Published in final edited form as:
J Expo Sci Environ Epidemiol. 2012 September ; 22(5): 468–475. doi:10.1038/jes.2012.33.

Consumer product exposures associated with urinary phthalate levels in pregnant women

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Abstract

Human phthalate exposure is ubiquitous, but little is known regarding predictors of urinary phthalate levels. To explore this, 50 pregnant women aged 18–38 years completed two questionnaires on potential phthalate exposures and provided a first morning void. Urine samples were analyzed for 12 phthalate metabolites. Associations with questionnaire items were evaluated via Wilcoxon tests and t-tests, and r-squared values were calculated in multiple linear regression models. Few measured factors were statistically significantly associated with phthalate levels. Individuals who used nail polish had higher levels of mono-butyl phthalate (p=0.048) than non-users. Mono-benzyl phthalate levels were higher among women who used eye makeup (p=0.034) or used makeup on a regular basis (p=0.004). Women who used cologne or perfume had higher levels of di-(2-ethylhexyl) phthalate metabolites. Household products, home flooring or paneling, and other personal care products were also associated with urinary phthalates. The proportion of variance in metabolite concentrations explained by questionnaire items ranged between 0.31 for mono-ethyl phthalate and 0.42 for mono-n-methyl phthalate. Although personal care product use may be an important predictor of urinary phthalate levels, most of the variability in phthalate exposure was not captured by our relatively comprehensive set of questionnaire items.

Keywords

Phthalates; pregnancy; biomonitoring; urine; personal care products

Introduction

Phthalates are synthetic diesters of phthalic acid used in a variety of industrial and consumer products. High molecular weight phthalates are added to plastics to enhance flexibility and

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Conflict of Interest The authors declare no conflicts of interest.

durability. Low molecular weight phthalates are used in adhesives, detergents, and solvents. Sources of phthalate exposure in consumer products are varied and include polyvinyl chloride (PVC) plastics, building materials, medical devices, pharmaceuticals, automotive components, toys, food packaging, cosmetics, fragrances, and pesticides (Schettler, 2006). Biomonitoring studies have demonstrated ubiquitous human exposure to phthalates in the developed world. Three phthalate metabolites, mono-ethyl, mono-n-butyl, and mono-benzyl, were present in more than 97% of urinary samples analyzed in the 1999–2000 National Health and Nutrition Examination Survey (NHANES) (Silva et al., 2004).

Widespread phthalate exposure has prompted investigations of their potential adverse health effects. Fetal exposures are of particular concern because phthalate metabolites cross the placenta and have been measured in amniotic fluid (Silva et al., 2004), placental tissue (Mose et al., 2007), cord blood (Latini et al., 2003), and neonatal meconium (Kato et al., 2006). Experimental animal studies have reported adverse reproductive and developmental effects and suggest that phthalates may have endocrine-disrupting properties (Lyche et al., 2009). Human *in utero* exposure has been linked to altered gestational duration, reduced anogenital distance in boys, and impaired behavior and executive functioning skills (Adibi et al., 2009; Engel et al., 2010; Latini et al., 2003; Swan et al., 2005; Swan, 2008; Whyatt et al., 2009; Wolff et al., 2008). Reproductive, respiratory, metabolic, and thyroid effects in children and adults have also been reported (Bornehag and Nanberg, 2010; Duty et al., 2003; Hatch et al., 2008; Hauser et al., 2006; Huang et al., 2007; Stahlhut et al., 2007).

Phthalates are quickly metabolized and excreted in urine, with elimination half lives of less than 24 hours (Koch et al., 2005). Urinary biomarkers are widely used to assess human exposure. However, biomarkers represent total exposure and cannot differentiate the contribution of particular exposure sources or routes. Several studies have assessed the correlation between urinary biomarkers of phthalate exposure and specific consumer products, such as baby care items, medical devices and medications, foods, fragrances, and personal care products (Adibi et al., 2003; Berman et al., 2009; Calafat et al., 2004; Colacino et al., 2010; Duty et al., 2005; Hernandez-Diaz et al., 2009; Just et al., 2010; Kwapniewski et al., 2008; Romero-Franco et al., 2011; Sathyanarayana et al., 2008). These previous studies provide evidence that urinary biomarkers incorporate phthalate exposure from various consumer products. However, none have quantified the degree to which urinary phthalate levels can be explained by consumer product exposure. The aim of this project was to design a questionnaire to predict urinary phthalate exposures in a population of pregnant women, who have a greater potential risk of adverse effects.

