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The Association between Urinary Bisphenol-A, Phthalate Metabolites and Body Fat Composition in US Adults Using NHANES

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**The Association between Urinary Bisphenol-A, Phthalate Metabolites and Body Fat
Composition in US Adults Using NHANES**

A Thesis Presented

By

IRIS CORBASSON

Submitted to the Graduate School of the
University of Massachusetts Amherst in partial fulfillment
of the requirements for the degree of

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Epidemiology

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Composition in US Adults Using NHANES**

A Thesis Presented

By

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DEDICATION

To my father, who contributed to my achievements in so many different ways.

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I would like to thank my advisor, Katherine W Reeves, for her wonderful guidance and support all throughout the thesis preparation process but also during the last two years. Without her encouragement, her dedication as a teacher, as well as her tireless patience, this would not have been possible. I would also like to thank my committee members, Susan E Hankinson and Edward J Stanek, for their valuable feedback and suggestions that helped create this manuscript.

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Lastly, I wish to thank my friends and family, near and far, for their belief in my potential and their unlimited support during this process.

ABSTRACT

THE ASSOCIATION BETWEEN URINARY BISPHENOL-A, PHTHALATE METABOLITES AND BODY FAT COMPOSITION IN US ADULTS USING NHANES

SEPTEMBER 2014

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Due to the widespread use of the endocrine disruptors Bisphenol-A (BPA) and phthalates in many plastic consumer goods, medical equipment, and personal care products, more than 95% of the US population show detectable levels of urinary BPA and phthalate metabolites. Both have been linked to increased body mass index (BMI in kg/m^2), an inexpensive diagnostic tool for obesity, which may however not reflect body fatness. Since excess body fat is associated with cardiovascular diseases, cancer and type II diabetes, it is important to understand the relationship between body fat composition and exposure to BPA and phthalates, a relationship that is still unknown. Using NHANES 1999-2006 data on adults aged >20 years, we investigated the relationship between urinary BPA (N=2,534), monoethyl-phthalate (mEP, N=5,431), monobutyl-phthalate (mBP), monoethylhexyl-phthalate (mEHP) and monobenzyl-phthalate (mBzP, each N=5,436) measured by high-performance liquid chromatography tandem mass spectrometry, and body fat composition measured as lean mass (LM, grams), fat mass (FM, grams) and percent body fat (%BF) using Dual Energy X-ray Absorptiometry. A multivariable linear regression analysis yielded that independently of BMI, BPA, mBP, and mBzP were inversely associated with LM (quartile 4 $b=-862.16$ (354.65), -731.76

(248.89), -909.13 (252.32), respectively; all $p < 0.02$, $p\text{-trend} < 0.02$); mEHP and FM were inversely associated (quartile 4 $b = -297.98$ (144.87), $p = 0.04$, $p\text{-trend} < 0.02$); BPA, mBP, and mBzP were positively associated with %BF but not clinically significant. These results provide novel insights in the relationship between urinary BPA, phthalates and LM independent of BMI, and it highlights the need for prospective studies establishing temporality of this relationship.

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CHAPTER 1

INTRODUCTION

Endocrine disruptors such as Bisphenol-A (BPA) and phthalates are pervasive in our environment and we are almost constantly exposed to them through dermal exposure, diet and inhalation of household dust.^{1,2} BPA is used in many plastic consumer products, dental sealants, thermal receipts, and Polyvinyl chloride (PVC).¹ Phthalates are used in numerous household hardware products, plastic medical equipment, medications and personal care products.²⁻⁵ Once phthalates enter the human body, they are rapidly metabolized into monoesters, which are known to act as endocrine disruptors.⁶

According to the National Health and Nutrition Examination Survey (NHANES), urinary BPA is detectable in 95% of the US adult population and several kinds of urinary phthalate metabolites are detectable in 97% of the total US population.^{3,4,7} It is important to understand how exposure to these compounds is related to excess body fat, because BPA and phthalate metabolites are known endocrine disruptors that interfere with energy use and metabolism regulation, which might lead to weight gain. Given that obesity is a serious public health problem in the US, as 78 million adults were obese in 2009-2010,⁸ it is crucial to identify potentially modifiable obesity risk factors, such as exposure to endocrine disruptors BPA and phthalates.

The biological mechanism underlying the positive relationship between urinary BPA and obesity could be explained by its estrogen-like effect that is known to induce insulin resistance and weight gain.^{7,9} Also, obese individuals might have a higher energy diet than non-obese individuals, implying that a higher BPA concentration is due to a

higher intake of BPA contaminated packaged foods.¹⁰ Moreover, as BPA is known to be lipophilic, higher body fat may imply higher BPA concentration storage in adipose tissue which might lead to higher urinary BPA levels.⁹ However, this mechanism remains controversial, as studies were unable to find a significant correlation between Body Mass Index (BMI in kg/m²) and BPA concentration in adipose tissue¹¹.

There is evidence that the biological mechanism underlying the effect of phthalates on obesity may differ by the type of phthalates.² Ingested phthalates diethyl-phthalate (DEP), di-n-butyl-phthalate (DBP), benzylbutyl-phthalate (BBzP), and di-2-ethylhexyl-phthalate (DEHP) rapidly metabolize into the monoesters mEP, mBP, mBzP, and mEHP respectively, which are known to interfere with the regular endocrine functions.⁶ The metabolite mEHP has been found to strongly affect biological pathways that regulate fatty acid storage and glucose metabolism; mBzP strongly affects the thyroid function, which controls energy use and hormone balance; and all four metabolites have been found to have antiandrogenic effects.²

Overall, most previously conducted epidemiological studies investigating the relationship between either urinary BPA or urinary phthalate metabolites and body fatness are limited to BMI and waist circumference (WC) as obesity measures, but they do not accurately reflect body fatness or body fat composition.^{12,13} A better body fatness measurement is the use of dual-energy X-ray absorptiometry (DXA) scans that estimate fat mass (FM), lean mass (LM) and percent body fat (%BF).¹² Since excess body fat has been shown to be linked to a number of adverse health outcomes,^{8,13} it is important to assess the relationship between body fatness and possible modifiable risk factors such as exposure to BPA and phthalates. Previous cross-sectional studies have shown that that

urinary BPA, mEP, mBP, and mBzP, are positively related to obesity when measured by BMI and WC,^{2,9,10,14,16} but it remains unclear how those compounds are related to FM, lean mass LM or percent body fat %BF. Some investigators found a positive yet weak relationship between BPA and body fat composition measures using DXA, but the study samples used were limited to pre-menopausal non-obese women of the elderly.^{5, 15} Therefore, the relationship between urinary BPA or phthalate metabolites and DXA measures in the general US population remains unknown.¹⁵

NHANES data includes Dual Energy X-ray Absorptiometry (DXA) measures for subjects describing the individual's body fat distribution in FM, LM and %BF. To our knowledge, the relationship between either urinary BPA or urinary phthalate metabolites and DXA measures has not been studied in a large population-based sample. Therefore, we evaluated the association between urinary BPA, urinary phthalate metabolites and body fat measures, assessed by DXA scans, among adults using NHANES data. We hypothesized that there is a positive association between urinary BPA quartiles and FM and %BF, and a negative association between BPA and LM. We further hypothesized that there is a positive relationship between each urinary phthalate metabolite measured in quartiles and FM, and %BF, and a negative association with LM.

CHAPTER 2

METHODS

Study Design

This analysis employs a cross-sectional study design using data from the National Health and Nutrition Examination Survey (NHANES). NHANES is designed to produce health statistics for the US population by assessing the health and nutritional status of non-institutionalized adults and children in the United States. More specifically, nearly 7000 residents are randomly selected each year and invited to participate. The NHANES interview includes demographic, socioeconomic, dietary, and health-related questions. Examinations comprise medical, physiological measurements and laboratory tests of specimens. The National Center for Health Statistic's Institutional Review Board (IRB) has reviewed and approved the NHANES protocol.¹⁶

To examine the association between urinary phthalate metabolites and DXA measures (LM, FM, %BF), we combined data from four NHANES survey cycles (1999-2000, 2001-2002, 2003-2004, 2005-2006) as those are the years when DXA body fat composition measures were performed. In addition, to examine the association between urinary BPA and DXA measures, we used NHANES data from 2003-2004 and 2005-2006, as urinary BPA measures were only taken during these two survey cycle during which DXA measures are also available.

Study population

Because there are substantial differences in the biology of environmental exposures and body fat composition between children and adults, we restricted our

analysis to adults aged 20 or older for the purpose of the proposed analysis. BPA and phthalate measurements were performed on a randomly selected one third subsample in the respective NHANES survey cycle. We only included participants for whom BPA and/or phthalate measurements as well as DXA measures are available.

For the BPA analysis, we had 2,534 eligible participants and excluded 84 (3.19%) with missing BPA levels and 32 (1.21%) with highly variable imputed DXA measures. Out of the remaining 2,534 (96.20%), about 28% had imputed DXA measures (see Appendix Table 13).

We had 5,688 eligible participants for all phthalate metabolite analyses and excluded 202 (3.55%) with missing mEP measures and 197 (3.46%) with missing mEHP, mBP, and mBzP measures. We further excluded 103 (1.81%) with highly variable DXA measures. Out of the total 5,431 (95.48%) participants for the mEP analysis and the 5,436 (95.57%) participants for the mEHP, mBP and mBzP analyses, about 23% had imputed DXA measures (see Appendix Table 13).

Exposure Assessment

Urinary BPA concentrations:

Total urinary BPA concentration was measured in spot urine samples using online solid-phase extraction coupled to isotope dilution high performance liquid chromatography-tandem mass spectrometry (SPE-HPLC-MS/MS).^{17,18} The precision of this method was evaluated by repeated measures in two quality control pools over time. Depending on the concentration, the coefficient of variations (CV) ranged from 12.1% - 18.6% in 2003-2004, and from 11.2%-12.6% in 2005-2006.^{17,18} Urinary creatinine also

was measured in each urine sample and was used in this analysis in order to adjust for urinary dilution.

Urinary phthalate concentration:

We focused on the four most prevalent phthalate metabolites: monobutyl phthalate (mBP), monoethylhexyl phthalate (mEHP), monoethyl phthalate (mEP), and monobenzyl phthalate (mBzP).³ For the NHANES 1999-2000 and 2001-2002 survey cycles, the urine samples were analyzed using high-pressure liquid chromatography tandem mass spectrometry (HPLC-MS/MS).^{19,20} The precision of this method was evaluated by repeated measures of quality control pools over time. Depending on concentration and measurement period, the CV in NHANES 1999-2000 range from 7.2 - 22.1% (mBP), 10.5 - 18.2% (mEHP), 4.9 - 10.0% (mEP), and 9.6 - 13.8% (mBzP).¹⁹ The CV in NHANES 2001-2002 range from 4.0 - 17.2% (mBP), 8.6 - 15.8% (mEHP), 4.6 - 10.6% (mEP), 5.4 - 14.2% (mBzP).²⁰

For the NHANES 2003-2004 and 2005-2006 survey cycles, the urine samples were analyzed using high performance liquid chromatography-electrospray ionization-tandem mass spectrometry (HPLC-ESI-MS/MS).^{21,22} The CV range from 7 - 7.4% (mBP), 7.6 - 10.5% (mEHP), 5.1 - 6% (mEP), 6.3 - 6.4% (mBzP) in 2003-2004,²¹ and from 7.5 - 17.4% (mBP), 6.3 - 12.0% (mEHP), 2.9 - 5.2% (mEP), 6.8 - 8.9% (mBzP) in 2005-2006.²² Urinary creatinine also was measured in each urine sample and was used in this analysis in order to adjust for urinary dilution.

