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Phthalates, non-phthalate plasticizers and bisphenols in Swedish preschool dust in relation to children's exposure

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ABSTRACT

Children are exposed to a wide range of chemicals in their everyday environments, including the preschool. In this study, we evaluated the levels of phthalates, non-phthalate plasticizers and bisphenols in dust from 100 Swedish preschools and identified important exposure factors in the indoor environment. In addition, children's total exposure to these chemicals was determined by urine analysis to investigate their relation with dust exposure, and to explore the time trends by comparing with children who provided urine fifteen years earlier. The most abundant plasticizers in preschool dust were the phthalates di-isononyl phthalate (DiNP) and di-(2-ethylhexyl) phthalate (DEHP) with geometric mean levels of 450 and 266 μg/g dust, respectively, and the non-phthalate plasticizers bis(2-ethylhexyl) terephthalate (DEHT) and diisononylcyclohexane-1,2-dicarboxylate (DiNCH) found at 105 and 73 μg/g dust, respectively. The levels of several substitute plasticizers were higher in newer preschools, whereas the levels of the strictly regulated phthalate di-n-butyl phthalate (DnBP) were higher in older preschools. The presence of foam mattresses and PVC flooring in the sampling room were associated with higher levels of DiNP in dust. Children's exposure from preschool dust ingestion was below established health based reference values and the estimated exposure to different phthalates and BPA via preschool dust ingestion accounted for 2–27% of the total exposure. We found significantly lower urinary levels of BPA and metabolites of strictly regulated phthalates, but higher levels of DiNP metabolites, in urine from the children in this study compared to the children who provided urine samples fifteen years earlier.

1. Introduction

Humans are exposed to chemicals in dust via ingestion, inhalation and dermal uptake. Children are known to be more exposed to dust than adults due to their proximity to the floor and frequent hand-to-mouth behavior (Mercier et al., 2011). Young children spend up to one third of their weekdays in the preschool, thus the preschool environment accounts for a considerable part of children's daily exposure to chemicals in dust. Phthalates have been suggested as a chemical group of high priority for dust exposure in children and a few previous studies have measured phthalates in preschool dust (Bergh et al., 2011; Bonvallot et al., 2010; Fromme et al., 2013; Gaspar et al., 2014; Langer et al., 2010; Morgan et al., 2004; Wilson et al., 2001). Only one previous study has analyzed non-phthalate plasticizers (Fromme et al., 2016) and no study has analyzed BPA analogues in preschool dust. Thus, there is need for more exposure data to follow the time trends of plasticizers in preschool environments as previously commonly used chemicals are replaced by alternatives.

Abbreviations: ATBC, tributyl *O*-acetylcitrate; BBzP, butylbenzyl phthalate; BPA, 4,4″-(propane-2,2-diyl)diphenol; BPAF, 4,4′-(hexafluoroisopropylidene)diphenol; BPF, 4,4′-methylenediphenol; BPS, 4,4″-sulfonyldiphenol; DEHA, bis(2-ethylhexyl) adipate; DEHP, di-(2-ethylhexyl) phthalate; DEHT, bis(2-ethylhexyl) terephthalate; DEP, diethyl phthalate; DiBP, diisobutyl phthalate; DiDP, diisodecyl phthalate; DiNCH, diisononylcyclohexane-1,2-dicarboxylate; DiNP, di-isononyl phthalate; DMP, dimethyl phthalate; DnBP, di-n-butyl phthalate; DPHP, di(2-propyl heptyl) phthalate; MBzP, monobenzyl phthalate; MCiNP, monocarboxyisononyl phthalate; MCiOP, mono(carboxyisooctyl) phthalate; MCMHP, Mono[2-(carboxymethyl)hexyl] phthalate; MECPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MEHHP, mono-(2-ethyl-5-hydroxylhexyl) phthalate; MEHP, mono-(2-ethylhexyl) phthalate; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; MEP, monoethyl phthalate; MHiDP, monohydroxyisodecyl phthalate; MHiNP, mono(hydroxyisononyl) phthalate; MnBP, monobutyl phthalate; MOiNCH, 2-4-methyl-7-oxyooctyl-oxycarbonyl-cyclohexane carboxylic acid; MOiNP, mono(oxoisononyl) phthalate.

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Phthalates, non-phthalate plasticizers and bisphenols are semi-volatile organic compounds present in indoor dust. Phthalates are the most commonly used plasticizers in the world and are mainly used for production of polyvinyl chloride (PVC) plastics and to a lesser extent for non-PVC applications, such as glues, paints and cosmetics (Frederiksen et al., 2007; KEMI, 2015; Wittassek et al., 2011). Phthalates can migrate from products and humans are exposed via food, water, air, dust and direct contact with consumer products (Janjua et al., 2008; Wittassek and Angerer, 2008; Wormuth et al., 2006).

Di-(2-ethylhexyl) phthalate (DEHP) was introduced in the 1940s and was the most commonly used phthalate for decades. However, when concern arouse for the reproduction toxicity of DEHP, the use of other phthalates that were considered less toxic increased. Some of these phthalates, such as di(2-propyl heptyl) phthalate (DPHP), di-isononyl phthalate (DiNP) and diisodecyl phthalate (DiDP) are the most commonly used phthalates in the EU today, whereas DEHP still dominates the global market (KEMI, 2014). The phthalates that are considered the most toxic have successively been phased out in the EU by applying gradually stricter regulations. For example, the use of DEHP, di-n-butyl phthalate (DnBP) and butylbenzyl phthalate (BBzP) were banned in toys and childcare articles in 2007, whereas DiNP and DiDP were banned from toys intended for mouthing (EC, 2005). After 2015, DEHP, DnBP, BBzP and diisobutyl phthalate (DiBP), which are classified as reproduction toxic category 1B, cannot be used for any application within the EU without permission (ECHA, 2016a). Although these four phthalates are strictly regulated within EU today, they are abundant in products and materials still in use, and will be so for a long time to come.

As previously commonly used phthalates have been subjected to stricter regulations, substituting non-phthalate plasticizers have become more widely used (Bui et al., 2016; Calafat et al., 2015). Currently, the most commonly used non-phthalate plasticizer is diisononylcyclohexane-1,2-dicarboxylate (DiNCH), which was introduced in the EU in 2002 and made up approximately 70% of the alternative plasticizer market in Sweden by 2012 (Bui et al., 2016). Other commonly used non-phthalate plasticizers are bis(2-ethylhexyl) terephthalate (DEHT), bis(2-ethylhexyl) adipate (DEHA) and tributyl *O*-acetylcitrate (ATBC). Applications for these plasticizers include food packaging, PVC flooring, toys and childcare articles, etc. (ChemSystems, 2008; ECHA, 2016b; KEMI, 2014). These plasticizers are currently considered as non-toxic substitutes for phthalates (Bui et al., 2016; Maag et al., 2010). However, exposure monitoring of these compounds is currently insufficient, not the least in young children (Bui et al., 2016).

4,4″-(propane-2,2-diyl)diphenol (BPA) is used in the production of polycarbonate plastics, epoxy resins and thermal paper, which are used in e.g. CDs and DVDs, inner coatings of cans and cash receipts, respectively. BPA is a known endocrine disrupting chemical. In addition, animal studies of BPA have shown effects on development and function of the reproductive organs as well as the nervous system and behavior (Richter et al., 2007). However, the level at which effects occur in humans is much debated (Beronius et al., 2010). The ban of BPA from the production of baby bottles and cosmetics within the EU, as well as the media focus and public concern about human health effects, has urged the industry to find BPA substitutes (EC, 2009; EC, 2011). Thus, structural analogues to BPA, such as 4,4″-sulfonyldiphenol (BPS), 4,4′-methylenediphenol (BPF) and 4,4′-(hexafluoroisopropylidene)diphenol (BPAF), are now used as substitutes for BPA. However, these substitutes are not necessarily better alternatives since animal and in vitro studies have shown that BPS, BPF and BPAF have endocrine disrupting properties in the same order of magnitude as BPA (Chen et al., 2016; Grignard et al., 2012; Rochester and Bolden, 2015).

Aiming to achieve the Swedish governmental goal of a "non-toxic environment" for children, preschools have received recommendations for interventions to reduce the amount of harmful chemicals in the preschool environment. However, the effectiveness of such interventions is currently unknown as little research evaluating the impact of specific products, furnishing and other preschool characteristics on chemical concentrations in indoor environments has been performed.

The purpose of this study is to evaluate the levels of phthalates, non-phthalate plasticizers and bisphenols in dust from 100 Swedish preschools and identify products and preschool characteristics that are important for the exposure. In addition, levels of chemical metabolites are measured in urine from preschool children to assess the overall chemical exposure and to evaluate the impact of preschool dust on children's total exposure. Also, time trends of chemical exposure in children are studied.

2. Method

2.1. Selection of preschools and recruitment of children

The study was performed in two stages. In a first pilot project, dust samples from 30 preschools were collected between February and April 2015. In the continuation of the study, dust samples from 70 additional preschools were collected between September and November 2015.

The 100 preschools in the study were located in six areas of Stockholm municipality. Most preschools were located in detached buildings, whereas only one fifth were located in apartment buildings. The preschools were built between 1890 and 2015, with the majority built between 1970 and 1989. The number of children attending the entire preschool ranged from 12 to 115, with a median of 50 children per preschool and the number of children in the department where the sample was collected ranged from 7 to 44 children, with a median of 18 children.

