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Distribution and predictors of urinary concentrations of phthalate metabolites and phenols among pregnant women in the Healthy Start Study

Kristen J. Polinski[a], **Dana Dabelea**[a], **Richard F. Hamman**[a], **John L. Adgate**[b], **Antonia M. Calafat**[c], **Xiaoyun Ye**[c], and **Anne P. Starling**[a]

[a]Department of Epidemiology, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO

[b]Department of Environmental and Occupational Health, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, Aurora, CO

[c]Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

Abstract

Background—Phthalates and phenols are suspected endocrine disrupting chemicals that may adversely impact fetal outcomes following *in utero* exposure. Understanding predictors of exposure to phthalates and phenols during the prenatal period is important.

Methods—We measured urinary concentrations of 15 phthalate metabolites and 11 phenols in 446 pregnant women enrolled in the Healthy Start pre-birth cohort. Creatinine-adjusted geometric means (GM) for each urinary biomarker were compared across categories of potential sociodemographic and dietary predictors. To assess the independent relationship between each significant food group predictor and biomarker we used multivariable models, adjusted for sociodemographic predictors.

Results—The phthalate metabolites with the highest concentrations were monoethyl phthalate (GM: 41.1 μg/g creatinine) and monocarboxyisooctyl phthalate (GM: 20.5 μg/g creatinine). Benzophenone-3 (GM: 124.6 μg/g creatinine) and methyl paraben (GM: 119.9 μg/g creatinine) were the phenols with the highest concentrations. Concentrations of the metabolites of di-n-butyl phthalate and di(2-ethylhexyl) phthalate were significantly higher in younger, unmarried or unemployed mothers, those who were overweight or obese, those with lower educational

Corresponding author: Anne P. Starling, Department of Epidemiology, Colorado School of Public Health, University of Colorado Anschutz Medical Campus, 12474 E 19th Ave, Campus Box F426, Aurora, CO 80045, [anne.starling@ucdenver.edu], 303-724-8483.

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attainment, or those of minority race/ethnicity (p-values <0.05). Metabolites of di-n-butyl phthalate concentrations were 18% lower in those who consumed milk ≥ 7 times per week (95% CI: 30–4%). Benzophenone-3 and triclosan concentrations were significantly higher in older, married, or employed mothers, those with normal body mass index, higher educational attainment, higher household income, or who were non-Hispanic white (p-values <0.05). Benzophenone-3 concentrations were 62% higher in those who consumed seafood ≥ 5 times per month (95% CI: 16–127%).

Conclusions—We observed differences in urinary concentrations of phthalates and phenol biomarkers by sociodemographic predictors in an ethnically diverse cohort of pregnant women. These results and future analyses from this prospective cohort will help inform targeted interventions to reduce exposure to these potential endocrine disrupting chemicals during pregnancy.

Keywords

Phthalate metabolites; phenols; benzophenone-3; triclosan; DBP; DEHP; human biomonitoring; pregnancy; predictors

1. Introduction

Due to their widespread use in numerous consumer and food packaging products, exposure to multiple phthalates and phenols is ubiquitous and has prompted concerns about potential adverse health effects (1, 2). Previous human studies suggest that some of these compounds may adversely impact human health, particularly during sensitive periods in the life course, such as *in utero* (3–9).

Evidence suggests that select phthalates and phenols may act as endocrine disrupting chemicals (EDCs) also during pregnancy (10, 11). A recent pregnancy cohort study observed an association between butyl paraben and decreased estradiol (11), a reproductive hormone involved in developing oxytocin receptors in the myometrium, which may play a role in preterm birth(11, 12). Another study found that urinary concentrations of first trimester mono-n-butyl phthalate (MBP) were inversely associated with thyroxine, a key thyroid hormone involved in fetal neuronal development (10). Phthalates and phenols acting as EDCs may also influence the development of metabolic disorders in humans, such as type 2 diabetes and overweight/obesity (13–15). Therefore, understanding the extent of exposure to phthalates and phenols during pregnancy and their sources is of public health relevance.

Several previous studies quantified urinary concentrations of phthalate and/or phenol biomarkers during pregnancy (16–26). Some similarities among sociodemographic and dietary predictors of phthalate and/or phenol biomarker concentrations exist; however, predictors vary depending on the study population, and the exposure assessment approach and questionnaire used. The variation in urinary concentrations is likely related to geographical variation in the composition of consumer products, cultural differences regarding diet and behavior, and study design (e.g., year and season of data collection, timing of urine sample collection, time interval between repeated measures). Exposure characterization is essential for informing any intervention aimed at reducing/eliminating

EDC exposure, such as a recent community-based participatory intervention that was developed to reduce EDCs exposures in adolescent girls (27). In sensitive populations, such as pregnant women and their offspring, identifying sociodemographic and dietary patterns of exposure to phenols and phthalates may provide insight into how to reduce exposure during pregnancy.

The present study examined the distribution of urinary concentrations of biomarkers of phthalates and phenols in a cohort of pregnant women in Colorado. We explored potential sociodemographic predictors and dietary sources to identify exposure patterns. We also used multivariable models to assess the independent relationship between each significant food group predictor and exposure biomarker.

2. Methods

2.1 Study population and design

We used data obtained from the Healthy Start study, a prospective cohort of pregnant women and their offspring in Colorado. The study design has been previously described (28–30). Briefly, women 16 years or older and less than 24 weeks gestation at their first prenatal visit were recruited from the University of Colorado obstetric clinics from 2009–2014. Participants were excluded if they were expecting multiple births, had a previous stillbirth, pre-existing diabetes, asthma managed with steroids, cancer, or had a serious psychiatric illness. The present analysis included a convenience sample of 446 pregnant women who provided spot urine samples during an in-person visit at 24–32 weeks gestation (median 27 weeks). Additionally, 24 participants had three spot urine samples collected at two week intervals. All samples were collected into sterile collection cups and were stored at −80 °C until ready for shipment to the laboratory for their analysis. The study was approved by the Colorado Multiple Institutional Review Board and all participants provided written informed consent prior to the first study visit. The involvement of the Centers for Disease Control and Prevention (CDC) laboratory was determined not to constitute engagement in human subjects research.

