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Author(s)	Ait Bamai, Yu; Shibata, Eiji; Saito, Ikue; Araki, Atsuko; Kanazawa, Ayako; Morimoto, Kanehisa; Nakayama, Kunio; Tanaka, Masatoshi; Takigawa, Tomoko; Yoshimura, Takesumi; Chikara, Hisao; Saijo, Yasuaki; Kishi, Reiko
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Exposure to house dust phthalates in relation to asthma and allergies in both children and adults

Yu Ait Bamai[a], Eiji Shibata[b], Ikue Saito[c], Atsuko Araki[d], Ayako Kanazawa[d], Kanehisa Morimoto[e], Kunio Nakayama[e], Masatoshi Tanaka[f], Tomoko Takigawa[g], Takesumi Yoshimura[h], Hisao Chikara[h], Yasuaki Saijo[i], Reiko Kishi[d,*]

[a] Hokkaido University Graduate School of Medicine, Department of Public Health Sciences, Kita 15, Nishi 7, Kita-ku, Sapporo 060-8638, Japan; [b] Aichi Medical University School of Medicine, 21 Yazakokarimata, Nagakute, Aichi 480-1195, Japan; [c] Department of Environmental Health and Toxicology, Division of Environment Health, Tokyo Metropolitan Institute of Public Health, 3-24-1 Hyakunincho, Shinjyuku-ku, Tokyo 169-0073, Japan;[d] Hokkaido University Center for Environmental and Health Sciences, Kita 12, Nishi 7, Kita-ku, Sapporo 060-0812, Japan; [e] Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita 565-0871, Japan; [f] Fukushima Medical University, 80-6 Yagita-Shinnmei, Fukushima-city, 960-8164, Japan; [g] Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan; [h] Fukuoka Institute of Health and Environmental Sciences, 39 Mukaizano, Dazaifu 818-0135, Japan; [i] Asahikawa Medical University, 1-1-1 Midorigaoka Higashi 2 jo, Asahikawa 078-8510, Japan

*Corresponding author: Reiko Kishi, Professor, MD, PhD, MPH

Hokkaido University Center for Environmental and Health Sciences

Kita 12, Nishi 7, Kita-ku, Sapporo 060-0812, Japan

Tel.: +81-11-706-4748, Fax: + 81-11-706-4725

E-mail: rkishi@med.hokudai.ac.jp

Abstract

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

Abbreviations:

BBzP, benzyl butyl phthalate

DBP, dibutyl phthalate

DEHA, di-2-ethylhexyl adipate

DEHP, di-2-ethylhexyl phthalate

DEP, diethyl phthalate

DiBP, di-iso-butyl phthalate

DiNP, di-iso-nonyl phthalate

DMP, dimethyl phthalate

DnBP, di-n-butyl phthalate

ETS, environmental tobacco smoke

GC/MS, gas chromatography/mass spectrometry

LOD, limit of detection

MBzP, mono benzyl phthalate

MDL, method detection limits

PVC, polyvinyl chloride

SVOC, semi-volatile organic compounds

Highlights

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

Key words

Phthalates

House dust

Children

Bronchial asthma

Allergic conjunctivitis

Atopic dermatitis

1. Introduction

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

Dust ingestion contributes to most to the ingestion of high-molecular-weight phthalates such as DEHP and BBzP in children (Beko et al., 2013). Because phthalates are not chemically bound to products, they can easily diffuse within materials, leach out, and then disperse into the air or adhere to airborne particles and settled dust (Fujii et al., 2003). Therefore, phthalates easily penetrate into house dust that settles on phthalate-containing products (Seto and Saito, 2002). We previously reported that high levels of DEHP in dust were detected in dwellings with polyvinyl chloride (PVC) flooring (Ait Bamai et al., 2013). The same findings were reported in previous epidemiological studies (Bornehag et al., 2005; Kolarik et al., 2008a). However, compared to other previous studies, the levels of DEHP in house dust in Japan were higher than in studies from Sweden (Bornehag et al., 2005), Bulgaria (Kolarik et al., 2008), Germany (Abb et al., 2009; Fromme et al., 2004), Denmark (Langer et al., 2010) (Clausen et al., 2003), Taiwan (Hsu et al., 2012), China (Guo and Kannan 2011), and the USA (Guo and Kannan 2011; Rudel et al., 2003), and thus, DEHP exposure is of particular concern for Japan (Ait Bamai et al., 2013).