Six preschools were Waldorf orientated which is associated with several characteristics that could influence the levels of chemicals in the indoor environment. For example, Waldorf preschools use primarily wooden and textile toys and furnishing while avoiding plastic materials, including PVC flooring. Also, the children sleep on sheepskin instead of foam mattresses.

Children attending a subset of 28 preschools were recruited for urine sampling via a written invitation addressing the parents. Urine samples were collected between March and May 2015, within a month from when the dust sample was collected at respective preschool. Children were only included if they were born between June 2010 and November 2011 and attended preschool >20 h/week. The parents signed an informed consent before the sample collection. Ethical permit was granted by the regional ethical review board in Stockholm (Dnr 2015/128-31/1).

A mean number of 4 (range 1–13) children from each of the 28 preschools provided urine samples, resulting in a total of 113 participating children. Among these children there were 59% boys and 41% girls, all except two children were born in Sweden and the age ranged between 40 and 58 months with a mean age of 50 months. The children had started preschool at the age of 18 months in average (range 12–48 months) and attended preschool between 24 and 45 h/week, with a mean of 36 h/week.

To study time trends of the studied compounds in urine, we analyzed spot urine samples that had been collected between 1998 and 2000 from 50 boys and 50 girls who lived in Stockholm and were between 45 and 55 months (mean 49 months) at the time. These urine samples were collected within the on-going prospective longitudinal birth cohort BAMSE (Wickman et al., 2002). The samples had been stored at −80 °C from the collection to analysis. Ethical permit for the analysis was granted by the regional ethical review board in Stockholm (Dnr 2014/448-32/1).

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2.2. Sampling

One settled dust sample from a play room at each preschool was collected, using a modified method previously described in Björklund et al., 2009. The sample was collected using a cellulose filter fixed in a styrene-acrylonitrile container, which was inserted in a holder made of polypropylene (Krim. Teknisk Materiel AB, Bålsta, Sweden) and mounted on the nozzle of a vacuum cleaner. Prior to sampling, the cellulose filters were washed with 10 mL methanol (>99.9%, Sigma-Aldrich) to remove possible contamination. Dust was collected from elevated surfaces between 50 and 250 cm above the floor, primarily from painted wood surfaces, such as shelves and window frames. Each sample was collected from different areas of the room, aiming to obtain an integrated measure of the entire room. After sampling, the filter container was wrapped in aluminum foil and sealed in a polyethylene plastic bag. The samples were stored at −20 °C until analysis.

The field workers filled in an inspection questionnaire covering information about the preschool characteristics as well as presence of certain products in the sampling room. The preschool personnel were asked to estimate the age of particular products, such as floors, upholstered furniture and mattresses. The floor type was determined by visual inspection of the floors.

Urine samples were collected on Thursday mornings because the children should have attended preschool at least two days before the sampling. To study if the urinary metabolite levels differed between Mondays and Thursdays, an additional sample was collected on a Monday morning from 24 children. The parents were provided sampling instructions, paper cups and polypropylene tubes (Sarstedt, Numbrecht, Germany) to collect the child's first morning urine. The parents answered a questionnaire about e.g. socioeconomics and home characteristics, as well as a questionnaire about the urine sampling (e.g. time of sampling and time for the last urination before sampling). The urine samples were stored at −20 °C until analysis.

2.3. Chemical analysis

2.3.1. Phthalates, non-phthalate plasticizers and bisphenols in dust

The dust samples were analyzed at the Swedish Environmental Research Institute (IVL). Dust samples from the preschools were spiked with deuterated internal standards (IS; d4-DMP, d4-DnBP and d4-DEHP for plasticizers and Bisphenol A-(diphenyl-d8) for bisphenols) and extracted using a modified method from Bergh et al. (2012) with organic solvent and microwave-assisted extraction (MAE; Milestone Ethos UP, Sweden) under controlled pressure and temperature program. The dust clean-up was performed with ENVI-Florisil SPE cartridges (ISOLUTE FL 500 mg/3 mL from Biotage, Uppsala), and before analysis a pre-injection IS was added. Bisphenols have been derivatized prior GC–MS analysis. All samples were analyzed with the use of GC–MS/MS (Agilent 7000; Agilent Technologies, Inc., Santa Clara, CA, USA). The instrument was equipped with an auto injector (Agilent 7683B) and the injection was in pulsed splitless mode. The detector was used in MRM mode with electron impact ionization mode (EI), and integration was made with MassHunter software version B.04.00 for quantitative analysis (Agilent Technologies, Inc. 2008). The limits of detection (LOD) presented in Table 1 were calculated based on three times the standard deviation of the lab blank values. The Standard reference material (SRM) 2585 from National Institute of Standard and Technology (NIST, USA) was analyzed in duplicate in order to evaluate the analytical method for the determination of the selected analytes (Table S1).

2.3.2. Phthalates and bisphenols in urine

The urine samples, both from 1998-2000 and 2015, were analyzed by a modified method for phthalate metabolites (Bornehag et al., 2015) at Lund University. The analyzed compounds and their eventual parent compounds are included in Table 4. Briefly, urine were added with ammonium acetate (pH 6.5) and glucoronidase (*E. coli*) and thereafter incubated at 37 °C in 30 min. Then a water and acetonitrile solution of labelled (^{3}H or ^{13}C) internal standards of all analyzed compounds was added. The samples were thereafter analyzed without any further work-up.

A C_{18} column was used prior to the injector to reduce the interferences of contaminants in the mobile phase. The phthalate metabolites and the bisphenols in the samples were separated on a C_{18} column. The samples were analyzed on a Shimadzu UFLC system (Shimadzu Corporation, Kyoto, Japan) coupled to a QTRAP5500 triple quadrupole linear ion trap mass spectrometer equipped with a TurboIon Spray source (LC–MS/MS; AB Sciex, Foster City, CA, USA). The samples were analyzed in duplicate (see Table S2 for the between batch precision expressed as the coefficient of variation; CV) and all samples were analyzed in a randomized order.

For quality control of the analyses, chemical blanks and in-house prepared quality control samples were analyzed in all sample batches. The LODs for all analyzed compounds are presented in Table 4. The between run precision of the method expressed as the CV of the quality control sample was between 2 and 10% for the analyzed metabolites (Table S2).

The laboratory at Lund University was a reference laboratory for analyses of urinary phthalate metabolites and Bisphenol A in a European biomonitoring project (www.eu-hbm.info/cophes). Moreover, the laboratory participates in the Erlangen inter-laboratory comparison program for those compounds where this is possible.

Urine density was determined using a hand refractometer.

2.4. Statistical analysis

The data was analyzed using the statistical software SPSS 22 (IBM Inc.) and STATA 13 (Statacorp TX, USA). Dust and urinary concentrations below respective LOD were replaced by LOD/2. Due to low dust sample weight with resulting high LOD, 2 samples were excluded from the BPS analysis. One value of DEHP in dust was excluded due to suspected contamination.

The distribution of data was skewed. Thus, the non-parametric Mann Whitney *U* test and Spearman's rank correlation test were used to analyze the associations between chemicals in dust and factors in the preschool environment. Diethyl phthalate (DEP) was not included in these analyses due to the relatively low percentage (60%) of samples above the LOD. The univariate analysis included the following factors in the preschools: type of building, year the building was built, preschool funding year, Waldorf preschool, cleaning and spring cleaning frequency, inventory of plastics (i.e. if the preschool had actively removed old plastics from the indoor environment), walls in sampling room painted in last 12 months, room size of sampling room, presence of mattresses, pillows, furniture with plastic covers, plastic toys, electronic devices and PVC floors in the sampling room as well as installation year of the floor. Variables with significance level < 0.1 in the univariate analysis were included in stepwise backward multivariable median regression models performed on 100 bootstrap samples for each compound separately. The stepwise procedure used a significance level of 0.10 for removal from the model and a significance level of 0.09 for addition to the model. The variables that were selected by the stepwise procedure in at least 50 of the 100 bootstrap samples were included in the final models. The variables for Waldorf preschools, installation year of PVC floor and preschool funding year were not included in the multivariate analysis due to multicollinearity with other variables.

All statistical analyses of urinary metabolite concentrations were performed using Thursday's samples only. To correct for dilution, levels of urinary metabolites were adjusted to the mean density level of 1.023 kg/L. ΣDEHP (MEHP + MEHHP + MEOHP + MECPP + MCMHP) and ΣDiNP (MHiNP + MOiNP + MCiOP) in urine were calculated by summing molar concentrations of each metabolite. To enable comparison to other metabolite levels, ΣDEHP and ΣDiNP are expressed

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as μg/L after multiplying the sum molar concentration with the average molecular weight of the DEHP and DiNP metabolites, respectively (Zota et al., 2014). The metabolite MCMHP was not included in the calculation of ΣDEHP used in the comparison between the sampling rounds 1998–2000 and 2015.

Associations between urinary chemical levels and questionnaire data (child characteristics, home and preschool variables) were analyzed with Mann Whitney *U* test. Correlations between dust and urinary levels were analyzed by calculating the Spearman's rank-correlation coefficient between the median of the urinary chemical levels in each preschool and the dust level in that preschool. Differences in urinary metabolite levels between the Monday's and Thursday's samples were analyzed using the Wilcoxon's matched pairs test. Differences between urinary levels in 1998–2000 and 2015 were analyzed with Mann Whitney *U* test.