2.2 Predictors

Potential predictors of urinary biomarker concentrations were selected based on previous studies exploring human exposure to phthalates and phenols (20–22, 26, 31–34). Maternal socio-demographic variables (i.e., age, race/ethnicity, education level, household income, marital status, employment status) and parity were self-reported at the first in-person visit at 15–23 weeks gestation (median 17 weeks). Pre-pregnancy body mass index (BMI) was calculated using maternal pre-pregnancy weight from the medical record or self-report and maternal height measured at the in-person visit. During the second in-person visit at 24–32 weeks gestation (median: 27 weeks), when urine samples were collected, a food propensity questionnaire was administered. The dietary assessment captured patterns of dietary intake during the previous three months. We considered nine food groups: milk, cheese, yogurt, ice cream, soft drinks, processed meat, red meat, seafood, and tofu, based on their importance as predictors in previous studies(6, 20, 21). In addition to the food propensity questionnaire, participants were asked at the same study visit about current fish oil supplement use. Fish oil

supplement use was included as a potential predictor because phthalates can be used to minimize aftertaste and produce the soft gelatin capsules (34). While urine samples were taken from pregnant women, we explored whether the sex of the fetus is associated with urinary concentrations of the phthalate metabolites and phenols. Previous studies have found that concentrations may vary by sex, and evidence suggests that in utero exposure influences future outcomes in the child (35, 36). We also selected smoking status at the time of urine sample collection and gestational age at urine sample collection as additional predictors.

2.3 Laboratory analyses

Fifteen phthalate metabolites were measured using previously published laboratory methods (37): mono-n-butyl phthalate (MBP), monobenzyl phthalate (MBzP), mono carboxyisononyl phthalate (MCNP), mono carboxyisooctyl phthalate (MCOP), mono-3-carboxypropyl phthalate (MCPP), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), monoethyl phthalate (MEP), mono-hydroxybutyl phthalate (MHBP), mono-hydroxyisobutyl phthalate (MHiBP), mono-isobutyl phthalate (MiBP), monomethyl phthalate (MMP), and mono-isononyl phthalate (MNP).

Ten phenols were measured using previously published laboratory methods (38): 2,4-dichlorophenol, 2,5-dichlorophenol, bisphenol A, bisphenol S, benzophenone-3, methyl paraben, ethyl paraben, propyl paraben, butyl paraben, and triclosan. Urine creatinine concentrations were measured at the CDC using a Roche/Hitachi Cobas 6000 Analyzer (Roche Diagnostics, Indianapolis, IN).

2.4 Statistical analysis

Descriptive statistics of sociodemographic characteristics for the 446 participants were calculated. Geometric means and 5^{th} and 95^{th} percentiles of the creatinine-adjusted urinary chemical concentrations (μg/g of creatinine) were calculated to describe the distribution of these metabolites.

All urinary chemical concentrations were natural log-transformed to normalize right skewed distributions for the purpose of linear regression analysis and calculation of the intraclass correlation coefficients (ICCs). Concentrations of the individual biomarkers and the molar sums were divided by creatinine concentrations to account for urinary dilution. For phthalate metabolite and phenol concentrations below the method limit of detection (LOD; Supplemental Table 1), we obtained instrument values when possible. For values reported as ‘zero’ concentration, we substituted one-half the minimum reported value for that biomarker (17). We calculated five molar sums, representing classes of chemicals or parent compounds, by dividing each individual metabolite by its molar mass and summing the resulting scaled concentrations (39): ΣLMWP (sum of metabolites of low molecular weight phthalates: MMP, MEP, MiBP, MBP, MHiBP, and MHBP), ΣDBP (sum of dibutyl phthalates metabolites: MBP, MiBP, MHBP, and MHiBP), ΣHMWP (sum of metabolites of high molecular weight phthalates: MBzP, MEHP, MNP, MEOHP, MEHHP, MECPP, MCOP, and MCNP), ΣDEHP (sum of di(2-ethylhexyl) phthalate metabolites (MEHP, MEOHP, MEHHP,

and MECPP), and Σparaben (sum of methyl paraben, ethyl paraben, butyl paraben, and propyl paraben).

Potential predictors were dichotomized based on median values or inherent groupings, with the exception of race/ethnicity, which was categorized as Hispanic, non-Hispanic white, non-Hispanic African American, and other. For the binary predictors, t-tests were performed with each biomarker concentration. For race/ethnicity, ANOVA was used to test if there was a significant difference among race/ethnicity categories for each biomarker or molar sum. Multivariable linear regression was used to identify if the association between potential food sources of chemical exposure and the urinary biomarker concentrations persisted after adjustment for potential sociodemographic confounders (i.e., race, maternal age, BMI, income, education, marital status, employment status). Potential food group predictors were examined in multivariable analysis if the bivariate relationship from the t-test/ANOVA was significant at the $p< 0.05$ level. In-text, the beta coefficients are interpreted as percent change in biomarker concentrations using $(e^{\beta}-1)*100$ to account for the log transformed biomarker concentrations (40). For these analyses, creatinine-adjusted phthalate metabolite sums are presented on a molar basis (log-nmol/g of creatinine) and phenols are presented as log-μg/g of creatinine. A sensitivity analysis of our multivariable models with unadjusted concentrations and creatinine as a covariate did not differ notably from our creatinine-adjusted urinary concentration multivariable models.

In the sample of 24 participants with three urine samples, we calculated ICCs to estimate between- and within-subject variability of the log-transformed urinary biomarker concentrations using the %INTRACC macro (41, 42). The confidence intervals were calculated according to the method described in Shrout and Fleiss (41). We only estimated ICCs for biomarkers with 100 percent detectable concentrations in all three samples. Repeated measures were not included in the main analysis. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc. Cary, NC).

3. Results

The majority of participants were 25 years of age or older, college-educated, non-smokers, and non-Hispanic whites, but with substantial African-American and Hispanic representation (Table 1). The distribution of socio-demographic characteristics in our sample of study participants is similar to the full Healthy Start eligible cohort (Table 1). The phthalate metabolites with the highest concentrations were MEP (GM: 41.1 μg/g creatinine) and MCOP (GM: 20.5 μg/g creatinine). Benzophenone-3 (GM: 124.6 μg/g creatinine) and methyl paraben (GM: 119.9 μg/g creatinine) were the phenols with the highest concentrations in our sample. Supplemental Table 1 provides LODs, detection frequencies, geometric means and 5^{th}, 95^{th} percentiles of creatinine-adjusted and unadjusted urinary concentrations for our participants.