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

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

2. Materials and methods

Details of the study design and methods used for the environmental measurements have been reported previously (Araki et al., 2010; Kanazawa et al., 2010; Kishi et al., 2009; Takigawa et al., 2010); therefore, only a brief description is provided here.

2.1. Study population

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

2.2. Questionnaire

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

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

2.3. Measurement of phthalate concentrations in settled dust

Dust collection, gas chromatography/mass spectrometry (GC/MS) analytical methods, and quality assurance measures have been previously reported (Araki et al., 2013; Kanazawa et al., 2010; Saito et al., 2007). Briefly, dust samples were categorised as one of two types: floor dust or multi-surface dust. Floor dust samples were collected from all surfaces of the living room floor for 1 min/㎡. Samples of multi-surface dust were collected from the surface of objects that were more than 35 cm above the living room floor, such as shelves, cupboards, doorframes, window frames, TV sets, audio sets, and personal computers. The same type of hand-held vacuum cleaner (National HC-V15, 38W, Matsushita Electric Works, Ltd., Osaka, Japan) equipped with a paper dust bag (Nichinichi Pharmaceutical Co., Ltd., Mie, Japan) was used in all dwellings. To avoid cross-contamination between samples, vacuum nozzles were washed in an ultrasound bath, and vacuum cleaners were wiped with ethanol after each sample was collected. The collected dust was stored in stoppered glass test tubes that had been cleaned with acetone. The tubes were sealed with fluoric-tape, wrapped with aluminium foil, and kept at −20 °C until the day of analysis. Using tweezers, unwanted substances, such as human and animal hair, insects, food scraps, and scrap paper, were removed from the dust samples. One millilitre of acetone per 25 mg dust was added to each sample (25-50 mg dust/sample). The dust collected in the test tubes was subjected to ultrasonic extraction with residue analysis-grade acetone (Wako Pure Chemical Industries, Ltd., Osaka, Japan) for 20 minutes and allowed to stand overnight. An internal standard (IS), 0.1 lg/ml DnBP-d4 was added to each sample for monitoring and quantification. After centrifugation at 2500 g for 10 min, the supernatants were injected onto a Ultra-1 column (Agilent J&W Scientific Inc., Folsom, CA, USA) for GC/MS (Agilent Technologies Inc., Palo Alto, CA, USA) at the Tokyo Metropolitan Institute of Public Health in Tokyo, Japan. The operating conditions for GC/MS are shown in Table S1. Seven phthalates and DEHA were analysed using GC/MS in SIM mode at a temperature of 280°C. The quantification ion of DnBP-d4 was 153, and the quantification and confirmation ions of target compounds were as follows: DMP, 163, 194; DEP, 149, 177; DiBP, 149, 223; DnBP, 149, 223; BBzP, 149, 206; DEHP, 149, 167; DiNP, 149, 167; DEHA, 129, 147.

2.4. Quality assurance and quality control

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

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

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

2.5. Other environmental measurements

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

2.6. Data analysis

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

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

2.7. Ethical considerations

The study protocol was approved by the ethics board for epidemiological studies at the Hokkaido University Graduate School of Medicine and by the ethics boards at all of the regional universities involved in the study. All participants and their parents, when relevant, provided written informed consent to participate in the study.