Materials and Methods

Population

The parent study for this phthalate exposure assessment project was the *Right From the Start (RFTS)* study, a geographically-based, prospective study of the relationship between tap water disinfection byproducts and spontaneous pregnancy loss. Women in three U.S. cities who were in early pregnancy (less than 12 weeks gestation) or who were trying to become pregnant were recruited by advertisement, direct mailing, pregnancy test coupons, and referrals from prenatal care sites. Interested women were screened by telephone for eligibility. The study was conducted from 2000 to 2004 and is described elsewhere (Hoffman et al., 2008; Promislow et al., 2004; Savitz et al., 2006).

A subcohort of women from each of the three *RFTS* sites was recruited for the phthalates protocol. Included women were approximately gestational weeks 22–24, did not use assisted reproductive technology to conceive, had a singleton gestation, intended to carry the pregnancy to term, were 18 years of age or older, and had, at minimum, conversational

English skills. The women also had to have completed a first-trimester study ultrasound by 10 weeks estimated gestational age. Women eligible for the phthalate subcohort completed a detailed mailed questionnaire prior to their baseline study visit, and were mailed materials to collect a first morning urine specimen on the day of their visit. Participants completed a 48-hour recall questionnaire during the baseline study visit. Demographic data were obtained during the *RTFS* screening call.

Questionnaires

The mailed questionnaire was designed to capture information on a variety of potential phthalate exposures including housing characteristics, building materials, cleaning products, cosmetics, prepared food, fragrances, and medical equipment. Questions focused on ascertaining potential phthalate exposure in the past year. The 48-hour recall questionnaire contained yes/no questions about exposures in the past 48 hours, including home renovations, chemicals, cosmetics, personal care items, nail care, and medical exposures. This questionnaire also included four global questions aimed at determining whether participants regularly wore makeup, used cosmetics or household products that contain fragrance, ate prepackaged foods or foods prepared at fast food restaurants, or did cleaning that involved using household cleaners at least 2 hours per week.

Biological Samples

First morning void urine samples were divided into 3.0 ml aliquots, stored at −20°C and shipped frozen to the Centers for Disease Control and Prevention for analysis. Urine samples were analyzed for phthalate monoesters and creatinine using methods described previously (Blount et al., 2000). Specifically, mono-butyl phthalate (MBP), mono-benzyl phthalate (MBZP), mono-cyclohexyl phthalate (MCHP), mono-ethyl phthalate (MEP), mono-ethylhexyl phthalate (MEHP), mono-n-methyl phthalate (MMP), mono-isononyl phthalate (MINP), monon-octyl phthalate (MOP), mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono-isobutyl phthalate (MIBP), and mono-3-carboxypropyl phthalate (MCPP) were measured. Samples were spiked with $^{13}C_4$-labeled phthalate monoesters and 4-methylumbelliferone glucuronide. They were then treated with β-glucuronidase to release the phthalate monoesters from their conjugated forms. Deconjugated urine samples were extracted twice with Oasis HLB solid phase extraction and resuspended in mobile phase. Chromatographic separation by high pressure liquid chromatography was followed with tandem mass spectrometry on a triple quadrupole instrument using atmospheric pressure chemical ionization (Finnigan Inc., San Jose, CA). Levels of 4-methylumbelliferone were monitored as quality control for the deconjugation step. Method blanks, laboratory quality control samples (spiked human urine) and standards were analyzed along with the study urine samples. Urinary creatinine was measured using an ASTRA analyzer (Beckman Inc., Brea, CA) based on a Jaffe rate reaction. Samples were analyzed in batches and at least one quality assurance sample and one duplicate were included in each batch. These quality assurance samples and duplicates were labeled and handled in an identical manner to actual samples with the laboratory unaware of sample status.

Statistical Analysis

Fifty women from May 2002 through September 2003 contributed both complete questionnaire and urinary phthalate data for the analyses. Observations below the limit of detection (LOD) were assigned a value of half the detection limit. Phthalate concentrations are reported as the absolute concentration in urine (ng/ml) and the concentration adjusted for urinary creatinine (μg/g creatinine) to account for urine dilution. Phthalate levels were divided by the creatinine level and then multiplied by 100 to obtain creatinine-adjusted

levels. MBZP and MEP levels were corrected for inaccurate phthalate standards in place at the time of laboratory analysis (multiplied by 0.66 and 0.72, respectively).

To evaluate associations between urinary phthalate concentrations and product use questionnaire responses, mean natural log transformed creatinine-adjusted phthalate levels were compared using Satterthwaite T tests. If a phthalate's distribution was not log-normal, median creatinine-adjusted phthalate levels were compared with Wilcoxon rank-sum tests. Statistical significance was determined at an alpha level of 0.05.

