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An Analysis of the Effects of Lifestyle Factors and Positive Marijuana Drug Screen upon Maternal Phthalate Exposure

By

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Bachelors of Science
University of Georgia
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Abstract

An Analysis of the Effects of Lifestyle Factors and Positive Marijuana Drug Screen upon Maternal Phthalate Exposure

By

Natalie Duke

Introduction: Phthalates are a ubiquitous environmental exposure in the United States. Maternal exposure to these compounds have been previously stated to cause adverse health effects to developing children. African American women have historically been faced with environmental injustice and may have higher prevalence of this exposure. The aim of this study is to explore the nature of the relationship between maternal phthalate exposure, positive marijuana drug screens along with other lifestyle factors present in an Atlanta, Georgia cohort of pregnant African American women through analysis of maternal urine.

Methods: Pregnant African American women were recruited at Emory University Hospital, Emory University Hospital Midtown, and Grady Memorial Hospital during the eight to fourteenth week of pregnancy. All participants provided written informed consent in accordance with the requirements of the Institutional Review Board of Emory University. Each participant was given a self-administered survey that inquired about lifestyle factors, previous health history and concerns. A spot maternal urine sample was collected from each of the study participants. This urine sample was then analyzed with high performance liquid chromatography and tandem mass spectrometry. Each sample had proper quality control methods to control for error. Correlations were assessed between covariates, and then each covariate was assessed for an association with phthalate concentrations at the bivariate level. Multivariable linear models were used to investigate the relationship of each phthalate concentration to each covariate controlled for all others.

Results: Low maternal income was positively correlated with a positive urine drug screen (P=0.01). Condom usage during vaginal intercourse was a significant predictor of MiBP concentration at the bivariate level and the full adjusted model (P=0.01). Vitamin usage was also found to be a significant predictor for MECPP (P=0.01), MEHHP (P=0.01), MEOHP (P= 0.02), and MEHP (0.01). Maternal BMI was a significant predictor for MEP (P=0.05) concentration in the fully adjusted model. Maternal income was also a significant predictor of MBZP concentration (P=0.04) in the bivariate analysis and marginally significant in the fully adjusted analysis (P=0.09).

Conclusion: There are significant relationships between maternal phthalate levels and certain covariates, many of which represent environmental justice concerns. Positive marijuana urine drug screens are correlated to other covariates that are significant predictors for phthalate concentration, which implies a complicated relationship and a need for additional research to understand the true effects. Phthalate exposure has implications in child health and associations between covariates must be explored to fully understand its effects.

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Introduction

Maternal exposures to environmental chemicals affects the quality of life for the mother and her offspring with potentially long-term adverse effects upon infant and child health. Phthalates were first introduced into the manufacturing process in the United States in the 1920s and are a prominent chemical exposure because of their widespread use as a plasticizer in the manufacturing process of poly-vinyl chloride (PVC) plastics and as solvents in industrial production (Barceló, 2012) (Heudorf, Mersch-Sundermann, & Angerer, 2007) (Schettler, 2006). Phthalates allow plastic products to be soft and malleable (Schettler, 2006). Due to their ubiquitous use in the plastics industry, phthalates are commonly found in PVC coated products, hair care products, makeup products, hospital tubing and condoms (M. J. Silva et al., 2004) (Kambia et al., 2001) (Lambert et al., 2013). Their wide use in society and potential for harm defines a great need to identify potential exposure routes and associated health effects.

It is commonly thought that African American women are more frequently exposed to phthalates due to cultural differences in product usage, as well as disparities in their exposure potential and knowledge of sources of exposure and health consequence. Prior studies have shown African American women to have a higher mean concentration of urinary phthalate metabolites (M. J. Silva et al., 2004) in comparison to Non-Hispanic Whites and Mexican Americans. These differences may be attributed to a higher incidence of usage of certain personal care products such as perfumes and certain hair care products (N'Dri, White-Newsome, Corbin-Mark, & Shepard, 2015). Furthermore, socioeconomic factors such as income or education may modify an individual's risk for increased phthalate exposure due to the increased amount of environmental exposures

that socioeconomically disadvantaged individuals face. Income is an important factor in the environmental plight of African American women due to increased poverty levels (Brah & Phoenix, 2013) leading to reduced access to safer products. In addition, African American women oftentimes live closer to areas where phthalates are being used in manufacturing processes (Jones & Jacques, 2014). Together these socioeconomic and cultural factors may play an important role in the disparities of exposure observed in the African American community.

Phthalates are commonly formed from oxidation of benzene derivatives (Reim, Lubbe, & Langer, 2006), produced by reacting phthalate anhydrides and alcohols in esterification reactions (Ellington, Park, & Brennecke, 1994). Phthalates are commonly divided into categories based on molecular weight. Low molecular weight phthalates such as diethyl phthalate (DEP) and dibenzyl phthalate (DPB) are commonly used in personal care products (Gomez-Hens & Aguilar-Caballos, 2003). High molecular weight phthalates such as di(2-ethylhexly) phthalate (DEHP) are commonly used as plasticizers in industrial production of PVCs and other types of plastic compounds (Gomez-Hens & Aguilar-Caballos, 2003). The high lipophilic properties and the fact that they are generally not chemically bound to compounds in products where they are found allows phthalates to leach out into the environment (Schettler, 2006).