3.1 Phthalates

Urinary concentrations of ΣDEHP and ΣDBP were significantly higher among participants with younger maternal age (≤29 years), overweight or obese BMI (≥25 kg/m^2), lower educational attainment (high school or less), lower income (≤$40,000), or in mothers who

were unmarried or unemployed (Table 2). Furthermore, ΣDEHP and ΣDBP significantly differed by race ethnicity and the lowest concentrations were observed in non-Hispanic white women. There were no significant bivariate associations between ΣDEHP and ΣDBP concentrations with smoking status, gestational age at time of urine collection, previous pregnancies or infant sex. The ΣLMWPs and ΣHMWPs followed the same general trend with the potential predictors as ΣDEHP and ΣDBP; however, the associations were largely statistically non-significant, with the exception of significantly higher concentrations of ΣHMWPs in women with pre-pregnancy BMI ≥ 25 kg/m^2.

Individual metabolites concentrations showed trends consistent with the sums of metabolites, with the exception of MCNP and MCOP; therefore, only the creatinine-adjusted molar sums are presented in the main text of the paper. MCNP and MCOP concentrations tended to be higher in women with higher educational attainment, higher income, those who were employed or who were non-Hispanic mothers. See Supplemental Table 2 for all tested associations between each individual phthalate metabolite and potential predictor.

3.2 Phenols and Parabens

We found a significant bivariate association of higher Σparaben concentrations with lower BMI (<25 kg/m^2) (Table 3). Race/ethnicity was also a significant predictor with the lowest Σparaben concentrations observed in non-Hispanic whites. The Σparaben was not significantly associated with education, income, marital status, employment status, gestational age at urine sample collection, infant sex or previous pregnancies in our cohort. Individually, higher concentrations of the four parabens (i.e., methyl, ethyl, propyl, butyl) were observed in women with higher levels of education (≥some college), income (> $40,000), lower BMI (<25 kg/m^2) or in those who were employed; although not all associations were statistically significant. Additionally, higher concentrations of ethyl paraben and butyl paraben were significantly associated with lower maternal age (≤29 years); methyl and propyl paraben were not significantly associated with maternal age. Methyl, ethyl and propyl paraben concentrations significantly differed by race/ethnicity with the highest concentrations observed in the non-white “other” group composed primarily of Asian, south Asian and Native American race/ethnicities.

In the bivariate analyses of the non-paraben phenols, higher triclosan and benzophenone-3 concentrations had significant associations with older maternal age (>29 years), higher levels of education (≥some college), higher levels of income (>$40,000), gestational age at urine sample collection of 20–27 weeks, or were higher among women who were married, employed or had lower pre-pregnancy BMI (<25 kg/m^2). Additionally, concentrations differed by race/ethnicity, with higher concentrations of urinary triclosan and benzophenone-3 observed in non-Hispanic white mothers. In contrast, higher concentrations of 2,5-dichlorophenol were significantly associated with younger maternal age (≤29 years), lower levels of education (≤high school), lower levels of income (≤$40,000), gestational age at urine sample collection of ≥28 weeks, or were higher among unmarried women or unemployed. Bivariate associations with 2,4-dichlorophenol followed a similar pattern as 2,5-dichlorophenol although the statistical tests were non-significant, with the exception of higher concentrations observed in unmarried women. Concentrations of 2,5 dichlorophenol

and 2,4-dichlorophenol significantly differed by race/ethnicity, with the higher concentrations observed in Hispanics. Furthermore, higher concentrations of bisphenol S were also significantly associated with lower educational attainment, lower levels income or women who were unmarried. Of note, bisphenol A did not have statistically significant associations with any of the potential predictors. See Supplemental Table 3 for all tested associations between each phenol or paraben and potential predictors.

3.3 Multivariable Analysis of Dietary Predictors

In the bivariate analysis several food groups stood out as significant potential predictors of ΣDEHP, ΣDBP, or ΣHMWPs concentrations, including: tofu, seafood, fish oil supplements, yogurt, milk and processed meat. After adjustment for sociodemographic characteristics, the associations of the food groups with urinary phthalate metabolite concentrations were no longer significant, with the exception of milk consumption. Participants who consumed milk ≥ 7 times per week had 18% (95% CI: −30% to −4%) lower ΣDBP concentrations than those who consumed milk fewer than 7 times per week. (Table 4). The ΣLMWPs did not have significant bivariate associations with the food groups and thus was not tested in multivariable models.

Among the phenols, benzophenone-3, triclosan, and 2,5 dichlorophenol had significant bivariate associations with several potential predictor food groups, including: tofu, seafood, fish oil supplements, yogurt, ice cream and red meat. After adjustment for sociodemographic characteristics, the associations of the food groups with urinary phenol concentrations were no longer significant, with the exception of seafood consumption. Those who consumed seafood 5 times per month or more had 62% (95% CI: 16% to 127%) higher concentrations of benzophenone-3 than those who consumed seafood 3 to 4 times per month or less (Table 4). The Σparaben did not have any significant bivariate associations with the food groups and thus was not tested in multivariable models.

3.4 Variability

The ICCs for urinary phthalate metabolite concentrations were low to moderate in our sample of 24 repeats (Table 5). The ICCs were below 0.6 with the exception of MMP which had an ICC of 0.73; however, our calculated ICC for MMP used repeated measures from only 9 participants due to relatively low detection frequency. The ΣHMWP had low reproducibility of 0.25; whereas, the ΣLMWP had a moderate ICC of 0.43. The ICCs for urinary phenols concentrations had moderate to high reproducibility (Table 5). The ICCs were greater than 0.53 with the exception of bisphenol S and bisphenol A with 0.39 and 0.25 ICCs, respectively. The Σparaben had an ICC of 0.62.

4. Discussion

In this ethnically diverse cohort of pregnant women, we observed varying trends in urinary concentrations of phthalate metabolites and phenols in relation to sociodemographic characteristics. Overall, urinary phthalate metabolite concentrations tended to be higher in samples from younger mothers, those who were overweight or obese, had lower educational attainment, lower income, unmarried, or unemployed. Phthalate metabolite concentrations

also differed by maternal race/ethnicity, and tended to be lowest among non-Hispanic white women compared with other racial/ethnic groups. Some urinary phenols such as 2,5-dichlorophenol, bisphenol S, and the four parabens also tended to have higher concentrations in samples from younger mothers, those who were overweight or obese, had lower educational attainment, lower income, unmarried, or unemployed, and tended to be lowest in non-Hispanic white mothers. In contrast, triclosan and benzophenone-3 concentrations tended to be higher in samples from older mothers, those with normal BMI, higher educational attainment, higher household income, who were married, or those who were employed. Triclosan and benzophenone-3 concentrations also differed by race/ethnicity and tended to be highest among non-Hispanic white women. We evaluated potential food sources of chemical exposure, but did not identify any clear patterns.