We also assessed the proportion of variance in phthalate metabolite levels explained by items in the two questionnaires. This analysis was conducted in two stages in order to screen a large number of items and obtain a parsimonious model. In the first stage, the association between each log creatinine-adjusted phthalate metabolite and questionnaire item was assessed in a bivariate linear regression model. In the second stage, items with $p<0.1$ in the bivariate models were entered into multiple linear regression models for each phthalate and the proportion of variance explained (R^2) was computed. This analysis was limited to metabolites detected in >70% of samples, and the di-(2-ethylhexyl) phthalate (DEHP) metabolites MEHHP, MEHP, and MEOHP were examined as a molar sum (ΣDEHP). Significance was evaluated at an alpha level of 0.1 in order to include all important predictors of phthalate metabolite levels in the multiple regression models. All analyses were conducted using SAS version 9.2 (Cary, NC) and only questionnaire items reported by at least 5 women were assessed.

Results

Characteristics of this sample of pregnant women are described in Table 1. Women were predominantly white or black non-Hispanic, never smokers, and had at least some college education. Phthalate concentrations with and without creatinine-adjustment are reported in Table 2. Urinary levels of MCHP, MINP, and MOP were below the limits of detection for all or nearly all women. Creatinine-adjusted phthalate distributions were log-normal except for MBP and MBZP; thus, results for these two metabolites are presented as medians rather than arithmetic means. Median phthalate levels reported in this study are comparable to U.S. population levels but lower than levels among pregnant women estimated by the National Health and Nutrition Examination Survey (NHANES) during a similar time period (Table 3).

Frequencies of product use reported on the 48-hour recall and mailed questionnaires and their associations with phthalate metabolites are reported in Tables 4 and 5, respectively. Products most commonly used by women in the past 48 hours were makeup and personal care items, particularly eye makeup, lipstick, and hand creams or lotions.

Women who reported using makeup most days of the week had higher levels of MBZP than women who did not (medians: 10.4 vs 5.2 μg/g creatinine, p=0.004). Use of eye shadow, eyeliner, or mascara in the past 48 hours was associated with higher levels of MBP (medians: 26.3 vs 12.8 μg/g creatinine, p=0.013), MBZP (medians: 7.9 vs 5.2 μg/g creatinine, p=0.034), MIBP (means: 3.7 vs 1.4 μg/g creatinine, p=0.022), and MEOHP (means: 23.6 vs 15.4 μg/g creatinine, p=0.045). Sunscreen use in the past 48 hours was associated with higher levels of MBP (medians: 50.7 vs 15.2 μg/g creatinine, p=0.024) and MMP (means: 3.2 vs 1.6 μg/g creatinine, p<0.001). Women who reported using bath oil, bath gel, or bubble bath in the past 48 hours had higher levels of MMP (means: 2.2 vs 1.5 μg/g creatinine, p=0.009). Using hair nutrient products in the past 48 hours was associated with increased urinary levels of MEP (means: 136.5 vs 124.7 μg/g creatinine, p=0.036) and MMP (means: 2.9 vs 1.6 μg/g creatinine, p=0.002). Women who applied or removed nail

polish in the past 48 hours had statistically significantly higher levels of MBP (medians: 30.2 vs 15.1 μg/g creatinine, p=0.048) than women who were not exposed to nail polish. In contrast, urinary MEP concentrations were statistically significantly lower among women who applied or removed nail polish (means: 33.2 vs 138.7 μg/g creatinine, p=0.002).

Women who normally tried to buy fragrance-free products had lower levels of both MEHP (means: 6.8 vs 17.4 μg/g creatinine, p=0.037) and its secondary phthalate metabolite, MEHHP (means: 14.4 vs 37.6 μg/g creatinine, p=0.032). Use of cologne or perfume was associated with higher levels of MIBP (means: 3.6 vs 2.0 μg/g creatinine, p=0.011) and the DEHP metabolites MEHP (means: 17.2 vs 8.1 μg/g creatinine, p=0.007), MEHHP (means: 36.7 vs 18.1 μg/g creatinine, p=0.007), and MEOHP (means: 26.3 vs 13.8 μg/g creatinine, p=0.011).

Few women reported using household chemicals or cleaning products in the 48-hour recall questionnaire. In the mailed questionnaire, regular fabric softener use was associated with higher levels of MEP (means: 176.7 vs 95.0 μg/g creatinine, p=0.039). Air freshener use was associated with higher levels of MBP (medians: 23.9 vs 8.9 μg/g creatinine, p=0.015), MBZP (medians: 8.9 vs 3.5 μg/g creatinine, p=0.003), and MEP (means: 147.7 vs 70.7 μg/g creatinine, p=0.026).