Phthalate esters enter the body and are metabolized to the corresponding monoester after undergoing biotransformation processes. Initially, esterases and lipases will cleave the parent compound into a hydrolytic monoester that corresponds to its parent compound (Meeker, Calafat, & Hauser, 2012). Furthermore, phase I biotransformation will allow monoesters to be further metabolized and potentially

oxidized depending upon the side chain that is present for the compound (Du Yeon Bang & Lee, 2011). Phase II biotransformation will allow phthalates to be further metabolized by reacting with glucuronic acid which increases the water solubility of the phthalate metabolite (Du Yeon Bang & Lee, 2011). This increased solubility will allow the metabolite to be expelled from the body through urine.

Phthalates have been found in soil and in runoff in Western countries (Przybylińska & Wyszkowski, 2016), and have contributed to concerns about phthalate exposure through agricultural products. These concerns originate from vegetation uptake of environmental pollutants. There is evidence that phthalates have the ability to enter a plant's root system and enter above ground portions of plants (Saeidnia & Abdollahi, 2013). Not only would this effect plants used as food sources but also those consumed through smoking, such as tobacco or marijuana. Unfortunately, phthalate concentrations of marijuana plants have been difficult to quantify due to the commonly illicit nature of production. Given the growing recreational use of marijuana, including in pregnant women, and the changes in laws regarding use and distribution, this may be a growing area of concern for environmental toxicant exposure.

Phthalate compounds are highly lipophilic, which makes these compounds a particular concern to women who have more body fat. Previous studies have correlated phthalate exposure to obesity; however, there is still a need to investigate causality (Latini, 2005). In previous rat models, there have been some associations between adipose tissue concentrations of phthalates and insulin resistance (Latini, 2005). In previous studies, there have been associations between exposure to MnBP, MiBP, MBzP,

MCPP, and DEHP the development of insulin resistance after attenuation for BMI (James-Todd et al., 2012).

Previous studies have indicated that some individuals are exposed to phthalates via orally received medications, as low molecular weight phthalates are sometimes used to plasticize the coatings of pills (Hernández-Díaz et al., 2013). These studies indicated that the number of times an individual has consumed the pill is an important contributor to the body load of phthalates (Hernández-Díaz et al., 2013).

Phthalates are commonly used as plasticizers in the industrial processes of making condoms (Jayawardena, Godakumbura, & Prashantha, 2016). Additionally, in industrially produced latex products, phthalates have been found to be mobile, thereby allowing an additional route of exposure (Jayawardena et al., 2016). Of additional note, colorants present in the condom may also contain phthalates due to the use of these chemicals in the industrial setting of colorant production (Motsoane, Bester, Pretorius, & Becker, 2003).

Phthalates are able to effect developmental health outcomes due to their activity as endocrine disruptors. Animal studies have shown that phthalates have endocrine disrupting capabilities (Sen, Liu, & Craig, 2015). Some studies have shown that this class of compounds has both anti-androgenic and estrogenic properties (Ferguson, McElrath, Cantonwine, Mukherjee, & Meeker, 2015). For example, in rodent studies that DEHP can alter sexual differentiation in male rats due to disruption of androgens (Abdel-Maksoud, Leasor, Butzen, Braden, & Akingbemi, 2015). Previous studies that were conducted in a diverse cohort of pregnant women have shown significant associations between maternal phthalate exposure and 8-hydroxydeoxyguanosine and 8-isoprostane

(which are urinary biomarkers of oxidative stress) (Ferguson, McElrath, Chen, Mukherjee, & Meeker, 2014). Furthermore, in previous studies, elevated maternal urinary phthalates have been linked to preeclampsia and preterm birth (Prins, Gomez-Lopez, & Robertson, 2012). In women of reproductive age, there has been evidence that high concentrations of DEHP are prevalent in women with endometriosis (Cobellis et al., 2003). Phthalate exposure during pregnancy may also play a role in free T_4 levels as shown in previous cross-sectional analysis (Johns, Ferguson, McElrath, Mukherjee, & Meeker, 2016).

Phthalate exposure can adversely impact human health and can likely contribute to the burden of disease among pregnant women. Phthalates are pervasive throughout the environment, and have the potential to act adversely towards children's health. Because of the increased cultural acceptance and incidence of marijuana use, it is important to provide a proper assessment of the potential for phthalate contamination through the assessment of urinary metabolites. Furthermore, other lifestyle factors will be considered in this fully adjusted analysis. Ultimately, the associations between phthalate exposure and marijuana usage with the inclusion of lifestyle factors will be quantified using bivariate and multivariate analysis.