4.1 Phthalates: Comparison to Previous Studies

Urinary phthalate metabolite concentrations of women enrolled in Healthy Start tend to differ from those observed in previous studies during pregnancy (20–22, 26, 33, 43, 44). Healthy Start participants had lower creatinine-adjusted urinary concentrations of MEHP, MBzP, and MBP compared to a Swedish pregnancy cohort(43), lower concentrations of MECPP compared to the Healthy Baby Cohort in China (33), and lower concentrations of MEP, MBP, MiBP, MBzP, MEHP, MEHHP, MEOHP, and MECPP than a Netherlands pregnancy cohort (43). Additionally, Healthy Start mothers had higher average urinary concentrations of methyl and propyl paraben compared to a Swedish cohort (43) and higher MEP concentrations compared to the Healthy Baby Cohort (33). Furthermore, the average creatinine-adjusted urinary concentration of ΣDEHP was lower in Healthy Start compared to a Spanish study (75.0 vs 86.6 μg/g) (26). The lower ΣDEHP concentrations observed in Healthy Start may be related to the replacement of DEHP in consumer plastics (45–47). The Spanish cohort collected samples between 2004 and 2006, whereas, Healthy Start samples were collected in 2014. Unadjusted average phthalate metabolite urinary concentrations from the Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) cohort of pregnant women tended to be higher than average concentrations from Healthy Start, with the exception of MCNP and MCOP (20, 22). Of note, the unadjusted phthalate concentrations in the PROTECT study were not statistically different from the specific gravity-adjusted concentrations (20, 22). Compared to a representative sample of U.S. pregnant women from the 2003–2004 NHANES, average urinary concentrations unadjusted for creatinine of MBP, MBzP, MEP, MEHP, MEHHP, MEOHP and MECPP were lower in Healthy Start and MiBP concentrations were higher (48). The variations in average urinary concentrations of phthalate metabolites among the different pregnancy populations is likely to due to year of sample collection (as in the Spanish cohort and NHANES 2003–2004 comparison) and geographical differences with associated cultural variations in diets and product use.

The trends we observed among phthalate metabolite predictors were also similar to other birth cohorts. For example, the Spanish birth cohort observed that lower education and social class were associated with higher ΣDEHP and MEP concentrations (26). Furthermore, higher ΣDEHP concentrations have also been observed in minority groups (44). Similar to trends observed in Healthy Start, the Netherlands cohort observed that MBP and MBzP were

associated with younger age (<30 years), lower educational attainment, lower income levels and belonging to a minority race/ethnicity (44). Likewise, the PROTECT study found increases in maternal age were significantly associated with lower MBP and MBzP concentrations (20, 22). However, PROTECT did observe that greater maternal age was associated with higher concentrations of MCPP, MCNP and MCOP (20). Furthermore, previous studies have indicated that overweight and/or obese pre-pregnancy BMI is related to overall higher phthalate metabolite concentrations (20, 26, 49), while in the present study we observed higher concentrations of ΣHMWP and ΣDBP only among overweight or obese women compared with normal weight or underweight women. While these observed trends in sociodemographic-type predictors is intriguing, we do not have the ability to determine potential exposure sources – outside of our measures of potential food groups – which may underlie these patterns in our cohort. However, a recent review article suggests that older housing and the purchasing of inexpensive products made with high amounts of phthalates are additional reasons that may explain the increased phthalate concentrations in low-income populations (50).

Similar to the findings from a Spanish cohort, we did not observe clear patterns among the food groups for phthalates (21, 26). We found that concentrations of ΣDBP were significantly lower in those with higher milk consumption. While phthalates have been found in milk products (6), a previous study of phthalate esters in commercial whole milk did not find detectable levels of DBP (51). The inverse association observed here suggests that milk consumption may be a marker of other behaviors or characteristics related to lower phthalate exposure during pregnancy. Furthermore, PROTECT identified that those who consumed fish had lower concentrations of MCPP and MiBP than those who did not consume fish in both the unadjusted and adjusted models (20); however, we did not identify significant associations among phthalates and seafood consumption.

4.2 Phenols: Comparison to Previous Studies

Average urinary phenol concentrations of women enrolled in Healthy Start differ from those observed in previous birth cohort studies in pregnant mothers (17, 20–22, 26, 44). The average creatinine-adjusted urinary concentration of bisphenol A in Healthy Start of 1.0 μg/g was higher than the third trimester concentration of 0.6 μg/g in a Spanish cohort (26), but lower than 1.7 μg/g observed in a Netherlands cohort (44). Unadjusted average phenol urinary concentrations from the PROTECT cohort tended to be higher than average concentrations from Healthy Start, with the exception of benzophenone-3, a common ingredient in sunscreen (20, 22). Of note, the unadjusted phenol concentrations in the PROTECT study were not statistically different from the specific gravity-adjusted concentrations (20, 22). In the Canadian Maternal-Infant Research on Environmental Chemicals cohort (MIREC), average specific gravity-adjusted concentrations of triclosan, an antimicrobial agent, were lower than concentrations observed in Healthy Start and average bisphenol A concentrations were similar (17). Compared to a 2005–2010 NHANES sample of pregnant woman aged 16–44 years, unadjusted urinary concentrations of benzophenone-3 were higher in Healthy Start, whereas triclosan and 2,5 dichlorophenol were lower, and BPA, 2,4 dichlorophenol, methyl paraben and propyl paraben concentrations were similar.

Of note, the authors reported that their creatinine-adjusted and unadjusted mean concentrations in the 2005–2010 NHANES were comparable (52).