Outcome Assessment

Our outcomes of interests are lean mass (LM in gm), fat mass (FM in gm), and percent body fat (%BF) as assessed by Dual Energy X-ray Absorptiometry (DXA). From 1999 to 2004, DXA was administered to eligible participants aged 8 years or older. In 2005-2006, DXA was administered to eligible participants between the ages 8 to 59.²³ Exclusion criteria for DXA examination were: pregnancy, self-reported history of radiographic contrast material use in the past 7 days, self-reported nuclear medicine studies in the past 3 years, and self-reported weight over 300 pounds or a standing height over 6'5'' (limitation for examination table). The NHANES DXA data in all four survey cycles were collected with a Hologic QDR-4500A fan-beam densitometer (Hologic, Inc. Bedford Massachusetts). Up until mid-2005, Hologic software version 8.26:a3 was used to administer all scans; in 2005 the software was updated to Hologic Discovery v12.4.²³ The health technicians performing DXA measures are trained to follow detailed protocols on maintenance and calibration of the DXA equipment with specific quality control checks performed daily and weekly.²⁴

Because DXA measures were missing for about 21% of the population eligible for DXA scans, and missingness was related to age, BMI, height and weight, NHANES used multiple imputation techniques to create predicted DXA measures in order to avoid bias due to missingness not at random (MNAR).²⁵ We used these multiply imputed DXA measures for our analysis, but we excluded those subject with highly variable imputed DXA measures.²³

Covariate Assessment

Information on demographics, socioeconomic status, dietary habits and health-related issues was collected through NHANES interviews. Furthermore, medical, physiological and laboratory tests were conducted during NHANES examinations. Based on covariates selected by previous studies investigating the relationship between urinary BPA or urinary phthalate metabolites and obesity, we considered age, gender, race/ethnicity, marital status, income, education, physical activity, smoking, alcohol consumption, total calorie intake, total fat intake, total serum cholesterol, diabetes, hypertension, BMI, standing height, weight, and WC.^{2,5,9,10,14,26,27}

Data Analysis

In order to account for urinary dilution, we standardized BPA and phthalate metabolite levels by urinary creatinine. We cross-tabulated LM, FM, %BF and covariates by creatinine standardized urinary BPA and phthalate metabolite quartiles. Analysis of variance and chi-square tests were used for continuous and categorical variables respectively to assess potential confounders. In case of heteroscedasticity or small cell counts, Kruskal-Wallis and Fisher's exact test were used instead. We modeled the association between the raw urinary BPA levels, raw urinary phthalate metabolites (continuous and quartiles) and LM, FM and %BF separately using linear regression with adjustment for urinary creatinine as an independent variable in order to adjust for urinary dilution. Because urinary creatinine is known to be associated with age, gender and race/ethnicity,²⁸ we included these covariates in all of our multivariable analyses. We created three separate multivariable models: First with adjustment for creatinine, age,

gender, and race/ethnicity (model 1); second with additional adjustment for BMI (model 2), and third we applied the Hosmer-Lemeshow model building process (model 3). For the third model, covariates were evaluated with each of the three outcomes separately in order to assess potential confounders. Further, all covariates with p-values of at least 0.25 were included in the full model and their individual effect on the full model was evaluated using partial F-test. For borderline significant effects, the variable was kept in the model, if other regression coefficient were changed by more than 15%. In addition, we reported each final model stratified by BMI category using the cut-off points for normal weight (BMI= 18.5-24.99 kg/m²), overweight (BMI= 25-29.99 kg/m²), and obese (BMI>= 30 kg/m²) as defined by the World Health Organization.²⁹ Due to a small number of people, we grouped those subjects with a BMI<18.5 kg/m² together with the normal weight subjects. In order to check for correlation between BMI and the outcome measures LM, FM, and %BF, we performed a correlation analysis using Pearson's correlations coefficients in both the total population and in the subpopulation consisting of subjects with only non-imputed DXA measures. The latter was performed because of the concern that BMI might be highly related to the imputed DXA measures due to the use of BMI in the multiple imputation models.

For all of our statistical analyses, we used STATA Statistical Software (StataCorp. 2013, Release 13. College Station, TX: StataCorp LP).

CHAPTER 3

RESULTS

In both the BPA and the phthalate metabolite analyses, our study population consisted of nearly 51% men and 49% women. The race/ethnicity distribution was similar in both samples; 49.5%-50.5% were non-Hispanic white, 20.9%-22.0% were non-Hispanic black, 19.4%-21.7% were Mexican American, 3.7%-4.4% were other Hispanic, and 3.5%-4.4% were other/multiethnic. The mean age was 47.7 (sd=17.5) years and 48.9 (sd=18.5) years in the BPA and the phthalate metabolite analysis, respectively.

Within the respective study samples, the total population geometric means were 2.04 $\mu\text{g/g}$ creatinine (95%CI=1.97-2.12) for BPA, 131.87 $\mu\text{g/g}$ creatinine (95%CI=127.12-136.80) for mEP, 2.89 $\mu\text{g/g}$ creatinine (95%CI=2.80-2.98) for mEHP, 18.35 $\mu\text{g/g}$ creatinine (95%CI=17.92-18.79) for mBP, and 7.74 $\mu\text{g/g}$ creatinine (95%CI=7.53-7.95) for mBzP.

A cross-tabulation of each covariate by creatinine standardized BPA quartile yielded that LM, and %BF, as well as gender, age, height, weight, and WC, differed significantly between the BPA comparison groups, while FM, race/ethnicity, and BMI appeared to be similar across all groups (Table 1). Within the crude creatinine standardized mEP analysis, LM, FM, %BF, as well as gender, age, race/ethnicity, BMI, height, weight, and WC differed significantly between the four comparison groups (Table 2). The outcome measures LM, and FM, as well as age, BMI, height, weight, and WC differed significantly between the mEHP comparison groups, while %BF, gender, and race/ethnicity appeared to be similar (Table 3). The outcome measures LM, and %BF, as well as age, race/ethnicity, BMI, height, weight, and WC, differed significantly between

the mBP comparison groups, while FM and gender appeared to be similar across all groups (Table 4). All three outcome measures LM, FM, %BF, as well as age, gender, height differed significantly between the mBzP comparison groups, while weight, BMI, and WC appeared to be similar (Table 5). A Pearson correlation analysis yielded that BMI and FM are highly correlated (coefficient=0.92) in the total population of both the BPA and phthalate analyses; BMI and LM as well as %BF were moderately correlated (coefficient= 0.51-0.59). In the sub-population of subjects with only non-imputed DXA measures, the Pearson correlation analysis between BMI and the outcome measures yielded a coefficient of 0.88 for FM, 0.43-0.44 for LM, and 0.54-0.56 for %BF.

The multivariable linear regression analysis using BPA as a continuous variable only showed a significant negative association with LM in model 2 ($b=-21.51$ (10.31), $p=0.037$) (Table 6). All other associations between urinary BPA and FM, as well as %BF were non-significant. Moreover, there was no significant association between any phthalate metabolite for each of the three outcomes LM, FM, and %BF when the phthalate metabolites were analyzed as a continuous variable (Table 6-8).

The following analyses model the exposure measures as categorical variables using quartiles (Q1-Q4) with the first quartile (Q1) used as the reference group:

Results of the Lean Mass analysis:

Using linear regression with adjustment for creatinine, age, gender, and race/ethnicity, we only observed a significant 1,154.85 (524.14) gm mean increase of LM for Q2. However, when the model was further adjusted for BMI, we observed a significant 1,263.23 gm (356.77) decrease in mean LM for Q4, with a p-trend of <0.001 .

Our final model adjusted for creatinine, age, gender, race/ethnicity, BMI, family income, vigorous physical activity, moderate physical activity, WC, total calorie intake, serum cholesterol. It showed 862 gm (354.65) mean LM decrease for Q4, with a p-trend=0.017 (Table 6).

Within the mEP analysis, the linear regression with adjustment for age, gender and race/ethnicity yielded a significant increase in LM of 887.91 gm (363.87) for Q4. When additionally adjusting for BMI, there was a borderline significant decrease in LM of 414.95 gm (222.68) for Q4 (p=0.062), with a p-trend= 0.022. There was not significant association between any of the mEP quartiles and LM in the full model, but it showed a significant trend of lower LM with increasing mEP (p-trend=0.035) (Table 6).

Within the mBP analysis, the model adjusted for age, gender and race/ethnicity showed a mean decrease of 1,319.47 gm (404.05) in LM for Q4. When further adjusting for BMI, we observed a decrease of 881.64 gm (246.48) in LM between Q4 and Q1. We observed a highly significant decrease of 731.76 gm (246.48) in LM for Q4 in the full model (Table 6).

Within the mEHP analysis, we did not observe a significant association between mEHP and LM in any of the three models (Table 6).

Within the mBzP analysis, there was no significant association with LM when adjusting for age, gender and race/ethnicity. There was a significant 592.98 gm (22.6.46) decrease for Q3 and a 1,070.43 gm (248.06) decrease for Q4 (p-trend<0.001) when the model was further adjusted for BMI. The full model showed a 707.35 gm (223.25)

decrease in LM for Q3, and a 909.13 gm (252.32) decrease in LM for Q4 (p-trend<0.001) (Table 6).

Results of the Fat Mass analysis:

When adjusting for age, gender and race/ethnicity, we observed a significant mean increase in FM for each BPA quartile with a mean 2,106 gm (736.83) in Q4 (p-trend= 0.009). When further adjusting for BMI, we only observed non-significant increases in mean FM for each BPA quartile. The full model adjusted for creatinine, age, gender, race/ethnicity, BMI, education, diabetes, WC, total calorie intake and total fat intake and only showed non-significant increases in FM for each BPA quartile (Table 7).

When adjusting the mEP model for age, gender, race/ethnicity, we observed a mean increase in FM of 1,995.70 gm (474.43) (p<0.001). When we further adjusted for BMI as well as additionally for education, marital status, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake and total fat intake, there was no significant association between mEP quartile and FM (Table 7).

There was no significant association between mBP and FM in any of the models (Table 10b).

There was no significant association between mEHP and FM in the model adjusted for age, gender and race/ethnicity. When we further adjusted for BMI, we observed a significant decrease in FM of 394.87 gm (155.61) for Q4. The full model was additionally adjusted for education, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake and total fat intake and showed a significant decrease in FM of

319.91 gm (140.90) for Q3 and a decrease in FM of 297.98 gm (144.87) for Q4 (p-trend=0.016) (Table 7).

Within the mBzP analysis, the model adjusted for age, gender, and race/ethnicity showed a mean increase in FM of 1,771.72 gm (529.45) for Q4. The models that further adjusted for BMI as well as the fully adjusted model did not show a significant association between mBzP and FM (Table 7).

