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Bisphenol A Exposure is Associated with Decreased Lung Function

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Abstract

Objective—To examine the associations of bisphenol A (BPA) exposure with lung function measures and exhaled nitric oxide (FeNO) in children.

Study design—We performed a cross-sectional analysis of a subsample of US children age 6–19 years who participated in the 2007–2010 National Health and Nutrition Examination Survey. We assessed univariate and multivariable associations of urinary BPA concentration with the predicted pulmonary function measures for age, sex, race/ethnicity and height (forced expiratory function in 1 second – FEV1, forced vital capacity – FVC, forced expiratory flow 25–75% – FEF2575, and FEV1/FVC) and with FeNO.

Results—Exposure and outcome data were available for 661 children. Median BPA was 2.4 ng/ml (IQR: 1.3, 4.1). In multivariable analysis a larger urinary BPA concentration was associated with significantly decreased %FEF2575 (3.7%, 95% CI 1.0, 6.5) and %FEV1/FVC (0.8%, 95% CI 0.1, 1.7) but not %FEV1, %FVC, or FeNO. A child in the top quartile of BPA compared with the

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bottom quartile had a 10% decrease in %FEF2575 (95% CI −1, −19) and 3% decrease in %FEV1/FVC (95% CI −1, −5).

Conclusions—BPA exposure was associated with a modest decrease in %FEF2575 (small airway function) and %FEV1/FVC (pulmonary obstruction) but not FEV1, FVC, or FeNO. Explanations of the association cannot rule out the possibility of reverse causality.

Keywords

bisphenol A; BPA; cotinine; pulmonary function; asthma; exhaled nitric oxide

Asthma prevalence has risen dramatically over the past decades, and currently it affects nearly one in ten children.(1, 2) Although many risk factors have been identified, the reason for the rising prevalence remains poorly understood.(3, 4) It is possible that novel environmental exposures may partially explain the rising prevalence.(5–8) Bisphenol A (BPA) is a chemical used in the manufacture of some plastics and epoxy resins found in many consumer products including the lining of canned foods. BPA exposure is pervasive, largely via food; over 90% Americans have detectible BPA in their urine.(9)

Animal studies suggest that BPA may adversely affect lung development. Animal models have identified an association of prenatal BPA exposure with the development of an experimental model of asthma, and one study noted that rhesus macaques exposed to BPA had accelerated development of secretory cells in the proximal airways.(10–12) However, another animal study demonstrated that maternal exposure to BPA has only subtle effects on allergic inflammation which did not lead to significant airway responsiveness.(13)

Epidemiologic studies have suggested that BPA may contribute to the development of asthma or bronchial obstruction in children.(14) The human studies note a similar association of BPA and asthma, but the timing of exposure and associated risks are conflicting. We previously reported that prenatal BPA exposure was associated with increased odds of developing parent reported wheeze in young children.(15) However, one study reported a postnatal association of BPA exposure with child asthma and wheeze but did not find an association of prenatal BPA exposure.(14) Using 2005–2006 NHANES data, Vaidya reported an association of urinary bisphenol A and allergic asthma primarily in females.(16) Yet, no study has examined whether BPA exposure is associated with objective measures of lung function such as spirometry, a tool used for diagnosing and monitoring lung diseases.(17–19) This is a gap in knowledge because most asthma guidelines recommend using spirometry and the measurement of forced expiratory volume in one second (FEV1) for assessing respiratory status.(19) A newer measure, exhaled nitric oxide (FeNO), has been proposed as potential noninvasive method to diagnose asthma and monitor the response to anti-inflammatory therapy, yet no study has examined BPA exposure and its relationship to FeNO.(20)

We therefore examined associations of urinary BPA with pulmonary function and FeNO in a large, representative sample of US children, the 2007–2010 National Health and Nutrition Examination Survey (NHANES).

Methods

We analyzed a concatenated set of data for children ages 6–19 years who participated in the 2007–2010 NHANES, a nationally representative survey which includes demographic, socioeconomic, and health questions and an examination component consisting of medical, dental, and physiological measurements. The New York University School of Medicine Institutional Review Board exempted this project from review on the basis of its analysis of already collected and deidentified data.

