Correlates of exposure to phenols, parabens, and triclocarban in the Study of Environment, Lifestyle and Fibroids

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Abstract

We performed a cross-sectional analysis to identify correlates of urinary concentrations of seven phenols (bisphenols A, F, and S, 2,4-dichlorophenol, 2,5-dichlorophenol, benzophenone-3, triclosan), triclocarban, and four parabens (butyl, ethyl, methyl, and propyl). We analyzed baseline data from 766 participants in the Study of Environment, Lifestyle, and Fibroids, a prospective cohort study of 1,693 Black women aged 23–34 years residing in Detroit, Michigan (2010–2012). We collected data on demographic, behavioral, and anthropometric factors via telephone interviews, clinic visits, and self-administered questionnaires. For each biomarker, we used linear regression models to estimate mean differences in log-transformed, creatinine-corrected concentrations across factors of interest. Each biomarker was detected in >50% of participants. Median creatinine-corrected concentrations were highest for methyl paraben (116.8 μg/g creatinine), propyl paraben (16.8 μg/g creatinine), and benzophenone-3 (13.4 μg/g creatinine). Variables most strongly associated with biomarker concentrations included season of urine collection, education, and body mass index (BMI). BMI was positively associated with bisphenol
A and S and triclocarban concentrations and inversely associated with butyl and methyl paraben concentrations. In this cohort of Black women, exposure to phenols, parabens, and triclocarban was prevalent and several factors were associated with biomarker concentrations.

Keywords
endocrine disruptors; epidemiology; personal exposure; population-based studies

INTRODUCTION

Endocrine disrupting chemicals (EDCs) are naturally occurring or synthesized compounds that can alter functioning of the endocrine system. Exposure to EDCs in the United States (U.S.) population is ubiquitous, with reproductive-aged women and non-Hispanic Blacks having higher urinary or serum concentrations of several EDCs than men and non-Hispanic Whites. EDCs are common ingredients in personal care and consumer products that are often used more frequently among women. Moreover, several EDCs have lipophilic and obesogenic properties. These characteristics may influence the sex distribution of biomarker concentrations, possibly due to different patterns of fat deposition in men and women. Higher concentrations of some EDCs have also been observed among individuals with lower socioeconomic status, greater body mass index, and exposure to cigarette smoke. In adults, exposure to non-persistent EDCs has been associated with a variety of health effects, including waist circumference, obesity, Type 2 diabetes, and cardiovascular disease, as well as altered levels of reproductive hormones, thyroid hormones, and markers of oxidative stress and inflammation. These potential health effects, with others under active investigation, add evidence that exposure to EDCs is an important public health concern.

Bisphenol A (BPA) is widely-used in polycarbonate plastics and epoxy resins, such that the general population is exposed through consumption of packaged, bottled, and canned foods and beverages, dermal exposure to personal care products, and ingestion or inhalation of contaminated dust. The use of thermal paper, such as cash register receipts, is another source of BPA exposure. BPA is non-persistent, with a half-life of approximately 4 to 6 hours. In the U.S. National Health and Nutrition Examination Survey (NHANES) 2013–2014, a nationally representative cross-sectional study, 95.7% of individuals in the U.S. population had detectable concentrations of BPA in their urine. Detection of BPA in populations is also widespread globally. BPA concentrations in NHANES have been highest among non-Hispanic Black individuals. Studies comparing urinary BPA concentrations by sex have been inconsistent, with some but not all studies observing higher concentrations among women than men. Studies comparing BPA exposure among Black and White women have also reported inconsistent findings, with some finding higher BPA concentrations among Blacks, some finding higher BPA concentrations among Whites, and some finding no difference. Recent attention to the potential health effects of BPA has resulted in increased use of replacement compounds, including bisphenol F (BPF) and bisphenol S (BPS), and regulatory bans to reduce use of BPA. Some replacement
compounds have similar chemical structures and half-lives as BPA and preliminary studies suggest that these analogous chemicals may have similar health effects.\textsuperscript{35–47}

2,4- and 2,5-dichlorophenol are by-products of waste water treatment, waste incineration, and wood pulp bleaching and metabolites of some organochlorine pesticides. Non-occupational exposure of 2,4-dichlorophenol occurs primarily through inhalation of contaminated air and ingestion of contaminated food or water, while exposure to 2,5-dichlorophenol occurs via ingestion or dermal contact with chlorinated water. 2,4-dichlorophenol can also be produced as a byproduct of triclosan and 2,5-dichlorophenol is a metabolite of 1,4-dichlorobenzene.\textsuperscript{48, 49} As their precursors have short half-lives, 2,4- and 2,5-dichlorophenol have estimated half-lives of 30 minutes to 3 days.\textsuperscript{18, 50, 51} In a combined analysis of NHANES 2005–2006 and 2007–2008 data, urinary concentrations of 2,4- and 2,5-dichlorophenol were higher among women than men and among non-Hispanic Blacks than non-Hispanic Whites.\textsuperscript{20}

Benzophenone-3 is a chemical ultraviolet filter found in products such as sunscreen, lotion, plastic packaging, and paints. Benzophenone-3 absorbs ultraviolet rays thereby protecting against sun exposure and/or degradation\textsuperscript{35, 52–54} and is non-persistent with a half-life of 4 to 8 hours.\textsuperscript{55} In NHANES 2003–2004, urinary concentrations of benzophenone-3 were higher among women than men and among non-Hispanic Whites than non-Hispanic Blacks.\textsuperscript{56} Benzophenone-3 concentrations are likely lower among non-Hispanic Blacks due to less frequent use of sunscreen,\textsuperscript{54} a primary source of benzophenone-3 exposure.

Triclosan and triclocarban are common additives in personal care products due to their antimicrobial properties.\textsuperscript{48, 52, 53} Both are non-persistent compounds with triclosan having a urinary half-life of approximately 11 hours and triclocarban having a urinary half-life of 10–28 hours.\textsuperscript{57–59} Urinary concentrations of triclosan were similar among men and women and higher among non-Hispanic Whites than non-Hispanic Blacks in NHANES 2003–2004.\textsuperscript{50} In NHANES 2013–2014, urinary concentrations of triclocarban were too low for the calculation of the median or geometric mean among women, men, or non-Hispanic Whites, but, among non-Hispanic Blacks, the median concentration of triclocarban was 0.17 μg/g creatinine.\textsuperscript{61} Because of concerns about efficacy and potential health effects, the U.S. Food & Drug Administration ruled that consumer antiseptic washes containing triclosan and triclocarban could not be marketed after September 2017.\textsuperscript{62} In 2017, a scientific consensus statement recommended limiting production and use of both triclosan and triclocarban.\textsuperscript{63} However, these chemicals remain in other commonly-used personal care products, including some toothpastes.\textsuperscript{53}

Parabens are estrogenic preservatives that are widely-used in personal care products, food and beverage processing, and pharmaceutical products\textsuperscript{35, 52} and have a half-life of less than 24 hours.\textsuperscript{64–66} In NHANES 2005–2006 participants, urinary concentrations of methyl paraben and propyl paraben, two commonly-used parabens, were higher among women than men and among non-Hispanic Blacks than non-Hispanic Whites.\textsuperscript{67} Non-Hispanic Black women had the highest concentrations of propyl paraben. The high proportion of individuals with butyl paraben and ethyl paraben concentrations below the limit of detection precluded comparisons across sex and race.\textsuperscript{67}
The present cross-sectional analysis evaluated the distribution of urinary concentrations of triclocarban and selected phenols and parabens and examined demographic, behavioral, and anthropometric factors as potential correlates of these biomarkers within a cohort of reproductive-age Black women. We focused our analysis on factors that have been shown to be associated with EDC concentrations in previous studies. Our cohort is uniquely positioned to explore these associations because exposure to EDCs is understudied in Black women, who may be disproportionately exposed to these chemicals compared to the general population, and few studies that include Black participants present race-specific data.

SUBJECTS AND METHODS

Study population

The Study of Environment, Lifestyle and Fibroids (SELF) is a prospective cohort study of 1693 Black women ages 23–34 years recruited from the Detroit, Michigan metropolitan area during 2010–2012. The study has been described in detail elsewhere.68 Eligible participants had an intact uterus, no prior diagnosis of uterine leiomyomata (fibroids), cancer, or autoimmune disease requiring regular medication, and were willing to remain in the study for a period of 5 years. Interviews and questionnaires elicited data on educational attainment, cigarette smoking, alcohol consumption, and other variables of interest. At the baseline visit, weight and height were measured by technicians and participants provided blood and urine samples. If participants had not collected a first-morning urine or their sample was <30 mL, then a spot urine sample was collected during the baseline clinic visit. SELF participants completed follow-up study visits every 20 months. All participants signed an informed consent form and the study was approved by the Institutional Review Boards of Henry Ford Health System, National Institute of Environmental Health Sciences, and Boston University Medical Campus. The involvement of the Centers for Disease Control and Prevention (CDC) laboratory was not considered engagement in human subjects research.

