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Original Contribution

Urinary Bisphenol A and Obesity in US Children

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Childhood obesity, a major public health problem, can lead to cardiovascular disease in adulthood. Studies have implicated exposure to bisphenol A (BPA), a commonly used chemical, in the development of obesity in adults. However, literature is limited on this association in children. We examined the association between urinary BPA and obesity in children aged 6–18 years from the National Health and Nutrition Examination Survey (2003–2008). The primary exposure was urinary BPA and the outcome was obesity, defined as the ≥95th percentile of body mass index specific for age and sex. We found a positive association between increasing levels of urinary BPA and obesity, independent of age, sex, race/ethnicity, education, physical activity, serum cotinine, and urinary creatinine. Compared with children in the lowest quartile of BPA (<1.5 ng/mL), children in the highest quartile (>5.4 ng/mL) had a multivariable odds ratio for obesity of 2.55 (95% confidence interval (CI): 1.65, 3.95) (P_{trend} < 0.01). The observed positive association was predominantly present in boys (odds ratio = 3.80, 95% CI: 2.25, 6.43) (P_{trend} < 0.001) and in non-Hispanic whites (odds ratio = 5.87, 95% CI: 2.15, 16.05) (P_{trend} < 0.01). In a representative sample of children, urinary BPA was associated with obesity, predominantly in non-Hispanic white boys, independent of major risk factors.

bisphenol A; body mass index; children; NHANES; obesity

Abbreviations: BPA, bisphenol A; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey.

Obesity is a risk factor for several health conditions including cardiovascular diseases, certain cancers, and respiratory ailments, and it adversely affects the health-related quality of life (1). In addition, obese children are at a much a higher risk of being obese in adulthood (1, 2). In 2009–2010, 16.9% of the US children and adolescents (2–19 years of age) were obese, suggesting that obesity is a severe public health problem in American children (3). Obesity is caused by a combination of genetic, behavioral, and environmental factors (4, 5). Several animal studies conducted to date show an association between exposure to endocrine-disrupting chemicals, such as bisphenol A (BPA), and obesity (6–11). BPA is a chemical manufactured in large quantities all over the world and used primarily as an intermediate in the production of polycarbonate plastic and epoxy resin that are used in plastic bottles, as lining for food cans, and for dental sealants (12).

In humans, epidemiologic studies examining this association in adults have generally found a positive association between BPA exposure and obesity (13–15). Recent studies have shown that infants and children have higher exposure to BPA than adults (16, 17). BPA intake is estimated to be highest in infants and children because they eat, drink, and breathe more per pound of their body weight, and they may ingest more BPA because they explore objects orally (12). Therefore, in addition to studies examining the association between BPA exposure and obesity in adults (13–15), we believe it is important to study this hypothesis separately in children also.

There is also a need to study if the association between BPA and obesity varies by gender and race/ethnicity. In animal studies, the effect of exposure to BPA, an environmental estrogen, on later body fat has been shown to be stronger in males (18). Similarly, because of the reported

differences in endogenous estrogen levels by race/ethnicity (19), it is possible that the contribution of BPA on obesity may vary by race/ethnicity also, in addition to gender.

In this context, we examined the association of urinary BPA and obesity among children aged 6–18 years by combining the National Health and Nutrition Examination Survey (NHANES) data from 2003 to 2008. We also analyzed this association between urinary BPA and obesity separately by race/ethnicity and gender.

MATERIALS AND METHODS

We examined the association between increasing levels of urinary BPA and obesity in children aged 6–18 years who participated in NHANES in 3 study cycles, 2003–2004, 2005–2006, and 2007–2008, where BPA measurements were available. NHANES is a cross-sectional study using a stratified, multistage probability sample, representative of noninstitutionalized civilians in the United States. A detailed description of the NHANES study design and methods is available elsewhere (20). NHANES was approved by the National Center for Health Statistics Research Ethics Review Board (21). Written child assent was obtained from children aged 7–11 years; written informed consent was obtained from children 12 years or older; and written parental consent was obtained for those younger than 18 years (20).

A random one-third subset of NHANES participants 6 years or older was selected for the measurement of urinary BPA levels. The current study sample consists of 2,664 children (6–18 years) from this subset. As recommended by the National Center for Health Statistics, specific sample weights for this BPA subsample were used when analyzing the data, to avoid potential selection bias.