BPA was measured in a spot urine specimen from a random, one-third subsample of participants (n=1625) and analyzed with high-performance liquid chromatography and tandem mass spectroscopy.(21) We substituted the limit of detection divided by √2 for BPA concentrations below the limit of detection (3.3%). We log transformed BPA (natural log) to account for skew and included urinary creatinine in all analyses to adjust for urinary dilution.(9)

Measures of Respiratory Function and FeNO

Spirometry procedures in 6–19 year olds followed American Thoracic Society (ATS) standards.(22–24) Participants made forced vital capacity (FVC) maneuvers to meet acceptability and reproducibility criteria. We focused our analyses on FEV1, FVC, forced expiratory flow 25–75% (FEF2575), and FEV1/FVC because these measures are widely used in clinical care. FEV1 is the most common measure of airway obstruction used for asthma management, FVC is a widely-used measure of lung volume, and FEF2575 is a measure of small airway function. Some investigators suggest that FEV1/FVC is a more appropriate measure of obstruction in children than FEV1.(25–28) We calculated percent predicted levels of each of these measurements (%FEV1, %FVC, %FEF2575, and %FEV1/FVC) for age, sex, race/ethnicity, and height, using standard methods and used these variables as our primary dependent variables.(29)

Health technicians measured FeNO with the NIOX MINO® (Aerocrine AB, Solna, Sweden) using an electrochemical sensor to detect exhaled nitric oxide levels (5 to 300 ppb).(30) Two valid, reproducible measurements were required, following ATS guidelines.(20) ATS recommends the use of cut-points rather than reference values for interpreting FeNO levels and recommends different thresholds for children < 12 years old. We used the NHANES variable average of two reproducible measurements, and we categorized children using the cut-point of 36 ppb (children 6–11 years) or 39 ppb (children ≥12 years).(20, 31) FeNO below the cut-point indicates less eosinophilic inflammation and good corticosteroid response, whereas FeNO above the cut-point indicates inflammation and poor steroid response.(20, 31)

Potential Confounders

Technicians collected data on height, weight, demographics, and medical history. Body mass index (BMI) was calculated and BMI z-scores were derived from the Centers for Disease Control and Prevention 2000 reference data.(32) We categorized overweight and obese (≥1.036 and ≥1.64) using BMI z-score. We grouped race/ethnicity into Mexican

American, other Hispanic, non-Hispanic White, and non-Hispanic Black. We categorized caregiver education as: <9th grade, 9th–12th grade, high school/graduate equivalency diploma, some college, ≥ college. We grouped the poverty-income ratio variable into quartiles. We categorized age into 6–11 and 12–19 years, to emulate NHANES prevalence reports. We included serum cotinine, a biomarker of tobacco exposure, as a covariate. We categorized cotinine into low (<0.015 ng/mL), medium (<2 and ≥0.015 ng/mL) and high (≥2 ng/mL) categories.(33) We accounted for recent respiratory illness using response to, "in the past 7 days, have you had a cough, cold, phlegm, runny nose or other respiratory illness? Do not count allergies or hay fever." We accounted for asthma diagnosis using response to, "has a doctor or other health professional ever told [you] that [study participant has] asthma?" We created "missing" categories for potential confounders (except BMI). Serum cotinine was missing in 9.2%; otherwise, <5% of values were missing for other covariates.

Statistical analyses

We calculated descriptive statistics for all demographic, exposure, and outcome data. We accounted for the complex survey sampling design using standard techniques, using Stata 12.0 (College Station, TX).(34) We employed two-sided, tests for statistical significance (defined as P≤0.05). We conducted linear regression analyses to examine the bivariate association of BPA and potential covariates with each pulmonary function outcome (%FEV1, %FVC, %FEF2575, and %FEV1/FVC) and logistic regression analysis to examine the associations with FeNO. To assess robustness of the bivariate associations we analyzed the association of BPA with pulmonary function using multivariable linear regression, and we used multivariable logistic regression for FeNO associations. We used the %FEV1 analysis to select covariates and applied the same covariates to each outcome. Because BPA has estrogenic effects, we tested interactions of BPA with sex. We also considered other biologically plausible covariate interactions including asthma diagnosis, race, cotinine, and obesity. Lastly, we tested strength of the findings by reprising the multivariable analysis of percent predicted lung function using Z-scores rather than % predicted pulmonary outcome, and we also examined the final multivariable percent predicted pulmonary outcome models without sample weights.