Results of the % Body Fat analysis:

There was a highly significant mean increase of 1.26% (0.37) -1.44% (0.40) in %BF for each BPA quartile compared to the lowest (p-trend=<0.001), when adjusted for age, gender, and race/ethnicity. After further adjusting for BMI, we observed a low statistically significant mean increase of 0.50% (0.24) in %BF for Q3 and an increase of 0.67% (se=0.26) in %BF for Q4. The fully adjusted model showed a similar increase in %BF as the previous model, but with only a statistically significant increase in %BF for Q4 (Table 8).

There was a significant increase in %BF in each of the mEP quartiles with the highest increase in %BF of 1.16% (0.26) for Q4 (p-trend <0.001), when adjusting for age, gender, and race/ethnicity. When further adjusting for BMI, only the increase of 0.41 %BF for Q3 remained significant. Similarly, the full model only showed a significant increase of 0.49% (0.16) in %BF for Q3, but it showed a significant trend of higher %BF with increasing mEP (p-trend=0.022) (Table 8).

We did not observe a significant association between mBP and %BF when adjusted for age, gender, race/ethnicity. When further adjusting for BMI, there was a

significant increase in BF of 0.35% (0.17) comparing the third to the lowest mBP quartile. Similarly, the full model adjusted for marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake and serum cholesterol and only showed a significant increase of 0.43% (0.17) in BF when comparing the third to the lowest mBP quartile (Table 8).

There was no significant association between mEHP and %BF in any of the models.

Within the mBzP analysis, we observed a significant increase of 1.20% (0.29) in BF for Q4 when adjusting for age, gender, race/ethnicity ($p\text{-trend}<0.001$). When further adjusting for BMI, the increase in %BF diminished to 0.43% (0.18) but remained significant ($p\text{-trend}=0.013$). The full model showed a significant increase of %BF of 0.61% (0.18) ($p\text{-trend}<0.001$) (Table 8).

Overall, after repeating the analyses of model 1 for each association between our exposures and outcomes within the sub-population of subjects with only non-imputed DXA measures, the results for LM were similar to those of the total population; the results for FM were closer to the null; and the results for %BF were slightly attenuated for mEP and mBzP, but similar to the total population results for BPA, mBP, and mEHP (Table 12).

CHAPTER 4

DISCUSSION

We found a significant inverse association between urinary BPA, mBP, mBzP and LM, independent of BMI. Surprisingly there was a negative association between mEHP and FM after adjustment for BMI. Moreover, all statistically significant associations in the %BF analysis were very small and did not seem to be clinically meaningful.

With regard to previous studies, only limited data are available on the relationship between urinary BPA and body fat composition measures. One cross-sectional study using DXA measures found a positive yet weak relationship between urinary BPA and FM after adjusting for age and BMI (partial correlation coefficient=0.193), but they did not find an association between BPA and fat free mass.¹⁵ Our findings differ from these, but the study population only consisted of pre-menopausal non-obese women, which makes it difficult to put our findings in perspective.¹⁵

We only observed a positive relationship between BPA and FM before adjustment for BMI, but not independent of BMI. This might be explained by the high correlation between BMI and FM, which results in an attenuation of the effect of BPA on FM after adjustment for BMI. Therefore, BMI and FM may essentially capture the same fatness measure and both seem to be individually related to high urinary BPA. These findings are in line with previous literature, as other cross-sectional studies with samples similar to ours have found a 28% to 76% increased risk of obesity measured by BMI for the highest BPA quartile.^{9,10,14}

The literature assessing the association between phthalate metabolites and body fat composition measures is limited, as most studies focus on fat measures and to our knowledge none have investigated the relationship between phthalates metabolites and LM. A positive and statistically significant association was found between urinary mBzP, mEP and abdominal obesity measures by WC with a male cohort, but results were not adjusted for BMI.²⁷ A strong positive association was found between urinary mBzP quartiles and BMI in men aged 20-59.² Conversely, a negative association has been found between urinary mEHP quartiles and BMI in women of the same age group.² A slight borderline significant negative association was found between serum mEHP and waist-hip ratio in men and a slight borderline significant positive association was found between monoisobutyl-phthalate (a structural isomer of monobutyl-phthalate (mBP)³⁰) and BMI in women.⁵ However this study was restricted to the elderly aged 70 and exposure was measured in blood instead of urine samples, which makes it difficult to compare their results to ours. Yet, overall these results are consistent with ours, as we found an association between mEP, mBzP and FM before BMI adjustment but not afterwards, which could imply that our initial results were confounded by BMI, but there is no association between mEP, mBzP and FM independent of BMI. With regard to mEHP, there seems to be a negative association between this phthalate metabolite and FM, which was also observed in previous literature that used different obesity measures. However, it has been found that the metabolite mEHP is not a good surrogate for the parent phthalate DEHP, because mEHP only accounts for a small proportion of its metabolites and the analysis of other metabolites such as mEOHP and mEHHP are a more appropriate measure of exposure to DEHP.³¹ Therefore, we believe that our

observed negative association between mEHP and FM could be due to its poor representation of the full exposure to DEHP.

Our study has several limitations. We are unable to make inferences about a causal relationship between exposure to BPA and phthalates and LM due to the cross-sectional study design and the inability to assess temporality. In addition, confounding can occur by unmeasured confounders such as medication use. We are unable to measure the use of medications that include phthalates, which could contribute to certain urinary phthalate metabolite levels,³ but might also be associated with high FM, if the medication is taken for obesity related health issues. However, since we did not find a positive association between BPA, phthalates and FM independent, we are confident that our results are not subject to confounding by medication.

In addition, BPA and phthalate metabolites were only measured in one single spot urine sample, which may not accurately represent an individual's typical exposure as studies have shown that urinary BPA levels vary considerably over longer periods of time.³² This type of misclassification is non-differential and we believe the impact of this is modest, possibly biasing the observed results towards the null. Moreover, studies have shown that urinary phthalate metabolite levels are relatively stable over time, probably because phthalates are ubiquitous in our environment, suggesting a rather continuous exposure.³³ Therefore, a single spot urine measurement may still be a close representation of typical exposure. This type of misclassification is non-differential and we believe the impact of this to be modest, biasing the observed results towards the null.

We restricted our analysis to non-pregnant adults without amputations, and used multiply imputed data for those who were unable to undergo a DXA scan due to e.g. high

body weight or the presence of pacemakers in their body. This allows us to generalize to men and women with high risk of obesity related health issues. However, we excluded those whose imputed DXA measure were highly variable, which occurred mostly among those with missing data on weight and WC.²³ The physiological mechanism linking urinary BPA and phthalate metabolites to body fat composition is likely the same among those excluded and included in the analysis. However, because body fat composition is highly variable among pregnant women, and the impact of BPA and phthalate on body composition may differ greatly due to hormonal differences, we should not generalize our findings to pregnant women.

Our secondary analysis of model 1 in the sub-population of subject with only non-imputed DXA measures showed attenuated effects of BPA, and phthalate metabolites on FM, but not on LM. We expected a bias towards the null within the secondary analysis after omitting subjects with multiple imputed DXA measures, because they were less likely to be eligible for a DXA scan examination due to an obesity related health concern (e.g. having a pace maker or body weight >300 pounds). These findings suggest that the use of multiply imputed DXA measures in analyses examining the association between BPA, phthalates and FM may be useful to avoid bias and to detect significant differences in FM between the comparison groups without adjustment for BMI.

Conclusion

Our results add to the current literature as we are the first to assess the relationship between urinary BPA, phthalate metabolites and DXA measures on a large population scale. Most previous studies assessed the relationship between BPA, phthalate metabolites and obesity using BMI and WC on the large population scale, but DXA

measures were only used in specific sub-populations. Our findings suggest that BPA, mBP, mBzP are inversely associated with LM independent of BMI, but not with FM. However, previous literature assessing the relationship between BPA, phthalates and LM is very limited and more studies should be conducted to analyze this relationship further. On the other hand, the positive relationship between BPA, phthalate metabolites and obesity can be explained by BMI, as we only found null results for FM independent of BMI. These findings suggest that BMI may indeed be an adequate fatness measure in order to assess the relationship between these endocrine disrupters and obesity. The relationship between mEHP and body fat composition measures remains unclear and a different metabolite of DEHP should be used as a surrogate of exposure to this parent phthalates in future studies. Prospective studies are needed in order to assess the timing between BPA or phthalates exposure and weight gain. Further research in this area is important because of the high obesity prevalence in the United States and the ubiquity of BPA and phthalates in our environment.

APPENDIX
SUMMARY TABLES AND REGRESSION COEFFICIENTS

Table 1: Means and standard deviations of Lean Mass, Fat Mass, % Body Fat and covariates according to creatinine standardized urinary BPA quartiles

	Q1 (n=634)	Q2 (n=650)	Q3 (n=616)	Q4 (n=633)	p-value
urinary BPA, $\mu\text{g/g}$ creatinine	<1.15	1.15-2.00	2.01-3.37	>3.37	
Lean mass, gm (sd)	52,891.20 (12,865.85)	51,716.01 (13,299.28)	49,807.63 (12,878.70)	49,718.33 (12,268.21)	<0.001
Fat mass, gm (sd)	27,504.30 (11,520.88)	28,617.54 (12,361.01)	27,763.37 (11,495.05)	29,084.37 (12,101.98)	<0.0639
Body fat, % (sd)	32.61 (8.83)	33.95 (8.92)	34.22 (8.52)	35.14 (8.64)	<0.001
Gender, n(%)					
Male	385 (60.73)	342 (52.62)	281 (52.62)	292 (45.62)	<0.0001
Female	249 (39.27)	308 (47.38)	335 (47.38)	341 (54.38)	
Age, years, m(sd)	48.72 (16.31)	47.58 (17.70)	45.67 (17.44)	48.62 (18.39)	<0.0029
BMI, kg/m ² , m(sd)	28.45 (6.33)	28.77 (6.55)	28.12 (6.35)	28.75 (6.52)	0.2426
Height, cm, m(sd)	169.82 (10.24)	168.61 (10.34)	167.59 (9.97)	166.94 (9.71)	<0.0001
Weight, kg, m(sd)	82.15 (20.10)	82.14 (21.50)	79.28 (20.34)	80.46 (20.39)	0.0348
Waist circumference, cm, m(sd)	98.00 (15.54)	98.35 (16.20)	96.09 (15.17)	98.21 (15.54)	0.0403
Race/ethnicity, n(%)					
Mexican American	140 (22.08)	136 (20.92)	106 (17.21)	109 (17.22)	0.125
Other Hispanic	16 (2.52)	27 (4.15)	24 (3.90)	26 (4.11)	
Non-Hispanic White	290 (45.74)	331 (50.92)	322 (52.27)	336 (53.08)	
Non-Hispanic Black	155 (24.45)	130 (20.00)	138 (22.40)	135 (21.33)	
Other/Multi-ethnic	33 (5.21)	26 (4.00)	26 (4.22)	27 (4.27)	
Income, n(%)					
\$0 - \$9,999	47 (7.87)	49 (7.90)	55 (9.29)	68 (11.30)	0.005
\$10,000 - \$19,999	88 (14.74)	108 (17.42)	105 (17.74)	132 (21.93)	
\$20,000 - \$34,999	124 (20.77)	141 (22.74)	125 (21.11)	131 (21.76)	
\$35,000 - \$54,999	118 (19.77)	115 (18.55)	129 (21.79)	109 (18.11)	
\$55,000 - \$74,999	65 (10.89)	79 (12.74)	67 (11.32)	60 (9.97)	
\$75,000 +	155 (25.96)	128 (20.65)	111 (18.75)	102 (16.94)	
Education, n(%)					
Below High School	180 (28.39)	180 (27.73)	152 (24.76)	158 (25.00)	0.36
High School Diploma	149 (23.50)	144 (22.19)	150 (24.43)	171 (27.06)	
Above High School	305 (48.11)	325 (50.08)	312 (50.81)	303 (47.94)	
Marital status, n(%)					
Married	386 (60.92)	354 (54.55)	347 (56.33)	310 (48.97)	0.009
Widowed	38 (6.01)	45 (6.93)	37 (6.01)	59 (9.32)	
Divorced	51 (8.07)	53 (8.17)	61 (9.90)	75 (11.85)	
Separated	11 (1.74)	24 (3.70)	22 (3.57)	17 (2.69)	
Never married	110 (17.41)	120 (18.49)	103 (16.72)	125 (19.75)	
Living with partner	37 (5.85)	53 (8.17)	46 (7.47)	47 (7.42)	
Moderate physical activity, n(%)	350 (55.21)	367 (56.46)	331 (53.73)	327 (51.66)	0.349
Vigorous physical activity, n(%)	225 (35.49)	217 (33.38)	199 (32.31)	169 (26.70)	0.006
Smoking status, n(%)					
Never	335 (52.92)	338 (52.08)	307 (49.92)	303 (47.94)	0.193
Past	162 (25.59)	149 (22.96)	141 (22.93)	158 (25.00)	
Current	136 (21.48)	162 (24.96)	167 (27.15)	171 (27.06)	
Diabetes, n(%)					
Yes	47 (7.42)	58 (8.94)	49 (7.95)	87 (13.74)	0.002
Borderline	10 (1.58)	6 (0.92)	5 (0.81)	11 (1.74)	
Hypertension, n(%)	227 (38.47)	213 (34.86)	178 (31.17)	235 (40.17)	0.007
Alcohol consumption (#drinks/month in past year), m(sd)	3.95 (7.10)	4.13 (7.12)	4.43 (7.36)	4.23 (7.39)	0.7116
Total calorie intake, kcal, m(sd)	2,216.43 (978.69)	2,241.17 (1062.55)	2,184.06 (1,057.16)	2,135.45 (994.08)	0.3022
Total fat intake, gm, m(sd)	83.24 (45.47)	85.73 (50.92)	81.26 (46.45)	79.52 (45.76)	0.1385
Total cholesterol, mg/dL, m(sd)	200.99 (41.42)	196.76 (44.11)	197.75 (40.40)	201.23 (46.55)	0.156
Urinary creatinine, mg/dL, m(sd)	143.25 (84.19)	137.66(85.69)	128.34 (83.36)	127.70 (80.33)	0.0015