2.5. Exposure assessment

To assess children's exposure to phthalates, non-phthalate plasticizers and bisphenols via preschool dust ingestion, daily intakes (μg/kg bw) via dust were calculated, based on the following equation:

$$Daily\ intake_{dust} = \frac{C_{dust} * I_{dust}}{BW}$$

C_{dust} is the concentration of respective chemical in dust (μg/g), and *BW* is the mean body weight (17.6 kg) of the four year old children in our study. I_{dust} is the assumed daily dust ingestion while attending the preschool (0.03 g). We base the daily dust intake on the assumption that children are exposed to 0.06 g (US EPA, 2011) dust per day during 16 waking hours, and that children spend half of this time in the preschool environment. We assumed 100% absorption rate after oral ingestion. Exposure from dust via dermal absorption was not calculated, because the contribution from this route is assumed to be negligible (Bekö et al., 2013; Guo and Kannan, 2011).

The total daily intakes of DEHP, DnBP, BBzP and DiNP were estimated with volume based back-calculation from urinary levels of phthalate metabolites (Bekö et al., 2013; Fromme et al., 2013; Giovanoulis et al., 2016; Wittassek et al., 2011), using the following equation:

$$Daily\ intake_{total} = \frac{\Sigma\left[\frac{C_u}{MW_m}\right] * MW_p * V_{excr}}{F_{UE}}$$

C_u is the concentration of respective metabolite in urine (μg/L). MW_m and MW_p are the molecular weights of the metabolite and parent phthalate, respectively. V_{excr} is the urinary volume excreted per day for children, which is assumed to be 0.0222 L/kg bw/day (Miller and Stapleton, 1989). F_{UE} is the molar fraction value, which explains the molar fraction of the monoester excreted in urine in relation to the intake of the parent compound. We used the F_{UE} presented by Wittassek et al., 2011. Also the total intake of BPA based on urinary concentrations was calculated. The F_{UE} for BPA was assumed to be 1, thus the equation for total daily intake of BPA only included C_u and V_{excr} (Morgan et al., 2011).

3. Results

3.1. Dust concentrations

Throughout this paper, the phthalates are divided into "banned phthalates" and "substitute phthalates" based on the recent European ban (unless permit is granted) on the production of the phthalates considered the most toxic (DEHP, BBzP, DnBP and DiBP). Summary statistics of phthalates, non-phthalate plasticizers and bisphenols in dust are presented in Table 1. The highest geometric mean level among the phthalates was seen for DiNP, followed by DEHP and DiDP, whereas DEHT and DiNCH were the non-phthalate plasticizers found at highest levels. The levels of the studied compounds in dust covaried significantly for approximately half of all possible combinations of compounds. No clear patterns of higher covariation between compounds within the same chemical group were observed (Table S3).

3.2. Factors in the preschool environment

The results from the univariate and multivariate analyses of associations between different factors in the preschool environment and levels of phthalates and non-phthalate plasticizers in preschool dust are presented in Tables 2 and 3, respectively. The analyses showed that preschool buildings built after year 2000 had higher levels of several substitute phthalates and non-phthalate plasticizers in dust, whereas the levels of the now banned phthalate DnBP were higher in older building. Box plots of plasticizer levels in dust in relation to the preschool building year are presented in Fig. 1.

The univariate analysis showed that presence of PVC floors, electronic devices, soft plastic toys, and foam mattresses in the sampling room were associated with higher levels of some substitute phthalates and non-phthalate plasticizers in dust. In the multivariate analysis, higher levels of DiNP in dust and the presence of foam mattresses and PVC flooring were significantly associated.

The levels of plasticizers in dust from Waldorf preschools were generally in the lower end of the concentration range compared to other preschools and the levels of DiNP were significantly lower in these preschools.

Bisphenols were not included in the analyses of potential exposure factors in the preschool environment presented in Tables 2 and 3 because these factors were generally not considered relevant for these compounds. However, the levels of BPA in dust were significantly higher in preschools built after year 2000 ($p = 0.004$), whereas BPS was not significantly associated with the building year. Furthermore, the levels of BPA and BPS in dust were not significantly altered by the cleaning frequency and were not significantly lower in Waldorf preschools compared to other preschools (data not shown).

3.3. Urinary levels

The levels of phthalate and DiNCH metabolites, BPA and BPS were above the LOD in all urine samples, whereas the levels of 4,4BPF and 2,2BPF were detected in 97% and 65% of the samples, respectively (Table 4). Density adjusted urinary levels of metabolites originating from the same parent phthalate (DEHP, DiNP or DiDP/DPHP) were strongly correlated (Spearman's rho 0.69–0.97). Weak or moderate correlations were seen between most of the measured metabolites originating from different parent compounds (data not shown).

There were no significant differences in urinary metabolite levels depending on the children's age or gender. However, children whose parents had a lower educational level had significantly higher levels of urinary metabolites of DEHP, DnBP, BBzP and DiNP in urine, compared to children of more highly educated parents (Table S4). Analysis of home characteristics showed that children living in homes with PVC floors had higher levels of DnBP and BBzP in urine.

Analysis of children's urinary levels in relation to preschool characteristics showed that children attending preschools built after year 2000 had higher levels of DiDP/DPHP metabolites in urine, whereas the levels of a DnBP metabolite were lower. The results for other factors in the preschool environment (mattresses, PVC flooring, cleaning frequency, Waldorf and inventory with removal of old plastics) in relation to urinary metabolite levels were not in concordance with the observed associations between these factors and levels of plasticizers in preschool dust (Table S4).

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Table 1
Levels (μg/g dust) of phthalates, non-phthalate plasticizers and bisphenols in preschool dust.

		N	LOD	% > LOD	AM (SD)	GM	Median	P95	Range
Banned phthalates	DEHP	99	0.27–0.39	99	470 (670)	260	290	1900	<LOD–4500
	BBzP	100	0.001–0.01	100	24 (42)	9.1	8.7	110	0.01–240
	DnBP	100	0.03–0.04	100	250 (2100)	21	21	140	1.2–21,000
	DiBP	100	0.03–0.04	100	12 (18)	7.2	6.4	46	1.0–130
Substitute phthalates	DEP	100	0.02–0.5	60	15 (51)	0.92	0.46	130	<LOD–390
	DMP	100	0.01–0.02	83	0.61 (2.0)	0.11	0.10	2.8	<LOD–12
	DiNP	100	0.01	100	1400 (6600)	450	380	3400	58–66,000
	DPHP	100	0.01–0.03	100	40 (260)	8.2	8.0	42	0.15–2600
	DiDP	70	0.01	100	110 (230)	57	50	430	11–1800
Non-phthalate plasticizers	DEHT	100	0.01–0.02	100	280 (560)	105	86	1500	6.8–3500
	DEHA	100	0.05–0.15	100	25 (51)	10	9.7	170	0.72–340
	ATBC	100	0.01–0.2	100	29 (120)	8.2	6.2	82	0.42–1200
	DiNCH	100	0.001–0.01	100	300 (750)	73	49	1300	4.7–5200
Bisphenols	BPA	100	0.06–0.09	95	2.3 (3.0)	1.2	1.3	11	<LOD–15
	BPS	98	0.12	80	0.77 (2.4)	0.26	0.24	3.8	<LOD–22
	BPF	100	0.06–0.12	35	.	.	.	4.4	<LOD–15
	BPAF	100	0.03–0.13	41	.	.	.	0.28	<LOD–2.8

LOD, limit of detection; AM, arithmetic mean; SD, standard deviation; GM, geometric mean; P95, 95th percentile.

Comparison between urinary metabolite levels in the Monday's and Thursday's samples, among the 24 children who provided samples at both time points, showed significantly higher levels of DEHP metabolites and BPA in the Monday's samples ($p = 0.001–0.040$ and 0.026, respectively), whereas the levels of MCiNP (metabolite of DiDP/DPHP) were significantly higher in the Thursday's urine samples ($p = 0.030$). For the other studied compounds, no significant differences between the Monday's and Thursday's samples were found (data not shown).

3.3.1. Correlation between urine and dust concentrations

The concentrations of the parent compound in dust and density adjusted levels of corresponding metabolite in urine were not significantly

Table 2
Univariate analysis of factors in the preschool environment. Median levels of plasticizers in dust (μg/g dust) for each binary category are presented and significant variables are indicated with asterisks (* ≤0.05, ** ≤0.01, *** ≤0.001). For all analyses, 100 dust samples were included, except for DEHP (N = 99) and DiDP (N = 70). Factors which were not significantly associated with any plasticizer were not included in the table (i.e. spring cleaning, type of building, presence of furniture with plastic cover and if the preschool had actively removed old plastics).