We further excluded participants with missing data ($n = 464$) on covariates included in the multivariable model, including body mass index, age, sex, race/ethnicity, parent/guardian education, physical activity, serum cotinine, and urinary creatinine. This resulted in the final sample of 2,200 participants (48.5% girls), 17.7% of whom were obese.

Measures of BPA concentration included BPA parent compound and conjugated metabolites. Urinary BPA was measured by using solid-phase extraction coupled on-line to high-performance liquid chromatography and tandem mass spectrometry (20). Rigorous quality assurance and quality control ensured that samples were not contaminated during collection, handling, and analysis (22).

Standing height was measured in centimeters to the nearest 0.1 cm by using an electronic stadiometer. Weight was measured in kilograms to the nearest 0.1 kg by using a Toledo self-zeroing weight scale (Seritex, Carlstadt, New Jersey). Body mass index was calculated (weight (kg)/height $(m)^2$). The Centers for Disease Control and Prevention (CDC) classifies the weight status categories used with children and teens according to percentile ranking relative to their age and sex (23). Following these guidelines, we defined obesity in children as age- and sex-specific body mass index greater than or equal to the 95th percentile (23).

Serum cotinine was measured in nanograms per milliliter by isotope dilution–high performance liquid chromatography. Urinary creatinine concentrations, a measure of urinary dilution, were collected from specimens by the clean-catch technique and measured in milligrams per deciliter. Information on other covariates, such as age, sex, race/ethnicity, parent/guardian education, and physical activity, was gathered from a standardized questionnaire.

Statistical analysis

The outcome variable, obesity, was defined as body mass index levels greater than or equal to the 95th percentile for age and gender (23). The main exposure of interest, urinary BPA, was categorized into quartiles (<1.5 ng/mL, 1.5–2.7 ng/mL, 2.8–5.4 ng/mL, >5.4 ng/mL) and also analyzed as a continuous variable, after log transformation due to skewed distribution. The odds ratio with 95% confidence interval of obesity for BPA was calculated by taking the lowest quartile (quartile 1) as the referent using multivariable logistic regression models. We used 2 models: the age- and sex-adjusted model and the multivariable-adjusted model, additionally adjusting for race/ethnicity (non-Hispanic whites, non-Hispanic blacks, Mexican Americans, and others), parent/guardian education (below high school, high school, above high school), urinary creatinine (mg/dL), serum cotinine (ng/mL), and moderate physical activity (absent, present). Linear trends in the odds ratio of obesity across increasing urinary BPA quartiles were determined by modeling BPA as an ordinal variable. We performed subgroup analysis by gender and race/ethnicity and tested for statistical interaction ($\alpha = 0.10$) by including multiplicative cross-product interaction terms between BPA quartiles and these stratifying variables in regression models. Sample weights that account for the unequal probabilities of selection, oversampling, and nonresponse were applied for all analyses by using SAS, version 9.3, software (SAS Institute, Inc., Cary, North Carolina); standard error values were estimated by using the Taylor series linearization method.

RESULTS

Table 1 presents the baseline characteristics of the study population. Among 2,200 children 6–18 years of age included in the current analysis, approximately half were girls (48.5%), and 62.4% were non-Hispanic whites. Over half (55.4%) of the parents/guardians had an education above high school, and over a third of the sample (34.4%) were overweight or obese.

Table 2 presents the association between increasing urinary BPA levels and mean change in body mass index in children. Overall, there was a positive association between increasing levels of urinary BPA and body mass index in both the age- and sex-adjusted model and the multivariable-adjusted model. Corresponding models evaluating linear trend in this association were statistically significant. We also found a similar positive association between urinary BPA levels and body mass index when BPA was analyzed as a continuous variable, with logarithmic transformation.

Table 3 presents the association of increasing levels of urinary BPA with obesity in children. Overall, there was a positive association between the increasing levels of urinary

Table 1. Characteristics of the Study Population, National Health and Nutrition Examination Survey, 2003–2008

Characteristics of the Study Population ($n = 2,200$[a])	%	Mean (SE)
Age, years		12.3 (0.1)
Girls	48.5	
Race/ethnicity		
Non-Hispanic white	62.4	
Non-Hispanic black	14.4	
Mexican American	12.5	
Other	10.7	
Parent/guardian education		
Below high school	20.1	
High school	24.5	
Above high school	55.4	
Moderate activity	36.9	
Body mass index[b]		21.3 (0.2)
Body mass index categories		
Underweight	2.9	
Healthy weight	62.7	
Overweight	16.7	
Obese	17.7	
Serum cotinine, ng/mL		10.3 (1.6)
Urinary creatinine, mg/dL		135.0 (2.2)
Urinary bisphenol A, ng/mL		4.8 (0.2)
Boys		5.0 (0.3)
Girls		4.6 (0.3)

Abbreviation: SE, standard error.
[a] Unweighted sample size.
[b] Body mass index: weight (kg)/height (m)^2.