The present analysis used data from a case-cohort substudy conducted within the SELF cohort. This “EDC substudy” was designed to investigate the relation of EDCs to risk of uterine fibroids. At baseline, approximately 22% of the SELF cohort had previously undiagnosed fibroids detected via ultrasound, so 594 participants were selected at random for inclusion in the substudy from among the participants who were at risk for fibroids. Among these 594 participants, 130 developed fibroids over follow-up. The random sub-cohort was supplemented with all remaining incident cases of fibroids (N = 172) that were detected via ultrasound through 60 months of follow-up. Participants included in the substudy did not differ appreciably from the other SELF participants (Supplementary Table 1).

Exposure assessment

Of the 1693 SELF participants enrolled at baseline, 1654 (97.7%) provided a first-morning urine sample and 41 (2.4%) provided a urine sample at the clinic visit.68 Urine samples for the 766 EDC substudy participants were collected in 2010–2012 during the baseline clinic visit. At the 20 month follow-up, a second urine sample was analyzed for 565 (73.8%) of the 766 EDC substudy participants. Urine samples were shipped on dry ice and stored at −80
degrees Celsius in the National Institute of Environmental Health Sciences (NIEHS) repository (Experimental Pathology Labs, Durham, NC).

Samples were analyzed for 12 biomarkers: BPA, 2,4-dichlorophenol, 2,5-dichlorophenol, benzophenone-3, triclosan, butyl paraben, ethyl paraben, methyl paraben, and propyl paraben. BPF, BPS, and triclocarban were only analyzed in 746 baseline samples because these biomarkers were added to the assay panel after the pilot phase of our study. Total concentrations of analytes were quantified at the CDC using methods based on online solid phase extraction coupled to high performance liquid chromatography-isotope dilution tandem mass spectrometry. Analytic measurements were conducted following strict Clinical Laboratory Improvement Amendments quality control guidelines, including analysis of proficiency testing samples. Along with the study samples, each analytic run included high- and low-concentration quality control materials (QCs) and reagent blanks to assure the accuracy and reliability of the data. Quality assurance also incorporated evaluation of blind duplicates within and across batches. The coefficients of variation of repeated measurements of the QCs, which reflect inter-batch precision, vary per analyte and concentration, but were typically <10% (range: 1.30–10.23%). Urinary creatinine was measured using a clinical analyzer at the NIEHS.

Potential Correlates

Women reported their age on the pre-enrollment questionnaire. During the computer-assisted telephone interview, participants reported their educational attainment; household income; marital status; smoking status; alcohol consumption; and reproductive, contraceptive, and medical history. Participants also provided data on their frequency of sunscreen use by responding to the question “When you spend time outside, how often do you wear sunscreen?” with never or hardly ever, sometimes, often, always or nearly always, or always wear sunscreen on face. Data on use of other personal care products were not available for this analysis.

We calculated body mass index (BMI, kg/m²) from technician-measured weight and height. We used simple imputation to the median for missing data on correlates: one participant was missing data on sunscreen use (set to “never/hardly ever”) and six participants were missing data on income (set to the median value within categories of education level). No other variables had missing data. The variables assessed as potential correlates were informed by previous research and included: age, season of urine collection, marital status, education, household income, smoking status, alcohol use, BMI, age at menarche, parity, and sunscreen use.

Data analysis

The limits of detection (LODs) varied by analyte and ranged from 0.1 to 1.7 μg/L (Table 1). We used instrumental reading values in the analyses, even for concentrations <LOD. Concentrations of zero were set to the lowest observed non-zero value to prevent biased estimates from log-transformation. To adjust for urine dilution, biomarker concentrations were divided by creatinine to obtain concentrations in μg/g creatinine. We compared the median and 75th percentile biomarker concentrations from our participants with the
distributions from publicly-available data for females and non-Hispanic Blacks (NHANES 2011–2012). To examine variability in biomarker concentrations at the baseline and the 20 month follow-up visits among the 565 women with urine samples at both time points, we calculated intraclass correlation coefficients (ICCs) and 95% confidence intervals (CIs) using the ‘ICC’ R package, which estimates ICCs using a one-way analysis of variance. We compared chemical concentrations across categories of each potential correlate using percentage difference in urinary biomarker concentrations. Each percentage difference compared a biomarker’s concentration among participants in a given a correlate category relative to the analogous concentration among those in the reference category of that correlate. We estimated the mean percentage difference (and 95% CIs) across levels of each correlate by fitting linear regression models of log-transformed creatinine-corrected biomarker concentrations, exponentiating regression coefficients for each correlate category, and transforming the exponentiated values into percentages. We used two-sided hypothesis tests for regression models. Multivariable models included all covariates considered as potential correlates. Only estimated percentage differences from the multivariable models are presented.

We conducted 3 separate sensitivity analyses. First, we fit models for biomarker concentrations that were not corrected for creatinine and included creatinine as a covariate in the model. The point estimates from these analyses did not materially differ from those of our primary analyses (data not shown). Second, we restricted the analysis to the random sub-cohort of 594 participants selected at baseline. Third, we fit models using an average of baseline and 20 month biomarker concentrations for each chemical with an ICC<0.20 among the participants with both baseline and 20 month follow-up measurements. Analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

The median age of participants at enrollment was 29 years (interquartile range: 26 to 31 years). Most participants were never married (58.7%), had at least a high school diploma or General Educational Diploma (GED) (78.2%), had an annual household income less than $50,000 (83.1%), or were never smokers (73.5%) (Supplementary Table 1). Alcohol use within the previous year (70.4%), obesity (≥30 kg/m², 59.6%), parity (60.9%), and “never/hardly ever” use of sunscreen (73.9%) were also prevalent.

Each biomarker was detected in more than half of the urine samples from SELF participants (Table 1). Median urinary concentrations were highest for methyl paraben (115.8 Mg/g creatinine), followed by propyl paraben (16.8 μg/g creatinine) and benzophenone-3 (13.3 Mg/g creatinine). The distributions of urinary concentrations in SELF were similar to those among females and non-Hispanic Blacks in NHANES (Table 1).

Table 2 presents the correlations among urinary concentrations of the biomarkers. Correlations between the urinary concentrations of the bisphenols were relatively weak (range of Spearman correlation coefficients (r)=0.12–0.22). Larger correlations were observed between urinary concentrations of 2,4-dichlorophenol and 2,5-dichlorophenol (r=0.51) and between 2,4-dichlorophenol and triclosan (r=0.45). Parabens were strongly
correlated with one another, with the strongest correlation observed between methyl paraben and propyl paraben (r=0.80).

When we evaluated variability in urinary concentrations of the individual biomarkers over 20 months of follow-up (Table 3), median urinary concentrations tended to be slightly lower at the 20 month follow-up than at baseline. The ICC demonstrated moderate reliability for BPA (0.59, 95% CI: 0.53, 0.64). However, reliability was poor for the other biomarkers (range: −0.01–0.36).

The multivariable-adjusted percentage differences in urinary bisphenol concentrations and 95% confidence intervals across categories of each correlate are shown in Table 4. BMI was positively associated with BPA and BPS. Compared with participants with BMI <25 kg/m², women with BMI ≥35 kg/m² had 19.8% (95% CI: 1.9%, 40.8%) higher concentrations of BPA and 39.7% (95% CI: 10.1%, 77.3%) higher concentrations of BPS. Parity was positively associated with BPS. Extremes of age at menarche (<10 and ≥14 years) were inversely associated with BPA and menarche at age 13 was associated with lower concentrations of BPF compared with menarche at age 12. Although not statistically significant, there was an inverse relationship between education and concentrations of BPF. Women with an annual household income of $20,000-$50,000 had lower concentrations of BPS than those with income <$20,000. BPF concentrations were higher in summer and autumn, while BPS concentrations were higher in summer, compared with winter. Sunscreen users had higher concentrations of BPF than nonusers of sunscreen (“often/always” vs. “never/hardly ever”: 35.4%, 95% CI: −15.0%, 115.7%). Compared with never smokers, BPS concentrations were non-significantly higher among current smokers.

Compared with never smokers, past smokers had 27.6% (95% CI: −1.1%, 64.6%) higher 2,4-dichlorophenol concentrations and 37.2% (95% CI: −9.6%, 108.1%) higher 2,5-dichlorophenol concentrations (Table 5). Age at menarche was positively associated with both 2,4-dichlorophenol and 2,5-dichlorophenol concentrations, though the associations were not statistically significant. Women with some college, an Associate’s degree, or Technical education had 20.8% (95% CI: −0.1%, 46.0%) higher concentrations of 2,4-dichlorophenol than those with a high school diploma/GED or less. Concentrations of urinary 2,4-dichlorophenol were 15.2% (95% CI: −27.9%, −0.2%) lower among participants who consumed 1–5 alcoholic drinks/day or ≥4 drinks once a month compared with non-drinkers. Sunscreen use had a positive relationship with 2,5-dichlorophenol concentrations (“often/always” vs. “never/hardly ever”: 41.7% higher, 95% CI: 0.0%, 100.8%). In addition, concentrations of 2,5-dichlorophenol were lower among married participants and were non-significantly higher with BMI ≥25 kg/m².