Similar to our findings, MIREC found that older maternal age, higher educational attainment and increased income were associated with higher triclosan concentrations (17). MIREC also identified associations of younger maternal age, lower educational attainment and decreased income with higher bisphenol A concentrations; whereas, no significant differences were detected in Healthy Start (17). The PROTECT study found that increases in maternal age were significantly associated with higher concentrations of triclosan and benzophenone-3 as observed in the present study (20, 22). Additionally, the PROTECT study observed higher concentrations of bisphenol A in those with higher pre-pregnancy BMI (21, 22), while we found no difference in bisphenol A concentrations between normal weight and overweight/obese women in Healthy Start. Furthermore, we found that greater concentrations benzophenone-3 in those who had higher levels of seafood consumption. Previous studies have detected the presence of benzophenone-3 in seafood, including shrimp (53, 54); although sunscreen use tends to be the major source of benzophenone-3 (55).

Notably, average benzophenone-3 concentrations in the present study were higher than NHANES 2011–2012 female only data and pregnant women only NHANES 2005–2010 data (52, 56). Used as an UV filter in sunscreens and a suspected EDC (57), higher urinary concentrations of benzophenone-3 have been associated with sunscreen use in NHANES, with stronger associations observed in women compared to men (58). We believe the benzophenone-3 concentrations may be higher in Healthy Start due to greater sunscreen use, perhaps owing to the approximately 300 sunny and partly sunny days in Colorado each year (59). However, we did not collect information on sunscreen use in our study population to formally test if its application is associated with the higher benzophenone-3 concentrations. In addition, other sources exist as benzophenone-3 can be used as an UV filter in non-sunscreen products such as packaging to shield content from UV radiation and textiles to prevent bleaching (60).

4.3 Implications for Future Studies

Phthalates and phenols rapidly metabolize and excrete in urine (61, 62). Urinary biomarker concentrations have been used in epidemiologic studies to estimate exposure to phthalates and phenols (45), but their relatively short half-life in the body makes it challenging to characterize exposure over time (62). Therefore, understanding how well a single urine sample captures typical urinary concentrations, particularly during windows of vulnerability, is important. Based on the 24 individuals with repeated measures, we found that urinary phenol concentrations, with the exception of bisphenol A and bisphenol S, have higher reproducibility than the urinary phthalate metabolites examined. Our findings are in accordance with previous literature examining the variability of chemical concentrations during pregnancy (20, 22, 23, 63). We found an ICC of 0.29 for ΣDEHP which was slightly higher than the ICC of 0.23 reported in a sample of 129 pregnant women from Brigham and Women's Hospital over four visits (63). The reproducibility of triclosan was higher (0.83) in Healthy Start compared to the PROTECT and SARAEH cohort from Mount Sinai in New York, ICCs of 0.47 and 0.58, respectively (22, 23). The low reproducibility for phthalates

and bisphenol A may have led to our inability to find strong patterns with predictors and suggests that multiple urine samples should be collected to obtain a more accurate representation of exposure. Overall, a single spot urine sample may be sufficient to assess individual exposure to most phenols, but not sufficient for phthalates or bisphenol A or bisphenol S during pregnancy.

The strengths of the present study include the use of an ethnically diverse cohort with detailed data on maternal characteristics and behaviors, including dietary habits during pregnancy. The present study did not collect information on the use of personal care products, such as sunscreen, or household cleaning products which have been examined in previous literature (18, 20, 22). Although we found few associations with usual intake from specific food groups over a three-month period, future studies may consider evaluating dietary intake via 24-hour recall at the time of urine sample collection due to the short-lived nature of these chemicals. Additionally, the food propensity questionnaire combined fresh, frozen and canned food group intake which may have limited our ability to detect associations with certain chemicals such as BPA, which is commonly used in aluminum can linings (64, 65). Other limitations were the use of single urine samples for bivariate and multivariable comparisons and the relatively small number of participants used to determine the reproducibility of certain urinary metabolite measurements.

5. Conclusion

We found detectable concentrations of phenols and phthalate metabolites in urine samples from a cohort of pregnant women in Colorado. Benzophenone-3, an ingredient commonly found in sunscreens, had the highest urinary concentrations in our cohort and were also high in comparison to NHANES females-only and pregnant women-only samples. This study highlights that urinary concentrations of phthalate metabolites and phenols vary with sociodemographic characteristics in this population. We found that younger maternal age, higher BMI, lower education attainment or lower income are associated with higher urinary phthalate metabolite and parabens concentrations. Whereas, older maternal age, lower BMI, higher educational attainment, higher household income, or non-Hispanic white race/ethnicity are related to higher non-paraben phenol concentrations, particularly benzophenone-3 and triclosan. We did not find strong evidence of specific dietary sources of exposure to phthalate metabolites and phenols in our population, so further exposure source characterization of these possible EDC biomarkers may provide insight into how to reduce exposure during pregnancy, a sensitive period in which exposures may have adverse impacts on health and development. Additional studies are needed to further evaluate sources of exposure to phthalates and phenols among pregnant women that may underlie these observed differences by sociodemographic predictors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- In a cohort of pregnant women, we observed differences in urinary concentrations of phthalates and phenol biomarkers by sociodemographic predictors.
- Younger maternal age, higher BMI, lower educational attainment or lower income tend to be associated with higher urinary phthalate metabolite and paraben concentrations.
- Older maternal age, lower BMI, higher educational attainment, higher household income or non-Hispanic white race/ethnicity tend to be associated with higher non-paraben phenol concentrations, particularly benzophenone-3 and triclosan.

Table 1

Healthy Start participant sociodemographic characteristics: comparison between the full cohort and the subsample used in this analysis

	Analytic sample N=446	Full Cohort N=1,382
Maternal age, years		
16–19	49 (11)	174 (13)
20–24	86 (19)	281 (20)
25–29	112 (25)	334 (24)
30–34	133 (30)	396 (29)
35–45	66 (15)	197 (14)
Race/ethnicity		
Non-Hispanic white	256 (57)	738 (53)
Hispanic	108 (24)	347 (25)
Non-Hispanic African American	53 (12)	210 (15)
All others	29 (7)	87 (6)
Education		
Less than 12th grade	61 (14)	200 (14)
High school or GED	72 (16)	253 (18)
Some college or associate's degree	98 (22)	325 (24)
Four years of college (BA, BS)	100 (22)	304 (22)
Graduate degree	115 (26)	300 (22)
Household income in the previous year		
Less than $40,000	113 (25)	404 (29)
$40,000-$70,000	93 (21)	256 (19)
Greater than $70,000	157 (35)	453 (33)
Don't know	83 (19)	269 (19)
Pre-pregnancy body mass index, kg/m^2		
<18.5	14 (3)	44 (3)
18.5–24.9	225 (51)	715 (52)
25.0–29.9	125 (28)	346 (25)
≥30	82 (18)	275 (20)
Previous pregnancies		
At least one	278 (62)	886 (64)
None	168 (38)	496 (36)
Smoking status at mid-pregnancy		
Any amount	26 (6)	99 (7)
None	420 (94)	1283 (93)
Marital status		
Married	283 (64)	838 (61)

