

Supplemental Material

**Urinary Phthalate Metabolites and Biomarkers of Oxidative Stress
in Pregnant Women: A Repeated Measures Analysis**

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Table S1. Demographic characteristics in weighted study population including only subjects with complete covariates included in adjusted regression models^a (N=464).

Characteristic	Percent
Race/ethnicity (N=464)	
White	60
African American	15
Other	25
Education (N=464)	
High school	14
Technical school	15
Junior college or some college	29
College graduate	41
Health insurance (N=464)	
Private/HMO/self-pay	82
Medicaid/SSI/MassHealth	18
Body mass index at visit 1 (N=461)	
<25 kg/m ² (underweight to normal)	53
25-30 kg/m ² (overweight)	27
≥30 kg/m ² (obese to morbidly obese)	20
Smoking during pregnancy (N=464)	
Some	6
None	94
Alcohol use during pregnancy (N=460)	
Some	5
None	95
Parity (N=464)	
Nulliparous	46
Parous	54

HMO, health maintenance organization, SSI, supplemental security income. Distributions of demographic characteristics created from inverse probability weightings for case-control status.

^aCovariates included in final statistical models were not the same as those described in Table S1.

Covariates for final models included: urinary specific gravity, gestational age at sample collection, race/ethnicity, education level, health insurance provider, body mass index (time-varying), time of day of urine sample collection, and parity of infant.

Table S2. Urinary phthalate metabolite concentrations (geometric mean and geometric standard deviation) by categorical demographic characteristics in all samples measured from weighted population (N=1678 samples, N=482 subjects).

Characteristic	MEHHP (µg/L)	MEOHP (µg/L)	MECPP (µg/L)	ΣDEHP (µmol/L)	MBzP (µg/L)	MiBP (µg/L)	MEP (µg/L)	MCPP (µg/L)
Race/ethnicity								
White (Ref.)	35.8 (2.11)	18.9 (2.03)	43.9 (2.02)	0.39 (1.91)	5.67 (1.63)	6.28 (1.33)	111 (3.06)	2.00 (1.78)
African-American	35.8 (2.13)	18.4 (2.16)	42.8 (2.22)	0.40 (2.05)	10.5 (1.90)*	11.2 (1.36)*	285 (3.04)*	2.49 (2.38)
Other	29.9 (2.11)	16.9 (2.06)	42.9 (2.27)	0.37 (1.98)	9.31 (2.15)*	9.44 (1.47)*	165 (3.26)*	2.13 (2.02)
Education								
High school (Ref.)	27.8 (1.76)	15.2 (1.79)	37.0 (1.94)	0.32 (1.74)	15.6 (2.30)	10.7 (1.25)	286 (3.22)	2.52 (2.04)
Technical school	30.0 (2.10)	15.5 (2.07)	34.7 (2.11)	0.32 (1.98)	8.18 (1.97)*	9.45 (1.44)	197 (3.01)	2.10 (1.90)
Junior college or some college	33.2 (2.29)	17.9 (2.21)	44.1 (2.23)	0.38 (2.01)	6.07 (1.72)*	6.43 (1.58)*	133 (3.10)*	1.99 (1.98)
College graduate	38.7 (2.10)	20.9 (2.00)	49.5 (2.06)	0.44 (1.93)	5.73 (1.59)*	7.05 (1.30)*	101 (3.04)*	2.06 (1.88)
Health insurance								
Private insurance/HMO/Self-pay (Ref.)	34.6 (2.21)	18.7 (2.13)	45.0 (2.18)	0.40 (2.00)	5.93 (1.66)	6.99 (1.43)	120 (3.20)	2.02 (1.92)
Medicaid/SSI/MassHealth	30.7 (1.76)	16.1 (1.78)	36.4 (1.85)	0.33 (1.73)	15.9 (2.12)*	11.4 (1.24)*	295 (2.79)*	2.39 (1.75)
BMI at visit 1								
Less than 25 kg/m ² (Ref.)	33.7 (2.09)	18.3 (1.99)	43.5 (2.14)	0.38 (1.95)	6.58 (1.86)	7.08 (1.30)	116 (2.90)	1.95 (1.82)
25 to less than 30 kg/m ²	34.0 (2.34)	17.7 (2.34)	41.4 (2.19)	0.38 (2.04)	6.08 (1.69)	7.89 (1.56)	162 (3.96)*	2.19 (2.06)
Greater than 30 kg/m ²	36.3 (1.94)	19.4 (1.90)	46.8 (1.96)	0.41 (1.82)	10.1 (1.88)*	8.88 (1.51)*	202 (3.18)*	2.38 (1.97)
Tobacco use								
Smoked during pregnancy (Ref.)	38.4 (1.71)	19.6 (1.65)	46.9 (1.64)	0.40 (1.64)	15.4 (1.75)*	9.06 (1.24)	177 (3.94)	3.55 (1.94)
No smoking during pregnancy	33.7 (2.15)	18.1 (2.08)	43.2 (2.15)	0.38 (1.97)	6.76 (1.83)	7.56 (1.42)	140 (3.26)	2.03 (1.91)*
Alcohol use								
Alcohol use during pregnancy (Ref.)	58.3 (1.84)	31.2 (1.78)	81.1 (2.05)	0.65 (1.87)	5.33 (1.41)	8.38 (1.53)	138 (2.88)	2.79 (2.72)
No alcohol use during pregnancy	32.9 (2.11)*	17.6 (2.05)*	41.8 (2.09)*	0.37 (1.93)	7.23 (1.89)*	7.61 (1.41)	143 (3.32)	2.07 (1.89)
Parity								
Nulliparous (Ref.)	36.4 (2.14)	19.7 (2.08)	46.3 (2.13)	0.41 (1.96)	6.21 (1.79)	7.26 (1.43)	149 (3.16)	2.04 (1.90)
Non-nulliparous	32.4 (2.10)	17.2 (2.03)	41.3 (2.09)	0.36 (1.93)	7.87 (1.89)*	7.91 (1.39)	136 (3.40)	2.15 (1.95)