			Banned phthalates				Substitute phthalates				Non-phthalate plasticizers			
		N[a]	DEHP	BBzP	DnBP	DiBP	DMP	DiNP	DPHP	DiDP	DEHT	DEHA	ATBC	DiNCH
Preschool characteristics	*Building year*													
	<1999	*79*	280	8.6	**26****	6.5	0.10	350	**6.8**	**43**	**84**	9.6	**6.1**	**47**
	>2000	*18*	300	11	**6.3**	5.5	0.07	640	**20*****	**110***	**230***	11	**16***	**120****
	Funding year													
	<1999	*64*	320	8.1	**28*****	6.6	0.10	450	6.4	43	70	10	6.1	**45**
	>2000	*35*	240	9.1	**9.3**	6.0	0.09	330	10	75	130	8.4	7.3	**65***
	Cleaning frequency													
	5 times/week	*86*	280	8	18	6.0	**0.09**	380	7.8	*NA*	**77**	9.9	6.1	47
	<4 times/week	*14*	460	13	27	7.5	**0.14***	360	9.1	*NA*	**240****	8.7	6.7	53
	Waldorf													
	Yes	*6*	150	5.8	48	4.4	0.24	**120**	6.6	*NA*	73	5.5	3.6	35
	No	*94*	290	9.2	20	6.6	0.10	**430****	8.1	*NA*	86	10	7.2	49
Sampling room	*Foam mattresses*													
	Yes	*31*	300	9.3	21	6.7	0.11	**560****	13	**76***	76	**13***	8.8	57
	No	*69*	280	8.0	19	5.6	0.09	**330**	7.2	**43**	89	**8.4**	6.1	48
	Old soft plastic toys													
	Yes	*57*	280	7.2	22	6.0	0.10	380	7.6	62	65	11	**6.1***	59
	No	*20*	210	6.0	14	7.6	0.10	350	6.6	37	45	6.2	**3.1**	38
	Amount of plastic toys													
	<1,5 crate	*11*	410	21	27	8.8	0.14	190	8.0	*NA*	280	8.5	**6.1**	56
	>2 crate	*19*	400	26	15	5.4	0.10	360	10	*NA*	280	12	**20****	43
	Floor type													
	PVC	*57*	320	9.8	16	6.0	**0.08**	**580*****	8.9	58	90	10	8.6	50
	Other	*43*	260	7.4	26	6.7	**0.13***	**250**	7.6	40	78	8.8	6.1	44
	Year of PVC floor													
	<1999	*11*	**591***	19	35	6.6	0.09	420	6.1	58	110	14	5.5	**28**
	>2000	*43*	**242**	8.3	14	5.0	0.07	740	10	59	89	10	8.6	**65***
	Room size													
	<32 m^2	*51*	230	7.2	19	6.0	0.10	380	6.8	43	84	9.2	**5.5**	39
	>32 m^2	*49*	320	9.8	24	6.7	0.10	360	8.7	66	99	10	**11****	61
	Recent wall paint													
	Yes	*12*	330	7.2	**44***	6.0	0.10	450	5.7	38	140	9.1	15	36
	No	*87*	280	9.2	**19**	6.6	0.10	380	8.1	59	84	10	6.1	49
	Electronic devices													
	Yes	*79*	300	10	21	6.5	0.10	**520*****	8.0	58	89	10	**7.3***	51
	No	*21*	160	4.6	19	5.0	0.10	**220**	7.6	43	51	8.4	**4.0**	34

NA, not applicable due to less than five preschools in any category.
[a] Maximum number of preschools per category.

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Table 3
Multivariate median regression of plasticizers in preschool dust and factors in the preschool environment. Intercept, beta and 95% confidence interval (CI) are presented in μg/g dust. Results for DEHP, BBzP, DiBP, DMP, DiDP, DEHA, DEHT, ATBC and DiNCH are not presented in the table as no significant factors were found for these compounds.

Compound		Intercept[a]	Beta[b] (95% CI)	p-Value
DnBP	–	26		
	Built after year 2000		−19 (−31, −7.1)	0.002
DiNP	–	185		
	PVC flooring		395 (181, 609)	<0.001
	Mattresses		379 (81, 676)	0.013
DPHP	–	6.8		
	Built after year 2000		14 (3.1, 25)	0.013

[a] Median level when all variables in the model are set to 0.
[b] Difference in median levels between binary groups.

correlated for phthalates (DEHP, BBzP, DnBP, DEP, DiNP, DPHP), DiNCH or BPA (Table S5).

3.3.2. Time trends of urinary levels

Aiming to evaluate time trends, the urinary levels of phthalate metabolites and bisphenols in our study were compared to the levels of the same compounds in urine samples collected between 1998 and 2000. There were significantly higher levels ($p < 0.001$) of BPA and metabolites of DEHP, DnBP, BBzP and DEP in urine samples collected in 1998–2000 compared to urine collected in 2015, whereas the levels of DiNP metabolites were higher in 2015 compared to 1998–2000 (Fig. 2). The levels of BPF were not significantly different between the two sampling rounds. Time trend evaluation of BPS was not possible due to the large number of samples below the LOD in 1998–2000, as an effect of a higher LOD in 1998–2000 (0.5 ng/mL) than in 2015 (0.07 ng/mL). Summary statistics of chemical metabolite levels in the urine samples collected in 1998–2000 are presented in Table S6.

3.4. Exposure from dust ingestion and total intake

Daily intakes from preschool dust based on the geometric mean and 95th percentile levels were below the health based reference values for all compounds with available reference values (Table 5). However, daily intake from preschool dust based on the highest measured dust concentration of DnBP and DiNP exceeded respective reference value.

To estimate the contribution of preschool dust intake to children's total exposure, the total daily intakes of DEHP, BBzP, DnBP, DiNP and BPA were calculated from urinary metabolite concentrations (Table 5). According to the calculated total daily intakes, two children exceeded the health based reference value for DnBP and one child exceeded the reference value for DiNP. At the geometric mean levels, the estimated intake from preschool dust contributed with 27%, 19%, 5%, 2% and 6% to the total intake of DiNP, DEHP, BBzP, DnBP and BPA, respectively.

4. Discussion

Our results in comparison with previous studies of preschool dust indicate that the levels of DEHP in European preschools have decreased over time, reflecting the phase-out of DEHP in the EU (Table S7; Bergh et al., 2011; Fromme et al., 2013; Gaspar et al., 2014; Langer et al., 2010). The time trends for other recently banned phthalates (DnBP, BBzP and DiBP) are less clear. Levels of non-phthalate plasticizers in preschool dust have only been measured in one previous European study (Fromme et al., 2016) and to the best of our knowledge DPHP, BPS, BPF and BPAF have not been measured in preschool dust in any previous study. More studies of children's exposure to substitute phthalates, non-phthalate plasticizers and BPA analogues are needed to better characterize children's exposure and to allow time trend evaluations of these emerging compounds.

In our study, the levels of substitute phthalates and non-phthalate plasticizers were generally higher in dust from preschools built after year 2000, whereas the banned phthalate DnBP was found in higher levels in older building, reflecting the shift in plasticizer use in the EU. These results indicate that the plasticizer content in dust partially originates from building materials. This is supported by the fact that the majority of the PVC annually produced in Europe is used within the construction industry, where PVC primarily is used in building facings, roofing, cables, floorings, wall coverings, door and window profiles, as well as in non-PVC applications, such as paints and adhesives (KEMI, 2015).

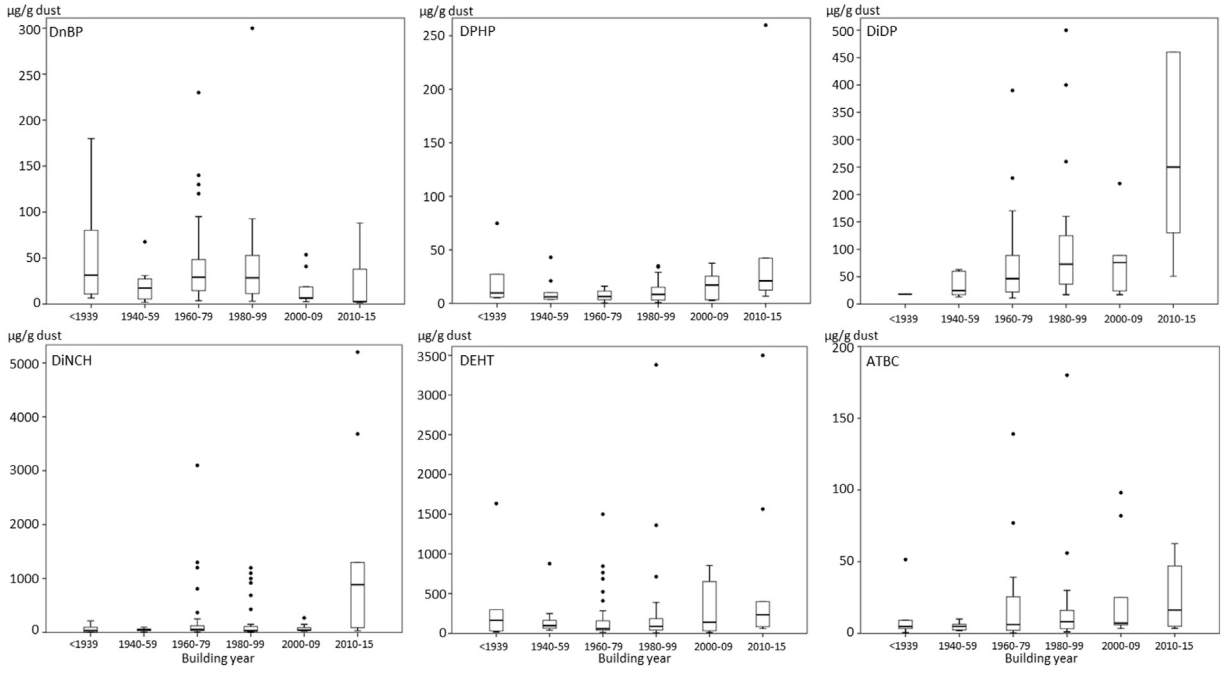

Fig. 1. Levels of phthalates and non-phthalate plasticizers in preschool dust in relation to preschool building year categories; <1939 (N = 6), 1940–59 (N = 10), 1960–79 (N = 35), 1980–99 (N = 28), 2000–09 (N = 9), 2010–15 (N = 10). To improve the readability, one extremely high value is not shown in the plots for DnBP, DPHP, DiDP and ATBC.