With the exception of three items on the mailed questionnaire, housing characteristics and building materials were not associated with urinary metabolite levels. Women who lived in a building with two or more units had higher levels of MIBP (means: 4.7 vs 2.5 μg/g creatinine, p=0.018) than women who lived in a house. Women who had vinyl flooring in their places of residence had significantly lower levels of MEHP (means: 8.6 vs 22.0 μg/g creatinine, p=0.016). Paneling in the home was associated with higher levels of MEP (means: 201.4 vs 113.8 μg/g creatinine, p=0.026).

Eating deli or “to go” foods three or more times a week was not associated with phthalate levels in this group of women. Analyses could not be completed on IV treatments or chemical products such as paints and solvents because our sample of women did not report exposure to these items. There were no statistically significant associations between consumer products and MCPP, MEOHP, or MMP.

The results of our exploratory analysis of predictive ability of the questionnaire variables are presented in Table 6. The R^2 values ranged between 0.31 for MEP and 0.42 for MMP. To a large extent, the predictors associated with each of the phthalates were personal care products, although different products were associated with different phthalates. While these models explained more variance than individual variables, there was no compelling pattern to the predictors identified. MMP had six products which overall explained 42% of the variance in creatinine adjusted MMP levels. Four of the products (sunscreen, bath oil, hair nutrient products, and hair styling gel) were positively associated with MMP, while two (spot cleaners and lipstick) were inversely associated. For MBP, seven items explained 39% of the variance and all were positively associated; four of these were personal care products used within the past two days and three where regular home activities within the past year (regular use of dryer sheets, air fresheners, and having interior walls painted).

Discussion

In this sample of pregnant women, questionnaire items related to product use were associated with urinary levels of some phthalate metabolites. Current use of personal care products and regular use of cleaning products in the home were associated with urinary phthalate concentrations. None of the four global questions about makeup, fragrance-free products, food, or household cleaners nor any of the specific product items explained

substantial variability in phthalate levels on their own. Given the complex patterns of exposure to phthalates, these analyses suggest that questionnaires are unlikely to predict urinary phthalate levels to an extent that would be adequate in epidemiologic studies of health effects.

The majority of pregnant women in this sample reported using makeup and personal care products. Because many of these products contain phthalates, frequent exposure may result in consistently elevated phthalate concentrations during pregnancy. In the current study, three personal care products were associated with higher levels of MMP: bath oil, bath gel, or bubble bath; hair nutrient products; and sunscreen. In other investigations of phthalate exposure sources, MMP was associated with baby lotion and shampoo in one study (Sathyanarayana et al., 2008), but was not significantly associated with personal care products in another (Duty et al., 2005). Although three prior studies reported increased urinary levels of MEP among those using personal care products or lotion (Berman et al., 2009; Romero-Franco et al., 2011; Sathyanarayana et al., 2008), the only positive association we observed for MEP was use of hair nutrient products in the past 48 hours. Mono-benzyl phthalate, which was anticipated to correlate with questions about plastic materials, was associated with using eye makeup in the last 48 hours and using makeup most days of the week. Other studies of personal care products have not reported positive associations with mono-benzyl phthalate.

In this study, the dibutyl phthalate metabolite MBP was positively associated with nail polish use. Dibutyl phthalate is an integral part of nail polishes (Koo and Lee, 2004). Occupational studies of phthalate exposure in manicurists have reported increased concentrations of dibutyl phthalate metabolites (Hines et al., 2009; Kwapniewski et al., 2008) and a previous study of phthalate exposure among pregnant women reported that nail polish use was associated with increased levels of dibutyl phthalate metabolites (Hines et al., 2009). We also observed an inverse association between MEP and applying or removing nail polish in the past 48 hours. Previous literature does not support this finding, which may have occurred by chance.

In our sample, MEP was positively associated with air freshener use but no other aspect of fragrance use or avoidance. MEP is the phthalate metabolite thought to be most associated with fragrances (Koo and Lee, 2004) and this finding is in contrast to two prior studies that reported dose dependent increases in urinary MEP levels with perfume, cologne, or aftershave use (Duty et al., 2005; Just et al., 2010). DEHP metabolites were positively associated with cologne or perfume use and inversely associated with buying fragrance-free products; DEHP has also been detected in perfumes (Koo and Lee, 2004). The association with DEHP but not MEP may reflect differences in the phthalate content of particular products and brands used by the women in this sample compared to other populations studied.

We used first morning voids to measure phthalate concentrations as these have been shown to be reliable and reproducible over time (Hoppin et al., 2002). While the variability in first morning voids is less than for spot urine samples, our study may have been unable to detect an association between phthalate metabolites and personal care products due to their short half lives and lack of product application prior to the first morning void. This may explain why we do not see associations with MEP that others have seen. By using first morning voids, we may have collected lower levels of MEP than other studies. Indeed, the median MEP concentration in our sample (61 ng/mL) was lower than reported by the Duty et al. (96 ng/mL, standard-corrected) and Just et al. (131 ng/mL, standard-corrected) studies.