3. Results

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

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

Table 3 shows the generalized liner mixed effects 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. As for floor dust, we obtained significantly positive liner associations between asthma and DiBP and DnBP, respectively. The prevalence of allergic rhinitis was significantly associated with DMP ($P = 0.002$), and a slightly positive liner association was observed for BBzP, however, it was not statistically significant ($P_{\text{trend}} = 0.058$). A significantly positive liner association was obtained between the prevalence of allergic conjunctivitis and DEHP. Significantly positive liner associations were also obtained between the prevalence of atopic dermatitis and DiBP, BBzP, and DEHP, respectively. Significant interaction effects were obtained between bronchial asthma and DiNP, and between allergic rhinitis and DMP. No significant associations were obtained in multi-surface dust.

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

Table 5 shows 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). There were no significant associations between the prevalence of asthma and allergies and any phthalates in multi-surface dust.

4. Discussion

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

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

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

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

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

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

Phthalate levels in house dust have been measured in several previously reported studies (Abb et al., 2009; Becker et al., 2004; Bornehag et al., 2005; Bornehag et al., 2004; Clausen et al., 2003; Guo and Kannan, 2011; Hsu et al., 2012; Kanazawa et al., 2010; Kang et al., 2012; Kolarik et al., 2008a; Kolarik et al., 2008b; Langer et al., 2010; Nagorka et al., 2005; Oie et al., 1997; Rudel et al., 2003). Comparing the levels of phthalates in our study to those of the other studies (Abb et al., 2009; Bornehag et al., 2004; Clausen et al., 2003; Fromme et al., 2004; Guo and Kannan, 2011; Hsu et al., 2012; Kang et al., 2012; Kolarik et al., 2008b; Langer et al., 2010; Nagorka et al., 2005), DEHP levels in our study were slightly higher than those reported in the other studies in both floor and multi-surface dust. In contrast, BBzP, DnBP, and DINP levels were lower in our study compared to the other studies. We previously reported that house dust levels of DEHP were higher and that BBzP levels were lower in Japan than in other countries, especially in comparison to the levels in Europe and the U.S. (Ait Bamai et al., 2013). Our results were consistent with our previous report.

There are several limitations in this study. First, since the participants in this study were those still remaining at the phase three follow-ups, selection bias may have occurred. Ultimately, this study was a cross-sectional study, and any causal relationships between phthalate levels and health outcomes were not discernible. Second, our study only included detached dwellings aged less than 8 years, thus our results may not be applicable to other types of dwellings. Selection bias of the population may be occurred. Moreover, since there are differences in the phthalate levels in house dust between newly built houses and old houses, the phthalate levels in this study will be generalizable only to relatively new dwellings. Third, environmental measurements were conducted only once. Seasonal and environmental factors affect the quantity and composition of house dust (Mercier et al., 2011). However, we consciously used the same sampling season between six regions from October to December in 2006. Moreover, pore size of the dust bag filter that we used for dust sampling was not measured. Therefore, it is possible that we missed those phthalates attached to smaller particles of dust when we collected the dust. Fourth, we could only measure a limited number of environmental factors related to allergies. Several environmental factors known to influence allergies such as mute allergens and mould were measured; however, other factors such as particle matter were not considered. Fifth, because many statistical analyses on the relation between phthalates and allergies were carried out, statistical significance may have occurred by chance. Thus, false positive associations are possible. Our sample size may also have been too small to evaluate interaction effects by age strata. Moreover, socio-economic status such as household income and educations were not assessed. However, because all participants lived in their own newly built detached house, it was considered that their socio-economic statuses was similar and belonged to the middle class (Saijo et al., 2004). Lastly, health outcomes were assessed using questionnaires of 2-years prevalence of bronchial asthma and allergies. Any biological markers to assess outcomes such as immunoglobulin E were not measured. On the other hand, Callesen et al. (2013) recently reported that DEHP in dust was associated with children's wheeze based on symptoms reported in a questionnaire, but not based on doctors' diagnoses (Callesen et al., 2013). Moreover, bronchial asthma is not diagnosed in the case of acute bronchial infections based on the 2012 Japan pediatric guidelines for the treatment and management of asthma (Hamazaki et al., 2012). Therefore, misclassification of health outcomes may have occurred. The cut-off point of the age categories used in this study was "below 15" for "children" and "more than 15 years old" for "adults" thus the association between house dust and allergies in toddlers could not be determined. The prevalence of bronchial asthma and allergies are different in toddlers, teenagers, and adults. We could not carry out multivariate analyses in three age categories (toddlers, teenagers, and adults) due to the small numbers of toddlers. Moreover, "pediatrics" is commonly defined as those under 15 year of age in Japan. Therefore, we used this definition in the present study and then adjusted for the influence of age using "age strata" in the analyses.

