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Urinary bisphenol A and age at menarche among adolescent girls: Evidence from NHANES 2003–2010

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Abstract

Background—Bisphenol A (BPA) is an environmental estrogen used in the manufacture of polycarbonate plastics and epoxy resins used to make food and beverage packaging. Increasing evidence suggests that BPA mimics estrogens in the body and may be associated with putative markers of breast cancer risk.

Objectives—We analyzed the National Health and Nutrition Examination Survey (NHANES) 2003–2010 data to investigate the association of BPA with age at menarche in adolescent girls. We hypothesized that urinary BPA, as a surrogate biomarker for BPA exposure, is associated with earlier age at menarche, and that body mass index (BMI) may modulate this association.

Methods—We conducted cross-sectional analyses of urinary BPA, BMI and age of menarche in a subsample of 987 adolescent girls aged 12–19, using pooled data from the 2003–2010 NHANES. Unconditional logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CI) for the association between urinary BPA and early onset of menarche, with adjustment for sampling design. We additionally assessed interaction of BPA with BMI.

Results—Adolescent girls with moderate BPA levels appeared to be less likely to have early onset of menarche than those with the lowest levels (OR=0.57; 95% CI=0.30, 1.08) after adjusting for age, race/ethnicity, parental education, country of birth, NHANES cycle, BMI and creatinine. BMI appeared to modify the BPA-menarche association.

Conclusions—Although a non-significant trend suggests increasing urinary BPA may be associated with delayed menarche in adolescent girls, these results are based on cross-sectional data. Results should be clarified in carefully designed longitudinal cohort studies.

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Competing Financial Interests

All authors declare they have no actual or potential competing financial interests.

Keywords

puberty; Bisphenol A; endocrine disruptors; breast cancer; menarche

1. Introduction

Bisphenol A (BPA) is an estrogen-like endocrine disrupting chemical (EDC) of phenolic nature that has been used for over 50 years in the manufacture of polycarbonate plastics and epoxy resins (Centers for Disease Control and Prevention, 2012). Polycarbonate plastics are used in food and drink packaging, while epoxy resins are used to coat the inside of metal cans. BPA can leach into food sources, particularly at high temperatures, thus dietary intake is suggested to be the main source of BPA exposure for the majority of the population (von Goetz et al., 2010). The Environmental Protection Agency (EPA) considers BPA a high production chemical, with the United States (US) volume of BPA totaling 2.4 billion pounds in 2007 (U.S. Environmental Protection Agency, 2010). Thus, due to its high volume production and ubiquitous application, human exposure to BPA is widespread. Data from the 2003–2004 National Health and Nutrition Examination Survey (NHANES) revealed detectable levels of BPA in 92.6% of individuals 6 years of age and older (Calafat et al., 2008).

There is little conclusive evidence of the health effects from BPA exposure in humans at low environmental doses. In animal studies, high dose BPA exposure has been shown to disrupt reproductive development including preputial separation (Ema et al., 2001; Tyl et al., 2002), delayed vaginal opening (Ashby and Tinwell, 1998) and delayed testicular descent (Nagao et al., 1999). Additionally, BPA exposure has demonstrated neurological effects including stimulation of neuronal differentiation and possible disruption of neonatal brain development (Kim et al., 2009). Animal studies conducted in rats suggest possible effects such as disruption to the hypothalamic-pituitary-gonadal axis (Rasier et al., 2006), changes to fetal mammary gland morphology (Moral et al., 2008), and carcinogenesis (Betancourt et al., 2010; Jenkins et al., 2009).

The adverse effects of EDCs such as BPA are especially prominent during puberty, with evidence from both animal and human studies (Parent et al., 2005). It has been suggested that at the onset of puberty, the neuroendocrine processes become highly vulnerable to environmental factors that can permanently affect the development and functionality of reproductive organs, growth spurt, and maturation of the brain (Roy et al., 2009). Epidemiological studies have shown associations with EDCs such as phthalates, dichlorodiphenyldichloroethylene (DDE), polybrominated biphenyls (PBB) and early onset of pubertal development in girls (Ozen and Darcan, 2011). BPA specifically has been shown to act as a hormonal agonist in animal models of reproductive development, thus accelerating pubertal development (Honma et al., 2002).