Phthalates are a primary component of PVC plastics. The amount of PVC used in floor and wall materials has been reported to correlate with benzyl butyl phthalate and DEHP levels in house dusts (Bornehag et al., 2005). Adibi et al. reported significant correlations between dust phthalate levels and urinary concentrations of MEP, MBP, and MBZP, demonstrating that inhalation may be an important exposure route (Adibi et al., 2003). While we observed positive associations between MIBP and living in a building with two or more units and between MEP and paneling in the home, there were no positive associations between plastic-containing materials in the home and DEHP metabolites. Contrary to expectations, living in a home with vinyl flooring was inversely associated with DEHP metabolites. One possible explanation for this finding is that homes without vinyl flooring may have been dustier, resulting in higher phthalate exposure via indoor air. Alternatively, this finding may be due to confounding if women with vinyl flooring in their homes had lower exposure to other sources of DEHP. The ability to detect associations with housing characteristics may also have been limited by our small sample size. Furthermore, dust phthalate levels may be a better metric for internal exposure to phthalates from plastics in housing materials than questionnaire data on the presence of PVC or vinyl materials in the home (Bornehag et al., 2005).

The proportion of variance in urinary phthalate metabolite levels explained by models including multiple product use items was moderate ($R^2 = 0.31 – 0.42$). These results suggest that a detailed questionnaire ascertaining the use of phthalate-containing products may have utility in predicting levels of some phthalate metabolites. However, the variation not explained by items on our questionnaires was substantial, indicating that major predictors of phthalate levels were not ascertained. It is therefore unlikely that these questionnaires could be used to classify phthalate exposures with enough discrimination for use in epidemiologic studies.

The consumer product questionnaires designed for this study aimed to capture potential phthalate exposures from home, cosmetic, medical, and cleaning product sources. However, we were unable to assess medical product or recent chemical use in relation to urinary phthalate levels because no women in our sample reported these exposures. Although comprehensive with respect to known phthalate sources, the questionnaires may not have ascertained information on important phthalate-containing products. Food is thought to be a primary exposure source due to the use of phthalates in packaging (Schettler, 2006). An analysis of urinary phthalate levels in relation to dietary intake in NHANES reported positive associations between DEHP and DEP metabolites and consumption of poultry and vegetables, respectively (Colacino et al., 2010). There was no association in our study between phthalate concentrations and eating deli or to go foods, which may be due to the use of first morning voids because exposure is unlikely to occur prior to sample collection. In addition, more detailed questionnaire data would be necessary for a full characterization of dietary phthalate exposure. More research on the phthalate content of foods would improve the ability to construct useful questionnaire items.

Phthalate metabolite concentrations were lower in this study than among pregnant women in NHANES, which may represent differences in exposures detectable by spot urine samples versus first morning voids. Because phthalates have a short half life and exposures are unlikely to occur within 8–10 hours prior to first morning voids, phthalate exposures may be underestimated in this sample limiting our ability to identify associations with product use. The small number of women in this sample limits the power to detect differences between product users and nonusers. Thus, questionnaire items that were significantly different between groups represent strong associations. It is also possible that some of the associations observed in the t-test comparisons are due to chance or to confounding, because the results of this analysis are unadjusted. Estimates of the proportion of variance explained

by questionnaire items were unable to support a large number of variables and may not have included all important predictors. The results of this study may not be generalizable to non-pregnant women due to differences in physiology and product use during gestation.

Correlations between questionnaire responses and phthalate levels were based on a single urine sample from each woman. Phthalate half lives are short with reproducibility of urinary phthalate metabolite levels measured on consecutive days ranging from 0.5 to 0.8, depending on the phthalate (Hoppin et al., 2002). Studies examining repeated urine samples over periods of up to 3 months reported intraclass correlations between 0.2 and 0.8, indicating that a single sample may be useful to project long term exposure to some phthalates but not others (Adibi et al., 2008; Fromme et al., 2007; Hauser et al., 2004; Marcus et al., 2010). Although creatinine is highly variable during pregnancy, the use of first morning voids collected during a short window of gestation (weeks 22–24) minimizes the potential bias from creatinine adjustment.

Use of questionnaire data for exposure assignment in epidemiologic studies of phthalates and health effects may be problematic for several reasons. Questionnaires are complicated to design and administer and they require open ended options to capture information on brands and products. Exposure sources are numerous and it may not be possible to construct a questionnaire that is able to ascertain all important sources of exposure. Finally, phthalate levels in products change over time and product labeling is not required in the United States, further limiting the ability to link specific products and exposure levels.