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Table 4
Levels (μg/L) of plasticizer metabolites and bisphenols in urine samples from 113 preschool children. White cells indicate unadjusted levels and grey cells indicate density adjusted levels.

	Parent compound	Measured metabolite	LOD	%>LOD	AM (SD)	GM	Median	P95	Range
Banned phthalates	DEHP	MEHP	0.4	94	2.0 (1.7)	1.5	1.5	5.6	<LOD-11
					1.9 (1.4)	1.5	1.5	5.0	<LOD-8.9
		MEHHP	0.07	100	22 (17)	17	17	56	1.8-133
					21 (16)	17	16	58	3.5-94
		MEOHP	0.04	100	15 (12)	11	12	37	1.5-82
					14 (11)	12	11	40	2.4-68
		MECPP	0.01	100	21 (17)	16	16	52	2.4-120
					20 (15)	16	16	56	4.2-100
		MCMHP	0.04	100	6.2 (4.3)	5.1	5.0	16	1.0-20
					6.1 (4.0)	5.1	5.0	17	1.6-20
	BBzP	MBzP	0.06	100	13 (15)	9.0	8.6	45	1.0-95
					13 (13)	9.1	8.4	39	1.4-76
	DnBP	MnBP	1.2	100	67 (42)	55	54	141	3.9-327
					65 (37)	56	55	128	7.5-237
Substitute phthalates	DEP	MEP	0.06	100	60 (146)	32	28	229	2.7-1400
					56 (127)	32	28	202	4.7-1200
	DiNP	MHiNP	0.01	100	30 (108)	12	12	93	1.3-1100
					27 (82)	12	11	78	1.5-838
		MOiNP	0.01	100	13 (44)	5.9	5.6	35	0.71-453
					12 (33)	6.0	5.4	29	0.71-339
		MCiOP	0.01	100	49 (221)	17	17	140	1.7-2300
					42 (166)	18	15	128	1.7-1700
	DiDP/ DPHP	MHiDP	0.02	100	6.2 (17)	2.6	2.4	16	0.47-140
					5.5 (13)	2.7	2.4	17	0.47-102
		MCiNP	0.03	100	1.8 (5.5)	0.76	0.74	5.3	0.05-54
					1.6 (4.2)	0.77	0.75	5.1	0.04-40
NP	DiNCH	MOiNCH	0.02	100	7.9 (27)	2.2	1.8	24	0.11-207
					6.9 (22)	2.2	1.8	21	0.15-171
Bisphenols	BPA		0.09	100	1.9 (2.4)	1.4	1.5	4.1	0.21-19
					1.8 (2.1)	1.4	1.4	3.7	0.27-18
	BPS		0.007	100	0.64 (3.1)	0.19	0.17	1.6	0.02-33
					0.78 (4.7)	0.20	0.16	1.6	0.03-50
	4,4BPF		0.02	97	0.64 (3.0)	0.16	0.15	2.6	<LOD-32
					0.57 (2.6)	0.16	0.15	2.1	<LOD-27
	2,2BPF		0.01	65	0.02 (0.01)	0.01	0.01	0.04	<LOD-0.07
					0.02 (0.01)	0.01	0.01	0.04	<LOD-0.07

LOD, limit of detection; AM, arithmetic mean; SD, standard deviation;GM, geometric mean; p95, 95th percentile; NP, non-phthalate plasticizers

Phthalates are not bound to the plastic polymer matrix and have been shown to migrate from vinyl materials, such as PVC floors (Afshari et al., 2004; Clausen et al., 2004; Fujii et al., 2003; Liang and Xu, 2014). In our study, PVC flooring was associated with higher levels of the substitute phthalate DiNP in dust. We also found that preschools with new PVC floors had higher levels of DiNCH, whereas preschools with old PVC floors had higher levels of DEHP in dust. This is expected as the non-phthalate plasticizer DiNCH has been substituting DEHP in PVC floors in recent years. However, in two previous studies of preschool environments (N = 40 and 63, respectively) no significant associations between PVC flooring and dust concentrations of phthalates were found (Fromme et al., 2013; Gaspar et al., 2014). In our study, presence of PVC flooring in the preschool sampling room was not associated with higher levels of phthalate metabolites in urine from children attending these preschools, which is in concordance with results from a previous German study of preschool exposure (Fromme et al., 2013). However, PVC flooring in the home environment was associated with higher levels of urinary metabolites of the now banned phthalates DnBP and BBzP among the children participating in our study. Previous studies of Swedish homes have reported that PVC flooring and wall material were correlated with DEHP and BBzP levels in indoor dust (Bornehag et al., 2005), and that infants living in houses with PVC flooring had higher levels of a BBzP metabolite in urine (Carlstedt et al., 2013).

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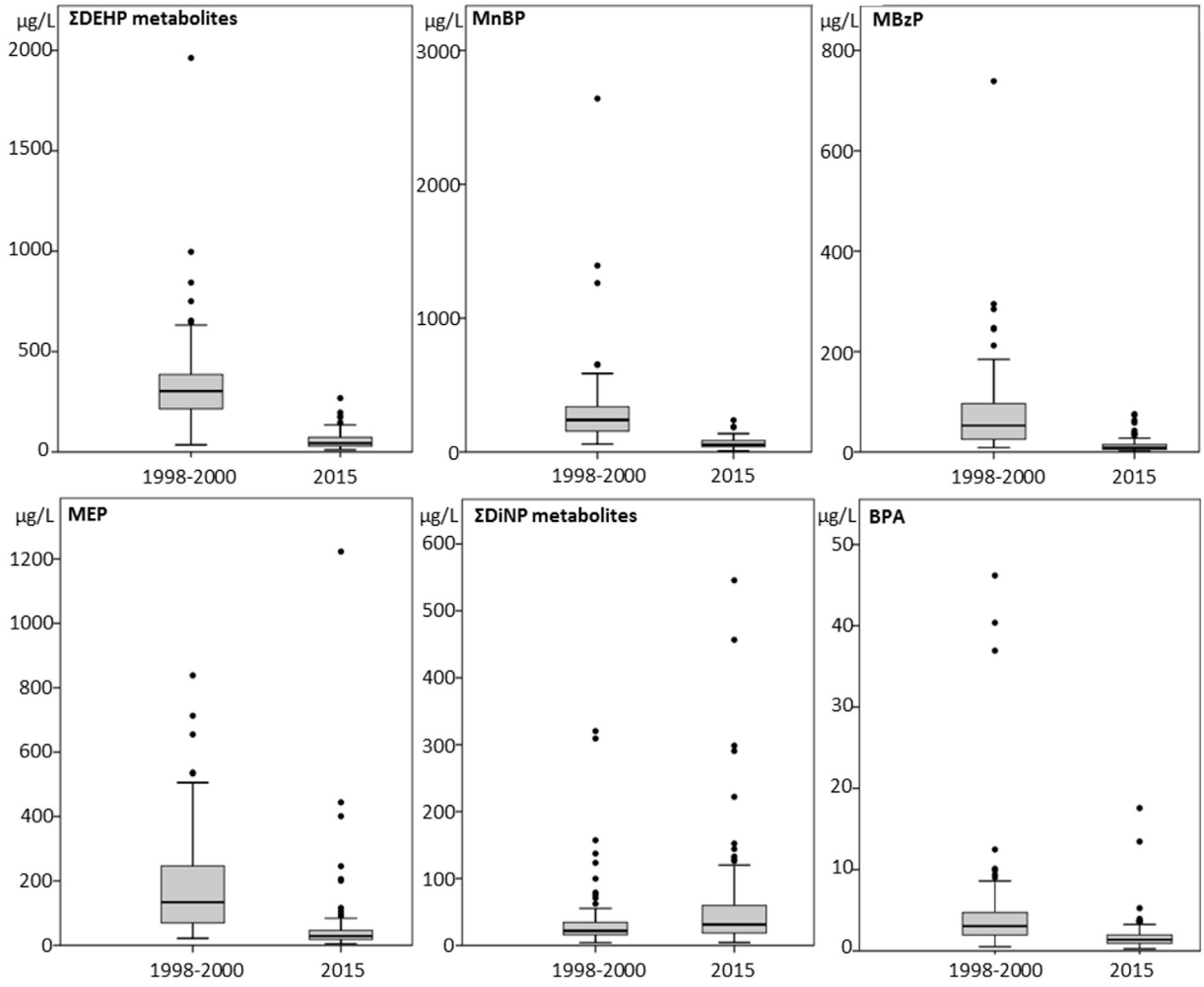

Fig. 2. Density adjusted levels (µg/L) of phthalate metabolites and BPA in urine collected from four year old children in 1998–2000 (N = 100) and 2015 (N = 113), respectively. To improve the readability, one extremely high value of DiNP is not shown.