Sunscreen use was strongly positively associated with benzophenone-3 concentrations (“often/always” vs. “never/hardly ever”: 223.3%, 95% CI: 124.2%, 366.5%). Education was positively associated with benzophenone-3 concentrations, while age at menarche had a U-shaped association with benzophenone-3 concentrations (Table 5). Benzophenone-3 concentrations were lower among smokers than never smokers and among primiparous women than nulliparous women. Benzophenone-3 concentrations tended to be highest in the summer (25.4%, 95% CI: −9.9%, 74.5%) and lowest in the autumn (−20.5%, 95% CI:
−43.3%, 11.5%) compared with winter. Obesity (BMI ≥30 kg/m²) had a non-significant positive relationship with benzophenone-3 concentrations.

Compared with urine collected in winter, triclocarban concentrations were higher in spring (126.6%, 95% CI: 33.3%, 285.2%). Women who were currently married had lower triclocarban concentrations (35.8%, 95% CI: −58.2%, −1.3%) than those who had never been married (Table 5). Triclocarban concentrations varied with age at menarche in a non-linear pattern and triclosan concentrations were higher among participants with ages at menarche ≤10, 11, and ≥14 years (relative to 12 years), though the results were only significant for age 11. BMI was positively associated with triclocarban with concentrations being 97.5% (95% CI: 16.1%, 236.1%) higher for BMI 25–29.9 kg/m² and 221.7 (95% CI: 98.0%, 422.8%) higher for BMI ≥35 kg/m² as compared with <25 kg/m². Alcohol use of 1–5 drinks/day or ≥4 drinks once per month or less was inversely associated with triclocarban concentrations (Table 5). Triclosan was positively associated with education and income, while triclocarban was inversely associated with income and had a non-significant inverse association with education. Triclosan was inversely associated with parity of ≥3 births. Concentrations of triclosan were also lower among current smokers compared with never smokers (−41.2%, 95% CI: −57.7%, −18.2%); triclocarban concentrations tended to be higher among past smokers (31.1%, 95% CI: −30.2%, 148.2%).

Concentrations of ethyl paraben were higher among “sometimes” users of sunscreen compared with non-users, though non-significant increases were observed for butyl, methyl, and propyl parabens (Table 6). Morbid obesity (BMI ≥35 kg/m²) was inversely associated with butyl and methyl paraben concentrations. For example, methyl paraben concentrations were 30.7% lower for BMI ≥35 vs. <25 kg/m² (−48.0%, −7.7%). Education was positively associated with methyl paraben and propyl paraben, with methyl paraben concentrations being 68.1% higher (95% CI: 15.7%, 144.2%) among women reporting at least a Bachelors degree compared with women reporting a high school diploma/GED or less. Education was positively associated with butyl paraben concentrations, though the association was not significant. Concentrations of butyl paraben were higher among women with annual household incomes >$50,000 relative to women with annual household incomes <$20,000. There was seasonal variability in methyl paraben concentrations with lower concentrations being observed in the autumn. Butyl paraben concentrations tended to be higher in the summer (30.3%, 95% CI: −5.6%, 79.8%). Methyl and propyl paraben concentrations were lower among past smokers, while butyl paraben concentrations were higher among past smokers relative to never smokers; these associations were not statistically significant. Alcohol use within the last year was strongly associated with ethyl paraben concentrations (125.5%, 95% CI: 52.8%, 232.9% comparing the highest and lowest categories of alcohol consumption). Ethyl paraben concentrations were also higher for primiparous women as compared with nulliparous women.

The results were generally similar in sensitivity analyses among the random sub-cohort of 594 participants (data not shown), although there were a few differences. In the random sub-cohort, positive associations were stronger for past (vs. never) cigarette smoking with 2,4-dichlorophenol concentrations (47.4%, 95% CI: 9.5%, 98.3%), having at least a Bachelors degree (vs. no high school diploma or GED) with benzophenone-3 concentrations (120%,
95% CI: 36.2%, 255.2%), being married previously (vs. never being married) with triclosan concentrations (54.6%, 95% CI: 5.3, 126.9%), and being previously married (vs. never married) with ethyl paraben concentrations (40.4%, 95% CI: −9.4, 117.5%). There was a weaker association for “often/always” sunscreen use (vs. “never/hardly ever”) with concentrations of butyl paraben (2.3%, 95% CI: −31.1, 51.9) and an inverse association between “often/always” sunscreen used compared to “never/hardly ever” sunscreen use with methyl paraben concentrations (−11.0%, 95% CI: −37.9%, 27.5%). In addition, a stronger inverse association was observed for annual household income over $50,000 (vs. <$20,000) with propyl paraben concentrations (−20.8%, 95% CI: −47.9%, 20.4%).

In the sensitivity analysis using the average of baseline and 20 month follow-up measurements for the 8 chemicals with an ICC<0.20, associations with biomarker concentrations tended to be slightly weaker for season of urine collection, BMI, and age at menarche and stronger for education, income, and parity (Supplementary Tables 2 and 3). The results were consistent with the main findings except for the following: a weak non-significant positive association for BMI ≥35 kg/m$^2$ and BPS concentrations, no association for urine collection in the summer and benzophenone-3 concentrations, no association for sometimes sunscreen use and ethyl paraben concentrations, and an inverse association for age at menarche at age 11 years (relative to age 12 years) and methyl paraben concentrations.

**DISCUSSION**

Exposure to triclocarban and selected phenols (or their precursors) and parabens was prevalent in this population of reproductive-aged Black women residing in Detroit, Michigan. Median urinary concentrations spanned several orders of magnitude and were highest for methyl paraben, but were similar to concentrations observed among women and non-Hispanic Black adults in NHANES 2011–2012. In SELF, concentrations of BPF, BPS, and triclocarban were lowest in the winter, while methyl paraben concentrations were highest in the winter. There was a moderate-to-strong positive relationship between education and concentrations of benzophenone-3, triclosan, methyl paraben, and propyl paraben, with an association that ranged from 51% to 77% for participants who reported having at least a Bachelors degree. Higher BMI was associated with higher concentrations of BPA, BPS, and triclocarban (range: 20%–222% for BMI ≥35 kg/m$^2$), while there was a weak inverse association between BMI and concentrations of butyl and methyl parabens (−31% for BMI ≥35 kg/m$^2$ for both biomarkers). The findings for the sensitivity analysis restricted to the random sub-cohort were generally similar to the results found using the full sample. Where differences seemed notable, we did not reach different conclusions.

Season of urine collection was correlated with concentrations of BPF, BPS, triclocarban, and methyl paraben. Although many studies report concentrations of EDCs by time of day of urine collection, few present data about month or season of data collection. In a cross-sectional study of 50 White, Black, and Hispanic adults aged 19–50 years in North Carolina in 2009, BPA concentrations were highest in winter and spring, while, in the Canadian Maternal-Infant Research on Environmental Chemicals (MIREC) study, a cohort study of 2,001 pregnant women (mean age: 32 years) recruited in 2008–2011, BPA concentrations...
were highest in fall and winter.\textsuperscript{74, 75} In an analysis of 177 pregnant women (mean age: 35.7 years; recruited in 2005–2011) from the Environment and Reproductive Health Study (EARTH), an open cohort study of mostly White women and men recruited from a fertility clinic in Boston, MA,\textsuperscript{76} adjustment for season of urine collection had no influence on paraben concentrations,\textsuperscript{9} indicating little association between season and methyl paraben concentrations. Our findings of higher concentrations of BPF and BPS in the summer, higher concentrations of triclocarban in the spring, and lower concentrations of methyl paraben in the fall could reflect seasonal changes in exposure through changes in personal care product use, diet, or travel\textsuperscript{45} or changes in levels of EDCs in environmental media.\textsuperscript{77}

In SELF, some post-secondary education was positively associated with 2,4-dichlorophenol concentrations, while an analysis of NHANES 2005–2008 data observed an inverse association between education and both 2,4-dichlorophenol and 2,5-dichlorophenol concentrations\textsuperscript{20} and an analysis of 466 pregnant women from the Healthy Start study, a cohort of White, Black, and Hispanic pregnant women aged 16–43 years recruited in Colorado in 2010–2014,\textsuperscript{78} observed an inverse association for 2,5-dichlorophenol concentrations.\textsuperscript{79} Higher education was positively associated with benzophenone-3 concentrations in SELF and in the Healthy Start study.\textsuperscript{79} Urinary triclosan concentrations were higher among participants with higher education in SELF, the Healthy Start study,\textsuperscript{79} the Health Outcomes and Measures of the Environment (HOME) Study, a cohort of 468 White and Black pregnant women (mean age: 29 years) recruited in 2003–2006 in Cincinnati, Ohio,\textsuperscript{80, 81} and in the National Children’s Study (NCS) Vanguard Study,\textsuperscript{82} a multi-site cohort study of 506 White, Black, and Hispanic pregnant women aged 18–49 years recruited in 2009, but there was no association in the MIREC study.\textsuperscript{74} We found a strong positive association between education and methyl paraben concentrations that, to our knowledge, has not been reported elsewhere. Since methyl paraben has been detected in seafood\textsuperscript{83} and, in the U.S., seafood consumption is higher among adults with greater educational attainment,\textsuperscript{84} this finding may reflect dietary patterns that differ by education.