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

5. Conclusion

This cross-sectional study showed the associations between the prevalence of bronchial asthma and allergies and levels of phthalates in house dust using interaction effects of age and exposure categories in a generalized liner mixed effect model. Interaction effects were obtained between DMP and allergic rhinitis in children and between DiNP and bronchial asthma in adults. Levels of DMP, DiNP, DEHP, DiBP, and BBzP in floor dust had liner associations with the prevalence of allergic rhinitis, conjunctivitis, and atopic dermatitis. Furthermore, a stronger association was seen in children compared to adults. No significant associations were found in phthalates levels collected from multi-surfaces. This may suggest that humans, especially children are exposed to phthalates from lower place rather than higher place. Elaborate assessments for metabolism of phthalates were not considered, and further studies are needed to advance our understanding of phthalate toxicity.

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References

Abb, M.; Heinrich, T.; Sorkau, E.; Lorenz, W. Phthalates in house dust. Environ Int. 35:965-970; 2009

Ait Bamai Y, Araki A, Kawai T, Tsuboi T, Saito I, Yoshioka E, et al. Associations of phthalate concentrations in floor dust and multi-surface dust with the interior materials in Japanese dwellings. Science of the Total Environment 2013; 468-469C:147-157.

Araki, A.; Kawai, T.; Eitaki, Y.; Kanazawa, A.; Morimoto, K.; Nakayama, K., et al. Relationship between selected indoor volatile organic compounds, so-called microbial VOC, and the prevalence of mucous membrane symptoms in single family homes. Sci Total Environ. 408:2208-2215; 2010

Araki, A.; Kanazawa, A.; Kawai, T.; Eitaki, Y.; Morimoto, K.; Nakayama, K., et al. The relationship between exposure to microbial volatile organic compound and allergy prevalence in single-family homes. Sci Total Environ. 423:18-26; 2012

Araki, A.; Saito, I.; Kanazawa, A.; Morimoto, K.; Nakayama, K.; Shibata, E., et al. Phosphorus flame retardants in indoor dust and their relation to asthma and allergies of inhabitants. Indoor Air; 2013

Asher, M.I.; Montefort, S.; Bjorksten, B.; Lai, C.K.W.; Strachan, D.P.; Weiland, S.K., et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet. 368:733-743; 2006

Becker, K.; Seiwert, M.; Angerer, J.; Heger, W.; Koch, H.M.; Nagorka, R., et al. DEHP metabolites in urine of children and DEHP in house dust. Int J Hyg Environ Health. 207:409-417; 2004

Beko, G.; Weschler, C.J.; Langer, S.; Callesen, M.; Toftum, J.; Clausen, G. Children's Phthalate Intakes and Resultant Cumulative Exposures Estimated from Urine Compared with Estimates from Dust Ingestion, Inhalation and Dermal Absorption in Their Homes and Daycare Centers. PLoS One. 8:e62442; 2013

Bertelsen RJ, Carlsen KC, Calafat AM, Hoppin JA, Haland G, Mowinckel P, et al. Urinary biomarkers for phthalates associated with asthma in Norwegian children. Environ Health Perspect 2013; 121: 251-6.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