Besides PVC floors, other products in the sampling room (foam mattresses, soft plastic toys and electronic devices) were associated with higher levels of some plasticizers in preschool dust. Furthermore, plasticizer levels in dust from Waldorf preschools, which avoid these kinds of products, were generally in the lower end of the concentration range, compared to other preschools.

Taken together, these results indicate that the concentration of plasticizers in dust is partially dependent on unattached plastics products, such as foam mattresses, which can easily be removed or replaced. However, the results showing detectable levels of plasticizers in Waldorf preschools as well as the importance of the preschool building year and PVC flooring indicate that the plasticizer content in dust partly originates from other sources, such as building materials, which is a more difficult problem to address when trying to reduce the levels of plasticizers in preschools.

We found no significant correlations between preschool dust levels of the studied compounds and corresponding metabolite levels in children's urine. The lack of correlations may be due to the low number of participating children per preschool and that morning urine may reflect exposure from the home rather than the preschool environment, due to the short half-lives of bisphenols and phthalates (ECHA, 2013a; Koch et al., 2012; Koch et al., 2006; Völkel et al., 2002). However, these results suggest that other exposure sources than preschool dust are relatively more important for children's total exposure. Few studies have investigated the association between plasticizers in dust and total exposure (urine or blood) in children. A German study found significant correlations between BBzP, DnBP, DEHP and DiNCH in preschool dust and corresponding metabolites in urine (Fromme et al., 2013; Fromme et al., 2016). In addition, a Danish study found significant correlations between BBzP, DnBP, DiBP and DEP levels in indoor dust from preschools and homes and corresponding urinary metabolites in children (Langer et al., 2014). Becker et al. (2004) exclusively studied exposure to DEHP in dust from German homes and did not observe any significant correlations between DEHP in house dust and corresponding metabolites in children's urine. In addition to the lack of correlations between dust and urinary levels in our study, factors in the preschool environment (mattresses, PVC flooring, Waldorf, etc.) were not significantly associated to levels of the same plasticizers in preschool dust and urine, respectively. This indicates that even if a certain factor in the preschool have impact on plasticizer levels in dust, it may not be significant for children's total exposure when all exposure sources from both the home and preschool environment are considered.

The estimated phthalate exposures via dust in relation to the total daily intake calculated from urinary phthalate metabolite concentrations showed that preschool dust ingestion contributes with 27%, 19%, 5% and 2% to the total intake of DiNP, DEHP, BBzP and DnBP, respectively. In a Danish study of 4–6 year old children, daily ingestion of indoor dust from preschools and homes contributed with 8%, 2% and 0.6% of the total intake of DEHP, BBzP and DnBP, respectively (Bekö et al., 2013). However, the calculations in the Danish study were adjusted for the excretion of phthalates during the time between the child left the preschool and the morning urine sample was collected. Also, the

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Table 5
Calculated daily intakes of plasticizers and bisphenols via dust ingestion based on measured levels in preschool dust. Daily intakes from dust are related to reference values using hazard quotients and to children's total daily intake calculated from urinary metabolite levels.

		Daily intake from dust (μg/kg bw/day)		Reference value (μg/kg bw/day)	Hazard quotient[a]		Total daily intake[b] (μg/kg bw)	
		GM	P95		GM	P95	GM	P95
Banned phthalates	DEHP	0.45	3.2	34 ($DNEL_{children}$)[1]	0.01	0.10	2.4	8.1
	BBzP	0.02	0.19	500 (TDI)[2]	0.00003	0.0004	0.34	1.4
	DnBP	0.04	0.22	7 ($DNEL_{children}$)[3]	0.005	0.03	2.3	5.2
	DiBP	0.01	0.06	–	–	–		
Substitute phthalates	DEP	0.002	0.12	–	–	–		
	DMP	0.0002	0.003	–	–	–		
	DiNP	0.77	5.5	75 ($DNEL_{children}$)[4]	0.01	0.07	2.8	19
	DPHP	0.01	0.06	–	–	–		
	DiDP	0.10	0.67	75 ($DNEL_{children}$)[4]	0.001	0.01		
Non-phthalate plasticizers	DEHT	0.18	2.3	1000 (TDI)[5]	0.0002	0.002		
	DEHA	0.02	0.16	300 (TDI)[6]	0.00006	0.001		
	ATBC	0.01	0.13	1000 (TDI)[7]	0.00001	0.0001		
	DiNCH	0.12	2.1	1000 (TDI)[8]	0.0001	0.002		
Bisphenols	BPA	0.002	0.01	4 (t-TDI)[9]	0.0005	0.003	0.03	0.08
	BPS	0.0004	0.006	–	–	–		

GM, geometric mean; P95, 95th percentile; TDI, Tolerable Daily Intake; t-TDI, temporary TDI; DNEL, Derived No-Effect Level.
[a] Ratio between daily intake from dust and respective reference value.
[b] Volume based back-calculation from urinary metabolite levels.
[1] ECHA, 2013b.
[2] EFSA, 2005a.
[3] ECHA, 2013c.
[4] ECHA, 2013a.
[5] EFSA, 2008.
[6] SCF, 2000.
[7] EFSA, 2005b.
[8] EFSA, 2006.
[9] EFSA, 2015.

calculations included dust from children's homes, in which the levels of DEHP, BBzP and DnBP were considerably lower than in preschool dust. The results from our and the Danish study are not consistent with previous studies reporting that humans are almost exclusively exposed to DEHP and DiNP via food whereas other sources (e.g. dust) are more important for phthalates with lower molecular weight, such as BBzP and DnBP (Fromme et al., 2007; Koch et al., 2013; Wittassek et al., 2011; Wormuth et al., 2006). However, these previous studies concerned exposure in adults, whereas our study assesses exposure in children, for whom dust ingestion is a more important exposure source.

The contribution from dust ingestion was 6% of the total BPA intake for the children in our study. These results are in line with previous research showing that the diet is the major contributor to the BPA intake (>90%), whereas dust is considered to be a minor exposure source (FAO/WHO, 2011; Gao et al., 2016; Geens et al., 2012; Loganathan and Kannan, 2011; Wang et al., 2015; Wilson et al., 2007).

The levels of phthalate metabolites in urine from the children in our study were generally in the same order of magnitude as urinary levels previously reported in studies of four year old children in Europe and North America, summarized in Table S8 (Becker et al., 2009; Casas et al., 2011; Fromme et al., 2013; Fromme et al., 2016; Health Canada, 2015; Langer et al., 2014; Myridakis et al., 2016; Watkins et al., 2014). However, the levels of DEHP metabolites in our study were lower than in the previous studies, which reflects the decreasing use of DEHP. The comparison between levels of phthalate metabolites and bisphenols in urine from a comparable group of children in 1998–2000 and 2015, respectively, showed that the levels of metabolites of the now banned phthalates have decreased over time, whereas the levels of the substitute phthalate DiNP have increased. Similar observations have been reported in previous studies (Gyllenhammar et al., 2016; Göen et al., 2011; Jönsson et al., 2010; Zota et al., 2014).

Levels of urinary BPA in our study were similar to levels reported in recent studies of four year old children, and somewhat lower than levels reported in older studies (Table S8; Becker et al., 2009; Casas et al., 2011; Health Canada, 2015; Myridakis et al., 2016; Stacy et al., 2016). Available biomonitoring data for BPA analogues is scarce and to the best of our knowledge, only one study has measured BPS in urine from young children (Liao et al., 2012) and no previous study has measured urinary BPF in children. In our study, we observed lower levels of BPA in urine from children in 2015 compared to 1998–2000. However, we did not observe significant differences for urinary BPS and BPF levels between the two time points. Data from the American NHANES study has shown a decreasing trend for urinary BPA levels between 2010 and 2014 and an increasing trend for BPS during the same time period, whereas no significant trend was observed for BPF (Ye et al., 2015). In addition, a study of Swedish women reported a decreasing trend of urinary BPA levels between 2009 and 2014, whereas the levels of BPF increased over the same period. No significant temporal trend was seen for BPS (Gyllenhammar et al., 2016).

5. Conclusions

In this study, we analyzed plasticizers and bisphenols in preschool dust and found that DiNP, DEHP, DEHT and DiNCH were the most abundant plasticizers in dust. The preschool building year was identified as the most important factor for the plasticizer concentrations in preschool dust, showing that substitute plasticizers are significantly more common in newer buildings. The results from this study indicate that the plasticizer concentrations in preschool dust partially are determined by the presence of visible plastics, such as mattresses, which easily can be removed or replaced, and partially are determined by other factors, such as building materials, which are more difficult to remove.

Children's estimated daily exposures to plasticizers and BPA via dust ingestion were below health based reference values, in all except two preschools and preschool dust ingestion accounted for 2–27% of the total daily intake of different phthalates and BPA in preschool children. Time trends in preschool dust and urine concentrations indicate decreasing levels of now banned phthalates and BPA, whereas there is little available data for substitute plasticizers and BPA analogues.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2017.02.006.