Table 2: Means and standard deviations of Lean Mass, Fat Mass, % Body Fat and covariates according to creatinine standardized urinary phthalate metabolite quartiles mEP (mono-ethyl phthalate)

	Q1 (n=1,358)	Q2 (n=1,358)	Q3 (n=1,358)	Q4 (n=1,357)	p-value
urinary BPA, µg/g creatinine	<50.34	50.34-119.09	119.10-317.25	>317.25	
Lean mass, gm (sd)	52,348.62 (12,431.54)	49,915.20 (12,976.91)	49,462.56 (11,876.04)	50,208.36 (12,311.00)	<0.001
Fat mass, gm (sd)	27,257.89 (11,399.70)	28,254.48 (12,024.26)	27,869.15 (11,256.42)	29,250.88 (12,240.59)	<0.001
Body fat, % (sd)	32.61 (8.83)	32.59 (8.46)	34.46 (8.93)	35.12 (8.80)	<0.001
Gender, n(%)					
Male	855 (62.96)	628 (46.24)	622 (45.80)	648 (47.75)	<0.001
Female	503 (37.04)	730 (53.76)	736 (54.20)	709 (52.25)	
Age, years, m(sd)	49.91 (18.57)	48.41 (18.28)	48.02 (17.97)	49.12 (17.28)	0.0335
BMI, kg/m ² , m(sd)	28.08 (6.07)	28.34 (6.49)	28.24 (5.99)	29.04 (6.51)	0.0004
Height, cm, m(sd)	169.89 (9.88)	167.48 (10.34)	167.12 (10.11)	166.82 (10.10)	<0.0001
Weight, kg, m(sd)	82.33 (20.08)	79.81 (20.72)	79.02 (18.61)	81.11 (20.33)	0.0084
Waist circumference, cm, m(sd)	97.87 (15.20)	96.72 (15.69)	96.05 (14.39)	98.25 (15.54)	0.0012
Race/ethnicity, n(%)					
Mexican American	228 (16.79)	274 (20.18)	338 (24.89)	340 (25.06)	<0.001
Other Hispanic	38 (2.80)	60 (4.42)	63 (4.64)	80 (5.90)	
Non-Hispanic White	802 (59.06)	713 (52.50)	607 (44.70)	562 (41.41)	
Non-Hispanic Black	212 (15.61)	273 (20.10)	313 (23.05)	337 (24.83)	
Other/Multi-ethnic	78 (5.74)	38 (2.80)	37 (2.72)	38 (2.80)	
Income, n(%)					
\$0 - \$9,999	149 (11.88)	141 (11.24)	135 (10.60)	129 (10.39)	0.1050
\$10,000 - \$19,999	219 (17.46)	226 (18.01)	231 (18.13)	261 (21.01)	
\$20,000 - \$34,999	273 (21.77)	285 (22.71)	297 (23.31)	295 (23.75)	
\$35,000 - \$54,999	208 (16.59)	223 (17.77)	254 (19.94)	222 (17.87)	
\$55,000 - \$74,999	132 (10.53)	133 (10.60)	135 (10.60)	125 (10.06)	
\$75,000 +	273 (21.77)	247 (19.68)	222 (17.43)	210 (16.91)	
Education, n(%)					
Below High School	377 (27.86)	387 (28.50)	432 (31.88)	471 (34.71)	<0.001
High School Diploma	300 (22.17)	327 (24.08)	316 (23.32)	317 (23.36)	
Above High School	676 (49.96)	644 (47.42)	607 (44.80)	569 (41.93)	
Marital status, n(%)					
Married	784 (58.81)	703 (53.66)	735 (55.43)	739 (55.82)	0.2290
Widowed	109 (8.18)	122 (9.31)	125 (9.43)	111 (8.38)	
Divorced	111 (8.33)	120 (9.16)	134 (10.11)	146 (11.03)	
Separated	38 (2.85)	44 (3.36)	45 (3.39)	51 (3.85)	
Never married	215 (16.13)	240 (18.32)	210 (15.84)	215 (16.24)	
Living with partner	76 (5.70)	81 (6.18)	77 (5.81)	62 (4.68)	
Moderate physical activity, n(%)	640 (47.13)	630 (46.43)	656 (48.38)	594 (43.84)	0.1120
Vigorous physical activity, n(%)	430 (31.66)	414 (30.51)	422 (31.12)	399 (29.42)	0.6220
Smoking status, n(%)					
Never	677 (49.93)	699 (51.51)	729 (53.80)	674 (49.67)	0.0820
Past	325 (23.97)	356 (26.23)	323 (23.84)	348 (25.64)	
Current	354 (26.11)	302 (22.25)	303 (22.36)	335 (24.69)	
Diabetes, n(%)					
Yes	134 (9.88)	121 (8.91)	135 (9.94)	127 (9.37)	0.1650
Borderline	21 (1.55)	26 (1.91)	10 (0.74)	23 (1.70)	
Hypertension, n(%)	440 (34.76)	447 (35.06)	426 (33.31)	469 (37.10)	0.2520
Alcohol consumption (#drinks/month in past year), m(sd)	4.57 (7.89)	3.82 (6.91)	4.05 (7.22)	3.85 (6.82)	0.2085
Total calorie intake, kcal, m(sd)	2,190.91 (1,089.84)	2,113.57 (988.60)	2,136.28 (1,054.41)	2,094.69 (1,034.55)	0.0559
Total fat intake, gm, m(sd)	81.61 (52.60)	78.78 (45.33)	79.56 (48.29)	77.74 (45.73)	0.4382
Total cholesterol, mg/dL, m(sd)	201.10 (44.94)	202.51 (42.78)	201.25 (40.68)	201.04 (43.21)	0.7870
Urinary creatinine, mg/dL, m(sd)	135.97 (84.67)	133.76 (85.60)	135.68 (83.95)	131.87 (80.42)	0.5484

Table 3: Means and standard deviations of Lean Mass, Fat Mass, % Body Fat and covariates according to creatinine standardized urinary phthalate metabolite quartiles mEHP (mono-2-ethyl-hexyl phthalate)