Methods

I. Subjects

This study examined the relationships of phthalate urinary metabolites to lifestyle factors among a cohort of forty-eight African American (American-borne) pregnant women**.** These women were recruited from Emory University Hospital-Midtown, Emory University Hospital or Grady Hospital as a part of the Center for Children's Health,

the Environment, the Microbiome, and Metabolomics (C-CHEM^2) at Emory University which employs a longitudinal cohort study to investigate prenatal and postnatal environmental exposures and their effects upon pregnancy and child health outcomes.

All women recruited into the larger study were African American (American Borne) women between 18-40 years old and were without chronic medical problems. The women recruited into the study were between 8 – 14 weeks' gestation. Additionally, each one of these women had four or fewer prior live or still-borne deliveries. Prior history of chronic illness, chronic medication usage, and history of incompetent cervix were criteria for exclusion from this study. All participants provided written informed consent in accordance with the requirements of the Institutional Review Board (IRB) of Emory University.

II. Measures

The study participants completed self-administered structured surveys regarding prenatal health and other lifestyle factors based on validated clinical instruments and measures. As part of routine prenatal care, urine drug screens were conducted for all study participants, results were obtained and validated from the review of medical records. Spot urine samples were collected from study participants during maternal prenatal visits scheduled for the study participants for phthalate quantification.

The urinary aliquots were collected and labeled with ^{13}C analogues of the target phthalate metabolites (Barr, 2017). These aliquots were mixed with β-glucuronidase in 1 mM ammonium acetate and incubated overnight at 37° C (Barr, 2017). Sodium phosphate was used to terminate enzyme activity. Furthermore, the aliquots were loaded onto preconditioned ABS Elut-NEXUS mixed mode polymeric solid phase extraction (SPE) cartridges (Agilent, Santa Clara, CA) (Barr, 2017). After the cartridges were

eluted with acetonitrile, the cartridges were dried and returned to the vials after being re-suspended in 0.1 % acetic acid solution. High performance liquid chromatography on a Betasil Phenyl column (3µ 150 x 2.1 mm, Thermo Scientific, San Jose, CA) was used to separate the extracts; subsequently, tandem mass spectrometry on an Agilent 6460 triple quadrupole mass spectrometer (Agilent, Santa Clara, CA) was used to analyze the extracts (Barr, 2017). To ensure proper quality assurance, each sample was run with two quality control materials (that fell between two standard deviations of the mean expected concentrations), one urine and one reagent blank along with a full calibration set (0.1 ng/mL to 400 ng/mL) (Barr, 2017). For the measurement to be considered valid, each of the target analytes had to coelute with the analog with the correct retention times. Additionally, each of the target analytes had to have the quantification and confirmation ion transitions to be considered valid (Barr, 2017).

III. Analysis Methods

The primary analysis of this study was to examine marijuana as a potential risk factor for phthalate exposure while also considering other sources of exposure, potential confounders.. Phthalate concentration values that were below the limit of detection were imputed by dividing the functional sensitivity for each respective phthalate metabolite by the square root of 2. Proc Standard was used to normalize the distribution of the data. Simple linear regression methods were used to analyze each continuous and two level categorical covariate and phthalate concentrations. A 95 % confidence interval and beta coefficient were generated with each simple linear regression. Correlation tests were used to analyze the correlation between each continuous variable.

A multivariate linear regression model was then generated with each dependent variable (phthalate metabolite) and all independent variables assessed in the bivariate analyses. Continuous covariates that were used include maternal age, and maternal body mass index (BMI) as determined by measured height and weight at the first prenatal visit between 8-14 weeks' gestation. Categorical covariates that were used include income level, condom usage, alcohol usage, tobacco usage, maternal educational attainment, all oral over the counter and prescription medication, and vitamin usage.

The overall F test was used to analyze the overall outcome. The significance of the t test was used to measure the marginal significance of the predictor within the model. All statistical procedures were conducted using SAS 9.4. An alpha level of 0.05 was considered statistically significant.

Results

Descriptive statistics of the cohort examined are provided in Table 2. The overall mean age of the women in the study was 25 years old. The overall mean BMI at the first prenatal visit was 29.10 kg/m^2. This is a socioeconomically diverse cohort, with 38% of women in the study reporting an income below 100% of the federal poverty line. Only 10 % of the pregnant women reported condom use during the month proceeding the survey. Additionally, 12 % of study participants reported tobacco usage and alcohol usage was present among 6 % of study participants. Most the study participants had not attended education higher than high school (62 %). Approximately 42% of study participants reported use of oral over the counter/ prescription medications, and 21% % of study participants reported usage of non-oral over the counter/ prescription pharmaceuticals. Additionally, 35 % of women self-reported the use of vitamins during pregnancy.

The relationship between the covariates is shown in Table 3. It was determined that maternal BMI at the first prenatal visit was negatively correlated with the presence of marijuana in the urine drug screen (P=0.02), all oral over the counter and prescription medications (P=0.01), and all other over the counter and prescription medications (P=0.05). Maternal education level was found to be negatively correlated with vitamin usage (P=0.04). Tobacco usage was found to be positively correlated with alcohol consumption (P<.0001). Low maternal income level was found to be positively correlated with a positive marijuana urine drug screen (P=0.01) and negatively correlated with vitamin usage (P=0.04). All oral over the counter and prescription medications was found to be positively correlated with all other over the counter and prescription medications (P=0.01) and vitamin usage (P=0.02).