We evaluated the specificity of associations of BPA and the respiratory outcomes by examining the association of urinary concentrations of two other structurally similar environmental phenols with the pulmonary outcomes. We evaluated benzophenone-3, a chemical found in non-food consumer products, and triclosan, a chemical added to soaps and other consumer products for antimicrobial function. Neither of these phenols is routinely used in food packaging, an important source of BPA exposure, thus the routes of exposure to these phenols have some differences from BPA.

Results

The analytic sample comprised 1625 participants with urinary BPA measurements out of the 5,096 children ages 6–19 who participated in NHANES for the study years. Out of the 1625 child participants with BPA samples, spirometry outcome data were available for 661. The mean age was 13 years, 39% were overweight or obese, 52% were male, and 19% reported a

doctor diagnosis of asthma (Table I). The geometric mean urinary BPA concentration was 2.5 ng/mL (95% CI 2.2, 2.8), the median BPA was 2.4 ng/ml (IQR: 1.3, 4.1). The mean percent predicted FEV1 was 102 (Table II). The mean FeNO was 18.8 ppb, and 10.6% of children were in the high FeNO category.

Bivariate Associations of Urinary BPA and Covariates with Respiratory Outcomes

Bivariate analyses failed to demonstrate association of BPA or any of the other potential covariates (sex, race/ethnicity, poverty-income ratio, parent education, serum cotinine, obesity, asthma diagnosis, recent respiratory infection, and age) with %FEV1 or %FVC (Table III; available at www.jpeds.com).

A larger BPA concentration was associated with decreased %FEV1/FVC (β=−0.01, 95% CI −0.003, −0.018; Table III); a child with a BPA in the top quartile compared with the bottom quartile had a 3% decrease in %FEV1/FVC (95% CI −1, −6). Similarly, a larger BPA concentration was associated with decreased %FEF2575 (β=−0.03, 95% CI −0.001, −0.057); a child with a BPA in the top quartile compared with the bottom quartile had an 8% decrease in %FEF2575 (95% CI −2, −17). Asthma diagnosis was associated with decreased %FEV1/FVC (β=−0.04, 95% CI −0.06, −0.03). Asthma diagnosis was also associated with a decreased %FEF2575 (β=−0.12, 95% CI −0.19, −0.04), and having had a recent cold had a borderline association with decreased %FEF2575 (β=−0.06, 95% CI −0.13, 0).

Although there was no bivariate association of BPA concentration with FeNO (OR=0.78, 95% CI 0.46, 1.3), having had a recent respiratory illness was associated with an increased odds of having a high FeNO (OR=2.94, 95% CI 1.25, 6.67). There was no association of BPA with asthma diagnosis, wheeze episode in the last year, or reported prescription of asthma medication.

Multivariable Association of Urinary BPA with Pulmonary Outcomes

In multivariable analysis, we found that urinary BPA concentration was associated with %FEF2575 and %FEV1/FVC, but BPA was not associated with %FEV1, %FVC, or FeNO (Tables IV and V). A log unit increase in BPA was associated with a 3.7% decrease in %FEF2575 (95% CI 1.0, 6.5) and 0.9% decrease in %FEV1/FVC (95% CI 0.1, 1.7). A child with a BPA in the top quartile compared with the bottom quartile had a 10% decrease in %FEF2575 (95% CI 2, 19) and 3% decrease in %FEV1/FVC (95% CI 1, 5). Increased urinary BPA concentration had a borderline association with a decrease in the log of FeNO (β=−0.07, 95% CI −0.144, 0.008) when treated as a linear variable.

There was no statistically significant interaction of BPA concentration with sex for any of the pulmonary function outcomes or FeNO (the strata did not differ by >10% and all interaction terms were p>0.05). There was also no statistically significant interaction of BPA with race, cotinine, obesity, or asthma diagnosis for any of the pulmonary function outcomes.

Sensitivity Analyses

When we removed asthma diagnosis from the same multivariable analyses, the associations were also similar: a larger urinary BPA concentration was associated with a decrease in %FEF2575 and %FEV1/FVC (data not shown), but BPA was not associated with differences in %FEV1, %FVC, or FeNO.