	Analytic sample N=446	**Full Cohort N=1,382**
Not married, but living with partner	85 (19)	271 (20)
Not married, and living alone	76 (17)	267 (19)
Don’t know	2 (<1)	6 (<1)
Employment status at mid-pregnancy		
Employed	290 (65)	755 (62)
Not employed	196 (35)	455 (38)
Gestational age at urine sample collection, weeks		
20–24	84 (19)	-
25–27	158 (35)	-
28–30	171 (38)	-
31–34	33 (7)	-

All values presented as n(%)

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Table 2

Associations of sociodemographic characteristics and sums of urinary phthalate metabolites (nmol/g creatinine): geometric means and 95% confidence intervals.

Characteristic		ΣLMWP			ΣHMWP			ΣDEHP			ΣDBP		
	N	GM	LL	UL	GM	LL	UL	GM	LL	UL	GM	LL	UL
Race													
Hispanic	108	493.5	399.5	609.5	243.9	206.3	288.5	90.2	77.3	105.1	119.6	103.7	137.8
NH white	256	320.1	279.1	367.2	206.9	185.6	230.7	66.5	60.1	73.4	85.1	77.6	93.3
NH African American	53	555.7	411.1	751.2	229.6	180.8	291.6	85.8	68.8	106.9	115.9	94.7	141.9
Other	29	559.9	372.5	841.5	235.3	170.3	325.1	88.5	65.9	119.1	103.9	79.1	136.7
p-value		<0.01			0.39			<0.01			<0.01		
Age, yrs													
≤29	247	432.1	374.8	498.1	236.2	211	264.3	83.6	75.2	93.0	108.5	99.1	118.8
>29	199	350.6	299.1	411	201.2	178.3	227	65.9	59.1	73.4	84.7	75.8	94.6
p-value		0.05			0.05			<0.01			<0.01		
BMI, kg/m^2													
<25	239	386.6	332.9	449	203.6	182	227.7	67.2	60.3	74.8	87.0	79.0	95.9
≥25	207	401.9	345.7	467.2	240.3	212.8	271.4	85.6	77.0	95.2	110.3	99.6	122.2
p-value		0.71			0.04			<0.01			<0.01		
Education													
≤High school	133	446.5	364.9	546.4	240.3	208	277.6	94.7	82.8	108.2	113.2	100.4	127.5
≥Some college	313	373.1	329.4	422.6	211.7	191.5	234.1	68.2	62.2	74.7	91.1	83.5	99.3
p-value		0.13			0.15			<0.01			<0.01		
Income													
≤$40,000	113	401.3	333	483.6	222.2	187.5	263.4	84.7	72.9	98.5	108.5	94.0	125.1
>$40,000	250	347	301.2	399.7	208.2	186.6	232.2	64.6	58.4	71.5	84.3	76.6	92.8
p-value		0.22			0.52			<0.01			<0.01		
Marital status													
Married	283	357.5	313.5	407.6	212.8	191.9	236	69.5	63.1	76.4	91.0	83.1	99.6
Not married	161	460.9	385	551.7	232.9	202.7	267.7	85.7	75.5	97.3	108.3	96.6	121.5

Characteristic		ΣLMWP			ΣHMWP			ΣDEHP			ΣDBP		
	N	GM	LL	UL	GM	LL	UL	GM	LL	UL	GM	LL	UL
p-value		0.02			0.30			<0.01			0.01		
Employment status													
Employed	290	370.4	325.2	422	231.6	208.1	257.8	71.2	64.6	78.5	90.0	82.4	98.4
Not employed	156	440.7	367.1	529.1	199.6	175.9	226.4	83.2	73.6	93.9	111.9	99.5	125.9
p-value		0.12			0.07			0.05			<0.01		
Gestational age at urine sample collection, wks													
20–27	242	378.6	330.7	433.4	204.6	184.3	227.1	72.4	65.6	80.0	93.7	85.2	103.0
≥28	204	412.2	348.4	487.8	239.4	210.1	272.9	78.5	69.7	88.6	101.4	91.1	113.0
p-value		0.43			0.06			0.30			0.27		
Time of day urine collection													
Morning	432	395.5	354.8	440.8	219	201.5	238	75.3	69.6	81.3	96.7	90.0	103.9
Afternoon	8	453	226	908	253.2	121.8	526.3	78.7	54.7	113.1	161.5	101.2	257.8
p-value		0.66			0.65			0.78			0.03		
Previous pregnancies													
None	168	415	349	493.3	230.3	202.3	262.2	73.8	65.1	83.7	99.3	89.1	110.6
Any amount	278	381.3	333.2	436.3	213.8	192.1	237.9	76.0	69.0	83.7	95.9	87.3	105.3
p-value		0.44			0.38			0.71			0.63		
Smoking status													
None	420	391	350.7	435.9	224	205.7	244	76.0	70.2	82.2	97.7	90.8	105.1
Any amount	26	439.1	265.7	725.6	162.4	119.6	220.5	63.4	47.5	84.5	89.0	62.7	126.2
p-value		0.64			0.04			0.22			0.59		
Child sex													
Girl	206	409.3	345.6	484.8	235.5	208.7	265.7	81.5	72.5	91.7	103.5	93.4	114.7
Boy	240	380.6	332.8	435.3	207.3	185.1	232.1	70.1	63.5	77.5	92.0	83.4	101.6
p-value		0.50			0.12			0.05			0.10		

ΣLMWP (sum of low molecular weight phthalates: MMP, MEP, MiBP, MBP, MHiBP, and MHBP)

ΣDBP (sum of di-n-butyl phthalate metabolites: MBP, MiBP, MHBP, and MHiBP)

ΣHMWP (sum of high molecular weight phthalates: MBzP, MEHP, MNP, MEOHP, MEHHP, MECPP, MCOP, MCNP)

ΣDEHP (sum of di(2-ethylhexyl) phthalate metabolites (MEHP, MEOHP, MEHHP, and MECPP)

N indicates sample size; GM indicates geometric mean; LL indicates lower limit; UL indicates upper limit; NH indicates non-Hispanic

Satterthwaite p-value from t-tests presented for dichotomous variables. Overall F-test p-values from ANOVA presented for race/ethnicity.