References

Afshari, A., Gunnarsen, L., Clausen, P.A., Hansen, V., 2004. Emission of phthalates from PVC and other materials. Indoor Air 14 (2), 120–128.

Becker, K., Seiwert, M., Angerer, J., Heger, W., Koch, H.M., Nagorka, R., et al., 2004. DEHP metabolites in urine of children and DEHP in house dust. Int. J. Hyg. Environ. Health 207 (5), 409–417.

Becker, K., Göen, T., Seiwert, M., Conrad, A., Pick-Fuss, H., Muller, J., et al., 2009. GerES IV: phthalate metabolites and bisphenol A in urine of German children. Int. J. Hyg. Environ. Health 212 (6), 685–692.

Bekö, G., Weschler, C.J., Langer, S., Callesen, M., Toftum, J., Clausen, G., 2013. 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 (4), e62442.

Bergh, C., Torgrip, R., Emenius, G., Östman, C., 2011. Organophosphate and phthalate esters in air and settled dust - a multi-location indoor study. Indoor Air 21 (1), 67–76.

Bergh, C., Luongo, G., Wise, S., Ostman, C., 2012. Organophosphate and phthalate esters in standard reference material 2585 organic contaminants in house dust. Anal. Bioanal. Chem. 402 (1), 51–59.

Beronius, A., Rudén, C., Håkansson, H., Hanberg, A., 2010. Risk to all or none? A comparative analysis of controversies in the health risk assessment of Bisphenol A. Reprod. Toxicol. 29 (2), 132–146.

Björklund, J.A., Thuresson, K., De Wit, C.A., 2009. Perfluoroalkyl compounds (PFCs) in indoor dust: concentrations, human exposure estimates, and sources. Environ. Sci. Technol. 43 (7), 2276–2281.

Bonvallot, N., Mandin, C., Mercier, F., Le Bot, B., Glorennec, P., 2010. Health ranking of ingested semi-volatile organic compounds in house dust: an application to France. Indoor Air 20 (6), 458–472.

Bornehag, C., Lundgren, B., Weschler, C., Sigsgaard, T., Hagerhed-Engman, L., Sundell, J., 2005. Phthalates in indoor dust and their association with building characteristics. Environ. Health Perspect. 113 (10), 1399–1404.

Bornehag, C.G., Carlstedt, F., Jönsson, B.A., Lindh, C.H., Jensen, T.K., Bodin, A., et al., 2015. Prenatal phthalate exposures and anogenital distance in Swedish boys. Environ. Health Perspect. 123 (1), 101–107.

Bui, T.T., Giovanoulis, G., Cousins, A.P., Magner, J., Cousins, I.T., de Wit, C.A., 2016. Human exposure, hazard and risk of alternative plasticizers to phthalate esters. Sci. Total Environ. 541, 451–467.

Calafat, A.M., Valentin-Blasini, L., Ye, X., 2015. Trends in exposure to chemicals in personal care and consumer products. Curr Environ Health Rep 2 (4), 348–355.

Carlstedt, F., Jönsson, B.A.G., Bornehag, C.G., 2013. PVC flooring is related to human uptake of phthalates in infants. Indoor Air 23 (1), 32–39.

Casas, L., Fernández, M., Llop, S., Guxens, M., Ballester, F., Olea, N., et al., 2011. Urinary concentrations of phthalates and phenols in a population of Spanish pregnant women and children. Environ. Int. 37 (5), 858–866.

ChemSystems, 2008. Developments in Non-Phthalate Plasticizers. PERP07/08S4. .

Chen, D., Kannan, K., Tan, H., Zheng, Z., Feng, Y.L., Wu, Y., et al., 2016. Bisphenol analogues other than BPA: environmental occurrence, human exposure, and toxicity-a review. Environ. Sci. Technol. 50 (11), 5438–5453.

Clausen, P.A., Hansen, V., Gunnarsen, L., Afshari, A., Wolkoff, P., 2004. Emission of di-2-ethylhexyl phthalate from PVC flooring into air and uptake in dust: emission and sorption experiments in FLEC and CLIMPAQ. Environ. Sci. Technol. 38 (9), 2531–2537.

EC, 2005. Directive 2005/84/EC of the European Parliament and of the Council of 14 December 2005. Amending for the 22nd time Council Directive 76/769/EEC on the approximation of the laws, regulations and administrative provisions of the Member States relating to restrictions on the marketing and use of certain dangerous substances and preparations (phthalates in toys and childcare articles). Official Journal of the European Union L 344 (40).

EC, 2009. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products. Official Journal of the European Union L 342 (59).

EC, 2011. Commission directive 2011/8/EU of 28 January 2011 amending directive 2002/72/EC as regards the restriction of use of Bisphenol A in plastic infant feeding bottles. Official Journal of the European Union L 26 (11).

ECHA, 2013a. Evaluation of New Scientific Evidence Concerning DINP and DIDP. In Relation to Entry 52 of Annex XVII to REACH Regulation (EC) No 1907/2006. Helsinki.

ECHA, 2013b. RAC/24/2013/08 rev. 2. Agreed in Written Procedure. Authorisation, Establishing Reference DNELs for DEHP. Helsinki.

ECHA, 2013c. RAC/24/2013/09_rev 2. Agreed in Written Procedure. Authorisation – Establishing Reference DNELs for DBP. Helsinki.

ECHA, 2016a. Authorisation List Annex XIV of REACH [Internet]. [cited 2016 Oct 31]. Available from. https://echa.europa.eu/addressing-chemicals-of-concern/authorisation/recommendation-for-inclusion-in-the-authorisation-list/authorisation-list.

ECHA, 2016b. Information on Chemicals [Internet]. [cited 2016 Oct 31]. Available from. http://echa.europa.eu/information-on-chemicals.

EFSA, 2005a. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request from the Commission related to butylbenzylphthalate (BBP) for use in food contact materials. The EFSA Journal 241, 1–14.

EFSA, 2005b. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request related to a 10th list of substances for food contact materials. The EFSA Journal 273, 1–26.

EFSA, 2006. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request related to a 12th list of substances for food contact materials. The EFSA Journal 395–401, 1–21.

EFSA, 2008. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request related to a 18th list of substances for food contact materials. The EFSA Journal 628–633, 2–19.

EFSA, 2015. Scientific opinion on the risks to public health related to the presence of Bisphenol A (BPA) in foodstuffs: executive summary. EFSA J. 13 (1), 3978.

FAO/WHO, 2011. Joint FAO/WHO Expert Meeting to Review Toxicological and Health Aspects of Bisphenol A. Ottawa. .

Frederiksen, H., Skakkebaek, N.E., Andersson, A.M., 2007. Metabolism of phthalates in humans. Mol. Nutr. Food Res. 51 (7), 899–911.

Fromme, H., Gruber, L., Schlummer, M., Wolz, G., Bohmer, S., Angerer, J., et al., 2007. Intake of phthalates and di(2-ethylhexyl)adipate: results of the Integrated Exposure Assessment Survey based on duplicate diet samples and biomonitoring data. Environ. Int. 33 (8), 1012–1020.

Fromme, H., Lahrz, T., Kraft, M., Fembacher, L., Dietrich, S., Sievering, S., et al., 2013. Phthalates in German daycare centers: occurrence in air and dust and the excretion of their metabolites by children (LUPE 3). Environ. Int. 61, 64–72.

Fromme, H., Schutze, A., Lahrz, T., Kraft, M., Fembacher, L., Siewering, S., et al., 2016. Non-phthalate plasticizers in German daycare centers and human biomonitoring of DINCH metabolites in children attending the centers (LUPE 3). Int. J. Hyg. Environ. Health 219 (1), 33–39.

Fujii, M., Shinohara, N., Lim, A., Otake, T., Kumagai, K., Yanagisawa, Y., 2003. A study on emission of phthalate esters from plastic materials using a passive flux sampler. Atmos. Environ. 37 (39–40), 5495–5504.

Gao, C., Liu, L., Ma, W., Zhu, N., Jiang, L., Ren, N., et al., 2016. Bisphenol A in urine of Chinese young adults: concentrations and sources of exposure. Bull. Environ. Contam. Toxicol. 96 (2), 162–167.

Gaspar, F.W., Castorina, R., Maddalena, R.L., Nishioka, M.G., McKone, T.E., Bradman, A., 2014. Phthalate exposure and risk assessment in California child care facilities. Environ. Sci. Technol. 48 (13), 7593–7601.

Geens, T., Aerts, D., Berthot, C., Bourguignon, J.P., Goeyens, L., Lecomte, P., et al., 2012. A review of dietary and non-dietary exposure to bisphenol-A. Food Chem. Toxicol. 50 (10), 3725–3740.

Giovanoulis, G., Alves, A., Papadopoulou, E., Cousins, A.P., Schutze, A., Koch, H.M., et al., 2016. Evaluation of exposure to phthalate esters and DINCH in urine and nails from a Norwegian study population. Environ. Res. 151, 80–90.

Göen, T., Dobler, L., Koschorreck, J., Muller, J., Wiesmuller, G.A., Drexler, H., et al., 2011. Trends of the internal phthalate exposure of young adults in Germany–follow-up of a retrospective human biomonitoring study. Int. J. Hyg. Environ. Health 215 (1), 36–45.