	Q1 (n=1,359)	Q2 (n=1,359)	Q3 (n=1,359)	Q4 (n=1,359)	p-value
urinary BPA, µg/g creatinine	<1.29	1.29-2.67	2.68-5.61	>5.61	
Lean mass, gm (sd)	52,574.75 (12,263.75)	50,231.92 (12,383.51)	49,065.75 (12,539.45)	50,022.63 (12,358.59)	<0.001
Fat mass, gm (sd)	29,013.51 (11,873.93)	27,971.71 (11,511.11)	27,702.75 (11,750.71)	27,948.66 (11,847.01)	<0.0184
Body fat, % (sd)	33.88 (8.78)	34.17 (8.79)	34.45 (8.82)	34.18 (8.84)	<0.4209
Gender, n(%)					
Male	815 (59.97)	678 (49.89)	623 (45.84)	638 (46.95)	<0.001
Female	544 (40.03)	681 (50.11)	736 (54.16)	721 (53.05)	
Age, years, m(sd)	51.06 (17.98)	49.57 (18.47)	48.16 (17.67)	46.74 (17.79)	<0.0001
BMI, kg/m ² , m(sd)	28.98 (6.31)	28.29 (6.18)	28.11 (6.20)	28.33 (6.39)	0.0020
Height, cm, m(sd)	169.51 (9.92)	167.75 (10.15)	166.62 (9.99)	167.39 (10.42)	<0.0001
Weight, kg, m(sd)	82.15 (20.10)	83.34 (19.89)	79.87 (19.59)	78.40 (20.14)	<0.0001
Waist circumference, cm, m(sd)	99.57 (15.09)	97.16 (15.02)	95.61 (15.02)	96.54 (15.28)	<0.0001
Race/ethnicity, n(%)					
Mexican American	299 (22.00)	282 (20.75)	314 (23.11)	286 (21.04)	0.1170
Other Hispanic	46 (3.38)	51 (3.75)	72 (5.30)	72 (5.30)	
Non-Hispanic White	689 (50.70)	680 (50.04)	654 (48.12)	665 (48.93)	
Non-Hispanic Black	281 (20.68)	287 (21.12)	271 (19.94)	295 (21.78)	
Other/Multi-ethnic	44 (3.24)	59 (4.34)	48 (3.53)	40 (2.94)	
Income, n(%)					
\$0 - \$9,999	130 (10.21)	147 (11.76)	132 (10.45)	146 (11.75)	0.5980
\$10,000 - \$19,999	259 (20.35)	212 (16.96)	238 (18.84)	228 (18.34)	
\$20,000 - \$34,999	287 (22.55)	295 (23.60)	292 (23.12)	278 (22.37)	
\$35,000 - \$54,999	234 (18.38)	229 (18.32)	234 (18.53)	210 (16.89)	
\$55,000 - \$74,999	138 (10.84)	120 (9.60)	140 (11.08)	128 (10.30)	
\$75,000 +	225 (17.67)	247 (19.76)	227 (17.97)	253 (20.35)	
Education, n(%)					
Below High School	417 (30.71)	412 (30.32)	443 (32.69)	396 (29.20)	0.0780
High School Diploma	346 (25.48)	294 (21.63)	305 (22.51)	315 (23.23)	
Above High School	595 (43.81)	653 (48.05)	607 (44.80)	645 (47.57)	
Marital status, n(%)					
Married	782 (58.66)	725 (55.05)	739 (56.28)	718 (53.78)	0.0110
Widowed	110 (8.25)	138 (10.48)	118 (8.99)	101 (7.57)	
Divorced	141 (10.58)	113 (8.58)	130 (9.90)	128 (9.59)	
Separated	29 (2.18)	50 (3.80)	48 (3.66)	51 (3.82)	
Never married	199 (14.93)	214 (16.25)	207 (15.77)	260 (19.48)	
Living with partner	72 (5.40)	77 (5.85)	71 (5.41)	77 (5.77)	
Moderate physical activity, n(%)	645 (47.46)	628 (46.24)	617 (45.47)	631 (46.50)	0.7750
Vigorous physical activity, n(%)	975 (71.74)	930 (68.43)	948 (69.86)	913 (67.28)	0.0690
Smoking status, n(%)					
Never	645 (47.50)	695 (51.22)	714 (52.62)	727 (53.53)	0.0120
Past	370 (27.25)	359 (26.46)	314 (23.14)	311 (22.90)	
Current	343 (25.226)	303 (22.33)	329 (24.24)	320 (23.56)	
Diabetes, n(%)					
Yes	140 (10.31)	106 (7.81)	120 (8.84)	151 (11.12)	0.0860
Borderline	23 (1.69)	20 (1.47)	19 (1.40)	19 (1.40)	
Hypertension, n(%)	772 (60.69)	466 (36.55)	418 (32.76)	402 (31.75)	<0.001
Alcohol consumption (#drinks/month in past year), m(sd)	4.41 (7.63)	4.05 (7.27)	3.96 (6.95)	3.88 (7.02)	0.6500
Total calorie intake, kcal, m(sd)	2,097.97 (982.66)	2,128 (1,038.31)	2,127.41 (1,088.85)	2,180.86 (1,057.25)	0.3279
Total fat intake, gm, m(sd)	78.04 (45.13)	78.75 (47.90)	79.78 (52.57)	81.10 (46.33)	0.2205
Total cholesterol, mg/dL, m(sd)	202.52 (43.67)	201.88 (42.56)	202.84 (43.64)	198.68 (41.68)	0.0561
Urinary creatinine, mg/dL, m(sd)	152.32 (80.81)	131.24 (87.48)	125.26 (83.89)	128.48 (79.58)	0.0001

Table 4: Means and standard deviations of Lean Mass, Fat Mass, % Body Fat and covariates according to creatinine standardized urinary phthalate metabolite quartiles mBP (mono-n-butyl-phthalate)

	Q1 (n=1,359)	Q2 (n=1,360)	Q3 (n=1,358)	Q4 (n=1,359)	p-value
urinary BPA, $\mu\text{g/g}$ creatinine	<10.63	10.63-17.85	17.86-30.46	>30.46	
Lean mass, gm (sd)	54,244.93 (12,216.55)	52,163.99 (12,557.14)	49,442.78 (12,122.88)	46,041.35 (11,343.38)	<0.001
Fat mass, gm (sd)	27,494.85 (11,233.42)	28,292.54 (11,749.51)	28,703.40 (12,400.86)	28,146.15 (11,583.56)	<0.1423
Body fat, % (sd)	32.06 (8.61)	33.55 (8.67)	34.93 (8.77)	36.14 (8.65)	<0.001
Gender, n(%)					
Male	920 (67.70)	790 (58.09)	612 (45.07)	432 (31.79)	<0.001
Female	439 (32.30)	570 (41.91)	746 (54.93)	927 (68.21)	
Age, years, m(sd)	48.34 (17.57)	47.81 (17.92)	48.51 (18.20)	50.89 (18.36)	<0.0001
BMI, kg/m ² , m(sd)	28.47 (5.78)	28.73 (6.24)	28.54 (6.69)	27.99 (6.36)	0.0057
Height, cm, m(sd)	171.09 (9.90)	169.04 (10.00)	166.92 (9.94)	164.23 (9.58)	<0.0001
Weight, kg, m(sd)	83.51 (19.27)	82.22 (20.03)	79.76 (20.46)	75.73 (19.20)	<0.0001
Waist circumference, cm, m(sd)	98.44 (14.84)	98.15 (15.15)	96.89 (15.34)	95.39 (15.42)	<0.0001
Race/ethnicity, n(%)					
Mexican American	290 (21.34)	301 (22.13)	300 (22.09)	290 (21.34)	<0.001
Other Hispanic	35 (2.58)	53 (3.90)	60 (4.42)	93 (6.84)	
Non-Hispanic White	720 (52.98)	700 (51.47)	646 (47.57)	622 (45.77)	
Non-Hispanic Black	263 (19.35)	273 (20.07)	306 (22.53)	293 (21.56)	
Other/Multi-ethnic	51 (3.75)	33 (2.43)	46 (3.39)	61 (4.49)	
Income, n(%)					
\$0 - \$9,999	103 (8.09)	129 (10.13)	140 (11.17)	183 (14.88)	<0.001
\$10,000 - \$19,999	191 (15.00)	212 (16.65)	243 (19.39)	291 (23.66)	
\$20,000 - \$34,999	285 (22.39)	290 (22.78)	312 (24.90)	265 (21.54)	
\$35,000 - \$54,999	253 (19.87)	218 (17.12)	232 (18.52)	204 (16.59)	
\$55,000 - \$74,999	137 (10.76)	152 (11.94)	126 (10.06)	111 (9.02)	
\$75,000 +	304 (23.88)	272 (21.37)	200 (15.96)	176 (14.31)	
Education, n(%)					
Below High School	390 (28.74)	387 (28.46)	401 (29.59)	490 (36.14)	<0.001
High School Diploma	318 (23.43)	302 (22.21)	338 (24.94)	302 (22.27)	
Above High School	649 (47.83)	671 (49.34)	616 (45.46)	564 (41.59)	
Marital status, n(%)					
Married	816 (61.08)	786 (59.23)	712 (53.65)	650 (49.69)	<0.001
Widowed	94 (7.04)	91 (6.86)	118 (8.89)	164 (12.54)	
Divorced	98 (7.34)	118 (8.89)	147 (11.08)	149 (11.39)	
Separated	31 (2.32)	41 (3.09)	54 (4.07)	52 (3.98)	
Never married	230 (17.22)	219 (16.50)	224 (16.88)	207 (15.83)	
Living with partner	67 (5.01)	72 (5.43)	72 (5.43)	86 (6.57)	
Moderate physical activity, n(%)	641 (47.17)	676 (49.78)	632 (46.54)	572 (42.18)	0.0010
Vigorous physical activity, n(%)	485 (35.69)	446 (32.82)	396 (29.16)	339 (25.00)	<0.001
Smoking status, n(%)					
Never	725 (53.39)	692 (50.92)	691 (50.96)	673 (49.59)	<0.001
Past	380 (27.98)	344 (25.31)	338 (24.93)	292 (21.52)	
Current	253 (18.63)	323 (23.77)	327 (24.12)	392 (28.89)	
Diabetes, n(%)					
Yes	115 (8.47)	116 (8.54)	130 (9.57)	156 (11.49)	0.0350
Borderline	26 (1.91)	21 (1.55)	13 (0.96)	21 (1.55)	
Hypertension, n(%)	453 (35.70)	439 (34.24)	425 (33.62)	469 (36.81)	0.3260
Alcohol consumption (#drinks/month in past year), m(sd)	4.28 (7.21)	4.36 (7.54)	4.08 (7.26)	3.56 (6.84)	0.0034
Total calorie intake, kcal, m(sd)	2,254.08 (1,042.39)	2,196.81 (1,036.59)	2,094.63 (1,034.73)	1,986.12 (1,037.24)	<0.0001
Total fat intake, gm, m(sd)	84.19 (47.88)	82.24 (49.00)	77.94 (46.21)	73.20 (48.41)	<0.0001
Total cholesterol, mg/dL, m(sd)	202.31 (42.79)	199.73 (42.45)	202.84 (43.13)	201.09 (43.29)	0.2590
Urinary creatinine, mg/dL, m(sd)	129.55 (86.55)	144.69 (83.18)	134.99 (82.59)	128.05 (81.25)	<0.0001

Table 5: Means and standard deviations of Lean Mass, Fat Mass, % Body Fat and covariates according to creatinine standardized urinary phthalate metabolite quartiles mBzP (mono-benzyl-phthalate)