Abbreviations: mono-n-butyl phthalate (MBP), monobenzyl phthalate (MBzP), mono carboxyisononyl phthalate (MCNP), mono carboxyisooctyl phthalate (MCOP), mono-3-carboxypropyl phthalate (MCPP), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), monoethyl phthalate (MEP), mono-hydroxybutyl phthalate (MHBP), mono-hydroxyisobutyl phthalate (MHiBP), mono-isobutyl phthalate (MiBP), monomethyl phthalate (MMP), and mono-isononyl phthalate (MNP).

Table 3

Associations between sociodemographic characteristics and urinary phenols (nmol/g creatinine): geometric means and 95% confidence intervals.

Characteristic		ΣParabens			Benzophenone-3			Triclosan			2,5 Dichlorophenol		
	N	GM	LL	UL	GM	LL	UL	GM	LL	UL	GM	LL	UL
Race													
Hispanic	108	904.4	701.4	1166.1	78.8	57.6	107.9	8.3	5.6	12.4	7.9	5.6	11.0
NH white	256	895.1	758.8	1055.7	203.5	165.9	249.5	23.8	18.4	30.7	1.1	0.9	1.4
NH African American	53	1738.6	1209.6	2499.1	28.4	18.2	44.5	4.8	2.7	8.5	4.3	2.6	6.9
Other	29	2304.5	1411.1	3763.7	101.1	55.2	185.4	16.3	7.6	35.0	3.4	1.7	6.6
p-value		<0.01			<0.01			<0.01			<0.01		
Age, yrs													
≤29	247	1025.4	856.8	1227.2	69.8	57.1	85.3	10.4	7.8	13.8	3.8	3.0	4.9
>29	199	1041.5	868.7	1248.6	245.6	192.1	314.2	23.5	18.0	30.7	1.2	1.0	1.6
p-value		0.90			<0.01			<0.01			<0.01		
BMI, kg/m^2													
<25	239	1181.2	988.4	1411.7	163.2	128.5	207.3	19.2	14.6	25.3	2.1	1.6	2.7
≥25	207	884.0	736.8	1060.6	87.7	70.3	109.4	11.2	8.4	15.0	2.6	2.0	3.4
p-value		0.02			<0.01			<0.01			0.21		
Education													
≤High school	133	867.3	676.3	1112.2	46.5	36.9	58.7	5.9	3.9	8.8	5.7	3.9	8.3
≥Some college	313	1112.0	958.7	1289.9	184.5	151.2	225.2	22.2	17.9	27.6	1.6	1.3	1.9
p-value		0.09			<0.01			<0.01			<0.01		
Income													
≤$40,000	113	977.7	752.3	1270.7	70.4	51.4	96.6	8.3	5.6	12.3	3.4	2.4	4.8
>$40,000	250	1051.1	890.7	1240.4	220.1	177.7	272.6	27.3	21.7	34.2	1.3	1.0	1.5
p-value		0.64			<0.01			<0.01			<0.01		
Marital status													
Married	283	1013.8	866.6	1186.0	198.9	162.2	244.0	19.8	15.6	25.2	1.4	1.1	1.6
Not married	161	1052.6	842.2	1315.5	52.4	41.3	66.5	9.1	6.3	13.0	5.7	4.1	8.1
p-value		0.78			<0.01			<0.01			<0.01		

Characteristic		ΣParabens			Benzophenone-3			Triclosan			2,5 Dichlorophenol		
	N	GM	LL	UL	GM	LL	UL	GM	LL	UL	GM	LL	UL
Employment status													
Employed	290	1091.1	927.7	1283.4	167.0	136.4	204.4	24.8	19.8	30.9	1.8	1.5	2.2
Not employed	156	931.9	757.4	1146.6	68.6	52.3	90.0	5.8	4.1	8.4	3.7	2.6	5.2
p-value		0.23			<0.01			<0.01			<0.01		
Gestational age at urine sample collection, wks													
20–27	242	1143.3	961.8	1359.2	160.1	127.7	200.6	18.4	14.2	23.8	1.9	1.5	2.3
≥28	204	915.0	756.8	1106.2	88.9	69.9	113.1	11.7	8.5	16.0	3.0	2.2	4.0
p-value		0.08			<0.01			0.02			0.01		
Time of day urine collection													
Morning	432	1026.1	900.3	1169.6	122.9	103.8	145.5	14.7	12.0	18.0	2.3	1.9	2.8
Afternoon	8	982.3	413.3	2334.5	140.5	29.5	668.3	19.6	6.2	62.6	1.9	0.5	7.5
p-value		0.90			0.84			0.57			0.73		
Previous pregnancies													
None	168	1070.3	856.7	1337.2	138.4	105.1	182.2	16.1	11.3	23.0	2.7	2.0	3.6
Any amount	278	1010.4	864.7	1180.6	113.5	92.1	140.0	14.3	11.2	18.2	2.1	1.7	2.7
p-value		0.67			0.25			0.57			0.22		
Smoking status													
None	420	1037.7	911.6	1181.3	130.5	109.9	154.9	15.1	12.3	18.6	2.4	1.9	2.8
Any amount	26	952.8	477.1	1902.6	43.3	24.3	77.1	12.4	5.8	26.5	1.8	0.8	3.8
p-value		0.80			<0.01			0.60			0.47		
Child sex													
Girl	206	1017.4	838.2	1234.8	96.8	76.5	122.4	13.2	9.7	17.9	2.5	1.9	3.3
Boy	240	1045.8	881.6	1240.5	149.6	118.5	188.8	16.7	12.8	21.7	2.1	1.7	2.7
p-value		0.83			<0.01			0.25			0.39		

Σparaben (sum of Methyl Paraben, Ethyl Paraben, Propyl Paraben, Butyl Paraben)

N indicates sample size; GM indicates geometric mean; LL indicates lower limit; UL indicates upper limit

Satterthwaite p-value from t-tests presented for dichotomous variables. Overall F-test p-values from ANOVA presented for race/ethnicity.