Ref., reference category. HMO, Health Maintenance Organization. SSI, Supplemental Security Income. BMI, body mass index.

*p<0.05 for significant difference in biomarker concentration from reference category, estimated from weighted linear mixed model with random intercepts for subject ID. All biomarkers adjusted for urinary specific gravity.

Table S3. Percent difference (95% confidence intervals) in oxidative stress biomarker in association with interquartile range increase in phthalate metabolite level. Estimates from adjusted^a linear mixed effect models with random intercepts for subject ID, including cases (N=405 samples, N=127 subjects) or controls only (N=1199 samples, N=337 subjects).

Metabolite	Cases 8-OHdG % difference (95% CI)	p	Controls 8-OHdG % difference (95% CI)	p	Cases 8-Isoprostane % difference (95% CI)	p	Controls 8-Isoprostane % difference (95% CI)	p
MEHP	4.11 (-2.13, 10.8)	0.202	2.77 (-0.47, 6.11)	0.10	11.8 (1.27, 23.3)	0.028	14.3 (8.15, 20.7)	<0.001
MEHHP	6.90 (0.02, 14.3)	0.050	8.07 (4.74, 11.5)	<0.001	11.8 (0.69, 24.1)	0.038	15.2 (9.15, 21.5)	<0.001
MEOHP	6.22 (-0.33, 13.2)	0.064	7.15 (3.91, 10.5)	<0.001	10.9 (0.44, 22.5)	0.042	15.5 (9.61, 21.7)	<0.001
MECPP	6.14 (-0.76, 13.5)	0.083	4.90 (2.23, 7.64)	<0.001	14.8 (3.02, 28.0)	0.013	16.9 (11.9, 22.2)	<0.001
ΣDEHP	6.08 (-0.61, 13.2)	0.077	6.65 (3.22, 10.2)	<0.001	12.9 (1.92, 25.0)	0.021	19.1 (12.6, 25.9)	<0.001
MBzP	18.5 (7.60, 30.5)	0.001	19.5 (14.6, 24.5)	<0.001	50.3 (27.4, 77.4)	<0.001	39.8 (29.8, 50.6)	<0.001
MBP	8.92 (2.03, 16.3)	0.011	17.5 (13.1, 22.2)	<0.001	30.9 (15.8, 48.0)	<0.001	40.7 (31.0, 51.0)	<0.001
MiBP	20.3 (10.2, 31.3)	<0.001	30.3 (24.4, 36.5)	<0.001	52.5 (32.2, 76.0)	<0.001	56.4 (43.9, 69.9)	<0.001
MEP	19.2 (10.3, 28.8)	<0.001	11.2 (7.12, 15.4)	<0.001	15.2 (0.70, 31.8)	0.040	19.1 (11.5, 27.3)	<0.001
MCPP	5.28 (-0.73, 11.6)	0.087	7.11 (3.77, 10.6)	<0.001	19.2 (8.46, 31.1)	<0.001	19.9 (13.5, 26.6)	<0.001

8-OHdG, 8-hydroxydeoxyguanosine.^aAdjusted for urinary specific gravity, gestational age at sample collection, race/ethnicity, education level, health insurance provider, body mass index (time-varying), time of day of urine sample collection (before vs. after 1pm, time-varying), and parity of infant.

Table S4. Percent difference (95% confidence intervals) in oxidative stress biomarker in association with interquartile range increase in phthalate metabolite level. All metabolites were included as predictors of one oxidative stress biomarker in each model. Estimates from adjusted^a linear mixed effect models with random intercepts for subject ID (N=1604 samples, N=464 subjects).

Metabolite	8-OHdG % difference (95% CI)	p	8-Isoprostane % difference (95% CI)	p
ΣDEHP	2.98 (-0.53, 6.60)	0.10	9.49 (3.25, 16.1)	0.003
MBzP	13.3 (7.84, 19.1)	<0.001	21.8 (11.3, 33.2)	<0.001
MBP	9.08 (4.08, 14.3)	<0.001	20.4 (10.5, 31.2)	<0.001
MEP	8.46 (4.41, 12.7)	<0.001	12.0 (4.71, 19.7)	0.001
MCPP	1.60 (-1.92, 5.24)	0.38	7.75 (1.47, 14.4)	0.015

8-OHdG, 8-hydroxydeoxyguanosine.^aAdjusted for urinary specific gravity, gestational age at sample collection, race/ethnicity, education level, health insurance provider, body mass index (time-varying), time of day of urine sample collection (before vs. after 1pm, time-varying), and parity of infant. Models include inverse probability weights to adjust for case-control study design.