The average age of pubertal onset in girls has fallen over the years (Biro et al., 2010). Studies also suggest a decline in the age of onset of menarche in girls (Herman-Giddens, 2006; Kaplowitz, 2008). Early age of menarche in girls is associated with many adverse psychosocial and health outcomes later in life including obesity, depression, and breast

cancer (Black and Klein, 2012). Specifically, research supports about a 30% increase in the risk of breast cancer for early age of menarche (Biro and Wolff, 2011). Of increasing concern is the association between environmental exposures and early menarche, particularly for EDCs such as BPA (Biro et al., 2009).

There is very limited epidemiologic data on BPA exposure in children as it relates to pubertal development. The current study analyzed data from the 2003–2010 NHANES to investigate the association of urinary BPA with age at menarche in adolescent girls. We hypothesized that urinary BPA concentration is associated with earlier age at menarche. Additionally, obesity is a strong endogenous hormonal risk factor for pubertal development (Kaplowitz, 2008). We hypothesized that obesity, as measured by body mass index (BMI), may modify the association between urinary BPA concentrations and age at menarche.

2. Methods

2.1. Study population

Pooled data from the 2003–2004, 2005–2006, 2007–2008, and 2009–2010 NHANES was used to investigate the association between urinary BPA concentrations and age at menarche in adolescent girls. NHANES utilizes a complex, multistage, probability cluster design of the civilian, non-institutionalized US population. Four sets of NHANES data were selected (2003–2010) and merged in order to create more precise survey estimates. The sample was restricted to female adolescents (aged 12–19 years) in order to assess BPA exposure near the age of menarche (n=3,493). Female adolescents were included if they had completed the reproductive health questionnaire and had complete data on age at menarche (n=3,114). Urinary BPA concentrations were measured in a random, one-third subsample of all participants aged 6 years and up. The study sample was further restricted to those that had measurements of BPA. The final sample size consisted of 987 adolescent girls.

2.2. Urinary BPA concentrations

One spot urine samples were collected from participants in the 2003–2010 continuous NHANES. Urinary BPA concentrations were measured using online solid phase extraction (SPE) coupled with high performance liquid chromatography (HPLC) isotope dilution-tandem mass spectrometry (MS/MS). Analysis was conducted at the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention (CDC) (National Center for Health Statistics, 2010). Coefficients of variation for low and high-concentrations were 18.6% and 12.1% in 2003–2004, 12.6% and 11.2% in 2005–2006, 8.1% and 5.7% in 2007–2008, and 8.1% and 5.7% in 2009–2010, respectively. The lower limit of detection (LLOD) was uniform across all years of data collection: 0.36 in 2003–2004, 0.4 in 2005–2006, 0.4 in 2007–2008, and 0.4 in 2009–2010. We categorized urinary BPA concentrations into tertiles based on the distribution of BPA in girls who achieved menarche at or above age 12.

2.3. Age at menarche

Age at menarche was assessed using the reproductive health questionnaire by asking girls aged ≥16 years “How old were you when you had your first menstrual period?” For girls

aged 12–15, their parent or guardian was used as a proxy and completed the questionnaire for them.

Of the 987 adolescent girls, 59 had not reached menarche prior to urinary analysis. Of the 59 girls who had not reached menarche, 58 (98%) of them were aged 12–15. Age of menarche was categorized as <12 and ≥12 years of age based on the mean age among girls who attained menarche. Menarche was considered "early" if it was achieved before 12 years of age.

2.4. Potential confounders

Potential confounders were identified from the literature and include: age (continuous in years), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, other/multi-racial), poverty income ratio (PIR: ratio of income to the family's appropriate poverty threshold, categorized as <1, 1–2, 2–3, and ≥3), country of birth (assessed by asking "In what country were you born", categorized as U.S. born or not), level of guardian education (<high school, high school or equivalent, and college graduate), annual household income (< $20,000, $20,000 to $35,000, $35,000 to $65,000, and ≥$65,000), and body mass index (BMI). Centers for Disease Control and Prevention (CDC) 2000 growth charts were used to convert NHANES BMI values into age- and gender-specific BMI percentile levels (<50th, 50–85th, and ≥85th percentile).

2.5. Statistical analysis

In order to account for the complex sampling design used in NHANES, all analyses were adjusted for sampling strata and clusters. Corresponding weights for each round of the sample were used. Weighted estimates were computed in accordance with the NHANES Analytic and Reporting Guidelines, and the smallest subsample weights were used (urinary BPA subsamples B and C) (National Center for Health Statistics, 2006). Taylor series linearization was used to take into account clustering using the masked variance pseudo-psu and pseudo-stratum variables.

Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between urinary BPA and menarche before 12 years of age. We further examined if this association was modified by BMI by including an interaction term between urinary BPA and BMI and by using the Wald test. BMI was categorized as overweight (≥85th percentile) and not overweight (<85th percentile) for the interaction analyses. Chi-square tests were used to assess associations between urinary BPA tertiles and potential cofounders. If a covariate from the list of potential confounders changed the OR between tertiles of urinary BPA and age of menarche by 10 percent or more in a logistic regression model, then it was included in the final model as a confounder. Urinary BPA concentrations were positively skewed, thus, log-transformation was applied to the measurements to achieve a normal distribution. Linear trend of BPA exposure and age at menarche was assessed by using the log-transformed values of urinary BPA. The values presented in the tables were reverse-log-transformed. Statistical significance was defined by p-values <0.05. All statistical analyses were performed using Stata 11.0 (Stata Corp, LP,

College Station, TX). Finally, all models were adjusted for urinary creatinine to correct for urinary dilution (Barr et al., 2005).

3. Results

The study sample comprised of 987 adolescent girls aged 12–19 years in the 2003–2010 NHANES. The weighted study sample was primarily non-Hispanic white (62.5%), from a household that had an annual income greater than $65,000 (40.3%), and had parents with more than a high school degree (54.1%). There was a higher percentage of girls in the 50–85th (37.3%) and ≥85th (35.3%) BMI age- and sex-specific percentiles (Table 1). Higher urinary BPA concentrations were observed for non-Hispanic Whites, African Americans, and those in the ≥85th BMI percentile. Girls in the 12–15 year old age category had similar BPA concentrations compared to those in the 16–19 age category. PIR, annual household income, and level of guardian education were not associated with urinary BPA concentrations (Table 1).

The overall geometric mean of urinary BPA concentration was 2.64 ng/mL (95% CI 2.41, 2.89). The geometric means of urinary BPA were 3.49 ng/mL (95% CI 2.86, 4.26) in the 2003–2004 NHANES cycle, 2.39 ng/mL (95% CI 2.15, 2.66) in the 2005–2006 cycle, 2.78 ng/mL (95% CI 2.19, 3.52) in the 2007–2008 cycle, and 2.08 ng/mL (95% CI 1.75, 2.47) in the 2009–2010 cycle (data not shown).

Table 2 shows the mean age at menarche and percentage of menarche before 12 years of age. The mean age of menarche was 12.14 years and ranged from 8 to 17 years among girls who had already attained menarche. Overall, 27.8% of girls had obtained menarche before 12 years of age. Among girls who experienced menarche, mean age of menarche differed by age group at time of survey, race/ethnicity, and BMI. Considering all girls in the sample, the percentage of girls who experienced menarche before age 12 also differed by age at time of survey, race/ethnicity and BMI. No other differences were observed between potential confounders and age of menarche.

Table 3 presents odds ratios and 95% confidence intervals for the association between urinary BPA and age at menarche. In the model adjusted for creatinine, age, and NHANES cycle, adolescent girls with moderate BPA levels were 45 percent less likely to have early onset of menarche compared to those with the lowest levels (OR=0.55; 95% CI=0.31, 0.99). This association was no longer statistically significant after adjusting for race/ethnicity, parental education, country of birth, and BMI (OR=0.57; 95% CI=0.30, 1.08). In adjusted models, a 1-unit (ng/mL) increase in log-transformed continuous BPA was associated with a 15% decrease in the relative odds of early onset of menarche (OR=0.85; 95% CI=0.61, 1.18). Body size was significantly associated with early onset of menarche in adjusted analyses. Overweight girls were 52 percent more likely to have early onset of menarche compared to normal weight girls (OR=1.52; 95% CI=1.07, 2.16).

Overweight status additionally modified the association between BPA and age of menarche (p=0.08). Table 4 presents the odds ratios and 95% confidence intervals for the effect modification assessment with overweight status. Overweight girls in the lowest BPA tertile appear to be more likely to have early onset of menarche compared to normal weight girls in

the lowest BPA tertile, though there is considerable variation in the estimate of the odds ratio (OR=1.65; 95% CI=0.84, 3.23).

4. Discussion

We examined the association between exposure to BPA, a known EDC, and age of menarche, an endpoint in pubertal maturation. In this cross-sectional analysis of pooled NHANES 2003–2010 data, urinary BPA appears to be associated with overall delayed menarche, particularly for moderate levels of BPA exposure. However, while the magnitude of association remained virtually unchanged when likely confounders were considered, the result was no longer statistically significant. Further, the BPA-menarche association varied by levels of body size with overweight girls showing earlier development on average.