A multivariable analysis of Z-score outcomes failed to produce substantially different results (data not shown). Unweighted analyses of urinary BPA with %FEF2575 demonstrated similar results to the weighted analyses, but the relationships were attenuated. Urinary BPA was associated with a 2.3% decrease in %FEF2575 (95% CI 0, 4.6) and a 0.3% decrease in %FEV1/FVC (95% CI 0, 1.0). Additionally, the association of urinary BPA with FEV1 became significant; a log unit increase in BPA was associated with a 1.4% decrease in %FEV1 (95% CI 0.2, 2.6).

When we replaced BPA with the two different phenols (separately) in each of the models, there was no association of benzophenone-3 or triclosan with any of the pulmonary function outcomes or FeNO. We also added each of these phenols (separately) into multivariable models with BPA in the model, and it did not change any of the associations. Triclosan was measurable in 84% and benzophenone-3 was measurable in 99% of urine samples for the 661 participants.

Discussion

In a nationally representative sample, we found that BPA exposure was associated with a modest decrease in two lung function measurements – %FEF2575 and %FEV1/FVC but not %FEV1, %FVC, or FeNO. Although the associations we describe are modest, across a population these changes may have important implications in long term lung function and lung health. Lung capacity is maximal by the early 20s, so any reduction in pulmonary function in childhood, even if not consistent with statistically significant obstructive or restrictive disease, may confer a vulnerability to future lung disease.

There are several strengths and limitations to this study. First, even though the large representative sample is a strength of this study, urinary BPA concentration and pulmonary function data were not available for all participants which could limit the generalizability. Second, due to the variability of urinary BPA concentrations over time, using a single biomarker measure could result in exposure misclassification. Some investigators have suggested that a single urinary BPA sample is predictive of long-term category of exposure, but others have noted that BPA concentrations vary both within the day and between days. (35, 36) The poor reproducibility of BPA could translate to non-differential misclassification of exposure which likely would have biased the results towards the null. Third, the children for whom all data were available were older, had higher cotinine levels, more had a recent cold, and the mean BPA was higher compared with those for whom data was not available. Although we accounted for these variables in the adjusted models, these differences may decrease generalizability of the findings. Fourth, the analysis was cross-sectional and cannot establish causality. However, the association may suggest a possible mechanism of BPA effect – obstruction of small airways. Moreover, the lack of association of either of the other

phenols (triclosan and benzophenone-3) with pulmonary function adds weight to the BPA association. Fifth, reverse causality is a possibility in this analysis; however, the most common BPA exposure route is food, and reverse causality would imply that children with decreased pulmonary function are more likely to eat more BPA containing foods, which seems unlikely.

Spirometry is a frequently used tool for diagnosing and monitoring lung disease in children.(17–19) Most asthma guidelines recommend using spirometry and the measure of forced expiratory volume in one second (FEV1), a measure of airway obstruction, for assessing respiratory status.(19) However, some have suggested that it might be more appropriate to use FEV1/FVC (another measure of airway obstruction) or FEF2575 (a measure of small airway function) to assess asthma severity in children.(25, 26) It has been suggested that FEF2575 may be a more sensitive marker of small airway obstruction than FEV1.(27, 28) Our finding of an association of BPA with %FEF2575 and %FEV1/FVC may suggest that the BPA is associated with small airway obstruction rather than a child's overall lung volume (FVC). Future studies will be needed to confirm mechanistic associations.

Animal models have identified an association of prenatal BPA exposure with the development of an experimental model of asthma, and one study noted that rhesus macaques exposed to BPA had accelerated development of secretory cells in the proximal airways.(10–12) However, another animal study demonstrated that maternal exposure to BPA has only subtle effects on allergic inflammation which did not lead to significant airway responsiveness.(13) The human studies note a similar association of BPA and asthma, but the timing of exposure and associated risks are conflicting. We previously noted an association of prenatal urinary BPA and wheeze in young children.(15) However, a more recent study reported a postnatal association of BPA exposure with child asthma and wheeze but did not find an association of prenatal BPA exposure.(14) Using 2005–2006 NHANES data, Vaidya reported an association of urinary bisphenol A and allergic asthma primarily in females.(16) We did not find an association of urinary BPA concentration with asthma diagnosis in children in this analysis. When we removed asthma from our adjusted model, it did not affect the BPA and pulmonary function association suggesting that the associations are independent of any effects of asthma diagnosis. The association that we found may reflect the timing of exposure that was available (concurrent BPA levels), and we cannot comment on any windows of vulnerability or effects of prenatal BPA exposure.