Table 4

Parameter estimates for multiple regression analysis of frequency of intake from selected food groups with urinary phenol and phthalate metabolite sum concentrations[†]

	Phthalate sums^ (log-nmol/g creatinine)			Phenols^ (log-μg/g creatinine)		
Characteristic	**ΣHMWPs**	**ΣDEHP**	**ΣDBP**	**Benzophenone-3**	**Triclosan**	**2,5-Dichlorophenol**
Tofu						
Never	-	0	-	0	0	0
Any amount	-	−0.09 (−0.29, 0.12)	-	0.37 (−0.03, 0.77)	−0.01 (−0.49, 0.46)	0.34 (−0.05, 0.76)
Seafood						
≤3–4 times per month	0	0	-	0	-	-
≥5 times per month	−0.16 (−0.35, 0.02)	−0.09 (−0.26, 0.08)	-	0.48 (0.15, 0.82) *	-	-
Yogurt						
≤2 times per week	0	0	0	0	-	0
≥3times per week	−0.13 (−0.32, 0.06)	−0.12 (−0.30, 0.05)	−0.09 (−0.26, 0.07)	0.10 (−0.24, 0.44)	-	0.04 (−0.31, 0.39)
Ice cream						
≤1 times per week	-	-	-	-	0	-
≥2 times per week	-	-	-	-	0.29 (−0.10, 0.69)	-
Fish oil supplements						
None	-	0	0	0	0	0
Any amount	-	−0.13 (−0.38, 0.11)	−0.12 (−0.35, 0.10)	0.05 (−0.43, 0.53)	0.47 (−0.10, 1.03)	−0.13 (−0.62, 0.35)
Milk						
≤5–6 times per week	-	-	0	-	-	-
≥7 times per week	-	-	−0.20 (−0.36, – 0.04) *	-	-	-
Processed Meat						
≤2–3 times per month	-	-	0	-	-	-
≥1 time per week	-	-	0.09 (−0.07, 0.25)	-	-	-
Red Meat						
≤2 times per week	-	-	-	-	0	-
≥3 times per week	-	-	-	-	0.01 (−0.43, 0.44)	-

† Adjusted for race, maternal age, body mass index, income, education, marital status, and employment status.

^ All statistics presented as β (95% CI).

* Indicates significance at the 0.05 level.

Σ Paraben and ΣLMWP had no significant bivariate food group associations.

ΣDBP (sum of di-n-butyl phthalate metabolites: MBP, MiBP, MHBP, and MHiBP)

ΣHMWP (sum of high molecular weight phthalates: MBzP, MEHP, MNP, MEOHP, MEHHP, MECPP, MCOP, MCNP)

ΣDEHP (sum of di(2-ethylhexyl) phthalate metabolites (MEHP, MEOHP, MEHHP, and MECPP).

Abbreviations: mono-n-butyl phthalate (MBP), monobenzyl phthalate (MBzP), mono carboxyisononyl phthalate (MCNP), mono carboxyisooctyl phthalate (MCOP), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), mono-hydroxybutyl phthalate (MHBP), mono-hydroxyisobutyl phthalate (MHiBP), mono-isobutyl phthalate (MiBP), and mono-isononyl phthalate (MNP).

Table 5

Intra-class correlation coefficients (ICC) for urinary phthalate metabolite and phenol and paraben concentrations

Phthalate Metabolites	N	ICC	95% Confidence Interval
MBP	18	0.04	(0.00, 0.27)
MCNP	23	0.18	(0.00, 0.39)
MCPP	21	0.23	(0.02, 0.45)
MCOP	24	0.25	(0.06, 0.46)
ΣHMWP	20	0.25	(0.02, 0.47)
MNP	10	0.26	(0.00, 0.56)
ΣDBP	20	0.26	(0.08, 0.53)
MEHHP	23	0.28	(0.17, 0.57)
ΣDEHP	20	0.29	(0.09, 0.53)
MEOHP	23	0.31	(0.10, 0.52)
MECPP	24	0.39	(0.17, 0.57)
ΣLMWP	18	0.43	(0.20, 0.64)
MBzP	21	0.48	(0.26, 0.67)
MHBP	9	0.52	(0.19, 0.76)
MHiBP	24	0.57	(0.37, 0.72)
MEHP	11	0.58	(0.30, 0.78)
MiBP	24	0.59	(0.40, 0.73)
MEP	24	0.60	(0.41, 0.74)
MMP	9	0.73	(0.45, 0.88)
Phenols and Parabens	N	ICC	95% Confidence Interval
Bisphenol S	19	0.25	(0.01, 0.48)
Bisphenol A	22	0.39	(0.16, 0.58)
Σparaben	12	0.62	(0.34, 0.79)
Butyl Paraben	12	0.67	(0.53, 0.88)
2, 4 dichlorophenol	19	0.74	(0.59, 0.85)
Propyl Paraben	21	0.79	(0.65, 0.87)
Methyl Paraben	24	0.82	(0.70, 0.89)
Triclosan	21	0.83	(0.72, 0.90)
2, 5 dichlorophenol	20	0.84	(0.58, 0.85)
Benzophenone-3	24	0.86	(0.76, 0.91)
Ethyl Paraben	8	0.95	(0.86, 0.98)

Abbreviations: mono-n-butyl phthalate (MBP), monobenzyl phthalate (MBzP), mono carboxyisononyl phthalate (MCNP), mono carboxyisooctyl phthalate (MCOP), mono-3-carboxypropyl phthalate (MCPP), mono-2-ethyl-5-carboxypentyl phthalate (MECPP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethylhexyl phthalate (MEHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP), monoethyl phthalate (MEP), mono-hydroxybutyl phthalate (MHBP), mono-hydroxyisobutyl phthalate (MHiBP), mono-isobutyl phthalate (MiBP), monomethyl phthalate (MMP), and mono-isononyl phthalate (MNP).

ΣLMWP (sum of low molecular weight phthalates: MMP, MEP, MiBP, MBP, MHiBP, and MHBP)

ΣDBP (sum of di-n-butyl phthalate metabolites: MBP, MIBP, MHBP, and MHiBP)

ΣHMWP (sum of high molecular weight phthalates: MBzP, MEHP, MNP, MEOHP, MEHHP, MECPP, MCOP, MCNP)

ΣDEHP (sum of di(2-ethylhexyl) phthalate metabolites: MEHP, MEOHP, MEHHP, and MECPP)

Σparaben (sum of parabens: Methyl Paraben, Ethyl Paraben, Propyl Paraben, Butyl Paraben)