Epidemiologic studies have suggested that exposure to EDCs may be associated with earlier breast development and age of onset of menarche, though much of the literature is inconsistent (Ozen and Darcan, 2011). More specifically, studies in humans have shown exposure to dioxin (Warner et al., 2004) and PBBs (Blanck et al., 2000) to be associated with earlier onset of menarche. In a recent study using NHANES data, researchers found that high polybrominated diphenyl ether (PBDE) concentrations were associated with earlier age of menarche (Chen et al., 2011). However, other studies have shown delayed pubertal maturation with exposure to these chemicals. Particularly, one study showed that exposure to polychlorinated biphenyls (PCBs) may delay breast development (Wolff et al., 2008). In another study, researchers found exposure to dioxin to be associated with delayed breast development (Den Hond et al., 2002).

No significant associations in human studies have been found with exposure to BPA and pubertal outcomes (Wolff et al., 2008; Wolff et al., 2010). A recent study assessed the association between EDCs, including BPA, and age of menarche using NHANES 2003–2008 (Buttke et al., 2012). This study found an inverse relationship between age of menarche and urinary phenols. When the authors assessed BPA specifically, however, they found no significant associations. Differences between this particular study and the current analysis include sample size (due to the addition of the NHANES 2009–2010 cycle in the current analysis), as well as different statistical techniques.

The findings of the association of BMI with earlier menarche are consistent with previous studies. Research has shown that those girls with a higher BMI are at an increased risk for earlier pubertal maturation (Biro et al., 2006). However, our study showed the association between urinary BPA and age at menarche may be even stronger among overweight/obese girls with lower levels of BPA. We evaluated potential effect modification of the BPA-menarche association by overweight status. The results from the modification analysis showed that the BPA-menarche association differed by body size. Since BPA has been shown to be an obesogen (Wang et al., 2012), it is hypothesized that exposure to BPA could lead to a higher BMI in some girls, which could contribute to early menarche. Consequently, a recent study in Shanghai found BPA to be associated with more than a 2-fold risk of obesity in girls aged 9–12 (Li et al., 2013). Consequently, our model adjusting for body size may have been over-adjusted if body size truly mediates the effect of BPA. Obesogens are

chemicals that can interfere with lipid metabolism and can potentially lead to obesity. The obesogen hypothesis supports that early life exposures to endocrine disrupting chemicals can predispose individuals to obesity (Janesick and Blumberg, 2011).

There are a few potential limitations in this analysis. The cross-sectional nature of this design limits the potential to examine causal associations. Further, a single, one-spot urine sample was collected for urinary BPA exposure. BPA is believed to have a short half-life in the human body, most of which is eliminated within 24 hours of exposure (Volkel et al., 2002). However, studies have shown that single spot urine samples of BPA may be representative of long-term averages and that spot samples can be used to characterize population distribution of intakes (Christensen et al., 2012; Teitelbaum et al., 2008; Vandenberg et al., 2007). It is not likely that this limitation contributed to our observed findings.

It is possible that there are other markers of pubertal maturation that may be related to BPA exposure. Breast development and presence of pubic hair are known to be the first markers of pubertal maturation. Pubertal maturation ends with the onset of menarche, which occurs approximately two years after breast development. In addition, earlier breast development may not lead to an earlier age of menarche (Biro et al., 2013). Thus, assessing onset of menarche does not allow one to examine changes in breast and pubic hair development. Earlier markers of pubertal maturation, such as thelarche and pubarche, may be more closely related with exposure to BPA. Additionally, age of menarche was assessed by recall, which may have introduced bias. Recall bias of age of onset of menarche may have been present, yet unlikely due to the short interval in recall (Koo and Rohan, 1997). There may have also been uncontrolled or residual confounding of other factors associated with the BPA exposure and menarche. We used post-pubertal BMI as a proxy for pre-pubertal BMI in our analysis. Although there is potential that some girls may have changed their overweight status based on categories of BMI, we do not believe this introduced significant bias. Finally, the current analysis was unable to adjust for genetic components of menarche, or mother’s age of menarche.

5. Conclusions

The current study takes advantage of a rich population based dataset with national biomonitoring data to examine the hypothesis that BPA, measured as urinary BPA, is associated with early onset of menarche in adolescent girls and the association is modulated by obesity status, measured as increased BMI. This study found urinary BPA was associated with overall delayed menarche in this sample of 987 adolescent girls from NHANES 2003–2010. Although a non-significant trend suggests increasing urinary BPA may be associated with delayed menarche in adolescent girls, these results are based on cross-sectional data. Results should be verified in carefully designed longitudinal cohort studies.