BPA and obesity in both the age- and sex-adjusted models and in the multivariable adjusted model. Models evaluating linear trend in this association were statistically significant.

Tables 4 and 5 present the association of increasing levels of urinary BPA with obesity in children, within the subgroups of gender and race/ethnicity. In Table 4, we found that the association between increasing urinary BPA levels and obesity was of strong magnitude and statistically significant among boys, but weak and statistically nonsignificant in girls ($P_{\text{interaction}} = 0.07$). In Table 5, we found that the association between increasing urinary BPA levels and obesity was strongly present among non-Hispanic whites, but it was weak and statistically nonsignificant in nonwhites ($P_{\text{interaction}} = 0.05$).

In order to further clarify these observed differences in Tables 4 and 5 and to examine any potential synergistic interaction, we created joint exposure categories of sex and race/ethnicity on the association between increasing urinary BPA levels and obesity in Table 6. We found that the observed positive association between BPA quartiles and obesity in children was predominantly present among non-Hispanic white boys (odds ratio = 18.89, 95% confidence interval (CI): 3.97, 89.89). In contrast, the BPA–obesity association was weak and statistically nonsignificant in the other subgroups.

We also performed several supplementary analyses. First, to examine the influence of adding higher order polynomial terms for age, we included a quadratic term for age in the multivariable model; the results were found to be essentially similar (Web Table 1 available at http://aje.oxfordjournals.org/). Second, to examine the possibility that sex differences in maturation may influence the association between BPA and obesity, we incorporated an age (continuous)–sex interaction term in the multivariable logistic regression model. The *P* value for the age–sex interaction was 0.2709. Third, to examine age differences in the BPA–obesity association in more detail, we performed a stratified analysis by age group; the BPA–obesity association was found to be essentially similar in prepubertal (6–11 years) and postpubertal (12–18 years) children (Web Table 2).

Fourth, to further examine the potential of selection bias, we compared the demographic characteristics of the entire NHANES sample of 6,559 children with the sample of 2,200 children included in the current study (who had BPA data available); the demographic characteristics were found to be essentially the same in the 2 samples (Web Table 3). Fifth, we performed a sensitivity analysis to examine the BPA–obesity association in 464 children who were excluded from the analyses because of missing data on covariates. The results showed a similar magnitude of association as the main findings, albeit not statistically significant because of the small sample size, where the odds ratio of obesity associated with log-transformed BPA was 1.12 (95% CI: 0.90, 1.39).

Sixth, to examine whether the use of gender-specific and race/ethnicity-specific BPA quartiles made any difference to our findings, we repeated the main analyses using gender-specific (Web Table 4) and race/ethnicity-specific BPA quartiles (Web Table 5); the odds ratios for the BPA–obesity association were essentially the same as those from the main analyses using full-sample BPA quartiles. Seventh, we calculated prevalence proportion ratios instead of odds ratios as a measure of the magnitude of the BPA–obesity association in this cross-sectional study. This analysis used a Cox proportional hazards model (which has complex survey options in SAS/SUDAAN) by assuming that the risk period is constant (by assigning an equal follow-up period for each observation) (24). The resultant prevalence proportion ratios were essentially similar in magnitude to the odds ratios in the main analysis, but with wider standard errors (Web Table 6). In a final supplementary analysis, we examined whether there were differences in demographic factors between gender and race/ethnicity subgroups. We found that age and urinary BPA levels were similar across these subgroups, but that body mass index was different; it was higher in nonwhite girls, but similar in the other subgroups (Web Table 7).

DISCUSSION

In a large, nationally representative sample of US children, we found an independent positive association between

Table 2. Association Between Urinary BPA Levels and Body Mass Index Levels in Children, National Health and Nutrition Examination Survey, 2003–2008

	Sample Size	Age- and Sex-Adjusted Change in BMI[a]		Multivariable-Adjusted Change in BMI[b]	
		Mean Change	95% CI	Mean Change	95% CI
BPA quartiles[c]					
1	547	0.00	Referent	0.00	Referent
2	544	0.91	0.33, 1.49	0.82	0.19, 1.45
3	556	0.67	0.05, 1.28	0.52	−0.19, 1.23
4	553	1.34	0.74, 1.93	1.17	0.50, 1.84
P_{trend}		0.0004		0.0056	
Log BPA	2,200	0.38	0.16, 0.60	0.30	0.05, 0.55

Abbreviations: BMI, body mass index; BPA, urinary bisphenol A; CI, confidence interval.