Our finding of a lack of association of BPA with FeNO levels is contrary to the findings from Donohue et al.(14) In their study, Donohue et al noted that at age 7 years of age BPA was associated with FeNO collected between age 7 and 11 years. There are several dissimilarities between that study and this NHANES analysis, which could account for this difference: (1) the collection method they used was an offline device and NHANES was online; (2) they analyzed FeNO as a linear variable only; (3) their BPA levels may have been collected at different ages than the FeNO measurement; and (4) their cohort was primarily African American and Dominican. The lack of an association of BPA with FeNO may suggest that the mechanism for the BPA and pulmonary function association may be via a pathway other than eosinophilic inflammation; this should be evaluated in future mechanistic studies.

In summary, we found that urinary BPA concentration was associated with a decrease in two key lung function measurements in children – %FEF2575 and %FEV1/FVC but not %FEV1, %FVC, or FeNO. While the analysis was cross-sectional and cannot establish causality, it suggests a possible mechanism of BPA effect (obstruction of small airways), which merits additional evaluation. Moreover, these decrements in pulmonary function projected across a population may have important implications in long term lung function and lung health.

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Abbreviations

ATS	American Thoracic Society
BPA	Bisphenol A
FEV1	Forced Expiratory Volume in one second
FEV1/FVC	Forced Expiratory Volume in one second divided by Forced Vital Capacity
FEF2575	Forced Expiratory Flow 25–75%
FVC	Forced Vital Capacity
FeNO	Fraction of Exhaled Nitric Oxide
NHANES	National Health and Nutrition Examination Survey
%FEV1	Percent Predicted FEV1
%FEV1/FVC	Percent Predicted FEV1/FVC
%FEF2575	Percent Predicted FEF2575
%FVC	Percent Predicted FVC

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Table 1

Study Population Characteristics and Exposures for the Children with BPA levels (n=1625).

	Spirometry Data Available N=661 N (Weighted %)	Spirometry Data Not Available Weighted N=964 N (Weighted %)	p-value Comparing Weighted Percentages or Means
Male sex	345 (51.6)	501 (50.9)	NS
Race/ethnicity			
Hispanic-Mexican	178 (13.4)	250 (14.6)	
Hispanic-Other Hispanic	93 (6.8)	123 (9.4)	NS
Non-Hispanic White	197 (64.6)	293 (60.5)	
Non-Hispanic Black	193 (15.2)	207 (15.5)	
Poverty-income ratio			
1st quartile (< 0.83)	140 (16.5)	250 (15.4)	
2nd quartile (0.83 to 1.59)	137 (14.5)	123 (20.0)	0.04
3rd quartile (1.60 to 3.09)	190 (28.5)	293 (21.0)	
4th quartile (at least 3.1)	150 (36.5)	207 (34.7)	
Missing	44 (4.0)	91 (8.9)	
Parent/caregiver education			
Less than 9th grade	69 (8.7)	112 (7.9)	
9th–12th grade	127 (12.5)	177 (13.5)	NS
High school or GED	146 (20.0)	226 (21.4)	
Some college	191 (30.5)	257 (28.7)	
College or greater	102 (24.9)	164 (25.7)	
Missing	26 (3.4)	28 (2.8)	
Serum cotinine (ng/mL)			
< 0.015	101 (14.3)	200 (21.0)	
0.015–1.9	397 (59.2)	524 (52.6)	0.01
≥ 2.0	90 (17.3)	106 (12.1)	
Missing	73 (9.2)	134 (14.3)	
Weight category			
Not overweight	406 (65.6)	576 (64.0)	NS
Overweight	96 (13.6)	173 (17.8)	
Obese	159 (20.8)	200 (18.2)	
Doctor diagnosed asthma	125 (18.3)	183 (17.9)	NS
Respiratory illness in last week	131 (20.8)	25 (2.4)	0.001
Age (years), mean (SD)	13.0 (5.4)	12.4 (7.6)	0.02
BPA (ng/mL), geometric mean (95% CI)	2.5 (2.2, 2.8)	2.0 (1.9, 2.2)	0.009

NS = Not significant (<0.05)

Table 2

Mean of the Percent Predicted Pulmonary Function or FeNO for the Study Population

	Mean	25th Percentile	75th Percentile
FEV1	102	92	110
FVC	103	94	111
FEF25–75	99	80	115
FEV1/FVC	98	94	102
FeNO (ppb)	12.0	8.0	20.5

Table 3

Unadjusted Association of the Participant Characteristics and Exposures with Pulmonary Function and FeNO (n=661).

