 1.85 | (0.47,7.34) | 1.03 | (0.33,3.2) |
| High | 129 | 4.58 | (0.68,30.95) | 0.57 | (0.11,2.97) | 1.84 | (0.52,6.48) | 0.94 | (0.31,2.87) | 6.66 | (0.72,61.53)† | 0.70 | (0.20,2.39) | 1.84 | (0.52,6.48) | 0.94 | (0.31,2.87) |
| P for trend | | 0.118 | | 0.500 | | 0.343 | | 0.912 | | 0.094 | | 0.563 | | 0.343 | | 0.912 | |
| DEHP | | | | | | | | | | | | | | | | | |
| Low | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 0.50 | (0.09,2.85) | 2.29 | (0.43,12.18) | 1.53 | (0.32,7.29) | 2.88 | (0.91,9.12) | 0.24 | (0.05,1.2) | 1.41 | (0.37,5.34) | 1.53 | (0.32,7.29) | 2.88 | (0.91,9.12) |
| High | 128 | 1.19 | (0.23,6.24) | 1.02 | (0.14,7.57) | 3.02 | (0.66,13.7 ₁) | 1.54 | (0.44,5.36) | 0.62 | (0.15,2.69) | 2.01 | (0.55,7.43) | 3.02 | (0.66,13.7 ₁) | 1.54 | (0.44,5.36) |
| P for trend | | 0.835 | | 0.986 | | 0.152 | | 0.497 | | 0.526 | | 0.293 | | 0.152 | | 0.497 | |
| DiNP | | | | | | | | | | | | | | | | | |
| Low | 131 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| Medium | 130 | 0.99 | (0.19,5.26) | 1.13 | (0.16,7.72) | 0.58 | (0.16,2.05) | 1.22 | (0.46,3.21) | 1.17 | (0.32,4.27) | 1.62 | (0.54,4.83) | 0.58 | (0.16,2.05) | 1.22 | (0.46,3.21) |
| High | 128 | 0.28 | (0.03,2.45) | 2.57 | (0.51,12.94) | 0.73 | (0.19,2.77) | 1.21 | (0.40,3.7) | 0.52 | (0.08,3.44) | 0.37 | (0.07,2.08) | 0.73 | (0.19,2.77) | 1.21 | (0.4,3.70) |
| P for trend | | 0.246 | | 0.252 | | 0.639 | | 0.735 | | 0.496 | | 0.260 | | 0.639 | | 0.735 | |
| DEHA | | | | | | | | | | | | | | | | | |
| Low | 197 | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | | 1.00 | |
| High | 192 | 0.84 | (0.24,2.97) | 3.47 | (0.60,19.93) | 0.86 | (0.42,1.77) | 0.66 | (0.25,1.76) | 0.39 | (0.11,1.36) | 0.54 | (0.17,1.67) | 1.00 | (0.34,2.95) | 1.02 | (0.41,2.54) |

^a: Adjusted for gender (male, female), age strata (= <14, +15 years old), environmental tobacco smoke (current smoker/ non-smoking, ETS/ non-smoking, non-ETS), dampness index (0-5), furry pets inside the home (yes, no), and Der1 (continuous).^b: a categorical variable of "absence / presence".

†: P< 0.1; *: P< 0.05; **: P< 0.01