[a] BMI: weight (kg)/height (m)^2.

[b] Adjusted for age (years); sex (boys, girls); race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, other); education (below high school, high school, above high school); moderate activity (absent, present); urinary creatinine (mg/dL); and serum cotinine (ng/mL).

[c] BPA quartiles: quartile 1 (<1.5 ng/mL); quartile 2 (1.5–2.7 ng/mL); quartile 3 (2.8–5.4 ng/mL); quartile 4 (>5.4 ng/mL).

increasing levels of urinary BPA and obesity. In subsequent subgroup analyses, this BPA–obesity association was found to be present predominantly among non-Hispanic white boys, while the association was weak and not statistically significant in other gender and race/ethnicity subgroups. Our study on the relationship between urinary BPA and obesity in children extends the previously reported positive relation between BPA exposure and obesity in adults (13–15) to children also. However, because of the cross-sectional nature of the current study, the time sequence in the association between BPA and obesity cannot be ascertained.

The current study found a positive association between increasing urinary levels of BPA and obesity. Our results are consistent with 3 available epidemiologic studies in adults. In the NHANES 2003–2004 study sample that included 694 men and 761 women, Lang et al. (14) found a linear, positive, and statistically significant relationship between urinary BPA and body mass index. Pooling NHANES 2003–2004 and 2005–2006 data on 2,747 adult US participants, Carwile and Michels (15) reported a similar positive association of urinary BPA with general and central obesity in the adult population. Another study by Wang et al. (13) among 3,390 Chinese adults also reported a positive and significant association of urinary BPA concentration with generalized and abdominal obesity.

As mentioned above, most of the studies to date on the association between BPA exposure and obesity have been in adults. We believe it is important to study the BPA–obesity association separately in children because recent studies have shown that infants and children have the highest exposure to BPA (16, 17). In addition, childhood obesity is a strong independent risk factor for accelerated atherosclerosis

Table 3. Association Between Urinary BPA Levels and Obesity in Children, National Health and Nutrition Examination Survey, 2003–2008

	Sample Size	Weighted %	Age and Sex Adjusted		Multivariable Adjusted[a]	
			OR	95% CI	OR	95% CI
BPA quartiles[b]						
1	547	10.0	1.00	Referent	1.00	Referent
2	544	20.9	2.40	1.59, 3.63	2.35	1.56, 3.53
3	556	16.8	1.83	1.20, 2.77	1.78	1.13, 2.79
4	553	22.9	2.66	1.80, 3.93	2.55	1.65, 3.95
P_{trend}			<0.0001		0.0022	
Log BPA	2,200	17.7	1.28	1.14, 1.44	1.25	1.09, 1.43

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

[a] Adjusted for age (years); sex (boys, girls); race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, other); education (below high school, high school, above high school); moderate activity (absent, present); urinary creatinine (mg/dL); and serum cotinine (ng/mL).

[b] BPA quartiles: quartile 1 (<1.5 ng/mL); quartile 2 (1.5–2.7 ng/mL); quartile 3 (2.8–5.4 ng/mL); quartile 4 (>5.4 ng/mL).

Table 4. Association Between Urinary BPA Levels and Obesity in Children, by Gender, National Health and Nutrition Examination Survey, 2003–2008

	Girls			Boys		
	Sample Size	Multivariable Adjusted[a]		Sample Size	Multivariable Adjusted[a]	
		OR	95% CI		OR	95% CI
BPA quartiles[b]						
1	265	1.00	Referent	282	1.00	Referent
2	279	1.75	1.00, 3.09	265	3.00	1.71, 5.24
3	274	1.26	0.63, 2.51	282	2.25	1.41, 3.59
4	266	1.48	0.88, 2.49	287	3.80	2.25, 6.43
P_{trend}		0.4786			0.0002	
Log BPA	1,084	1.03	0.85, 1.23	1,116	1.42	1.19, 1.70

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

[a] Adjusted for age (years); race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, other); education (below high school, high school, above high school); moderate activity (absent, present); urinary creatinine (mg/dL); and serum cotinine (ng/mL). $P_{interaction} = 0.0660$.