Conclusion

This study characterized usage of phthalate-containing products among a sample of pregnant women and assessed associations with urinary phthalate metabolites. The findings suggest that application of personal care products may be an important predictor of urinary phthalate levels; however, the metabolites associated with questionnaire items were not always the phthalates that were anticipated. Using these two detailed questionnaires we were able to explain more of the variance in urinary phthalate levels than by using one question alone, but it is unclear how consistent these predictors will be over time. The major predictors of urinary phthalate levels in pregnant women have yet to be identified.

Acknowledgments

Jessie Buckley and Jeanine Matuszewski were supported by a National Institute of Environmental Health Sciences training grant (T32 ES007018). Amy Herring and Katherine Hartmann were supported by the American Water Works Association Research Foundation under Contract #2579. This work was supported in part by the Intramural Research Program of the National Institute of Environmental Health Sciences, NIH, DHHS (Z01ES049003). The authors thank CDC for phthalate analysis.

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Table 1

Demographic characteristics of the 50 pregnant study participants, 2000–2004

Characteristic	*n*	(%)
Maternal Age (years)		
18–24	8	(16)
25–29	16	(32)
30–34	20	(40)
35+	6	(12)
Race		
White	23	(46)
Black	20	(40)
Other	7	(14)
Hispanic		
Yes	6	(12)
No	44	(88)
Education		
High school or less	7	(14)
Some college	14	(28)
College or more	29	(58)
Income[1]		
≤$40 000	13	(26)
$4 001–$80 000	21	(42)
> $80 000	12	(24)
Maternal BMI (kg/m^2)[1]		
< 24.9	24	(48)
25–29.9	15	(30)
30+	10	(20)
Smoking Status[1]		
Never	34	(68)
Former	8	(16)
Current	0	(0)
Total number of pregnancies[1]		
1	9	(18)
2	18	(36)
3+	21	(42)
Total number of births[1]		
0	16	(32)
1	21	(42)
2+	11	(22)

[1]Numbers do not sum to 50 due to missina values.

Table 2

Unadjusted and creatinine-adjusted urinary phthalate levels among 50 pregnant women[1]

Phthalate	Limits of detection (LOD)	Number (%) below LOD		Unadjusted values (ng/ml)					Creatinine-adjusted values (μg/g creatinine)				
				Mean	SD	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum
MBP	1.07	5	(10)	27.6	29.4	18.2	0.5	135.0	24.7	23.0	17.9	1.6	121.2
MBZP	0.18	5	(10)	15.9	27.5	7.6	0.1	139.5	11.8	12.4	7.7	0.1	63.3
MCHP	0.28	49	(98)	0.1	0.0	0.1	0.1	0.3	0.2	0.1	0.1	0.1	0.8
MCPP	0.37	15	(30)	3.1	9.0	1.3	0.2	64.1	2.2	3.4	1.2	0.1	21.5
MEHHP	0.95	3	(6)	28.3	32.7	17.1	0.5	167.7	28.5	36.4	18.7	0.8	215.8
MEHP	0.98	9	(18)	13.4	18.5	6.2	0.5	84.6	13.2	18.6	5.3	0.5	94.5
MEOHP	1.07	3	(6)	21.3	24.2	14.0	0.5	124.2	20.8	21.9	14.0	0.9	111.3
MEP	N/A	0	(0)	157.0	279.9	61.5	6.5	1611.1	126.1	155.9	68.7	6.5	763.2
MIBP	1.04	23	(46)	3.5	6.4	1.3	0.5	35.3	2.9	4.1	1.6	0.3	19.4
MINP	0.85	49	(98)	0.4	0.1	0.4	0.4	1.0	0.6	0.5	0.4	0.1	2.3
MMP	0.23	13	(26)	2.0	2.3	1.5	0.1	13.1	1.8	1.6	1.3	0.1	8.2
MOP	1	50	(100)	0.5	0.0	0.5	0.5	0.5	0.7	0.5	0.5	0.2	2.7

[1]For those values which were below the limits of detection (LOD), the limit of detection divided by 2 replaced the zero value for the analyses. Phthalate levels were divided by the creatinine level and then multiplied by 100 to obtain the creatinine-adjusted levels.