	%FEV1		%FVC		%FEV1/FVC		%FEF2575		FeNO*	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	Odds Ratio	95% CI
Male sex	0.003	−0.014, 0.02	0.019	−0.002, 0.04	−0.004	−0.016, 0.008	−0.008	−0.051, 0.035	0.69	0.29, 1.64
Race/ethnicity										
Hispanic-Mexican	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Hispanic-Other Hispanic	−0.073	−0.119, −0.026	−0.044	−0.078, −0.01	−0.031	−0.053, −0.008	−0.113	−0.199, −0.027	0.61	0.17, 2.17
Non-Hispanic White	0.007	−0.017, 0.031	0.006	−0.035, 0.023	0.012	−0.007, 0.03	0.058	−0.006, 0.123	0.74	0.36, 1.52
Non-Hispanic Black	−0.008	−0.049, 0.034	−0.0004	−0.032, 0.032	−0.018	−0.036, 0.001	−0.033	−0.111, 0.046	1.96	0.92, 4.35
Poverty-income ratio										
1st quartile (< 0.83)	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
2nd quartile (0.83 to 1.59)	0.035	−0.006, 0.075	0.043	0.006, 0.079	−0.011	−0.031, 0.01	0.017	−0.057, 0.091	1.09	0.38, 3.13
3rd quartile (1.60 to 3.09)	0.025	−0.012, 0.061	0.034	−0.003, 0.071	−0.006	−0.03, 0.018	−0.001	−0.088, 0.086	1.33	0.51, 3.57
4th quartile (at least 3.1)	0.009	−0.032, 0.05	0.001	−0.043, 0.044	0.006	−0.018, 0.03	0.037	−0.058, 0.131	1.0	0.45, 2.22
Missing	−0.031	−0.083, 0.021	−0.013	−0.07, 0.044	−0.017	−0.044, 0.011	−0.083	−0.176, 0.011	0.48	0.08, 2.86
Parent/caregiver education										
Less than 9th grade	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
9th–12th grade	0.010	−0.086, 0.105	0.004	−0.071, 0.078	0.005	−0.026, 0.035	0.028	−0.128, 0.185	2.70	0.68, 11.11
High school or GED	−0.017	−0.089, 0.055	−0.026	−0.098, 0.045	0.013	−0.003, 0.029	0.006	−0.088, 0.1	1.18	0.32, 4.35
Some college	−0.012	−0.0866, 0.063	−0.038	−0.109, 0.034	0.023	0.004, 0.042	0.057	−0.035, 0.149	0.47	0.09, 2.44
College or greater	−0.006	−0.075, 0.063	−0.019	−0.084, 0.046	0.015	0.001, 0.029	0.039	−0.073, 0.151	1.37	0.31, 6.25
Missing	−0.00	−0.086, 0.085	0.012	−0.08, 0.103	−0.009	−0.048, 0.03	−0.034	−0.153, 0.084	0.61	0.13, 3.03
Serum cotinine (ng/mL)										
< 0.015	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
0.015–1.9	0.036	0.003, 0.068	0.023	−0.015, 0.061	0.012	−0.002, 0.027	0.045	−0.036, 0.125	0.64	0.20, 2.08
≥ 2.0	0.011	−0.029, 0.051	0.011	−0.038, 0.059	−0.0004	−0.024, 0.023	−0.021	−0.103, 0.061	0.82	0.22, 3.03
Missing	−0.006	−0.006, 0.019	−0.039	−0.081, 0.003	0.018	−0.008, 0.044	0.088	−0.11, 0.128	0.83	0.14, 4.76
Weight category										
Not overweight	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.