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Highlights

- Bisphenol A (BPA) may be associated with putative markers of breast cancer risk.
- Girls with moderate BPA levels were less likely to have early onset of menarche.
- Body mass index appeared to modify the BPA-menarche association.
- Results should be clarified in carefully designed longitudinal cohort studies.

Table 1

Sample characteristics across urinary BPA tertiles in 2003–2010 NHANES

	Total N (%)[a]	Urinary BPA concentrations (ng/mL)			*p-value*[b]
		Low (<1.9) (%)	Moderate (1.9–4.1) (%)	High (>4.1) (%)	
Total	987	336 (34.0)	324 (32.8)	327 (33.1)	
Age (years)					
12–15	482 (49.0)	164 (33.8)	169 (35.7)	149 (30.5)	0.77
16–19	505 (51.0)	172 (35.4)	155 (32.9)	178 (31.7)	
Race/ethnicity					
Non-Hispanic Whites	293 (62.5)	95 (33.8)	96 (35.0)	102 (31.2)	0.03
African Americans	296 (14.7)	69 (25.6)	95 (34.3)	132 (40.1)	
Mexican Americans	278 (11.2)	125 (43.4)	94 (36.6)	59 (20.1)	
Other	120 (11.6)	47 (41.9)	39 (27.7)	34 (30.4)	
Annual household income					
<$20,000	229 (15.6)	77 (33.1)	65 (28.7)	87 (38.3)	0.74
$20,000–$35,000	225 (18.2)	76 (34.2)	74 (35.2)	75 (30.6)	
$35,000–$65,000	234 (21.3)	77 (33.1)	86 (36.4)	71 (30.5)	
≥ $65,000	259 (40.3)	88 (35.1)	88 (36.0)	83 (29.0)	
Missing	40 (4.6)	18 (44.5)	11 (24.5)	11 (31.0)	
Poverty income ratio					
<1.0	299 (21.8)	96 (33.0)	99 (35.3)	104 (31.8)	0.24
1.0–1.9	258 (20.0)	92 (34.8)	80 (34.8)	86 (30.5)	
2.0–2.9	134 (15.1)	36 (23.9)	52 (37.1)	46 (39.1)	
≥3	246 (37.7)	93 (39.2)	78 (33.9)	75 (26.8)	
Missing	50 (5.5)	19 (38.2)	15 (23.0)	16 (38.8)	
U.S. born					
Yes	862 (91.4)	277 (33.1)	293 (35.3)	292 (31.6)	0.01
No	125 (8.6)	59 (50.5)	31 (23,2)	35 (26.3)	
Level of guardian education					
<High school	311 (20.2)	101 (35.1)	102 (28.3)	108 (36.6)	0.39
High school or equivalent	215 (20.6)	76 (33.2)	64 (32.0)	75 (34.8)	

	Total	Urinary BPA concentrations (ng/mL)			
	N (%)[a]	Low (<1.9) (%)	Moderate (1.9–4.1) (%)	High (>4.1) (%)	*p-value*[b]
>High school	415 (54.1)	139 (33.6)	142 (37.2)	134 (29.3)	
Missing	46 (5.1)	20 (49.4)	16 (35.9)	10 (14.8)	
BMI age- and sex-specific percentile					
<50th	238 (27.4)	91 (35.8)	73 (35.5)	74 (28.7)	0.78
50–85th	349 (37.3)	132 (36.6)	107 (32.7)	110 (30.7)	
≥85th	400 (35.3)	113 (31.6)	144 (34.9)	143 (33.5)	

Abbreviations: BPA, bisphenol A; BMI, body mass index (kg/m^2).

[a] Percentages are weighted using population weights for the BPA subsample.

[b] Calculated using a Chi-square test.