Bivariate analysis was conducted for each compound and covariate and summarized in Tables 4,5,6, 7. We also observed a significant increase in the concentration of MBZP with lower income (P=0.04) (Table 4). There was a small but significant increase in MiBP concentration with condom use during vaginal intercourse (P=0.01) (Table 5). Increasing maternal age was associated with a significant increase in MEHHP concentration (P=0.04) (Table 6). All other relationships were shown to be insignificant at the bivariate level of analysis (*$P>0.05$).*

A regression including all potential covariates was created for each of the phthalate exposure measures in table 8, 9, 10, 11. Maternal BMI (P=0.07), over the counter and oral prescription medications usage (P=0.10) were marginally significant predictors of exposure to MBP (Table 8). Income level (P=0.09) and all oral over the counter and prescription medications (P=0.09) are marginally significant predictors of

MBZP concentration (Table 8). Maternal age (P=0.05) and Maternal BMI (P=0.05) were significantly associated with MEP concentration (Table 9). Condom usage (P= 0.01) was determined to be a significant predictor for MIBP concentration (Table 9). Vitamin use (P=0.01) was shown to be significant predictor of MECPP urinary metabolite concentration, while low income level (P= 0.09) and Maternal BMI (P= 0.1) were found to be marginally significant predictors of MECPP concentration (Table 10). Alcohol use (P= 0.02) and vitamin use (P=0.01) were both significantly associated with MEHPP concentration, while age (P=0.09), maternal BMI (P=0.08), and low maternal income were shown to be marginal predictors of MEHPP concentration (Table 10). Low maternal income (P=0.02) and vitamin usage (P=0.01) were significant predictors of MEHP concentration, with condom use (P= 0.06) and alcohol use (P=0.09) are demonstrating a marginal association with MEHP concentration (Table 11). Alcohol use (P=0.04) and vitamin use (P=0.02) were significantly associated with MEOHP concentration, while maternal BMI (P=0.08) and low income level (P=0.06) are marginally significant predictors of MEOHP concentration (Table 11).

Discussion

Maternal BMI was found to be a marginally significant predictor of MBP urinary phthalate concentration. Di-n-butyl phthalate (DBP**)** which is the parent compound to MBP, has been previously associated with lower birth weights in women that experience environmental exposure to this compound (Hinckley, Bachand, & Reif, 2005). Maternal MBP concentration has also been previously associated with anti-androgenic effects (Sen et al., 2015). Furthermore, the relationship of maternal BMI and MBP concentration

necessitates inquiry concerning the use of personal care products due to the potential for increased dermal exposure due to increased body mass (Hatch et al., 2008).

Benzyl butyl phthalate (BzBP) is the parent compound of monobenzyl phthalate (MBzP) (CDC, 2016). This compound was found to be marginally associated with income level **(**P=0.09**)** and usage of oral pharmaceuticals (P=0.09**).** Additionally, previous studies have found that individuals who are at a lower socioeconomic status are more frequently exposed to phthalates and it is likely a factor in environmental injustice (Adamkiewicz et al., 2011). The beta effect estimate **(**β =-0.31**)** of oral pharmaceuticals implies that there is a negative trajectory for the concentration of MBZP even after increasing usage of these products. However, previous studies have suggested that there is likely some type of interaction with income level and prescription drug use where individuals with lower incomes tend to not be able to afford medications (Bloch, Rozmovits, & Giambrone, 2011).

In the univariate analysis of MBZP, a positive urine drug screen (P=0.07**)** was shown to be a marginally significant predictor of exposure. However, this effect was not seen in the multivariate analysis. This could potentially be explained by the significant correlation between a positive urine drug screen and having an income below 100 % of the federal poverty line (P=0.01), and confounding of the relationship. This is consistent with previously collected data which indicates that individuals that have been exposed to poverty are at a greater risk of drug use (Gilliard-Matthews, Stevens, & Medina, 2016), and suggests a complicated relationship between these risk factors and this exposure.

Diethyl phthalate (DEP) is the parent compound to monoethyl phthalate (Hatch, Nelson, Stahlhut, & Webster, 2010). Maternal age (P=0.05) and BMI (0.05) were found

to be significant predictors of metabolite concentrations. As maternal age increases, the concentration of maternal MEP metabolites are expected to increase. Maternal age is an important factor in the exposure of MEP due to likely associated increases in usage of certain products; however, this would call for additional research (M. J. Silva et al., 2004). Maternal BMI is an important predictor of MEP; however, it is surprising that the beta coefficient for this compound is negative because it implies that individuals with higher BMIs will have lower concentrations of DEP.