Findings on the relation of household income to BPA concentrations in NHANES are inconsistent with three studies observing higher BPA concentrations among participants with low household incomes\textsuperscript{19, 43, 85} and another finding no association.\textsuperscript{86} The latter concurs with our finding of no association for BPA, although the MIREC study observed an inverse association with BPA concentrations.\textsuperscript{74} Consistent with the Healthy Start study, we observed an inverse association between household income and BPS concentrations.\textsuperscript{79} In NHANES 2013–2014, household income was positively associated with BPF concentrations, but not BPS concentrations.\textsuperscript{19} Inconsistency across analyses of NHANES data may relate to differences in how income variables were modeled. In SELF, the NCS Vanguard Study,\textsuperscript{82} and the Korean National Human Biomonitoring Survey (KNHBS),\textsuperscript{87} a cross-sectional study of 1 865 women and men aged 18–69 years recruited in 2009, no relation was observed between 2,4-dichlorophenol or 2,5-dichlorophenol concentrations and income, while higher concentrations of 2,5-dichlorophenol were observed among low-income Healthy Start study participants.\textsuperscript{79} One analysis of NHANES 2001–2008 data observed higher concentrations of 2,4-dichlorophenol and 2,5-dichlorophenol among both low income and high income non-Hispanic Blacks compared with high income non-Hispanic Whites,\textsuperscript{88} while an analysis of NHANES 2005–2008 observed an inverse association with education and income for both
compounds. A systematic assessment of NHANES 1999–2006 found little association of 2,4-dichlorophenol or 2,5-dichlorophenol with household income and no association of benzophenone-3 and household income. Our study also found no association between benzophenone-3 and household income, differing from NHANES 2001–2010, which observed a positive association between benzophenone-3 concentrations and the poverty income ratio (a measure of household income relative to poverty), and the Healthy Start study, which observed higher benzophenone-3 concentrations among high-income participants. However, each study characterized income differently, which makes direct comparisons difficult. Although a systematic assessment of NHANES 1999–2006 and analyses in the MIREC study and the NCS Vanguard Study found no association between household income and urinary triclosan concentrations, concentrations were higher among participants with higher income in SELF, the HOME Study, and the Healthy Start study. Triclosan concentrations were also higher among participants with higher income in NHANES 2003–2004. Methyl paraben concentrations did not vary by income in SELF and the Healthy Start study. However, in NHANES 2001–2008 data, low-income non-Hispanic Blacks had higher concentrations of methyl paraben than non-Hispanic Whites. The analysis used poverty-income ratio to approximate socioeconomic status and did not assess education, which may account for the differences in findings.

In SELF, BMI was positively associated with concentrations of BPA and BPS and the association was particularly strong for BPS. In a multi-ethnic cohort of 1,396 pregnant women (mean age: 31 years) recruited in the Netherlands during 2003–2005, BMI ≥30 kg/m² was associated with higher levels of BPS, but not BPA or BPF. However, in NHANES 2013–2014, BPA was the only bisphenol associated with higher BMI. These findings are consistent with evidence that bisphenols are lipophilic and may be obesogenic. In NHANES 2005–2008, 2,5-dichlorophenol concentrations were positively associated with BMI, but BMI was not associated with 2,5-dichlorophenol concentrations in SELF, the Healthy Start study, or the KNHBS. Our findings on BMI and triclosan also differed from those of other studies: we found no association between BMI and triclosan concentrations, but, in NHANES 2003–2010, the Healthy Start study, and the MIREC study, triclosan concentrations were inversely associated with BMI. In NHANES 2013–2014, having a higher body surface area was associated with higher levels of triclocarban. Although body surface area differs from BMI, the two measures are highly correlated ($r>0.97$) such that the finding of a positive association between BMI and triclocarban in SELF can be considered consistent with NHANES. In the Healthy Start study, BMI ≥25 kg/m² was associated with lower concentrations of butyl, methyl, and propyl parabens. An inverse association between BMI and concentrations of methyl paraben was also observed in SELF and in EARTH. Since several EDCs are suspected obesogens, findings of a positive association with BMI could be due to reverse causation.

Most of the research on EDCs and age at menarche has modeled EDCs as the exposure of interest and age at menarche as the outcome. However, the results can still be informative for the present study. We found lower BPA concentrations among SELF participants with an age at menarche ≤10 or ≥13 years, relative to 12 years. BPA was not associated with age at menarche among adolescent girls in NHANES 2003–2010, or in the multiethnic Breast Cancer and Environment Research Program Puberty Study (BCERP), a multi-site cohort.
study of 1,239 girls aged 6–8 years enrolled in 2004–2007. We found non-significant positive associations of age at menarche with 2,4-dichlorophenol and 2,5-dichlorophenol concentrations, while, in NHANES 2003–2008, greater concentrations of 2,5-dichlorophenol were associated with later age at menarche. In the BCERP and among 200 girls from the Growth and Obesity Cohort Study, a cohort study of children recruited at ages 3–4 years in 2006 in Santiago, Chile, greater concentrations of 2,5-dichlorophenol were associated with earlier age at menarche. Although there was no association between benzophenone-3 and age at menarche in the BCERP, benzophenone-3 concentrations were inversely associated with age at menarche among girls in the Growth and Obesity Cohort Study and age at menarche and benzophenone-3 levels in SELF seemed to have a U-shaped relationship. In SELF, triclosan concentrations were higher among participants with age at menarche ≥14 years, in contrast with NHANES 2003–2008 and the BCERP where there was no association. Enzymes such as cytochromes p450 and sulfotransferase are involved both in estrogen metabolism and in biotransformation and bioactivation of EDCs. Thus, associations with age at menarche could reflect varying levels of endogenous estrogen or differences in estrogen metabolism that could influence urinary concentrations of EDCs. Age at menarche is strongly correlated with childhood body fat, childhood body fat distribution, and adult obesity. Although we adjusted for BMI, our results for age at menarche may reflect differences in body fat or be due to residual confounding.

Consistent with other studies, sunscreen use was strongly positively associated with benzophenone-3 concentrations in SELF. In NHANES 2009–2012, triclosan concentrations were higher among participants who reported always using sunscreen. We did not observe higher triclosan concentrations among sunscreen users in SELF, but occasional sunscreen users had higher concentrations of ethyl paraben. An analysis of NHANES 2009–2012 found a strong positive association between sunscreen use and urinary concentrations of methyl, butyl, ethyl, and propyl paraben among women. These findings may not accurately represent the non-Hispanic Blacks in NHANES, as the study did not stratify by race and had a low prevalence of “always use” of sunscreen among Blacks (5.5%).

Low-to-moderate ICCs indicated high within-subject variability and that baseline and 20 month follow-up measures are weakly correlated for these biomarkers. In SELF, reliability in BPA concentrations (ICC=0.59) was higher than that reported in other studies of non-pregnant adults in the U.S., which have observed low reliability (range of ICCs: 0.04–0.26). The ICC for BPF, which was negative, could be a spurious finding. Compared with an ancillary study of 143 participants from the BioCycle Study, which collected urine samples from White, Black, and Asian women aged 18–44 years in Buffalo, New York over a period of 2 months in 2005–2007, there was lower reliability for 2,4-dichlorophenol in SELF (ICC=0.16 and 0.38, respectively), but similar findings for 2,5-dichlorophenol (ICC=0.31 and 0.33, respectively). For benzophenone-3, our results (ICC=0.09) indicated lower reliability than previously reported (range of ICCs: 0.67–0.92). Similarly, the ICC for triclosan (0.15) was much lower in SELF than in other studies (range of ICCs: 0.50–0.96). For parabens, the ICC for propyl paraben (0.36) was slightly lower than the range observed in other studies of non-pregnant adults in the U.S. (0.43–0.54). However, reliability for butyl, ethyl, and methyl paraben in SELF (0.02, 0.16, and 0.10, respectively) was much lower than reported in these studies, which found ICCs in the range
of 0.39–0.49 for butyl paraben,\textsuperscript{96,106} 0.38–0.82 for ethyl paraben,\textsuperscript{106,108} and 0.42–0.71 for methyl paraben.\textsuperscript{96,106,108} Sensitivity analyses in which we averaged the baseline and 20 month measurements for EDCs with ICCs <0.20 produced slightly different associations for some EDCs. However, use of this alternative measure did not lead to materially different conclusions about the relation of correlates of interest to biomarker concentrations with the exception of slightly weaker associations for season of urine collection, BMI, and age at menarche and stronger associations for education, income, and parity.