Grignard, E., Lapenna, S., Bremer, S., 2012. Weak estrogenic transcriptional activities of Bisphenol A and Bisphenol S. Toxicol. in Vitro 26 (5), 727–731.

Guo, Y., Kannan, K., 2011. Comparative assessment of human exposure to phthalate esters from house dust in China and the United States. Environ. Sci. Technol. 45 (8), 3788–3794.

Gyllenhammar, I., Glynn, A., Jönsson, B.A.G., Lindh, C.H., Darnerud, P.O., Lignell, S., 2016. Concentrations of phthalate metabolites and phenolic substances in urine from first-time mothers in Uppsala, Sweden: temporal trends 2009–2014. Report to the Swedish EPA (The Health-Related Environmental Monitoring Program).

Health Canada, 2015. Third report on human biomonitoring of environmental chemicals in Canada. Results of the Canadian Health Measures Survey Cycle 3 (2012–2013) Ottawa.

Janjua, N.R., Frederiksen, H., Skakkebaek, N.E., Wulf, H.C., Andersson, A.M., 2008. Urinary excretion of phthalates and paraben after repeated whole-body topical application in humans. Int. J. Androl. 31 (2), 118–130.

Jönsson, B.A.G., Axmon, A., Lindh, C.H., Rignell Hydbom, A., Axelsson, J., Giwercman, A., et al., 2010. Tidstrender för och halter av persistenta fluorerade, klorerade och bromerade organiska miljögifter i serum samt ftalater i urin hos unga svenska män - Resultat från den tredje uppföljningsundersökningen år 2009–2010. Rapport till Naturvårdsverket.

KEMI, 2014. Kartläggning av ftalater i varor i Sverige [in Swedish]. PM 2/14. Stockholm. Available from:. www.kemi.se.

KEMI, 2015. Phthalates which are toxic for reproduction and endocrine-disrupting – proposals for a phase-out in Sweden. Report 4/15 Stockholm. Available from:. www.kemi.se.

Koch, H.M., Preuss, R., Angerer, J., 2006. Di(2-ethylhexyl)phthalate (DEHP): human metabolism and internal exposure – an update and latest results. Int. J. Androl. 29 (1), 155–165.

Koch, H.M., Christensen, K.L., Harth, V., Lorber, M., Bruning, T., 2012. Di-n-butyl phthalate (DnBP) and diisobutyl phthalate (DiBP) metabolism in a human volunteer after single oral doses. Arch. Toxicol. 86 (12), 1829–1839.

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Koch, H.M., Lorber, M., Christensen, K.L., Palmke, C., Koslitz, S., Bruning, T., 2013. Identifying sources of phthalate exposure with human biomonitoring: results of a 48 h fasting study with urine collection and personal activity patterns. Int. J. Hyg. Environ. Health 216 (6), 672–681.

Langer, S., Weschler, C.J., Fischer, A., Bekö, G., Toftum, J., Clausen, G., 2010. Phthalate and PAH concentrations in dust collected from Danish homes and daycare centers. Atmos. Environ. 44 (19), 2294–2301.

Langer, S., Bekö, G., Weschler, C.J., Brive, L.M., Toftum, J., Callesen, M., et al., 2014. Phthalate metabolites in urine samples from Danish children and correlations with phthalates in dust samples from their homes and daycare centers. Int. J. Hyg. Environ. Health 217 (1), 78–87.

Liang, Y., Xu, Y., 2014. Emission of phthalates and phthalate alternatives from vinyl flooring and crib mattress covers: the influence of temperature. Environ. Sci. Technol. 48 (24), 14228–14237.

Liao, C., Liu, F., Guo, Y., Moon, H.B., Nakata, H., Wu, Q., et al., 2012. Occurrence of eight bisphenol analogues in indoor dust from the United States and several Asian countries: implications for human exposure. Environ. Sci. Technol. 46 (16), 9138–9145.

Loganathan, S.N., Kannan, K., 2011. Occurrence of bisphenol A in indoor dust from two locations in the eastern United States and implications for human exposures. Arch. Environ. Contam. Toxicol. 61 (1), 68–73.

Maag, J., Lassen, C., Brandt, U.K., Kjølholt, J., Molander, L., Mikkelsen, S.H., 2010. Identification and assessment of alternatives to selected phthalates. Environmental Project No. 1341 2010. COWI A/S Denmark.

Mercier, F., Glorennec, P., Thomas, O., Le Bot, B., 2011. Organic contamination of settled house dust, a review for exposure assessment purposes. Environ. Sci. Technol. 45 (16), 6716–6727.

Miller, L.A., Stapleton, F.B., 1989. Urinary volume in children with urolithiasis. J. Urol. 141 (4), 918–920.

Morgan, M.K., Sheldon, L.S., Croghan, C.W., Chuang, J.C., Lordo, R.A., Wilson, N.K., et al., 2004. A Pilot Study of Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants (CTEPP). Contract Number 68-D-99-011. Task Order 0002. U.S. EPA National Exposure Research Laboratory, Research Triangle Park, NC Available from:. https://cfpub.epa.gov/si/si_public_file_download.cfm?p_download_id=525063.

Morgan, M.K., Jones, P.A., Calafat, A.M., Ye, X., Croghan, C.W., Chuang, J.C., et al., 2011. Assessing the quantitative relationships between preschool children's exposures to bisphenol A by route and urinary biomonitoring. Environ. Sci. Technol. 45 (12), 5309–5316.

Myridakis, A., Chalkiadaki, G., Fotou, M., Kogevinas, M., Chatzi, L., Stephanou, E.G., 2016. Exposure of preschool-age Greek children (RHEA cohort) to bisphenol A, parabens, phthalates, and organophosphates. Environ. Sci. Technol. 50 (2), 932–941.

Richter, C.A., Birnbaum, L.S., Farabollini, F., Newbold, R.R., Rubin, B.S., Talsness, C.E., et al., 2007. In vivo effects of bisphenol A in laboratory rodent studies. Reprod. Toxicol. 24 (2), 199–224.

Rochester, J.R., Bolden, A.L., 2015. Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes. Environ. Health Perspect. 123 (7), 643–650.

SCF, 2000. Opinion of the Scientific Committee on Food on a survey on dietary intake of the food contact material di-2-(ethylhexyl) adipate (DEHA). SCF/CS/PM/3276 Final/31920 Brussel.

Stacy, S.L., Eliot, M., Calafat, A.M., Chen, A., Lanphear, B.P., Hauser, R., et al., 2016. Patterns, variability, and predictors of urinary bisphenol A concentrations during childhood. Environ. Sci. Technol. 50 (11), 5981–5990.

US EPA, 2011. Exposure Factors Handbook: 2011 Edition. Washington. Available from:. www.epa.gov.

Völkel, W., Colnot, T., Csanady, G.A., Filser, J.G., Dekant, W., 2002. Metabolism and kinetics of bisphenol A in humans at low doses following oral administration. Chem. Res. Toxicol. 15 (10), 1281–1287.

Wang, W., Abualnaja, K.O., Asimakopoulos, A.G., Covaci, A., Gevao, B., Johnson-Restrepo, B., et al., 2015. A comparative assessment of human exposure to tetrabromobisphenol A and eight bisphenols including bisphenol A via indoor dust ingestion in twelve countries. Environ. Int. 83, 183–191.

Watkins, D.J., Eliot, M., Sathyanarayana, S., Calafat, A.M., Yolton, K., Lanphear, B.P., et al., 2014. Variability and predictors of urinary concentrations of phthalate metabolites during early childhood. Environ. Sci. Technol. 48 (15), 8881–8890.

Wickman, M., Kull, I., Pershagen, G., Nordvall, S.L., 2002. The BAMSE project: presentation of a prospective longitudinal birth cohort study. Pediatr. Allergy Immunol. 13 (Suppl. 15), 11–13.

Wilson, N.K., Chuang, J.C., Lyu, C., 2001. Levels of persistent organic pollutants in several child day care centers. J. Expo. Anal. Environ. Epidemiol. 11 (6), 449–458.

Wilson, N.K., Chuang, J.C., Morgan, M.K., Lordo, R.A., Sheldon, L.S., 2007. An observational study of the potential exposures of preschool children to pentachlorophenol, bisphenol-A, and nonylphenol at home and daycare. Environ. Res. 103 (1), 9–20.

Wittassek, M., Angerer, J., 2008. Phthalates: metabolism and exposure. Int. J. Androl. 31 (2), 131–138.

Wittassek, M., Koch, H.M., Angerer, J., Bruning, T., 2011. Assessing exposure to phthalates - the human biomonitoring approach. Mol. Nutr. Food Res. 55 (1), 7–31.

Wormuth, M., Scheringer, M., Vollenweider, M., Hungerbuhler, K., 2006. What are the sources of exposure to eight frequently used phthalic acid esters in Europeans? Risk Anal. 26 (3), 803–824.

Ye, X., Wong, L.Y., Kramer, J., Zhou, X., Jia, T., Calafat, A.M., 2015. Urinary concentrations of bisphenol A and three other bisphenols in convenience samples of U.S. adults during 2000–2014. Environ. Sci. Technol. 49 (19), 11834–11839.

Zota, A.R., Calafat, A.M., Woodruff, T.J., 2014. Temporal trends in phthalate exposures: findings from the National Health and Nutrition Examination Survey, 2001–2010. Environ. Health Perspect. 122 (3), 235–241.

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