Condom use during vaginal sex was found to be a significant predictor of MiBP phthalate concentration for both bivariate (P=0.01**)** and fully adjusted analysis (P=0.01). Di-isobutyl phthalate (DiBP) is the parent compound of MiBP. It is not surprising that condom use would be a significant predictor of MiBP metabolite concentration due to its usage in industrially produced latex products (Jayawardena et al., 2016). DiBP is a highly lipophilic compound that has been implicated in the contamination of dairy products and breast milk (Wu et al., 2015) (Kim et al., 2015). Condom usage is likely an important source of exposure due to the potential for dermal exposure to DiBP (Koniecki, Wang, Moody, & Zhu, 2011). Exposure to this compound likely has important implications for prenatal development due to its potential ability to impact sexual differentiation during early development due to endocrine disruption (Furr, Lambright, Wilson, Foster, & Gray, 2014).

MECPP exposure was marginally associated with maternal BMI (P=0.10), income level (P=0.09), and vitamin usage (P=0.01)**.** Historically, income has been linked to higher levels of environmental exposure and it likely contributes to an increased burden of disease in lower income communities (Evans & Kantrowitz, 2002). This

association was also demonstrated in MEHHP **(**P=0.08**)** and MEOHP concentrations (P=0.08**)**. Additionally, maternal BMI is likely associated with this compound due to the lipophilicity of high molecular weight phthalates. This marginal association was also seen in MEHHP (P=0.07) and MEOHP (P=0.08).

Alcohol consumption has been shown to be a significant predictor of MEHHP (P=0.02) and MEOHP concentrations (P= 0.04). It is also a marginal predictor of MEHP concentrations (P=0.08). DEHP is the parent compound of MEHHP, MEOHP, and MEHP. Furthermore, DEHP has been previously associated with the improper storage of alcoholic beverages in plastic containers (M. Silva et al., 2006) (Jurica et al., 2016). Exposure to this compound is detrimental to human health because it has the potential to alter the normal circulation of thyroid hormone (Johns et al., 2016).

MECPP (P=0.01), MEHHP (P=0.01), MEHP (P=0.01), and MEOHP (P=0.02) are all significantly associated with vitamin usage. However, the beta effects for each of these compounds are negative (see table 10 and 11). This effect implies that individuals who do not take prenatal vitamins tend to be more exposed to phthalates. This result may be indicative of the low socioeconomic status of the research participants which could potentially influence nutrition and contact with certain consumer products that might be heavily contaminated with phthalates (Parlett, Calafat, & Swan, 2013).

This study is a useful preliminary study of maternal exposure to phthalates, providing a baseline assessment to allow for improved targeting of future studies. Expansion of this study would provide the needed statistical power and precision to better pinpoint sources of exposure, based on the preliminary results reported here.

A particular weakness of this study is the usage of spot urine analysis rather than first morning urine for measuring phthalate concentrations. This is an important issue because phthalates have a short half-life that occur between a few hours up to a few days (Casas et al., 2016). Additionally, this study had some issues with a small sample size and can be remedied by having more individuals included in the analysis at a later stage of the study.

Future studies should include examinations of the use of personal care products such as lotion, makeup and hair care products due to the usage of low molecular weight phthalates in the products (Parlett et al., 2013). Future studies should also include testing across different brands of products that are potentially associated with phthalate exposure. Furthermore, it would be useful to obtain first morning urine to get an improved analysis of phthalates by capturing the metabolite before it has an opportunity to succumb to its half-life. It may also be beneficial for future studies to include body size measurements in regards to area in square centimeters to calculate the risk of dermal exposure.

Public Health Message

Phthalate exposure is ubiquitous throughout the United States and has impacts across socioeconomic strata. It is important for future research to consider the implications that phthalates have upon human reproductive health. Additionally, it is important to consider the implications that socioeconomic factors and consumer product usage have upon exposure to phthalates. Ultimately, there must be additional research into this topic to help provide insight into the effects that environmental injustice can have upon women's health.

Tables and Figures

Table 1: Phthalates Metabolites Included in the Analysis and Their Associated Health Effects

Parent Phthalate	Metabolites	Source of Exposure	Health Effects	References
Low Molecular Weight				
Benzylbutyl phthalate (BzBP)	Monobenzyl phthalate (MBP)	Crops, PVCs and other types of plastics	Anti-androgenic effects Male rodent reproductive system development disruption	(CDC, 2016). (Aylward, Hays, Gagné, & Krishnan, 2009) (Borch, Axelstad, Vinggaard, & Dalgaard, 2006) (Swan, 2008)
Diethyl phthalate (DEP)	Monoethyl phthalate (MEP)	Personal care products	Some anti-androgenic activity	(M. J. Silva et al., 2004) (Hatch et al., 2010)
Di-isobutyl phthalate (DiBP)	Mono-isobutyl phthalate (MiBP)	Home upholsteries, medical plastics, fabric manufacturing, inks and dyes	Anti-androgenic effects	(Kent R. Carlson, 2010) (Borch et al., 2006)
Di-n-butyl phthalate (DBP)	Mono-Butyl phthalate (MBP)	Personal care products, dyes, pill coatings, latex adhesives and plastics	Anti-androgenic effects Previous rodent studies have shown negative reproductive health effects.	(Borch et al., 2006) (Sen et al., 2015)
High Molecular Weight				
Di(2-ethylhexyl) phthalate (DHP)	Mono(2-ethylhexyl) phthalate (MEHP) Mono(2-ethyl-5-carboxypentyl) phthalate (MECPP) Mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) Mono(2-ethyl-5-oxohexyl) phthalate (MEOHP)	Medical devices, food manufacturing applications and household plastics	Anti-androgenic effects	(Tickner, Schettler, Guidotti, McCally, & Rossi, 2001) (Swan, 2008)