This study is one of few investigations examining variability and correlates of urinary phenol, paraben, and triclocarban concentrations among Black women. We examined and controlled for a wide range of covariates associated with EDC concentrations in previous studies, including season of specimen collection, which may be an important confounder or modifier to consider in future exposure-disease investigations.\textsuperscript{111} We were unable to adjust for time of day of urine collection. All samples were processed and analyzed under a rigorous protocol at the CDC laboratory and scientific consensus suggests that urine is the appropriate matrix for non-persistent chemicals, like phenols.\textsuperscript{112} The present analysis relied upon baseline urine samples and these data represent only recent exposure. Although we had two urinary measurements for most women (74%), the biomarker concentrations, with the exception of BPA, showed evidence of variation over time. Additional measurements may be necessary to reduce potential exposure misclassification from variation in exposure over time\textsuperscript{113,114} and to collect samples most likely to reflect important windows of exposure.

SELF is a convenience sample of women from a single urban area of the U.S., which may not represent locations where other Black women reside. The convenience sample may explain differences between our findings and those of other studies. Another limitation is that, in this analysis, we did not consider use of personal care products as sources of exposure, with the exception of sunscreen use. We also did not assess dietary factors as potential correlates, although consumption of canned food and beverages is a common source of exposure to bisphenols. Examination of a full range of personal care products and dietary factors was beyond the scope of this analysis. Control for these additional variables likely would have attenuated the associations observed. Future analyses will incorporate these exposure sources as the relevant data become available. As with all studies based on self-reported variables, misclassification could have resulted in bias. Since SELF participants in this substudy, who were selected to be part of a case-cohort study design, did not materially differ from participants in the parent study (Supplementary Table 1), misclassification is likely to have been non-differential and to have biased associations toward the null. Finally, although multivariable models adjusted for numerous covariates, these models were not designed to address a causal framework for exposure to any particular exposure pathway and may be subject to an inflated false discovery rate due to the multiple correlates and analytes under study.\textsuperscript{115} We did not correct our results for multiple hypothesis testing. Despite these limitations, the findings provide an opportunity to generate hypotheses and suggest causal pathways for future investigation.

In the present cross-sectional analysis nested within a prospective cohort study of reproductive-aged Black women, exposure to phenols (or their precursors), parabens, and triclocarban was prevalent with relatively high within-person variability. We identified
several correlates of EDC biomarker concentrations with the most consistent findings observed for BMI as a correlate of BPA, BPS, triclocarban, butyl paraben, and methyl paraben concentrations; education as a correlate of benzophenone-3, triclosan, methyl paraben, and propyl paraben concentrations; and season of urine collection as a correlate of BPF, BPS, triclocarban, and methyl paraben concentrations. Although concentrations of EDC biomarkers in SELF participants were similar to the general population in NHANES, other studies have observed disparities and it is important to examine correlates of exposure, thereby identifying opportunities to reduce exposure and its potential health effects in this population. In addition, investigating correlates of EDC exposure across diverse populations may be useful for determining next steps in research and policy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Distribution of urinary concentrations of EDC biomarkers at baseline in a sample of SELF participants \(^1\) and in NHANES 2011–2012

| Biomarker       | SELF 2010–2012 | NHANES 2011–2012 |
|-----------------|----------------|------------------|
|                 | N   | LOD (μg/L) | % below LOD | Median (μg/g creatinine) | 75th percentile (μg/g creatinine) | Median (μg/g creatinine) | 75th percentile (μg/g creatinine) |
| Bisphenol A (BPA) | 766 | 0.2 | 0.1% | 1.71 | 2.82 | 1.75 | 2.93 |
| Bisphenol F (BPF) \(^2\) | 746 | 0.2 | 34.2% | 0.24 | 0.95 | -- | -- |
| Bisphenol S (BPS) \(^2\) | 746 | 0.1 | 4.3% | 0.30 | 0.63 | -- | -- |
| 2,4-dichlorophenol | 766 | 0.1 | 1.7% | 0.52 | 0.87 | 0.71 | 1.45 |
| 2,5-dichlorophenol | 766 | 0.1 | 0.4% | 2.38 | 6.03 | 3.39 | 13.10 |
| Benzophenone-3 | 766 | 0.4 | 0.6% | 13.31 | 45.05 | 30.10 | 186.00 |
| Triclocarban \(^2\) | 746 | 0.1 | 30.5% | 0.22 | 1.17 | -- | -- |
| Triclosan | 766 | 1.7 | 8.6% | 7.10 | 25.34 | 10.80 | 53.30 |
| Butyl paraben | 766 | 0.1 | 42.3% | 0.09 | 0.28 | <LOD | 1.56 |
| Ethyl paraben | 766 | 1.0 | 21.3% | 2.36 | 8.53 | 2.96 | 18.90 |
| Methyl paraben | 766 | 1.0 | 0.0% | 115.75 | 313.90 | 119.00 | 309.00 |
| Propyl paraben | 766 | 0.1 | 0.0% | 16.76 | 49.54 | 20.90 | 74.70 |

\(^1\) Abbreviations: EDC, endocrine-disrupting chemical; LOD, limit of detection; NHANES, U.S. National Health and Nutrition Examination Survey; SELF, Study of Environment, Lifestyle and Fibroids

\(^2\) This biomarker was not assessed in NHANES 2011–2012.
### Table 2.

Spearman correlations between baseline creatinine-corrected concentrations of EDC biomarkers among SELF participants

| Biomarker    | BPF  | BPS  | 2,4-dichlorophenol | 2,5-dichlorophenol | Benzophenone-3 | Triclocarban | Triclosan | Butyl paraben | Ethyl paraben | Methyl paraben | Propyl paraben |
|--------------|------|------|--------------------|--------------------|----------------|--------------|-----------|---------------|---------------|----------------|----------------|
| BPA          | 0.17 | 0.22 | 0.03               | 0.05               | 0.04           | 0.06         | −0.05     | 0.10           | 0.09           | 0.00           | 0.00           |
| BPF          | 0.12 | 0.01 | 0.03               | 0.00               | −0.01          | 0.00         | 0.02      | 0.11           | 0.02           | 0.02           | 0.05           |
| BPS          | −0.03| 0.05 | −0.05              | 0.08               | −0.09          | −0.04        | −0.03     | −0.03          | −0.01          | −0.02          |                |
| 2,4-dichlorophenol |      |      | 0.51               | 0.12               | 0.02           | 0.45         | 0.04      | 0.04           | 0.08           | 0.08           | 0.08           |
| 2,5-dichlorophenol |      |      | 0.05               | 0.06               | −0.03          | 0.02         | 0.09      | 0.06           | 0.08           | 0.08           |                |
| Benzophenone-3 |      |      | −0.06              | 0.20               | 0.17           | 0.14         | 0.16      | 0.16           | 0.16           |                |                |
| Triclocarban  |      |      | −0.08              | −0.07              | −0.05          | −0.07        | −0.07     | −0.06          |                |                |                |
| Triclosan     |      |      | 0.08               | −0.02              | 0.08           | 0.29         | 0.24      | 0.21           | 0.33           |                | 0.80           |
| Butyl paraben |      |      |                    |                    |                |              |           |                |                |                |                |
| Ethyl paraben |      |      |                    |                    |                |              |           |                |                |                |                |
| Methyl paraben|      |      |                    |                    |                |              |           |                |                |                |                |
Table 3.
Correlation between baseline and 20 month follow-up creatinine-corrected concentrations (μg/g creatinine) of EDC biomarkers among SELF participants