[b] BPA quartiles: quartile 1 (<1.5 ng/mL); quartile 2 (1.5–2.7 ng/mL); quartile 3 (2.8–5.4 ng/mL); quartile 4 (>5.4 ng/mL).

and cardiovascular disease early in adult life (25). Vandenberg et al. (26) reviewed over 80 biomonitoring studies including 41 premature infants, 909 children (3–11 years of age), and 883 adolescents (12–19 years of age) and concluded that neonates and young children have the highest exposures to BPA. Consistent with these observations, analyzing a sample of 2,517 participants from the NHANES 2003–2004 population, Calafat et al. (16) reported BPA concentrations higher in children than in adults.

In the current study, we found that higher urinary BPA was positively associated with obesity in children. The underlying biological pathways are still not clear, yet different hypotheses have been proposed that explain the mechanism of BPA exposure leading to obesity. First, in vitro studies have indicated that BPA exposure triggers the differentiation of fibroblasts into adipocytes (27). Fibroblasts treated with BPA showed an increase in triglyceride content, lipoprotein lipase activity, and glycerol phosphate dehydrogenase activity (27). BPA was also found to simulate and accelerate the adipocyte conversion process (27). Second, BPA enhances basal and insulin-stimulated glucose uptake (28). BPA exposure of cell suspensions causes lipid accumulation in adipocytes and hepatoma cell lines, associated with obesity and metabolic syndrome (29).

Confirming the results from in vitro studies, in vivo studies have also found an increase in body weight from BPA exposure in immature mice (7), in mice during the perinatal period (7, 8) that persisted long after the exposure ended (6, 11, 30–32), and in adult rats (10). This suggests that in vivo prolonged exposure to BPA might increase body fat mass, leading to the development of overweight and obesity. In addition, low-dose BPA exposure in mice has

Table 5. Association Between Urinary BPA Levels and Obesity in Children, by Race/Ethnicity, National Health and Nutrition Examination Survey, 2003–2008

	Non-White			White		
	Sample Size	Multivariable Adjusted		Sample Size	Multivariable Adjusted[a]	
		OR	95% CI		OR	95% CI
BPA quartiles[b]						
1	399	1.00	Referent	148	1.00	Referent
2	398	1.14	0.75, 1.73	146	5.29	2.02, 13.85
3	391	1.26	0.87, 1.82	165	3.06	1.04, 9.00
4	388	1.21	0.79, 1.86	165	5.87	2.15, 16.05
P_{trend}		0.3555			0.0031	
Log BPA	1,576	1.05	0.91, 1.22	624	1.46	1.17, 1.84

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

[a] Adjusted for age (years); sex (boys, girls); education (below high school, high school, above high school); moderate activity (absent, present); urinary creatinine (mg/dL); and serum cotinine (ng/mL). $P_{interaction} = 0.0549$.

[b] BPA quartiles: quartile 1 (<1.5 ng/mL); quartile 2 (1.5–2.7 ng/mL); quartile 3 (2.8–5.4 ng/mL); quartile 4 (>5.4 ng/mL).

Table 6. Association Between Urinary BPA Levels and Obesity in Children, by Gender and Race/Ethnicity, National Health and Nutrition Examination Survey, 2003–2008

	Race/Ethnicity Categories					
	Non-White			White		
	Sample Size	Multivariable Adjusted		Sample Size	Multivariable Adjusted[a]	
		OR	95% CI		OR	95% CI
			Girls			
BPA quartiles[b]						
1	195	1.00	Referent	70	1.00	Referent
2	208	1.41	0.82, 2.43	71	2.20	0.83, 5.82
3	191	1.30	0.71, 2.41	83	1.28	0.38, 4.31
4	185	1.09	0.61, 1.96	81	1.97	0.76, 5.08
P_{trend}			0.9762			0.3943
Log BPA	779	0.95	0.77, 1.17	305	1.14	0.81, 1.60
			Boys			
BPA quartiles[b]						
1	204	1.00	Referent	78	1.00	Referent
2	190	0.89	0.47, 1.67	75	15.56	3.43, 70.57
3	200	1.22	0.76, 1.96	82	8.47	1.83, 39.10
4	203	1.25	0.63, 2.47	84	18.89	3.97, 89.89
P_{trend}			0.3440			<0.0001
Log BPA	797	1.14	0.92, 1.41	319	1.70	1.30, 2.21

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

[a] Adjusted for age (years); education (below high school, high school, above high school); moderate activity (absent, present); urinary creatinine(mg/dL); and serum cotinine (ng/mL).