Table 2: Descriptive Statistics of the Atlanta, GA Pregnancy Cohort

Descriptive Statistics			
	Marijuana Users (n=16)	Non-Marijuana Users (n=32)	Overall
Median Age	25.13 (σ=4.51)	25.28 (σ=3.67)	25.23 (n=48)
Maternal BMI	25.33 (σ =5.66)	30.98 (σ =8.72)	29.10 (n=48)
Percent of Income Above the Federal Poverty Line			
<100%	10 (62.50%)	8 (25.00%)	18 (37.50%)
>100%	6 (37.50%)	24 (75.00%)	30 (62.50%)
Condom Usage			
Never	15 (93.75 %)	28 (87.50 %)	43(89.58%)
Sometimes/always	1 (6.25%)	4 (12.50 %)	5 (10.42%)
Past 30 days Tobacco Usage			
No	14 (87.50%)	28 (87.50 %)	42 (87.50 %)
Yes	2 (12.50 %)	4 (12.50 %)	6 (12.50 %)
Past 30 days Alcohol Consumption			
Yes	0 (0)	3 (9.38%)	3 (6.25 %)
No	16 (100 %)	29 (90.63 %)	45 (93.75%)
Maternal education level			
High school or less	11 (68.75%)	18 (56.25 %)	29 (60.42%)
More than high school	5 (31.25 %)	14 (43.75 %)	19 (39.58%)
All oral over the counter and prescription medications			
Yes	8 (50.00 %)	12 (37.50 %)	20 (41.67%)
No	8 (50.00%)	20 (62.50 %)	28 (58.33%)
All other over the counter and prescription medications			
Yes	4 (25.00%)	6 (12.50 %)	10(20.83%)
No	12(75.00%)	26 (81.25 %)	38 (79.17%)
Vitamin Use			
Yes	6 (37.50%)	11 (34.38%)	17 (35.42%)
No	10 (62.50 %)	21 (65.63%)	31 (64.58%)

Table 3. Pearson Correlation Examining Relationships Between Covariates

	1	2	3	4	5	6	7	8	9	10	11
1. Age	-										
2. Maternal BMI	0.14	-									
3. Maternal Education	-0.07	0.17	-								
4. Condom usage during vaginal Intercourse	0.01	0.01	-0.01	-							
5. Maternal tobacco use during the previous 30 days	-0.02	-0.11	0.18	0.08	-						
6. Maternal alcohol use during the previous 30 days	0.10	0.01	0.03	0.19	0.68***	-					
7. Maternal Income	-0.01	-0.01	0.19	-0.12	0.10	-0.02	-				
8. All oral prescriptions and over the counter medications	-0.16	-0.36*	-0.18	0.27	-0.06	-0.04	-0.04	-			
9. All other prescriptions and over the counter medications	0.04	-0.30 *	-0.01	0.16	-0.04	0.08	-0.19	0.40**	-		
10. Vitamin Usage	-0.13	-0.20	-0.29 *	0.03	-0.02	0.17*	-0.30*	0.35 *	0.26	-	
11. Positive Marijuana Urine Drug Screen	-0.02	-0.33 *	0.12	-0.10	0.00	-0.18	0.37 *	0.12	0.07	0.03	-
***p < .05. **p < .01. ***p < .001**											

Table 4. Bivariate Linear Regression Models of MBP and MBZP

	MBP				**MBZP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	-0.10	-1.00	0.51	0.52	-0.08	-0.95	0.56	0.61
Maternal BMI	-0.24	-0.64	0.06	0.10	0.00	-0.37	0.36	0.98
Maternal Education	-0.12	-8.45	3.47	0.40	-0.12	-8.30	3.63	0.44
Positive Urine Drug Screen for Marijuana Use	0.18	-2.26	9.98	0.21	0.26	-0.45	11.56	0.07
Condom Use	0.00	-9.53	9.69	0.99	-0.01	-10.02	9.21	0.93
Tobacco Use	0.01	-8.72	9.04	0.97	-0.09	-11.47	6.22	0.55
Alcohol Use	0.04	-10.37	13.88	0.77	-0.07	-14.98	9.22	0.63
Income Level	0.15	-2.85	9.13	0.30	0.29	0.22	11.82	**0.04**
All Oral Over the Counter and Prescription Medications	-0.11	-8.23	3.61	0.44	-0.17	-9.28	2.47	0.25
All Other Over the Counter and Prescription Medications	-0.18	-11.40	2.84	0.23	-0.15	-10.77	3.54	0.31
Vitamin Use	0.17	-2.61	9.50	0.26	0.03	-5.53	6.74	0.84

All significant associations have been bolded.