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Table 3

Comparison of median creatinine-adjusted urinary phthalate levels (μ/g creatinine) to a U.S. population-based sample

Phthalate	Present study (*n* = 50)	NHANES[1] total population (*n* = 2 782)	NHANES[2] pregnant women (*n* = 111)
MBP	17.9	17.4	22.7
MBZP[3]	7.7	9.7	15.7
MCHP	0.1	< LOD	
MCPP	1.2	2.5	3.5
MEHHP	18.7	16.6	22.8
MEHP	5.3	3.9	10.4
MEOHP	14.0	11.2	17.8
MEP[3]	68.7	98	306.4
MIBP	1.6	2.5	3.3
MINP	0.4	< LOD	
MMP	1.3	1.3	2.1
MOP	0.5	< LOD	0.7

[1] Data from the 2001–2002 National Health and Nutrition Examination Survey (NHANES) (Centers for Disease Control and Prevention, 2010).

[2] Data from the 2001–2002 National Health and Nutrition Examination Survey (NHANES) (Ye et al., 2009).

[3] NHANES levels for MBZP and MEP are standard-corrected. < LOD Below limit of detection

Table 4

Frequencies of product use reported in the 48 hour recall questionnaire and associations with phthalate metabolites[1]

Exposure Group / Product	*n*	(%)	MBP	MBZP	MBP	MEP	MMP	Any DEHP metabolite[2]
Global items								
Makeup most days of the week	29	(58)	+	+*				
Try to buy fragrance free products	19	(38)						−*
Deli or “to go” foods 3+ times a week	16	(32)						
Household cleaners at least 2 hours a week	30	(60)						
In the last 2 days (48 hours) …								
Cleaning products								
Laundry detergent with fragrance	30	(60)						+
Fabric softener or dryer sheet with fragrance	29	(58)						
Fabric starch	8	(16)						
Spot cleaners	12	(24)					−	
Carpet cleaners	2	(4)						
Furniture polish or wax	9	(18)						
Shoe cleaner or polish	2	(4)						
Interior car cleaner	1	(2)						
Creams and lotions								
Anti-aging or overnight cream	10	(20)						
Cleansing cream	21	(42)						
Facial masks	7	(14)						+
Sunscreen	5	(10)	+*				+*	
Baby oil	4	(8)						
Petroleum jelly or diaper ointment	18	(36)						
Hand cream or lotion	43	(86)						+
Other cream or lotion, including shaving cream	33	*(66)*	+					
Toiletries and cosmetics								
Lipstick, chapstick, or lip balm	42	(84)					−	
Foundation makeup	27	(54)						
Eye shadow, liner, or mascara	33	(66)	+*	+*	+*			+*

Exposure Group / Product	*n*	(%)	MBP	MBZP	MBP	MEP	MMP	Any DEHP metabolite[2]
Powder	25	(50)						
Cologne or perfume	28	(56)			+*			+*
Bath oil, bath gel, or bubble bath	15	(30)	+				+*	
Hair conditioner	29	(58)						−
Hair nutrient product	6	(12)				+*	+*	
Hair spray	23	(46)						
Hair styling gel, mousse, pomade, or grease	33	(66)					+	
Hair and nail grooming								
Visit a beauty salon	3	(6)						
Hair permed, straightened, or relaxed	0	(0)						
Permed, straightened, relaxed someone else's hair	0	(0)						
Colored or highlighted hair	0	(0)						
Colored or highlighted someone else's hair	0	(0)						
Nail polish applied or removed	8	(16)	+					
Applied or removed nail polish	6	(12)	+*			−*		
Artificial nails applied, filled, or removed	0	(0)						
Applied, filled, removed artificial nails	0	(0)						
Medical treatments								
Intravenous treatment for a medical problem	0	(0)						
Medicinal cream, lotion, or balm	5	(10)						
Renovations or repairs								
Interior paint or wood stain	3	(6)						
Exterior paint or wood stain	0	(0)						
New flooring, paneling, counter tops, or cupboards	0	(0)						
Wallpaper	0	(0)						
Interior grout	3	(6)						
New carpet	0	(0)						
Hardwood floor finish	0	(0)						
Chemical products								
Furniture refinishing chemicals	1	(2)						
Smelly glue	1	(2)						

Exposure Group / Product	*n*	(%)	MBP	MBZP	MBP	MEP	MMP	Any DEHP metabolite[2]
Spray adhesive	1	(2)						
Paint for furniture, fabric, ceramics, hobby	1	(2)						
Solvents (e.g., paint thinner, turpentine, degreaser)	1	(2)						

[1] Associations assessed using Wilcoxon rank-sum tests (MBP and MBZP) or Satterthwaite T tests (MIBP, MEP, MEHP, DEHP metabolites). Products used by fewer than 5 women were not tested.