	Q1 (n=1,359)	Q2 (n=1,360)	Q3 (n=1,358)	Q4 (n=1,359)	p-value
urinary mBzP, $\mu\text{g/g}$ creatinine	<4.35	4.35-7.74	7.75-14.01	>14.01	
Lean mass, gm, m(sd)	51,762.21 (12,454.52)	50,893.48 (12,179.48)	50,052.44 (12,537.41)	49,186.93 (12,492.92)	<0.001
Fat mass, gm, m(sd)	27,391.43 (10,755.54)	27,769.01 (11,657.82)	28,204.49 (11,752.60)	29,271.70 (12,698.52)	<0.003
%Body fat, m(sd)	33.15 (8.51)	33.66 (8.81)	34.40 (8.78)	35.48 (8.95)	<0.001
Gender, n(%)					
Male	795 (58.50)	721 (53.05)	652 (47.98)	586 (43.12)	<0.001
Female	564 (41.50)	638 (46.95)	707 (52.02)	773 (56.88)	
Age, years, m(sd)	50.37 (17.47)	48.66 (17.84)	48.06 (18.10)	48.45 (18.69)	0.0044
BMI, kg/m^2 , m(sd)	28.17 (5.72)	28.37 (6.19)	28.34 (6.30)	28.85 (6.84)	0.3198
Height, cm, m(sd)	169.14 (10.07)	168.15 (10.18)	167.66 (10.21)	166.32 (10.04)	<0.0001
Weight, kg, m(sd)	80.90 (19.04)	80.34 (19.51)	79.90 (20.10)	80.09 (21.15)	0.179
Waist circumference, cm, m(sd)	97.47 (14.52)	96.84 (15.22)	96.76 (15.26)	97.82 (15.89)	0.1968
Race/ethnicity, n(%)					
Mexican American	327 (24.06)	297 (21.85)	295 (21.71)	262 (19.28)	0.0630
Other Hispanic	53 (3.90)	59 (4.34)	65 (4.78)	64 (4.71)	
Non-Hispanic White	664 (48.86)	642 (47.24)	689 (50.70)	693 (50.99)	
Non-Hispanic Black	262 (19.28)	304 (22.37)	272 (20.01)	297 (21.85)	
Other/Multi-ethnic	53 (3.90)	57 (4.19)	38 (2.80)	43 (3.16)	
Income, n(%)					
\$0 - \$9,999	107 (8.47)	114 (9.13)	139 (10.96)	195 (15.61)	<0.001
\$10,000 - \$19,999	189 (14.95)	223 (17.87)	254 (20.03)	271 (21.70)	
\$20,000 - \$34,999	282 (22.31)	281 (22.52)	291 (22.95)	298 (23.86)	
\$35,000 - \$54,999	248 (19.62)	227 (18.19)	228 (17.98)	204 (16.33)	
\$55,000 - \$74,999	121 (9.57)	149 (11.94)	132 (10.41)	124 (9.93)	
\$75,000 +	317 (25.08)	254 (20.35)	224 (17.67)	157 (12.57)	
Education, n(%)					
Below High School	417 (30.71)	397 (29.23)	401 (29.55)	453 (33.43)	0.0470
High School Diploma (including GED)	293 (21.58)	311 (22.90)	333 (24.54)	323 (23.84)	
Above High School	648 (47.72)	650 (47.86)	623 (45.91)	579 (42.73)	
Marital status, n(%)					
Married	819 (61.30)	754 (56.91)	713 (53.93)	678 (51.56)	<0.001
Widowed	110 (8.23)	114 (8.60)	114 (8.62)	129 (9.81)	
Divorced	93 (6.96)	130 (9.81)	133 (10.06)	156 (11.86)	
Separated	36 (2.69)	40 (3.02)	46 (3.48)	56 (4.26)	
Never married	220 (16.47)	202 (15.25)	242 (18.31)	216 (16.43)	
Living with partner	58 (4.34)	85 (6.42)	74 (5.60)	80 (6.08)	
Mod. physical activity, n(%)	636 (46.83)	634 (43.72)	652 (48.05)	599 (44.08)	0.2050
Vig. physical activity, n(%)	434 (31.96)	428 (31.54)	423 (31.15)	381 (28.04)	0.1060
Smoking status, n(%)					
Never	713 (52.50)	730 (53.72)	691 (50.88)	647 (47.75)	<0.001
Past	382 (28.13)	326 (23.99)	321 (23.64)	325 (23.99)	
Current	263 (19.37)	303 (22.30)	346 (25.48)	383 (28.27)	
Diabetes, n(%)					
Yes	121 (8.92)	134 (9.86)	124 (9.13)	138 (10.16)	0.9080
Borderline	18 (1.33)	22 (1.62)	21 (1.55)	20 (1.47)	
Hypertension, n(%)	473 (37.51)	428 (33.44)	423 (33.12)	462 (36.35)	0.0500
Alcohol consumption (#drinks/month in past year), m(sd)	4.35 (7.57)	4.09 (7.04)	3.84 (7.09)	4.01 (7.18)	0.2074
Total calorie intake, kcal, m(sd)	2,146.90 (1,007.86)	2,160.20 (985.91)	2,137.78 (1,044.60)	2,088.73 (1,126.48)	0.0194
Total fat intake, gm, m(sd)	78.94 (45.81)	81.01 (47.46)	79.64 (46.10)	78.06 (52.61)	0.1059
Total cholesterol, mg/dL, m(sd)	202.04 (40.37)	201.10 (42.97)	201.29 (41.30)	201.55 (46.81)	0.6397
Urinary creatinine, mg/dL, m(sd)	119.51 (79.46)	135.98 (83.66)	139.92 (83.87)	141.88 (85.70)	0.0001

Table 6: Adjusted regression coefficients, standard errors and p-values for Lean Mass by urinary BPA and phthalate metabolites

Urinary BPA or phthalate metabolite concentration (µg/g creatinine)	N	Model 1 beta (se)	p-value	N	Model 2 beta (se)	p-value	N	Model 3 beta (se)	p-value
Bisphenol-A (BPA)	2,533			2,519			2,166		
continuous		-19.81 (17.07)	0.246		-21.51 (10.31)	0.037		-16.35 (9.97)	0.101
Q1: <1.15		(ref)	—		(ref)	—		(ref)	—
Q2: 1.15-2.00		1,154.85 (524.14)	0.028		-138.56 (321.85)	0.667		-38.42 (321.41)	0.905
Q3: 2.01-3.37		868.84 (546.23)	0.112		-398.97 (333.83)	0.232		-150.25 (330.43)	0.649
Q4: >3.37		15.12 (584.92)	0.979		-1,263.23 (356.77)	<0.001		-862.16 (354.65)	0.015
		p-trend: 0.872			p-trend: <0.001			p-trend: <0.017	
Monoethyl phthalate (mEP)	5,431			5,378			4,531		
continuous		0.05 (0.09)	0.585		-0.04 (0.05)	0.471		-0.04 (0.06)	0.422
Q1: <50.34		(ref)	—		(ref)	—		(ref)	—
Q2: 50.34-119.09		496.34 (338.49)	0.146		34.38 (207.65)	0.869		-56.17 (204.72)	0.784
Q3: 119.10-317.25		-56.14 (351.69)	0.873		-321.22 (215.34)	0.136		-355.63 (213.58)	0.096
Q4: >317.25		887.91 (363.87)	0.015		-414.95 (222.68)	0.062		-393.14 (221.49)	0.076
		p-trend: 0.067			p-trend: 0.022			p-trend: 0.035	
Monobutyl phthalate (mBP)	5,436			5,383			4,535		
continuous		-0.50 (0.60)	0.407		-0.32 (0.37)	0.379		-0.21 (0.34)	0.531
Q1: <10.63		(ref)	—		(ref)	—		(ref)	—
Q2: 10.63-17.85		-82.34 (344.03)	0.811		-98.73 (212.80)	0.643		-382.42 (207.22)	0.065
Q3: 17.86-30.46		-741.61 (372.95)	0.047		-680.65 (228.83)	0.003		-823.58 (226.84)	<0.001
Q4: >30.46		-1,319.47 (404.05)	0.001		-881.64 (246.48)	<0.001		-731.76 (248.89)	0.003
		p-trend: <0.001			p-trend: <0.001			p-trend: <0.001	
Monoethylhexyl phthalate (mEHP)	5,436			5,383			4,535		
continuous		-1.04 (2.92)	0.721		1.56 (1.83)	0.396		0.45 (1.74)	0.796
Q1: <1.29		(ref)	—		(ref)	—		(ref)	—
Q2: 1.29-2.67		-369.59 (340.02)	0.277		-143.83 (208.24)	0.490		-175.79 (204.79)	0.391
Q3: 2.68-5.61		-217.82 (336.35)	0.517		12.72 (206.85)	0.951		-142.57 (207.20)	0.491
Q4: >5.61		-401.54 (353.52)	0.256		-87.67 (217.68)	0.687		-130.65 (149.82)	0.545
		p-trend: 0.326			p-trend: 0.842			p-trend: <0.568	
Monobenzyl phthalate (mBzP)	5,436			5,383			4,535		
continuous		-0.50 (0.60)	0.407		-0.27 (0.31)	0.387		-0.05 (0.29)	0.858
Q1: <4.35		(ref)	—		(ref)	—		(ref)	—
Q2: 4.35-7.74		524.67 (342.31)	0.125		30.22 (209.76)	0.885		-97.74 (208.71)	0.640
Q3: 7.75-14.01		123.43 (369.01)	0.738		-592.98 (226.46)	0.009		-706.35 (223.25)	0.002
Q4: <14.01		0.96 (405.25)	0.998		-1,070.43 (248.06)	<0.001		-909.13 (252.32)	<0.001
		p-trend: 0.709			p-trend: <0.001			p-trend: <0.001	
Model 1: creatinine, age, gender, race									
Model 2: creatinine, age, gender, race, BMI									
Model 3 (BPA): creatinine, age, gender, race, BMI, family income, vigorous physical activity, moderate physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (mEP): creatinine, age, gender, race, BMI, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (mBP): creatinine, age, gender, race, BMI, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (mEHP): creatinine, age, gender, race, BMI, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (mBzP): creatinine, age, gender, race, BMI, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									

Table 7: Adjusted regression coefficients, standard errors and p-values for Fat Mass by urinary BPA and phthalate metabolites

Urinary BPA or phthalate metabolite concentration (µg/g creatinine)	N	Model 1 beta (se)	p-value	N	Model 2 beta (se)	p-value	N	Model 3 beta (se)	p-value
Bisphenol-A (BPA)	2,533			2,519			2,368		
continuous		-1.42 (21.61)	0.948		-3.35 (7.15)	0.639		-4.34 (6.53)	0.507
Q1: <1.15		(ref)	—		(ref)	—		(ref)	—
Q2: 1.15-2.00		2,243 (661.18)	0.001		349.20 (231.34)	0.132		123.02 (209.12)	0.557
Q3: 2.01-3.37		2,150.24 (688.93)	0.001		381.87 (235.59)	0.105		232.05 (212.90)	0.276
Q4: >3.37		2,106.20 (736.83)	0.004		303.09 (249.06)	0.224		236.58 (232.89)	0.310
			p-trend: 0.009			p-trend: 0.248			p-trend: <0.276
Monoethyl phthalate (mEP)	5,431			5,378			4,754		
continuous		0.13 (0.12)	0.275		0.13 (0.12)	0.275		-0.01 (0.08)	0.696
Q1: <50.34		(ref)	—		(ref)	—		(ref)	—
Q2: 50.34-119.09		753.03 (442.00)	0.089		-22.82 (150.36)	0.879		-73.38 (139.89)	0.600
Q3: 119.10-317.25		587.42 (456.46)	0.198		97.70 (152.98)	0.523		170.28 (143.26)	0.235
Q4: >317.25		1,995.70 (474.43)	<0.001		-98.92 (158.69)	0.533		-37.67 (149.82)	0.801
			p-trend: <0.001			p-trend: <0.714			p-trend: <0.779
Monobutyl phthalate (mBP)	5,436			5,383			4,759		
continuous		-0.24 (0.79)	0.761		0.04 (0.26)	0.862		0.02 (0.23)	0.922
Q1: <10.63		(ref)	—		(ref)	—		(ref)	—
Q2: 10.63-17.85		27.48 (447.99)	0.951		-11.88 (152.12)	0.938		-209.39 (141.21)	0.138
Q3: 17.86-30.46		-50.57 (438.48)	0.917		-51.16 (164.89)	0.756		-66.30 (152.79)	0.664
Q4: >30.46		-785.98 (526.48)	0.136		-144.10 (174.60)	0.409		-48.73 (169.65)	0.774
			p-trend: <0.141			p-trend: 0.495			p-trend: <0.984
Monoethylhexyl phthalate (mEHP)	5,436			5,383			4,886		
continuous		-2.35 (3.80)	0.537		1.33 (1.30)	0.308		0.55 (1.21)	0.646
Q1: <1.29		(ref)	—		(ref)	—		(ref)	—
Q2: 1.29-2.67		-429.28 (443.00)	0.333		-130.98 (146.75)	0.372		-78.01 (136.91)	0.569
Q3: 2.68-5.61		-630.09 (438.41)	0.151		-303.11 (148.78)	0.042		-319.91 (140.90)	0.023
Q4: >5.61		-806.72 (459.64)	0.079		-394.87 (155.61)	0.011		-297.98 (144.87)	0.040
			p-trend: <0.072			p-trend: <0.007			p-trend: <0.016
Monobenzyl phthalate (mBzP)	5,436			5,383			4,759		
continuous		-0.24 (0.79)	0.761		0.22 (0.22)	0.322		0.21 (0.20)	0.298
Q1: <4.35		(ref)	—		(ref)	—		(ref)	—
Q2: 4.35-7.74		714.00 (446.00)	0.109		-48.69 (147.28)	0.741		-143.55 (140.19)	0.306
Q3: 7.75-14.01		1,070.98 (479.96)	0.026		-95.71 (161.13)	0.553		-41.62 (152.15)	0.784
Q4: <14.01		1,771.72 (529.45)	0.001		69.25 (174.92)	0.692		48.51 (167.10)	0.772
			p-trend: <0.001			p-trend: <0.764			p-trend: <0.611
Model 1: creatinine, age, gender, race									
Model 2: creatinine, age, gender, race, BMI									
Model 3 (BPA): creatinine, age, gender, race, BMI, education, diabetes, waist circumference, total calorie intake, total fat intake									
Model 3 (mEP): creatinine, age, gender, race, BMI, education, marital status, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									
Model 3 (mBP): creatinine, age, gender, race, BMI, marital status, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									
Model 3 (mEHP): creatinine, age, gender, race, BMI, education, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									
Model 3 (mBzP): creatinine, age, gender, race, BMI, education, marital status, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									