Table 5. Bivariate Linear Regression Models of MBP and MBZP

	MEP				**MIBP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	0.27	-0.05	1.41	**0.07**	-0.18	-1.21	0.28	0.21
Maternal BMI	-0.22	-0.61	0.09	0.14	-0.21	-0.61	0.09	0.14
Maternal Education	-0.14	-8.87	3.01	0.33	-0.05	-7.11	4.88	0.71
Positive Urine Drug Screen for Marijuana Use	0.03	-5.66	6.80	0.85	0.01	-5.93	6.53	0.92
Condom Use	0.18	-3.52	15.38	0.21	0.36	2.83	20.74	**0.01**
Tobacco Use	-0.04	-10.17	7.57	0.77	0.12	-5.12	12.50	0.40
Alcohol Use	-0.02	-12.95	11.31	0.89	0.10	-8.04	16.10	0.50
Income Level	-0.06	-7.30	4.81	0.68	0.06	-4.73	7.37	0.66
All Oral Over the Counter and Prescription Medications	0.03	-5.33	6.58	0.83	0.10	-3.82	8.02	0.48
All Other Over the Counter and Prescription Medications	-0.10	-9.61	4.78	0.50	0.18	-2.75	11.48	0.22
Vitamin Use	-0.01	-6.45	5.83	0.92	0.17	-2.63	9.48	0.26

All significant associations have been bolded.

Table 6. Bivariate Linear Regression Models of MECPP and MEHHP

	MECPP				**MEHHP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	0.02	-0.71	0.80	0.91	0.30	0.03	1.48	**0.04**
Maternal BMI	-0.25	-0.66	0.04	0.08	-0.16	-0.55	0.17	0.29
Maternal Education	0.01	-5.87	6.14	0.96	-0.08	-7.57	4.40	0.60
Positive Urine Drug Screen for Marijuana Use	-0.01	-6.51	5.95	0.93	-0.03	-6.89	5.56	0.83
Condom Use	-0.06	-11.41	7.78	0.71	-0.14	-13.93	5.12	0.36
Tobacco Use	0.03	-7.98	9.77	0.84	0.10	-5.88	11.79	0.50
Alcohol Use	0.09	-8.49	15.68	0.55	0.22	-3.05	20.65	0.14
Income Level	-0.13	-8.76	3.26	0.36	-0.13	-8.64	3.40	0.39
All Oral Over the Counter and Prescription Medications	0.11	-3.77	8.08	0.47	-0.11	-8.07	3.77	0.47
All Other Over the Counter and Prescription Medications	0.15	-3.37	10.92	0.29	-0.06	-8.67	5.77	0.69
Vitamin Use	-0.24	-10.95	0.97	0.10	-0.24	-10.99	0.92	0.10

All significant associations have been bolded.

Table 7. Bivariate Linear Regression Models of MEHP and MEOHP

	MEHP				**MEOHP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	0.13	-0.41	1.08	0.37	0.25	-0.09	1.38	0.08
Maternal BMI	-0.16	-0.55	0.17	0.29	-0.18	-0.58	0.13	0.22
Maternal Education	0.01	-5.82	6.19	0.95	-0.07	-7.34	4.65	0.65
Positive Urine Drug Screen for Marijuana Use	-0.05	-7.18	5.27	0.76	0.00	-6.27	6.19	0.99
Condom Use	-0.13	-13.88	5.17	0.36	-0.14	-13.95	5.09	0.35
Tobacco Use	0.11	-5.51	12.14	0.45	0.09	-6.17	11.52	0.55
Alcohol Use	0.17	-5.19	18.73	0.26	0.18	-4.38	19.46	0.21
Income Level	-0.22	-10.48	1.35	0.13	0.13	-3.26	8.76	0.36
All Oral Over the Counter and Prescription Medications	0.05	-5.04	6.86	0.76	-0.07	-7.39	4.49	0.62
All Other Over the Counter and Prescription Medications	0.08	-5.36	9.07	0.61	-0.05	-8.56	5.88	0.71
Vitamin Use	-0.19	-9.95	2.10	0.20	-0.22	-10.52	1.46	0.14

All significant associations have been bolded.

Table 8. Multivariate Linear Regression Analysis of MBP and MBZP

	MBP				**MBZP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	-0.07	-0.97	0.60	0.64	-0.12	-1.10	0.47	0.43
Maternal BMI	-0.33	-0.82	0.03	**0.07**	0.02	-0.41	0.45	0.92
Maternal Education	-0.07	-8.14	5.13	0.65	-0.20	-10.76	2.58	0.22
Positive Urine Drug Screen for Marijuana Use	0.09	-5.40	9.34	0.59	0.24	-2.45	12.36	0.18
Condom Use	0.14	-5.88	14.62	0.39	0.14	-5.79	14.81	0.38
Tobacco Use	-0.15	-17.46	8.43	0.48	0.13	-16.80	9.21	0.56
Alcohol Use	0.12	-13.67	23.08	0.61	0.02	-17.58	19.35	0.92
Income Level	0.19	-3.14	10.92	0.27	0.30	-0.93	13.19	**0.09**
All Oral Over the Counter and Prescription Medications	-0.30	-13.32	1.32	0.11	-0.31	-13.64	1.08	**0.09**
All Other Over the Counter and Prescription Medications	0.26	-2.01	12.82	0.15	-0.05	-9.49	7.27	0.79
Vitamin Use	0.09	-5.40	9.34	0.59	0.24	-2.45	12.36	0.18

All covariates are included in each model. All significant and marginally significant values have been bolded.