[2] DEHP metabolites include MEHHP, MEHP, and MEOHP

+*/−* Positive/negative association between questionnaire item and metabolite at $p<0.05$

+/− Positive/negative association between questionnaire item and metabolite at $0.05 \leq p < 0.1$

Table 5

Frequencies of product use reported in the mailed questionnaire and associations with phthalate metabolites[1]

Product	*n*	(%)	MBP	MBZP	MIBP	MEP	MMP	Any DEHP metabolite[2]
Type of Home								
One family house, detached	35	(70)						
One family house, attached	6	(12)						
Building with 2+ units	9	(18)			+*			
Time frame in which home was built								
1969 or earlier	10	(20)						
1970–79	7	(14)						
1980–89	8	(16)						
1990–99	15	(30)						
2000 or later	8	(16)						
In the last 12 months …								
Interior car treatment for vinyl/leather	24	(48)						
Car purchased	11	(22)						
Fabric softener regularly used	19	(39)		+		+*		
Dryer sheets regularly used	34	(69)	+					+
Shoe wax or polish	2	(4)						
Shoe cleaner	2	(4)						
Wood cleaning products	36	(72)						
Air freshener	36	(72)	+*	+*	+	+*		+
Vinyl or linoleum floors in home	35	(70)						−*
Laminate flooring in home	10	(20)		+				+
Hardwood floors in home	16	(32)						
Walls painted in home	25	(50)						
Paneling in home	7	(14)		+		+*		+
Refinish furniture	2	(4)						
Perm, straighten, relax own hair	18	(36)						
Perm, straighten, relax someone else's hair	8	(16)						
Manicure or pedicure self	31	(62)						+

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Product	*n*	(%)	MBP	MBZP	MIBP	MEP	MMP	Any DEHP metabolite[2]
Manicure or pedicure someone else	3	(6)						

[1] Associations assessed using Wilcoxon rank-sum tests (MBP and MBZP) or Satterthwaite T tests (MIBP, MEP, MEHP, DEHP metabolites). Products used by fewer than 5 women were not tested.

[2] DEHP metabolites include MEHHP, MEHP, and MEOHP

+*/−* Positive/negative association between questionnaire item and metabolite at $p<0.05$

+/− Positive/negative association between questionnaire item and metabolite at $0.05 \leq p < 0.1$

Table 6

Multiple linear regression results and proportion of variance explained (R^2) for urinary phthalate metabolites and product use questionnaire items[1]

Phthalate	Questionnaire item	Regression coefficient	Standard error	R^2
MBP	Intercept	1.37	0.36	0.39
	Sunscreen (last 2 days)	0.74	0.45	
	Other cream or lotion (last 2 days)	0.30	0.32	
	Eye shadow, liner, or mascara (last 2 days)	0.20	0.31	
	Applied or removed nail polish (last 2 days)	0.42	0.36	
	Dryer sheets regularly used (last 12 months)	0.32	0.32	
	Air freshener (last 12 months)	0.63	0.33	
	Walls painted (last 12 months)	0.40	0.27	
MBZP	Intercept	0.76	0.39	0.32
	Makeup most days of the week (global item)	0.44	0.41	
	Eye shadow, liner, or mascara (last 2 days)	0.20	0.41	
	Applied or removed nail polish (last 2 days)	0.07	0.47	
	Air freshener (last 12 months)	1.35	0.40	
	Laminate flooring in home (last 12 months)	0.43	0.45	
MEP	Intercept	3.83	0.27	0.31
	Fabric starch (last 2 days)	0.89	0.36	
	Fabric softener regularly used (last 12 months)	0.36	0.28	
	Air freshener (last 12 months)	0.66	0.30	
	Paneling in home (last 12 months)	0.78	0.40	
MMP	Intercept	0.57	0.39	0.42
	Spot cleaners (last 2 days)	−0.77	0.33	
	Sunscreen (last 2 days)	0.45	0.49	
	Bath oil, bath gel, or bubble bath (last 2 days)	0.67	0.31	
	Lipstick, chapstick, or lip balm (last 2 days)	−1.25	0.40	
	Hair nutrient product (last 2 days)	0.82	0.44	
	Hair styling gel, mousse, pomade, or grease (last 2 days)	0.59	0.30	
ΣDEHP[2]	Intercept	3.08	0.47	0.34
	Try to buy fragrance free products (global item)	−0.45	0.31	
	Eye shadow, liner, or mascara (last 2 days)	0.54	0.29	
	Cologne or perfume (last 2 days)	0.50	0.31	
	Air freshener (last 12 months)	0.45	0.30	
	Vinyl or linoleum floors in home (last 12 months)	−0.40	0.31	

[1] Multiple linear regression models for each phthalate include questionnaire items statistically significant at $p<0.1$ in bivariate linear regression models

[2] Molar sum of the DEHP metabolites MEHHP, MEHP, and MEOHP