94:560-562; 2004

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

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

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

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

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

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

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

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

habits in the family. Atmos Environ. 42:8553-8559; 2008a
Kolarik, B.; Naydenov, K.; Larsson, M.; Bornehag, C.G.; Sundell, J. The association between phthalates in dust and allergic diseases among Bulgarian children. Environ Health Perspect. 116:98-103; 2008b
Lake, B.G.; Price, R.J.; Cunninghame, M.E.; Walters, D.G. Comparison of the effects of di-(2-ethylhexyl)adipate on hepatic peroxisome proliferation and cell replication in the rat and mouse. Toxicology. 123:217-226; 1997
Langer, S.; Weschler, C.J.; Fischer, A.; Beko, G.; Toftum, J.; Clausen, G. Phthalate and PAH concentrations in dust collected from Danish homes and daycare centers. Atmos Environ. 44:2294-2301; 2010
Larsen ST, Nielsen GD. The adjuvant effect of di-(2-ethylhexyl) phthalate is mediated through a PPARalpha-independent mechanism. Toxicol Lett 2007; 170: 223-8.
Larsson, M.; Hagerhed-Engman, L.; Kolarik, B.; James, P.; Lundin, F.; Janson, S., et al. PVC--as flooring material--and its association with incident asthma in a Swedish child cohort study. Indoor Air. 20:494-501; 2010
Mercier, F.; Glorennec, P.; Thomas, O.; Le Bot, B. Organic Contamination of Settled House Dust, A Review for Exposure Assessment Purposes. Environmental Science & Technology. 45:6716-6727; 2011
Nagorka, R.; Scheller, C.; Ullrich, D. Plasticizer in house dust. Gefahrst Reinhalt Luft. 65:99-105; 2005
OECD. Bis(2-ethylhexyl)adipate (DEHA) CAS N°: 103-23-1. In: OECD, ed; 2010
Oie, L.; Hersoug, L.G.; Madsen, J.O. Residential exposure to plasticizers and its possible role in the pathogenesis of asthma. Environ Health Perspect. 105:972-978; 1997
Rudel, R.A.; Camann, D.E.; Spengler, J.D.; Korn, L.R.; Brody, J.G. Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine-disrupting compounds in indoor air and dust. Environmental Science & Technology. 37:4543-4553; 2003
Saijo, Y.; Kishi, R.; Sata, F.; Katakura, Y.; Urashima, Y.; Hatakeyama, A., et al. Symptoms in relation

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

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

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

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

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

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

Stapleton, H.M., Klosterhaus, S., Eagle, S., Fuh, J., Meeker, J.D., Blum, A. and Webster, T.F. Detection of orga- nophosphate flame retardants in furni- ture foam and U.S. house dust, Environ. Sci. Technol., 43, 7490–7495; 2009

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

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

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

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

U.S.EPA. Exposure Factors Handbook. 2011 van den Eede, N., Dirtu, A.C., Neels, H. and Covaci, A. Analytical develop- ments and preliminary assessment of human exposure to organophosphate flame retardants from indoor dust, Environ. Int., 37, 454–461; 2011

Wang IJ, Lin CC, Lin YJ, Hsieh WS, Chen PC. Early life phthalate exposure and atopic disorders in children: a prospective birth cohort study. Environ Int 2014; 62: 48-54.

WHO. The public health implications of asthma-PUBLIC HEALTH REVIEWS. 2005

Wormuth, M.; Scheringer, M.; Vollenweider, M.; Hungerbuhler, K. What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? Risk Anal. 26:803-824; 2006

Table 1

Distribution of phthalate in house dust (μg/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 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 4)	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 (μ g/g)*
DMP	80.5 ± 1.6	0.10
DEP	89.9 ± 2.5	0.12
DiBP	97.9 ± 5.4	0.04
DnBP	90.2 ± 3.3	1.8
BBzP	95.3 ± 5.8	0.10
DEHP	87.3 ± 4.9	0.42
DiNP	99.9 ± 4.5	2.0
DEHA	92.7 ± 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 S3

Distribution of phthalate in house dust (μg/g dust) (n=112).

		Floor (n=112)					Multi-surface (n=112)					
	MDL	Min.	25%	Med.	75%	Max	Min.	25%	Med.	75%	Max	ρ[a]
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	(0.66,13.71)	1.54	(0.44,5.36)	0.62	(0.15,2.69)	2.01	(0.55,7.43)	3.02	(0.66,13.71)	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