[b] BPA quartiles: quartile 1 (<1.5 ng/mL); quartile 2 (1.5–2.7 ng/mL); quartile 3 (2.8–5.4 ng/mL); quartile 4 (>5.4 ng/mL).

been found to disrupt pancreatic β-cell function and subsequently result in insulin resistance, which is a risk factor for obesity (33). Animal studies have also shown that BPA exposure can interact with estrogen receptor β to cause insulin resistance and obesity (34). Very few animal studies have reported either no significant association (35–37) or negative association (38) of BPA with body weight.

It has also been reported that BPA levels (39) as well as obesity prevalence (3, 40) may vary by gender and race/ethnicity. Trends in obesity prevalence in the United States in the past decade have shown significant increases in men and boys (3, 40). Among adults, there was a significant increasing linear trend in obesity among men, but not in women during the period of 1999 through 2010 (40). Among children and adolescents, a significant increase in obesity prevalence was seen among males aged 6–19 years at the 97th percentile of body mass index between 1999–2000 and 2007–2008 (3). Biomonitoring studies that examined BPA levels in urine also report similar gender (higher levels in males) (16, 39, 41) and racial/ethnic differences (higher levels in non-Hispanics) (16).

In the current study, in a separate analysis by gender, we found a statistically significant positive association with obesity among boys but not in girls. Similarly, in a stratified analysis by race/ethnicity, we found that the observed association between urinary BPA and obesity is primarily present in non-Hispanic white boys. The exact reasons for these observed gender and racial/ethnic differences in the BPA–obesity association are not clear. First, our results on the gender difference are consistent with the findings by Xu et al. (18) that perinatal exposure to 0.1 mg/L of BPA in rats increased the body weight, body fat, and visceral fat percentage in male offspring, but not in females. Animal studies attribute this gender difference in BPA concentrations to a lower rate of BPA glucuronidation and subsequent renal clearance in male rats (42), potentially resulting in higher free serum BPA concentrations and therefore higher biological action (43, 44). Second, estrogens have been reported to have a role in the pathogenesis of obesity (45). It is possible that the relative estrogenic activity of BPA may vary by the levels of endogenous estrogen levels, which are known to vary by gender (lower in males) and race/ethnicity (lower in non-Hispanic whites (19)). It is possible that BPA may act as an estrogenic agonist in the presence of low endogenous estrogen levels (males and non-Hispanic whites), whereas as an antagonist in the presence of higher endogenous estrogen levels (females and other race/ethnicities) (18). It is also possible that the effect of BPA on mechanisms related to obesity, such as insulin resistance, adipocyte differentiation, or aromatase-mediated transformation of androgen into estrogen, is different by gender and race/ethnicity (18). Finally, these observed gender and racial differences in the BPA–obesity association could be due to unmeasured confounding or a chance finding. To our knowledge, ours is the

first study to show that there are potential differences among children in the association between urinary BPA and obesity by gender and race/ethnicity. There is a need for more prospective studies with adequate representation of minorities to confirm or disprove our findings.

The advantages of our study include its population-based nature, large, multiethnic sample to enable subgroup analysis by race/ethnicity and sex, the assessment of multiple confounding variables (including age, sex, race/ethnicity, parent/guardian education, physical activity, urinary creatinine, and serum cotinine), and a broad range of urinary BPA levels. All data were collected following a rigorous methodology. Another important strength of this study is that we examined the association in children, a subgroup relatively free from the cumulative effects of some of those confounding factors that can blur the true associations in adult samples.

The main limitation of the study is the cross-sectional nature of NHANES that does not permit the ascertainment of temporal associations between BPA and obesity; future longitudinal studies are needed to confirm or disprove our findings. Another limitation is that, due to insufficient sample size for minority racial/ethnic groups, we had to group all nonwhite groups together in the analysis for statistical power. These nonwhite groups may also be heterogeneous with respect to distributions of body mass index, dietary practices, birth outcomes, and timing of puberty, all of which may influence the BPA–obesity association. Future studies with adequate numbers of minority racial/ethnic groups are needed to examine the BPA–obesity association separately in these groups also.

In conclusion, in a large, nationally representative sample of US children, we found that increasing levels of urinary BPA are positively associated with obesity. This association was found to be independent of age, sex, race/ethnicity, parent/guardian education, physical activity, and serum cotinine. In subgroup analyses by race/ethnicity and gender, this positive association was found to be present mainly in non-Hispanic white boys. Future prospective studies in children are needed to confirm our findings.

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