Table 9. Multivariate Linear Regression Analysis of MEP and MiBP

	MEP				**MiBP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	0.32	0.02	1.61	**0.05**	-0.17	-1.23	0.36	0.27
Maternal BMI	-0.36	-0.87	0.00	**0.05**	-0.18	-0.65	0.22	0.32
Maternal Education	-0.04	-7.49	5.98	0.82	-0.06	-7.81	5.57	0.74
Positive Urine Drug Screen for Marijuana Use	-0.02	-7.82	7.14	0.93	-0.03	-8.04	6.83	0.87
Condom Use	0.23	-3.08	17.72	0.16	0.41	2.79	23.47	**0.01**
Tobacco Use	-0.08	-15.52	10.76	0.72	0.14	-8.93	17.19	0.53
Alcohol Use	-0.02	-19.39	17.90	0.94	-0.10	-22.69	14.38	0.65
Income Level	-0.06	-8.44	5.82	0.71	0.05	-6.07	8.10	0.77
All Oral Over the Counter and Prescription Medications	-0.01	-7.69	7.17	0.94	-0.20	-11.31	3.46	0.29
All Other Over the Counter and Prescription Medications	-0.26	-14.75	2.18	0.14	0.13	-5.21	11.62	0.44
Vitamin Use	-0.01	-7.67	7.37	0.97	0.15	-4.46	10.49	0.42

All covariates are included in each model. All significant and marginally significant values have been bolded.

Table 10. Multivariate Linear Regression Analysis of MECPP and MEHHP

	MECPP				**MEHHP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	-0.02	-0.81	0.71	0.90	0.25	-0.09	1.35	**0.09**
Maternal BMI	-0.28	-0.76	0.07	**0.10**	-0.29	-0.74	0.04	**0.08**
Maternal Education	0.01	-6.29	6.59	0.96	-0.06	-7.33	4.83	0.68
Positive Urine Drug Screen for Marijuana Use	0.03	-6.53	7.78	0.86	0.08	-5.17	8.34	0.64
Condom Use	-0.19	-15.94	3.95	0.23	-0.23	-16.73	2.05	0.12
Tobacco Use	-0.20	-18.49	6.64	0.35	-0.20	-17.98	5.74	0.30
Alcohol Use	0.35	-3.33	32.35	0.11	0.48	2.65	36.33	**0.02**
Income Level	-0.28	-12.59	1.05	**0.09**	-0.30	-12.56	0.32	**0.06**
All Oral Over the Counter and Prescription Medications	0.19	-3.20	11.01	0.27	0.07	-5.27	8.15	0.67
All Other Over the Counter and Prescription Medications	0.07	-6.34	9.86	0.66	-0.14	-10.97	4.32	0.38
Vitamin Use	-0.53	-18.15	-3.76	**0.01**	-0.45	-16.02	-2.43	**0.01**

All covariates are included in each model. All significant and marginally significant values have been bolded.

Table 11. Multivariate Linear Regression Analysis of MEHP and MEOHP

	MEHP				**MEOHP**			
	β	(95% CI)		*P*-Value	β	(95% CI)		*P*-Value
Age	0.11	-0.48	1.02	0.47	0.22	-0.19	1.29	0.14
Maternal BMI	-0.19	-0.64	0.19	0.27	-0.30	-0.77	0.04	**0.08**
Maternal Education	0.02	-5.92	6.81	0.89	-0.04	-7.09	5.44	0.79
Positive Urine Drug Screen for Marijuana Use	0.07	-5.57	8.58	0.67	0.10	-4.94	8.97	0.56
Condom Use	-0.29	-19.35	0.32	**0.06**	-0.23	-17.00	2.35	0.13
Tobacco Use	-0.10	-15.37	9.48	0.63	-0.19	-17.97	6.47	0.35
Alcohol Use	0.37	-2.32	32.96	**0.09**	0.44	0.71	35.40	**0.04**
Income Level	-0.40	-14.98	-1.49	**0.02**	-0.31	-13.06	0.21	**0.06**
All Oral Over the Counter and Prescription Medications	0.22	-2.52	11.53	0.20	0.10	-4.97	8.86	0.57
All Other Over the Counter and Prescription Medications	-0.01	-8.36	7.65	0.93	-0.15	-11.51	4.24	0.36
Vitamin Use	-0.46	-16.72	-2.49	**0.01**	-0.42	-15.79	-1.79	**0.02**

All covariates are included in each model. All significant and marginally significant values have been bolded.

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