| Biomarker                | N  | Baseline               | 20 month follow-up | Between follow-up ICC (95% CI) |
|--------------------------|----|------------------------|--------------------|-------------------------------|
|                          |    | Median     | 75th percentile | Median     | 75th percentile |                              |
| BPA                      | 565| 1.73       | 2.85            | 1.28       | 2.11            | 0.59 (0.53, 0.64)             |
| BPF                      | 553| 0.25       | 0.85            | 0.17       | 0.73            | -0.01 (-0.09, 0.08)           |
| BPS                      | 553| 0.31       | 0.64            | 0.36       | 0.70            | 0.04 (-0.04, 0.12)            |
| 2,4-dichlorophenol       | 565| 0.53       | 0.89            | 0.39       | 0.75            | 0.16 (0.07, 0.24)             |
| 2,5-dichlorophenol       | 565| 2.40       | 6.10            | 1.01       | 2.54            | 0.31 (0.23, 0.38)             |
| Benzophenone-3           | 565| 13.11      | 46.57           | 9.77       | 28.11           | 0.09 (0.01, 0.17)             |
| Triclocarban             | 553| 0.25       | 1.21            | 0.11       | 0.74            | 0.20 (0.12, 0.28)             |
| Triclosan                | 565| 6.65       | 25.38           | 6.41       | 27.26           | 0.15 (0.07, 0.23)             |
| Butyl paraben            | 565| 0.09       | 0.28            | 0.00       | 0.15            | 0.02 (-0.06, 0.10)            |
| Ethyl paraben            | 565| 2.43       | 8.40            | 2.11       | 10.66           | 0.16 (0.08, 0.24)             |
| Methyl paraben           | 565| 123.33     | 331.61          | 117.61     | 258.56          | 0.10 (0.02, 0.19)             |
| Propyl paraben           | 565| 17.27      | 50.21           | 13.65      | 44.82           | 0.36 (0.28, 0.43)             |
Table 4.

Percentage difference\(^1,2\) in creatinine-corrected bisphenol concentrations (μg/g creatinine) by baseline characteristics among SELF participants

| Characteristic                  | N  | %  | Unadj. pct. | Adj. pct. | Adj. 95% CI       | Adj. pct. | Adj. 95% CI       | BPA | BPF | BPS |
|--------------------------------|----|----|-------------|-----------|--------------------|-----------|--------------------|-----|-----|-----|
| **Age (yrs)**                  |    |    |             |           |                    |           |                    |     |     |     |
| 23–25                          | 184| 24.0| 4.2         | 7.8       | (−9.5, 28.4)       | −6.0      | (−41.1, 44.0)      |     |     |     |
| 26–28                          | 191| 24.9| 6.5         | 9.1       | (−7.7, 28.9)       | −33.7     | (−60.4, −6.5)      |     |     |     |
| 29–31                          | 204| 26.6| 3.3         | 1.9       | (−13.1, 19.4)      | −0.8      | (−42.8, 28.9)      |     |     |     |
| 32–35                          | 187| 24.4| 0.0         | 0.0       | Reference          | 0.0       | Reference          |     |     |     |
| **Season of urine collection** |    |    |             |           |                    |           |                    |     |     |     |
| Spring (March, April, May)     | 161| 21.0| −3.5        | −1.0      | (−17.3, 18.4)      | 51.0      | (−5.6, 132.7)      |     |     |     |
| Summer (June, July, August)    | 243| 31.7| 16.6        | 17.0      | (−0.7, 37.8)       | 94.3      | (26.7, 189.4)      |     |     |     |
| Autumn (September, October, November) | 224| 29.2| 7.0         | 6.9       | (−9.6, 26.3)       | 61.2      | (2.6, 142.8)       |     |     |     |
| Winter (December, January, February) | 138| 18.0| 0.0         | 0.0       | Reference          | 0.0       | Reference          |     |     |     |
| **Marital status**             |    |    |             |           |                    |           |                    |     |     |     |
| Never married                  | 439| 57.3| 0.0         | 0.0       | Reference          | 0.0       | Reference          |     |     |     |
| Currently married              | 217| 28.3| −0.1        | −1.0      | (−14.3, 14.3)      | 20.2      | (21.1, 64.2)       |     |     |     |
| Previously married             | 110| 14.4| 3.2         | 3.5       | (−12.6, 22.5)      | 20.3      | (−26.5, 75.4)      |     |     |     |
| **Education**                  |    |    |             |           |                    |           |                    |     |     |     |
| High school diploma/GED        | 163| 21.3| 0.0         | 0.0       | Reference          | 0.0       | Reference          |     |     |     |
| Some college/Associates/Technical | 393| 51.3| −12.6       | −9.0      | (−22.4, 6.6)       | −19.4     | (−47.8, 17.7)      |     |     |     |
| Bachelors degree               | 210| 27.4| −22.6       | −15.7     | (−31.7, 4.1)       | −38.6     | (−59.9, 17.4)      |     |     |     |
| **Household income**           |    |    |             |           |                    |           |                    |     |     |     |
| <$20,000                       | 351| 45.8| 0.0         | 0.0       | Reference          | 0.0       | Reference          |     |     |     |
| $20,000–$50,000                | 289| 37.7| −4.1        | 8.0       | (−6.0, 24.1)       | 14.0      | (−23.2, 56.5)      |     |     |     |
| >$50,000                       | 126| 16.5| −13.1       | 5.4       | (−13.3, 28.1)      | −28.2     | (−53.6, 25.3)      |     |     |     |
| **Smoking status**             |    |    |             |           |                    |           |                    |     |     |     |
| Never                          | 561| 73.2| 0.0         | 0.0       | Reference          | 0.0       | Reference          |     |     |     |
| Past                           | 60 | 7.8 | 22.3        | 16.7      | (−5.7, 44.5)       | −11.1     | (−50.4, 45.5)      |     |     |     |
| Current                        | 145| 18.9| 17.4        | 11.7      | (−5.5, 32.1)       | 12.9      | (−32.7, 59.1)      |     |     |     |
| Alcohol use within the last year|     |     |             |           |                    |           |                    |     |     |     |
| None                           | 217| 28.3| 0.0         | 0.0       | Reference          | 0.0       | Reference          |     |     |     |
| Characteristic | N   | %    | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95% CI | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95% CI | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95% CI |
|---------------|-----|------|-------------------|----------------|-------------|-------------------|----------------|-------------|-------------------|----------------|-------------|
| 1–5 drinks/day or ≥4 drinks once per month or less | 394 | 51.4 | −1.8             | 0.2            | (−12.5, 14.8) | −11.4            | −8.8          | (−35.5, 29.0) | 0.6               | 6.0            | (−13.2, 29.4) |
| 6 drinks/day or ≥4 drinks twice per month or more | 155 | 20.2 | 2.7              | −3.8           | (−18.8, 14.0) | 12.4             | 11.1          | (−27.9, 71.4) | 22.7              | 13.4           | (−11.7, 45.5) |
| Body mass index (kg/m²)                          |     |      |                   |                |             |                   |                |             |                   |                |             |
| <25.0        | 146 | 19.1 | 0.0              | 0.0            | Reference    | 0.0              | 0.0            | Reference    | 0.0              | 0.0            | Reference    |
| 25.0–29.9    | 160 | 20.9 | 15.0             | 15.6           | (−3.1, 38.0) | −3.2             | −15.2         | (−46.1, 33.2) | 20.9              | 21.6           | (−6.3, 57.8)  |
| 30.0–34.9    | 150 | 19.6 | 7.4              | 6.5            | (−11.4, 28.0) | 72.8             | 55.3          | (−2.8, 148.2) | 23.7              | 24.6           | (−4.9, 63.3)  |
| ≥35.0        | 310 | 40.5 | 23.1             | 19.8           | (19.4, 40.8) | 55.1             | 31.7          | (−129.9, 99.1) | 45.9              | 39.7           | (10.1, 77.3)  |
| Age at menarche                          |     |      |                   |                |             |                   |                |             |                   |                |             |
| ≤10          | 127 | 16.6 | −12.7            | −16.3          | (−29.8, −0.3) | 49.5             | 37.7          | (−119, 115.1) | −2.7              | −9.0           | (−29.7, 17.7) |
| 11           | 162 | 21.2 | −13.3            | −13.1          | (−26.1, 2.3) | −3.9             | −6.1          | (−37.9, 42.2) | −4.2              | −0.4           | (−21.6, 26.5) |
| 12           | 208 | 27.2 | 0.0              | 0.0            | Reference    | 0.0              | 0.0           | Reference    | 0.0              | 0.0            | Reference    |
| 13           | 132 | 17.2 | −15.1            | −13.7          | (−27.3, 2.4) | −46.6            | −43.8         | (−63.7, −12.8) | −4.3              | −3.9           | (−25.4, 23.7) |
| ≥14          | 137 | 17.9 | −17.0            | −16.6          | (−29.8, −0.9) | 10.8             | 15.0          | (−260, 78.5)  | −16.3             | −11.9          | (−31.7, 13.5) |
| Parity (births)                          |     |      |                   |                |             |                   |                |             |                   |                |             |
| 0            | 292 | 38.1 | 0.0              | 0.0            | Reference    | 0.0              | 0.0           | Reference    | 0.0              | 0.0            | Reference    |
| 1            | 208 | 27.2 | 6.2              | 6.7            | (−7.9, 23.6) | 22.9             | 15.3          | (−209, 68.0)  | 14.5              | 15.8           | (−6.8, 43.9)  |
| 2            | 130 | 17.0 | 9.4              | 5.2            | (−12.0, 25.7) | 53.1             | 31.9          | (−164, 108.2) | 39.4              | 37.5           | (5.7, 78.9)   |
| ≥3           | 136 | 17.8 | 21.0             | 17.5           | (−2.1, 41.1) | 7.0              | −12.2         | (−45.0, 40.2) | 45.8              | 40.8           | (7.5, 84.4)   |
| Sunscreen use                          |     |      |                   |                |             |                   |                |             |                   |                |             |
| Never/hardly ever                  | 575 | 75.1 | 0.0              | 0.0            | Reference    | 0.0              | 0.0           | Reference    | 0.0              | 0.0            | Reference    |
| Sometimes                               | 104 | 13.6 | −13.9            | −9.5           | (−23.6, 7.3) | 0.2              | 20.1          | (−22.4, 85.7) | −9.6              | 6.2            | (−17.4, 36.6) |
| Often/always                         | 87  | 11.4 | −9.6             | −3.1           | (−19.2, 16.1) | 28.4             | 35.4          | (−150, 115.7) | −9.3              | 4.7            | (−20.0, 36.9) |