Table 8: Adjusted regression coefficients, standard errors and p-values for % Body Fat by urinary BPA and phthalate metabolites

Urinary BPA or phthalate metabolite concentration (µg/g creatinine)	N	Model 1 beta (se)	p-value	N	Model 2 beta (se)	p-value	N	Model 3 beta (se)	p-value
Bisphenol-A (BPA) continuous	2,533	0.005 (0.01)	0.631	2,519	0.005(0.007)	0.503	2,256	0.001 (0.07)	0.838
Q1: <1.15		(ref)	—		(ref)	—		(ref)	—
Q2: 1.15-2.00		1.26 (0.37)	0.001		0.45 (0.24)	0.062		0.27 (0.24)	0.259
Q3: 2.01-3.37		1.29 (0.38)	0.001		0.50 (0.24)	0.039		0.40 (0.23)	0.085
Q4: >3.37		1.44 (0.40)	<0.001		0.67 (0.26)	0.009		0.64 (0.25)	0.011
		p-trend: <0.001				p-trend: 0.013			p-trend: 0.012
Monoethyl phthalate (mEP) continuous	5,431	<0.001 (<0.001)	0.420	5,378	<0.001 (<0.001)	0.875	4,537	<0.001 (<0.001)	0.704
Q1: <50.34		(ref)	—		(ref)	—		(ref)	—
Q2: 50.34-119.09		0.48 (0.24)	0.051		0.10 (0.15)	0.497		0.12 (0.15)	0.433
Q3: 119.10-317.25		0.65 (0.25)	0.009		0.41 (0.16)	0.010		0.49 (0.16)	0.002
Q4: >317.25		1.16 (0.26)	<0.001		1.19 (0.16)	0.225		0.27 (0.16)	0.093
		p-trend: <0.001				p-trend: 0.085			p-trend: 0.022
Monobutyl phthalate (mBP) continuous	5,436	<0.001 (<0.001)	0.790	5,383	<0.001 (<0.001)	0.341	4,542	<0.001 (<0.001)	0.420
Q1: <10.63		(ref)	—		(ref)	—		(ref)	—
Q2: 10.63-17.85		0.11 (0.25)	0.647		0.10 (0.16)	0.534		0.10 (0.15)	0.490
Q3: 17.86-30.46		0.30 (0.27)	0.264		0.35 (0.17)	0.044		0.43 (0.17)	0.011
Q4: >30.46		-0.17 (0.29)	0.552		0.12 (0.18)	0.492		0.38 (0.18)	0.039
		p-trend: 0.688				p-trend: 0.301			p-trend: 0.014
Monoethylhexyl phthalate (mEHP) continuous	5,436	<0.001 (0.002)	0.793	5,383	0.001 (0.001)	0.426	4,540	<0.001 (0.001)	0.480
Q1: <1.29		(ref)	—		(ref)	—		(ref)	—
Q2: 1.29-2.67		-0.19 (0.24)	0.439		-0.07 (0.15)	0.642		-0.3 (0.15)	0.828
Q3: 2.68-5.61		-0.23 (0.24)	0.349		-0.07 (0.15)	0.669		-0.04 (0.15)	0.800
Q4: >5.61		-0.42 (0.25)	0.095		-0.24 (0.16)	0.136		-0.12 (0.16)	0.437
		p-trend: 0.104				p-trend: 0.164			p-trend: 0.465
Monobenzyl phthalate (mBzP) continuous	5,436	<0.001	0.790	5,383	<0.001 (<0.001)	0.143	4,542	<0.001 (<0.001)	0.280
Q1: <4.35		(ref)	—		(ref)	—		(ref)	—
Q2: 4.35-7.74		0.41 (0.24)	0.091		0.06 (0.15)	0.702		0.05 (0.15)	0.718
Q3: 7.75-14.01		0.70 (0.26)	0.008		0.16 (0.16)	0.338		0.38 (0.16)	0.020
Q4: <14.01		1.20 (0.29)	<0.001		0.43 (0.18)	0.015		0.61 (0.18)	0.001
		p-trend: <0.001				p-trend: 0.013			p-trend: <0.001
Model 1: creatinine, age, gender, race									
Model 2: creatinine, age, gender, race, BMI									
Model 3 (BPA): creatinine, age, gender, race, BMI, vigorous physical activity, education, smoking status, diabetes, WC, total calorie intake, serum cholesterol									
Model 3 (mEP): creatinine, age, gender, race, BMI, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									
Model 3 (mBP): creatinine, age, gender, race, BMI, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									
Model 3 (mEHP): creatinine, age, gender, race, BMI, education, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									
Model 3 (mBzP): creatinine, age, gender, race, BMI, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									

Table 9: Regression coefficients of fully adjusted Lean Mass models* stratified by BMI category

Urinary BPA or phthalate metabolite concentration (µg/g creatinine)	BMI <24.99 kg/m ²			BMI 25-29.99 kg/m ²			BMI >30 kg/m ²		
	N	b (se)	p-value	N	b (se)	p-value	N	b (se)	p-value
Bisphenol-A (BPA)	679			726			761		
Q1: <1.15		(ref)	—		(ref)	—		(ref)	—
Q2: 1.15-2.00		-740.46 (0.124)	0.124		232.86 (523.77)	0.657		124.00 (666.30)	0.852
Q3: 2.01-3.37		-813.32 (55.22)	0.108		554.97 (567.68)	0.329		-553.00 (656.67)	0.400
Q4: >3.37		-1,530.16 (540.89)	0.005		-310.32 (611.33)	0.612		-756.20 (691.77)	0.275
			p-trend: 0.007			p-trend: 0.765			p-trend: 0.161
Monoethyl phthalate (mEP)	1,374			1,584			1,550		
Q1: <50.34		(ref)	—		(ref)	—		(ref)	—
Q2: 50.34-119.09		-2.08 (323.96)	0.995		160.90 (338.71)	0.635		-660.34 (411.63)	0.109
Q3: 119.10-317.25		45.66 (333.89)	0.891		-190.18 (354.37)	0.592		-858.19 (426.84)	0.045
Q4: >317.25		77.40 (367.52)	0.833		-219.18 (368.51)	0.552		-879.56 (417.55)	0.035
			p-trend: 0.811			p-trend: 0.373			p-trend: 0.045
Monobutyl phthalate (mBP)	1,398			1,587			1,550		
Q1: <10.63		(ref)	—		(ref)	—		(ref)	—
Q2: 10.63-17.85		-579.56 (327.40)	0.077		4.68 (335.95)	0.989		-940.24 (418.26)	0.025
Q3: 17.86-30.46		-1,110.82 (369.08)	0.003		-569.99 (364.91)	0.113		-1,054.40 (444.10)	0.018
Q4: >30.46		-807.06 (393.80)	0.041		-588.78 (418.30)	0.159		-1,170.24 (481.35)	0.015
			p-trend: 0.022			p-trend: 0.076			p-trend: 0.026
Monoethylhexyl phthalate (mEHP)	1,398			1,587			1,550		
Q1: <1.29		(ref)	—		(ref)	—		(ref)	—
Q2: 1.29-2.67		189.35 (322.91)	0.558		195.92 (344.63)	0.570		-595.14 (407.94)	0.145
Q3: 2.68-5.61		312.38 (337.24)	0.354		180.53 (337.86)	0.593		-997.75 (393.57)	0.011
Q4: >5.61		263.50 (351.11)	0.453		52.27 (359.87)	0.885		-635.22 (414.12)	0.125
			p-trend: 0.403			p-trend: 0.863			p-trend: 0.074
Monobenzyl phthalate (mBzP)	1,375			1,587			1,550		
Q1: <4.35		(ref)	—		(ref)	—		(ref)	—
Q2: 4.35-7.74		-325.79 (320.39)	0.309		289.71 (337.27)	0.390		-452.16 (436.16)	0.037
Q3: 7.75-14.01		-1,002.26 (360.00)	0.005		-280.54 (366.97)	0.445		-927.89 (444.14)	0.001
Q4: <14.01		-714.87 (407.35)	0.080		-681.00 (416.25)	0.102		-1,651.46 (485.29)	<0.001
			p-trend: 0.025			p-trend: 0.047			p-trend: <0.001
*Model 3 (BPA): creatinine, age, gender, race, family income, vigorous physical activity, moderate physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (mep): creatinine, age, gender, race, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (mbp): creatinine, age, gender, race, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (mehp): creatinine, age, gender, race, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									
Model 3 (model): creatinine, age, gender, race, family income, education, moderate physical activity, vigorous physical activity, WC, total calorie intake, serum cholesterol									

Table 10: Regression coefficients of fully adjusted Fat Mass models* stratified by BMI category