Table 2

Mean age at menarche and percentage of menarche <12 years of age, NHANES, 2003–2010

	N	Mean menarche age (95% CI)[a]	N	Menarche <12 years (%)[b]
Total	928	12.14 (12.04, 12.24)	987	301 (27.8)
Urinary BPA concentrations (ng/mL)				
Low (<1.9)	319	12.06 (11.85, 12.26)	336	111 (32.5)
Moderate (1.9–4.1)	316	12.34 (12.20, 12.47)	324	97 (23.1)
High (>4.1)	293	12.02 (11.82, 12.22)	327	93 (27.8)
Age (years) [#]				
12–15	424	11.75 (11.63, 11.87)	482	166 (32.1)
16–19	504	12.47 (12.33, 12.61)	505	135 (23.7)
Race/ethnicity[#]				
Non-Hispanic Whites	272	12.28 (12.12, 12.44)	293	68 (23.3)
African Americans	280	11.95 (11.75, 12.16)	296	110 (38.6)
Mexican Americans	262	11.91 (11.75, 12.07)	278	85 (34.6)
Other	114	11.88 (11.60, 12.17)	120	38 (32.2)
Annual household income				
<$20,000	223	12.24 (11.99, 12.49)	229	64 (26.4)
$20,000–$35,000	212	12.12 (11.91, 12.33)	225	73 (30.7)
$35,000–$65,000	214	12.03 (11.84, 12.21)	234	67 (24.6)
≥ $65,000	240	12.21 (12.04, 12.38)	259	83 (27.7)
Missing	39		40	
Poverty income ratio				
<1	289	12.13 (11.90, 12.35)	299	90 (29.5)
1-	237	12.20 (11.99, 12.41)	258	71 (24.1)
2-	123	11.89 (11.59, 12.19)	134	42 (32.0)
≥3	230	12.27 (12.09, 12.45)	246	79 (25.5)
Missing	49		50	
U.S. born				
Yes	807	12.14 (12.04, 12.25)	862	269 (27.5)
No	121	12.12 (11.83, 12.40)	125	32 (31.5)
Level of guardian education				
<High school	294	11.96 (11.77, 12.16)	311	88 (31.8)
High school or equivalent	198	12.23 (11.99, 12.47)	215	61 (23.3)
>High school	390	12.19 (12.05, 12.33)	415	132 (27.4)
Missing	46		46	
BMI age- and sex-specific percentile[#]				
<50th	217	12.52 (12.35, 12.69)	238	47 (16.5)
50–85th	330	12.04 (11.91, 12.17)	349	113 (29.1)
≥85th	381	11.97 (11.75, 12.19)	400	141 (35.2)

Abbreviations: BPA, bisphenol A; BMI, body mass index (kg/m).

[a] Excluding girls who had not experienced menarche (n=59).

[b] Percentages are weighted using population weights for the BPA subsample.

[#] P <0.05 for difference in percentage of menarche below 12 years of age.

Table 3

Association of urinary BPA concentrations and age at menarche <12 years, NHANES, 2003–2010

	Menarche <12/≥12	Model 1[a]	Model 2[b]
Urinary BPA concentrations (ng/mL)		**OR (95% CI)**	**OR (95% CI)**
Low (<1.9)	111/225	1.00 (ref)	1.00 (ref)
Moderate (1.9–4.1)	97/227	0.55 (0.31, 0.99)	0.57 (0.30, 1.08)
High (>4.1)	93/234	0.73 (0.39, 1.37)	0.77 (0.38, 1.55)
Log urinary BPA (ng/mL)	301/686	0.84 (0.62, 1.15)	0.85 (0.61, 1.18)
p for trend		0.27	0.32
Body size			
Under/normal weight		1.00 (ref)	1.00 (ref)
Overweight/obese		1.71 (1.20, 2.45)	1.52 (1.07, 2.16)

Abbreviations: BPA, bisphenol A; OR, odds ratio; CI, confidence interval.

[a]Model 1 is a logistic regression model adjusted for urinary creatinine (log-transformed mg/dL), age, and NHANES cycle.

[b]Model 2 is a logistic regression model adjusted for race/ethnicity (non-Hispanic white, African American, Mexican American, other), parental education, country of birth, and body size in addition to model 1 covariates.

Table 4

Association of urinary BPA concentrations and age at menarche in relation to body size, NHANES, 2003–2010

	Not overweight		Overweight/obese	
Urinary BPA concentrations (ng/mL)	**OR**	**95% CI**	**OR**	**95% CI**
Low (<1.9)	1.00	(ref)	1.65	0.84, 3.23
Moderate (1.9–4.1)	0.68	0.30, 1.53	0.74	0.41, 1.33
High (>4.1)	0.72	0.33, 1.58	1.36	0.60, 3.08

Abbreviations: BPA, bisphenol A; OR, odds ratio; CI, confidence interval.

ORs computed from model with interaction term (tertiles of BPA times body size), adjusted for age, urinary creatinine, race/ethnicity, parental education, NHANES cycle, and country of birth. *p*-interaction = 0.08