1 Abbreviation: GED, General Educational Diploma
2 Unadj models are bivariate models with each correlate modeled separately. Adj. models are adjusted for all correlates.
Table 5.
Percentage difference in creatinine-corrected concentrations (μg/g creatinine) of select EDC biomarkers by baseline characteristics among SELF participants

| Characteristic                              | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI   | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI   |
|---------------------------------------------|-------------------|-----------------|--------------|-------------------|-----------------|--------------|
| Age (yrs)                                   |                   |                 |              |                   |                 |              |
| 23–25                                       | 1.29              | 1.08            | (−0.7, 3.1)  | 2.53              | 2.27            | (−1.3, 7.1)  |
| 26–28                                       | −0.04             | 1.3             | (−17.0, 23.8) | 3.0               | 24.5           | (−11.2, 74.6) |
| 29–31                                       | −5.9              | −6.1            | (−20.6, 16.0) | 4.1               | 5.1            | (−2.2, 16.2)  |
| 32–35                                       | 0                 | 0               | Reference    | 0                 | 0               | Reference    |
| Season of urine collection                   |                   |                 |              |                   |                 |              |
| Spring (March, April, May)                  | −6.5              | −5.3            | (−21.9, 14.0) | 2.47              | −20            | (−45.3, 13.8) |
| Summer (June, July, August)                 | 4                 | 5.8             | (−13.4, 26.0) | 10.7              | 14.4           | (−6.5, 35.6)  |
| Autumn (September, October, November)       | 1.9               | 5.3             | (−13.8, 26.0) | 6.2               | 8              | (−21.4, 40.9) |
| Winter (December, January, February)        | 0                 | 0               | Reference    | 0                 | 0               | Reference    |
| Marital status                              |                   |                 |              |                   |                 |              |
| Never married                               | 0                 | 0               | Reference    | 0                 | 0               | Reference    |
| Currently married                           | −12.5             | −12.3           | (−26.2, 4.1)  | −25               | −14.9          | (−53.7, 12.2) |
| Previously married                          | 2.1               | 3.7             | (−15.2, 26.0) | −19               | 14             | (−30.5, 23.8) |
| Education                                   |                   |                 |              |                   |                 |              |
| ≤High school/diploma/ED                     | 0                 | 0               | Reference    | 0                 | 0               | Reference    |
| Some college/Associate/Technical            | 26.7              | 20.8            | (−81.4, 66.0) | −0.9              | 14.1           | (−15.9, 34.4) |
| <Bachelors degree                           | 21.2              | 6.6             | (−17.3, 37.0) | −11.5             | 6.4            | (−28.9, 5.9)  |
| Household income                            |                   |                 |              |                   |                 |              |
| <$20,000                                    | 0                 | 0               | Reference    | 0                 | 0               | Reference    |
| ≥$20,000–$50,000                            | 12.1              | 12.6            | (−46.3, 32.9) | −14.5             | −6.5           | (−26.8, 22.1) |
| >$50,000                                    | 15.7              | 18.7            | (−61.4, 40.9) | −25.2             | −16.2          | (−42.5, 21.9) |
| Smoking status                              |                   |                 |              |                   |                 |              |
| Never                                       | 0                 | 0               | Reference    | 0                 | 0               | Reference    |
| Past                                        | 15.8              | 27.6            | (−1.2, 68.6)  | 36.9              | 36.9           | (−6.1, 106.1) |
| Current                                     | −14.6             | −14.4           | (−21.7, 16.0) | 1.64              | 14.8           | (−16.8, 35.6) |
| Alcohol use within the last year            |                   |                 |              |                   |                 |              |
| None                                        | 0                 | 0               | Reference    | 0                 | 0               | Reference    |
| 1–5 drinks/day or 1–4 drinks once per month | −8.8              | −15.2           | (−27.9, 6.2)  | −14               | −19.7          | (−30.1, 1.2)  |
| 5–9 drinks/day or 5–14 drinks twice per month | −8.8            | −10.5           | (−20.9, 9.6)  | 8.8               | −5.1           | (−31.5, 3.3)  |

Body mass index (kg/m²)
| Characteristic | 2,4-dichlorophenol | 2,5-dichlorophenol | Benzophenone-3 | Triclocarban | Triclosan |
|----------------|--------------------|--------------------|----------------|--------------|----------|
| **Unadj. pct. diff.** | 0 | 2.5 (−17.0, 26.7) | 7.1 (−18.2, 61.5) | 4.9 (−31.8, 39.5) | 28 (−10.9, 106.5) |
| **Adj. pct. diff.** | 0 | 0 | 2.5 (−15.2, 78.2) | 21.4 (−12.4, 60.4) | 20.9 (−12.0, 63.4) |
| **Adj. 95 CI** | 0 | (−16.6, 22.5) | (−16.6, 55.3) | (−12.4, 60.4) | (−12.0, 63.4) |
| **Unadj. pct. diff.** | 0 | 0 | Reference | Reference | Reference |
| **Adj. pct. diff.** | 0 | 0 | Reference | Reference | Reference |
| **Adj. 95 CI** | 0 | Reference | Reference | Reference | Reference |

**Age at menarche**

| Age | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI |
|-----|------------------|----------------|----------|------------------|----------------|----------|
| <25.0 | −1.1 | 2.5 | (−17.0, 26.7) | 7.1 | 149 | (−18.2, 61.5) |
| 25.0–29.9 | 0 | 0 | Reference | 4.9 | 2.5 | (−15.2, 78.2) |
| ≥35.0 | −7 | 1 | (−16.6, 22.5) | 8 | 21.4 | (−12.4, 60.4) |

**Parity (births)**

| Parity (births) | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI |
|----------------|------------------|----------------|----------|------------------|----------------|----------|
| 0 | 0 | 0 | Reference | 0 | 0 | Reference |
| 1 | −16.3 | −4 | (−26.2, 4.8) | 147 | −4.6 | (−29.4, 24.1) |
| 2 | −17 | −11.3 | (−28.3, 9.9) | 261 | −22 | (−366, 59) |
| ≥3 | −24.8 | −17.9 | (−54.2, 2.2) | −14 | −5.2 | (−53.2, 34.7) |

**Sunscreen use**

| Sunscreen use | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95 CI |
|---------------|------------------|----------------|----------|------------------|----------------|----------|
| Never/hardly ever | 0 | 0 | Reference | 0 | 0 | Reference |
| Sometimes | 14.1 | 81 | (−117, 32.4) | 6 | 154 | (−46.7, 59.9) |
| Occasionally | 10.9 | 71 | (−157, 33.0) | 243 | 41.7 | (010, 100.8) |

Unadj models are bivariate models with each correlate modeled separately. Adj. models are adjusted for all correlates.