	%FEV1		%FVC		%FEV1/FVC		%FEF2575		FeNO*	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	Odds Ratio	95% CI
Overweight	0.025	−0.024, 0.074	0.038	0.003, 0.074	−0.016	−0.043, 0.01	0.007	−0.102, 0.117	1.59	0.54, 4.55
Obese	0.019	−0.023, 0.061	0.033	0.006, 0.061	−0.017	−0.046, 0.012	−0.014	−0.14, 0.111	1.06	0.28, 4.17
Doctor Diagnosed Asthma	−0.023	−0.062, 0.016	0.027	−0.004, 0.058	−0.043	−0.061, −0.025	−0.116	−0.191, −0.04	1.67	0.63, 4.55
Respiratory Illness in last week	−0.023	−0.057, 0.011	−0.012	−0.054, 0.031	−0.011	−0.033, 0.011	−0.062	−0.126, 0.003	2.94	1.25, 6.67
Age (years), mean (SD)	0.0004	−0.004, 0.005	0.002	−0.003, 0.006	0.002	0, 0.003	−0.005	−0.012, 0.001	1.04	0.98, 1.12
BPA (ng/mL), geometric mean (95% CI)	−0.006	−0.025, 0.013	0.004	−0.015, 0.022	−0.010	−0.018	−0.029	−0.057, −0.001	0.78	0.46, 1.3
BPA (ng/mL),										
Quartile 1	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref
Quartile 2	0.013	−0.027, 0.054	0.018	−0.029, 0.066	−0.007	−0.033, 0.019	0.008	−0.079, 0.096	1.61	0.56, 4.59
Quartile 3	−0.021	−0.066, 0.023	0.011	−0.037, 0.06	−0.036	−0.064, −0.009	−0.072	−0.171, 0.027	0.5	0.14, 1.73
Quartile 4	−0.005	−0.056, 0.046	0.024	−0.03, 0.077	−0.034	−0.058, −0.010	−0.075	−0.171, 0.021	0.72	0.18, 2.92

*This column represents the logistic regression model of being in the high FeNO category (i.e. an odds ratio over 1.0 suggests an increased odds of having high FeNO).

Table 4

Adjusted Associations* of linear BPA, asthma diagnosis, and recent respiratory illness with pulmonary function and FeNO (n=661)

	%FEV1		%FVC		%FEV1/FVC		%FEF2575		FeNO†	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	Odds Ratio	95% CI
BPA (ng/mL)	−0.010	−0.027, 0.007	0.0001	−0.017, 0.017	−0.009	−0.017, −0.001	−0.037	−0.065, −0.010	0.72	0.40, 1.28
Doctor Diagnosed Asthma	−0.026	−0.061, 0.009	0.022	−0.004, 0.048	−0.043	−0.062, −0.023	−0.114	−0.190, −0.037	2.28	0.80, 6.54
Respiratory Illness In the last week	−0.025	−0.062, 0.012	−0.014	−0.055, 0.028	−0.013	−0.032, 0.007	−0.058	−0.126, 0.009	3.15	1.36, 7.28

*Adjusted for urinary creatinine, body mass index, age, poverty-income ratio, sex, race, and serum cotinine.

†This column represents the logistic regression model of being in the high FeNO category (ie, an odds ratio over 1.0 suggests an increased odds of having high FeNO).

Table V

Adjusted Associations* of linear BPA in quartiles, asthma diagnosis, and recent respiratory illness with pulmonary function and FeNO (n=661)

	%FEV1		%FVC		%FEV1/FVC		%FEF2575		FeNO†	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	Odds Ratio	95% CI
BPA (ng/mL)										
Quartile 1	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Quartile 2	0.013	−0.023, 0.048	0.024	−0.015, 0.062	−0.008	−0.030, 0.013	−0.010	−0.097, 0.077	1.33	0.32, 5.48
Quartile 3	−0.027	−0.061, 0.006	0.013	−0.032, 0.058	−0.038	−0.063, −0.013	−0.106	−0.193, −0.020	0.47	0.11, 1.98
Quartile 4	−0.016	−0.060, 0.029	0.015	−0.035, 0.066	−0.030	−0.053, −0.006	−0.103	−0.191, −0.015	0.59	0.12, 2.94
Doctor Diagnosed Asthma	−0.027	−0.062, 0.009	0.021	−0.004, 0.047	−0.043	−0.063, −0.023	−0.115	−0.193, −0.038	3.13	1.35, 7.29
Respiratory Illness In the last week	−0.026	−0.063, 0.011	−0.014	−0.055, 0.027	−0.014	−0.033, 0.005	−0.061	−0.130, 0.008	2.23	0.74, 6.75

*Adjusted for urinary creatinine, body mass index, age, poverty-income ratio, sex, race, and serum cotinine.

†This column represents the logistic regression model of being in the high FeNO category (ie, an odds ratio over 1.0 suggests an increased odds of having high FeNO).