Urinary BPA or phthalate metabolite concentration (µg/g creatinine)	BMI <24.99 kg/m ²			BMI 25-29.99 kg/m ²			BMI >30 kg/m ²		
	N	b (se)	p-value	N	b (se)	p-value	N	b (se)	p-value
Bisphenol-A (BPA)	728			797			825		
Q1: <1.15		(ref)	—		(ref)	—		(ref)	—
Q2: 1.15-2.00		315.17 (312.14)	0.314		100.77 (318.61)	0.752		-121.33 (579.40)	0.834
Q3: 2.01-3.37		479.47 (328.64)	0.146		-60.94 (341.62)	0.858		-23.77 (580.07)	0.967
Q4: >3.37		357.07 (346.29)	0.303		-59.97 (373.94)	0.873		329.36 (613.17)	0.591
			p-trend: 0.246			p-trend: 0.762			p-trend: 0.533
Monoethyl phthalate (mEP)	1,492			1,651			1,611		
Q1: <50.34		(ref)	—		(ref)	—		(ref)	—
Q2: 50.34-119.09		107.24 (209.67)	0.609		162.01 (225.59)	0.473		-370.06 (410.78)	0.368
Q3: 119.10-317.25		306.33 (213.60)	0.152		648.25 (235.49)	0.006		-22.40 (416.41)	0.957
Q4: >317.25		219.42 (234.89)	0.350		218.82 (245.32)	0.373		239.66 (414.90)	0.564
			p-trend: 0.220			p-trend: 0.150			p-trend: 0.343
Monobutyl phthalate (mBP)	1,493			1,655			1,611		
Q1: <10.63		(ref)	—		(ref)	—		(ref)	—
Q2: 10.63-17.85		-311.87 (212.35)	0.142		-118.16 (226.87)	0.603		-837.51 (406.54)	0.040
Q3: 17.86-30.46		-407.64 (236.18)	0.085		65.45 (246.23)	0.790		39.87 (434.53)	0.927
Q4: >30.46		-107.76 (249.53)	0.666		97.75 (288.53)	0.735		-719.31 (472.48)	0.128
			p-trend: 0.617			p-trend: 0.607			p-trend: 0.431
Monoethylhexyl phthalate (mEHP)	1,534			1,701			1,651		
Q1: <1.29		(ref)	—		(ref)	—		(ref)	—
Q2: 1.29-2.67		-218.69 (208.30)	0.294		-114.39 (232.46)	0.623		309.93 (394.42)	0.432
Q3: 2.68-5.61		-470.07 (218.42)	0.032		-93.17 (228.15)	0.683		-367.01 (381.78)	0.337
Q4: >5.61		-416.27 (221.72)	0.061		-316.55 (242.02)	0.191		119.80 (397.12)	0.763
			p-trend: 0.034			p-trend: 0.234			p-trend: 0.867
Monobenzyl phthalate (mBzP)	1,493			1,655			1,611		
Q1: <4.35		(ref)	—		(ref)	—		(ref)	—
Q2: 4.35-7.74		-183.32 (204.06)	0.369		-134.56 (226.84)	0.553		-160.38 (418.25)	0.701
Q3: 7.75-14.01		-204.28 (232.49)	0.380		-287.61 (250.72)	0.252		287.75 (436.26)	0.510
Q4: <14.01		-487.25 (255.96)	0.057		-107.41 (284.03)	0.705		170.09 (463.36)	0.714
			p-trend: 0.075			p-trend: 0.583			p-trend: 0.487
*Model 3 (BPA): creatinine, age, gender, race, education, diabetes, WC, total calorie intake, total fat intake									
Model 3 (mep): creatinine, age, gender, race, education, marital status, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									
Model 3 (mbp): creatinine, age, gender, race, marital status, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									
Model 3 (mehp): creatinin, age, gender, race, education, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									
Model 3 (mbzp): creatinine, age, gender, race, education, marital status, vigorous physical activity, diabetes, WC, alcohol intake, total calorie intake, total fat intake									

Table 11: Regression coefficients of fully adjusted % Body Fat models* stratified by BMI category

Urinary BPA or phthalate metabolite concentration (µg/g creatinine)	BMI <24.99 kg/m ²			BMI 25-29.99 kg/m ²			BMI >30 kg/m ²		
	N	b (se)	p-value	N	b (se)	p-value	N	b (se)	p-value
Bisphenol-A (BPA)	705			758			793		
Q1: <1.15		(ref)	—		(ref)	—		(ref)	—
Q2: 1.15-2.00		0.58 (0.47)	0.217		-0.08 (0.34)	0.820		0.004 (0.38)	0.787
Q3: 2.01-3.37		0.74 (0.47)	0.116		-0.22 (0.38)	0.556		0.38 (0.37)	0.125
Q4: >3.37		0.89 (0.48)	0.066		-0.01 (0.40)	0.980		0.62 (0.40)	0.075
			p-trend: 0.062			p-trend: 0.925			p-trend: 0.066
Monoethyl phthalate (mEP)	1,407			1,580			1,550		
Q1: <50.34		(ref)	—		(ref)	—		(ref)	—
Q2: 50.34-119.09		0.23 (0.29)	0.430		0.11 (0.24)	0.658		0.06 (0.25)	0.820
Q3: 119.10-317.25		0.26 (0.29)	0.370		0.71 (0.25)	0.005		0.41 (0.26)	0.111
Q4: >317.25		0.23 (0.32)	0.472		0.30 (0.26)	0.253		0.40 (0.25)	0.117
			p-trend: 0.447			p-trend: 0.071			p-trend: 0.059
Monobutyl phthalate (mBP)	1,408			1,584			1,550		
Q1: <10.63		(ref)	—		(ref)	—		(ref)	—
Q2: 10.63-17.85		-0.07 (0.29)	0.800		0.17 (0.24)	0.756		0.09 (0.25)	0.709
Q3: 17.86-30.46		0.14 (0.33)	0.672		0.53 (0.26)	0.047		0.50 (0.26)	0.059
Q4: >30.46		0.38 (0.35)	0.275		0.64 (0.31)	0.042		0.21 (0.29)	0.457
			p-trend: 0.236			p-trend: 0.018			p-trend: 0.279
Monoethylhexyl phthalate (mEHP)	1,407			1,583			1,550		
Q1: <1.29		(ref)	—		(ref)	—		(ref)	—
Q2: 1.29-2.67		-0.47 (0.29)	0.102		-0.10 (0.25)	0.701		0.46 (0.25)	0.069
Q3: 2.68-5.61		-0.72 (0.30)	0.018		0.01 (0.24)	0.953		0.28 (0.24)	0.243
Q4: >5.61		-0.50 (0.30)	0.093		-0.17 (0.26)	0.512		0.23 (0.25)	0.362
			p-trend: 0.057			p-trend: 0.624			p-trend: 0.468
Monobenzyl phthalate (mBzP)	1,408			1,584			1,550		
Q1: <4.35		(ref)	—		(ref)	—		(ref)	—
Q2: 4.35-7.74		0.03 (0.28)	0.922		-0.18 (0.24)	0.448		0.04 (0.25)	0.867
Q3: 7.75-14.01		0.29 (0.32)	0.362		0.10 (0.27)	0.709		0.48 (0.27)	0.071
Q4: <14.01		0.03 (0.36)	0.923		0.56 (0.30)	0.064		0.71 (0.28)	0.012
			p-trend: 0.717			p-trend: 0.038			p-trend: 0.003
*Model 3 (BPA): creatinine, age, gender, race, vigorous physical activity, education, smoking status, diabetes, WC, total calorie intake, serum cholesterol									
Model 3 (mep): creatinine, age, gender, race, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									
Model 3 (mbp): creatinine, age, gender, race, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									
Model 3 (mehp): creatinine, age, gender, race, education, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									
Model 3 (mbzp): creatinine, age, gender, race, marital status, vigorous physical activity, smoking status, diabetes, WC, alcohol intake, total calorie intake, serum cholesterol									

Table 12: Adjusted* regression coefficients, standard errors and p-values for Lean Mass, Fat Mass, and %Body Fat by urinary BPA and phthalate metabolites in sub-population of subjects with non-imputed DXA measures

Urinary BPA or phthalate metabolite concentration (µg/g creatinine)	N	Lean Mass beta (se)	p-value	N	Fat Mass beta (se)	p-value	N	%Body Fat beta (se)	p-value
Bisphenol-A (BPA)	1,820			1,820			1,817		
continuous		-12.49 (14.27)	0.382		3.36 (17.33)	0.846		0.007 (0.01)	0.556
Q1: <1.15		(ref)	—		(ref)	—		(ref)	—
Q2: 1.15-2.00		315.23 (488.80)	0.519		1,543.87 (591.92)	0.009		1.20 (0.38)	0.002
Q3: 2.01-3.37		34.45 (514.19)	0.947		1,318.08 (622.67)	0.034		1.19 (0.40)	0.003
Q4: >3.37		-24.93 (552.25)	0.964		1,975.74 (668.76)	0.003		1.55 (0.43)	<0.001
			p-trend: 0.845			p-trend: 0.008			p-trend: <0.001
Monoethyl phthalate (mEP)	4,136			4,136			4,136		
continuous		0.08 (0.09)	0.369		0.04 (0.11)	0.693		- <0.001 (<0.001)	0.922
Q1: <50.34		(ref)	—		(ref)	—		(ref)	—
Q2: 50.34-119.09		309.33 (322.12)	0.337		400.16 (399.27)	0.316		0.30 (0.26)	0.249
Q3: 119.10-317.25		-11.40 (333.04)	0.973		442.95 (421.81)	0.283		0.55 (0.26)	0.038
Q4: >317.25		784.81 (348.85)	0.025		1,147 (33)	0.008		0.77 (0.28)	0.005
			p-trend: 0.069			p-trend: 0.011			p-trend: 0.004
Monobutyl phthalate (mBP)	4,140			4,140			4,140		
continuous		-0.04 (0.51)	0.940		0.21 (0.64)	0.746		0.002 (0.004)	0.546
Q1: <10.63		(ref)	—		(ref)	—		(ref)	—
Q2: 10.63-17.85		-176.60 (325.67)	0.588		-0.98 (404.14)	0.998		0.06 (0.26)	0.821
Q3: 17.86-30.46		-699.37 (350.56)	0.046		-42.08 (435.03)	0.923		0.30 (0.28)	0.276
Q4: >30.46		-1,177.64 (385.29)	0.002		-650.84 (478.14)	0.174		-0.19 (0.31)	0.540
			p-trend: 0.001			p-trend: 0.189			p-trend: 0.737
Monoethylhexyl phthalate (mEHP)	4,140			4,140			4,140		
continuous		1.10 (2.58)	0.669		-1.18 (3.20)	0.713		-0.009 (0.002)	0.672
Q1: <1.29		(ref)	—		(ref)	—		(ref)	—
Q2: 1.29-2.67		-174.19 (324.13)	0.591		-223.30 (401.75)	0.578		-0.20 (0.26)	0.430
Q3: 2.68-5.61		-16.64 (322.59)	0.959		-376.73 (399.84)	0.346		-0.24 (0.26)	0.349
Q4: >5.61		57.27 (336.81)	0.865		-622.23 (417.46)	0.136		-0.52 (0.27)	0.054
			p-trend: 0.793			p-trend: 0.131			p-trend: 0.064
Monobenzyl phthalate (mBzP)	4,140			4,140			4,140		
continuous		0.05 (0.43)	0.909		0.47 (0.54)	0.380		0.004 (0.003)	0.239
Q1: <4.35		(ref)	—		(ref)	—		(ref)	—
Q2: 4.35-7.74		354.67 (324.44)	0.274		579.36 (402.46)	0.150		0.32 (0.26)	0.214
Q3: 7.75-14.01		-356.46 (350.08)	0.351		407.12 (434.27)	0.349		0.43 (0.28)	0.119
Q4: <14.01		-613.23 (388.65)	0.115		848.62 (482.12)	0.078		0.86 (0.31)	0.005
			p-trend: 0.037			p-trend: 0.133			p-trend: 0.006

*adjusted for urinary creatinine, age, gender, and race

Table 13: Number and Percent in Final Sample: NHANES 1999-2006

	for BPA analysis (NHANES 03-06)	for phthalate analysis (NHANES 99-06)
Original Study Sample	2,634	5,688
<u>excluded:</u>		
Missing information on urinary Phthalate metabolites		197 (3.46%)
Missing information on urinary BPA	84 (3.19%)	
Highly variable DXA measures	32 (1.21%)	103 (1.81%)
Final sample size	2,534 (96.20%)	5,436 (95.57%)
DXA measures imputed:		
Fat Mass	713 (28.14%)	1,296 (22.78%)
Lean Mass	713 (28.14%)	1,296 (22.78%)
Percent Body Fat	716 (28.26%)	1,296 (22.78%)

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