Unadj. pct. diff. are unadjusted percent differences. Adj. pct. diff. are adjusted percent differences.
Table 6. Percentage difference in creatinine-corrected paraben concentrations (μg/g creatinine) by baseline characteristics among SELF participants

| Characteristic                        | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95% CI   | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95% CI   | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95% CI   | Unadj. pct. diff. | Adj. pct. diff. | Adj. 95% CI   |
|--------------------------------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-----------------|
| **Age (yrs)**                        |                   |                 |               |                   |                 |               |                   |                 |               |                   |                 |               |                 |
| 23–25                                | −27.8             | −17.7           | (−41.7, 16.2) | −18.5             | −12.6           | (−41.5, 30.8) | −11.9             | −9.8            | (−33.9, 23.2) | −6.9             | −3.0            | (−30.3, 35.1) |
| 26–28                                | −24.9             | −13.4           | (−37.7, 20.4) | −9.9              | −2.4            | (−33.5, 43.3) | −8.9              | −6.4            | (−30.4, 25.9) | −1.1             | −9.9            | (−34.3, 23.5) |
| 29–31                                | −29.5             | −21.6           | (−42.7, 7.2)  | −12.0             | −13.6           | (−40.0, 24.4) | −14.1             | −9.6            | (−31.8, 19.9) | −7.8             | −4.2            | (−20.0, 29.2) |
| 32–35                                | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     |
| **Season of urine collection**       |                   |                 |               |                   |                 |               |                   |                 |               |                   |                 |               |                 |
| Spring (March, April, May)           | −9.1              | −12.2           | (−38.3, 24.9) | −21.8             | −18.7           | (−46.1, 22.7) | −3.0              | −4.7            | (−30.7, 22.9) | 17.0             | 14.6            | (−18.2, 46.6) |
| Summer (June, July, August)          | 33.8              | 30.3            | (−56.7, 9.8)  | 17.9              | 22.0            | (−16.3, 77.7) | −3.5              | −5.3            | (−29.2, 26.7) | 23.2             | 20.4            | (−11.6, 63.9) |
| Autumn (September, October, November)| −5.3              | −5.0            | (−13.7, 32.3) | −12.5             | −11.0           | (−39.5, 30.7) | −28.4             | −27.3           | (−46.0, −2.2) | −8.8             | −7.1            | (−32.3, 23.4) |
| Winter (December, January, February) | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     |
| **Marital status**                  |                   |                 |               |                   |                 |               |                   |                 |               |                   |                 |               |                 |
| Never married                        | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     |
| Currently married                    | 17.2              | 3.0             | (−22.4, 36.8) | −24.6             | −25.7           | (−46.6, 3.4)  | −8.1              | −14.2           | (−33.5, 10.8) | −10.2             | −17.7           | (−37.2, 8.0)  |
| Previously married                   | 31.3              | 25.7            | (−58.8, 75.4) | 14.6              | 11.3            | (−24.5, 64.1) | 23.2              | 16.4            | (−43.8, 57.1) | 15.6             | 9.3             | (−20.5, 50.4) |
| **Education**                        |                   |                 |               |                   |                 |               |                   |                 |               |                   |                 |               |                 |
| ≤High school diploma/GED            | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     |
| Some college/Associate/Technical     | 41.6              | 10.9            | (−18.9, 91.6) | −24.1             | −23.1           | (−46.6, 10.8) | 61.8              | 51.4            | (14.2, 190.8) | 55.8             | 39.1            | (1.1, 87.7)   |
| ≥Bachelors degree                   | 136.3             | 37.9            | (−85.1, 108.6) | 0.2               | 4.9             | (−35.3, 70.1) | 89.6              | 68.1            | (157.1, 144.2) | 85.6             | 50.6            | (1.3, 124.0)  |
| **Household income**                |                   |                 |               |                   |                 |               |                   |                 |               |                   |                 |               |                 |
| <$20,000                             | 35.6              | 9.1             | (−17.0, 45.4) | −6.1              | −7.1            | (−32.5, 27.8) | 20.0              | −2.2            | (−23.6, 25.1) | 20.6             | −2.1            | (−24.7, 27.2) |
| ≥$50,000                            | 126.6             | 48.7            | (1.3, 118.2)  | 12.5              | 2.3             | (−34.6, 60.1) | 25.4              | −11.2           | (−37.2, 25.5) | 36.7             | −0.1            | (−30.8, 44.2) |
| **Smoking status**                  |                   |                 |               |                   |                 |               |                   |                 |               |                   |                 |               |                 |
| Never                                | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     |
| Past                                 | 9.2               | 36.4            | (−10.4, 107.5) | −6.3              | −6.9            | (−42.9, 52.0) | −29.2             | −23.5           | (−47.6, 11.8) | −34.7             | −29.2           | (−52.7, 5.8)  |
| Current                              | −39.9             | −14.2           | (−38.3, 19.4) | 16.7              | 1.9             | (−30.7, 49.7) | −27.9             | −10.8           | (−33.8, 20.1) | −33.4             | −16.3           | (−39.0, 14.9) |
| Alcohol use within the last year    |                   |                 |               |                   |                 |               |                   |                 |               |                   |                 |               |                 |
| None                                 | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     | 0.0               | 0.0             | Reference     |
| 1–5 drinks/day or ≥8 drinks once per month or less | 7.5               | −4.8            | (−27.1, 24.4) | 33.1              | 20.5            | (−5.2, 36.9)  | 8.5               | −0.6            | (−21.9, 26.5) | 18.5             | 9.7             | (−15.1, 41.7) |
| Characteristic | Butyl paraben | Ethyl paraben | Methyl paraben | Propyl paraben |
|----------------|---------------|---------------|----------------|----------------|
| ≥6 drinks/day or ≥4 drinks twice per month or more | −17.0 | −8.6 (−34.5, 27.7) | 127.1 | 125.3 (−18.4, 249.0) | 0.6 | 7.2 (−22.2, 47.5) |
| Body mass index (kg/m$^2$) | | | | | | |
| <25.0 | 0.0 | 0.0 | Reference | 0.0 | 0.0 | Reference | 0.0 | 0.0 | Reference |
| 25.0–29.9 | 2.4 | −2.1 (−30.9, 38.8) | −16.7 | −18.5 (−45.8, 22.4) | −20.2 | −19.6 (−41.3, 10.1) | −1.0 | −1.4 (−29.4, 37.7) |
| 30.0–34.9 | 1.0 | −4.4 (−30.4, 37.2) | 6.6 | 9.8 (−20.0, 76.5) | −6.5 | 2.0 (−26.4, 41.4) | 1.6 | 8.1 (−23.5, 52.9) |
| ≥35.0 | −34.9 | −30.6 (−49.6, −4.6) | −28.2 | −23.9 (−47.6, 10.3) | −38.8 | −30.7 (−48.0, −7.7) | −22.1 | −12.2 (−35.5, 19.1) |
| Age at menarche | | | | | | |
| ≤10 | −9.0 | 12.8 (−20.2, 39.3) | −5.7 | 10.5 (−26.2, 65.4) | −17.7 | −6.4 (−31.5, 27.8) | −10.3 | −3.4 (−30.7, 34.5) |
| 11 | −3.2 | 5.1 (−23.7, 44.8) | −0.4 | 1.9 (−29.9, 48.1) | −4.9 | −6.6 (−30.1, 24.6) | 4.9 | 3.2 (−24.1, 40.3) |
| 12 | 0.0 | 0 | Reference | 0.0 | 0 | Reference | 0.0 | 0 | Reference |
| 13 | 16.9 | 23.9 (−11.6, 73.6) | 17.0 | 16.3 (−21.6, 72.5) | 0.5 | −1.2 (−27.2, 33.9) | −2.6 | −1.9 (−29.0, 35.6) |
| ≥14 | −21.0 | −1.5 (−38.3, 21.4) | 23.6 | 22.1 (−17.8, 81.2) | 1.34 | 10.8 (−18.3, 50.4) | 12.5 | 13.2 (−18.2, 56.5) |
| Parity (births) | | | | | | |
| 0 | 0.0 | 0 | Reference | 0.0 | 0 | Reference | 0.0 | 0 | Reference |
| 1 | −17.1 | −10.7 (−33.2, 19.2) | 47.6 | 59.0 (13.5, 121.9) | 13.3 | 18.2 (−8.9, 53.4) | 10.2 | 18.5 (−10.2, 56.4) |
| ≥2 | −11.7 | −2.0 (−31.0, 39.7) | −9.0 | 8.9 (−27.8, 64.4) | −5.4 | −6.0 (−31.5, 29.1) | −21.6 | −8.9 (−34.9, 27.6) |
| ≥3 | −29.0 | −20.6 (−44.6, 13.8) | 3.3 | 20.3 (−21.0, 83.1) | −17.7 | −11.1 (−28.5, 36.9) | −48.5 | 1.4 (−28.2, 43.1) |
| Sunscreen use | | | | | | |
| Never/hardly ever | 0.0 | 0 | Reference | 0.0 | 0 | Reference | 0.0 | 0 | Reference |
| Sometimes | 61.6 | 29.9 (−20.8, 114.1) | 46.2 | 51.9 (29.2, 124.3) | 44.9 | 28.6 (−4.8, 73.8) | 41.5 | 29.7 (−5.8, 78.6) |
| Often/always | 63.4 | 29.6 (−9.3, 85.3) | 36.1 | 38.7 (−9.6, 110.5) | 22.7 | 7.5 (−22.1, 48.4) | 35.9 | 16.8 (−17.0, 64.5) |

Unadj models are bivariate models with each correlate modeled separately. Adj. models are adjusted for all correlates.