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Supplemental Material

Associations of Prenatal Urinary Bisphenol A Concentrations with Child Behaviors and Cognitive Abilities

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Table S1: Description of neurobehavioral tests administered to children or parents in the MIREC Study at approximately 3 years of age.

Test	Description	Composite/Scale Scores Examined
Behavioral Assessment for Children-2	These scales offer a comprehensive assessment of a child’s adaptive and problem behaviors in community, home, and school settings. Provides summary composite measures that are derived from clinical subscales. The BASC-2 assesses a variety of symptoms that are noted in the DSM-IV.	Composite scales include externalizing, internalizing, and total behavior problems. Clinical subscales include aggression, anxiety, attention, atypicality, depression, hyperactivity, somatization, and withdrawal.
Behavior Rating Inventory of Executive Function	This parent-reported survey assesses several executive functions: inhibition, ability to shift, emotional control, working memory, and planning/organization. The BRIEF is useful for assessing children with such medical, acquired neurologic, and developmental conditions as prematurity, emerging learning disabilities and attention disorders, language disorders, traumatic brain injuries, and lead exposure.	Working memory-ability to hold information while completing a task. Plan/organize-Anticipate future events, develop steps, set goals, grasp main ideas. These two scales measure emerging metacognitive abilities in young children.
Social Responsiveness Scale	Parent-reported instrument of children’s pervasive-developmental problem behaviors, autistic mannerisms, and reciprocal social behaviors. The SRS-2 is designed to assess symptoms of autism spectrum disorders. It is considered a sensitive and reliable screening tool for pervasive developmental disorders.	Includes single composite scale, as well as subscales of social awareness, social cognition, social communication, social motivation, and repetitive behaviors and restricted interests. Also has two DSM-V criteria subscales related to social communication/interaction and restricted interests and repetitive behaviors.
Wechsler Primary & Preschool Scales of Intelligence-III	Examiner-administered intelligence test (IQ). Assesses verbal, performance, working memory, and processing speed abilities. The test provides subtest and composite scores which represent intellectual functioning in specific cognitive domains as well as a composite score which represents general intellectual ability.	Composite scores include full scale, verbal, and performance IQ. Subscales include vocabulary, block design, information, object design, and picture completion.
NEPSY-II	The NEPSY-II is an examiner-administered test battery that is designed	The affect recognition test assesses a child’s ability to

	to assess a broad array of neuropsychological domains based on Luria's principals.	recognize affect from photograph's of children's faces. Low scores on this task may indicate poor visual attention, visual discrimination, and facial recognition.
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Table S2: Baseline maternal covariates among women whose children did not complete follow-up at 3 years of age (n=895), completed neurobehavioral assessments via questionnaire at 3 years of age (n=812), and completed in-person assessments of neurobehavior at 3 years of age (n=544).

Covariates	No Follow-Up (%)	Questionnaire Follow-Up (%)	In-Person Follow Up (%)
Maternal Age			
18-25 years	77 (8.6)	26 (3.2)	15 (2.8)
>25-35 years	531 (59.3)	493 (60.7)	342 (62.9)
>35 years	287 (32.1)	293 (36.1)	187 (34.3)
Maternal Race			
White	697 (77.8)	702 (86.5)	465 (85.5)
Asian/Pacific Islander	65 (7.4)	27 (3.3)	16 (2.9)
Other	88 (9.8)	49 (6.0)	39 (7.2)
Multi-Racial	45 (5.0)	34 (4.2)	24 (4.4)
Maternal Education			
Graduate Degree	212 (23.7)	229 (28.2)	146 (26.8)
University Degree	309 (34.5)	325 (40.2)	224 (41.2)
Some College, Trade School, or Diploma	278 (31.1)	214 (26.4)	149 (27.4)
High School or Less	96 (10.7)	44 (5.4)	25 (4.6)
Marital Status			
Married or Living with Partner	846 (94.5)	791 (97.4)	527 (96.9)
Not Married or Living Alone	49 (5.5)	21 (2.6)	17 (3.1)
Household Income (CAD)			
>\$100K	360 (40.2)	330 (40.6)	217 (39.9)
\$80K-100K	227 (25.4)	270 (33.3)	177 (32.5)
\$40K-<80K	167 (18.7)	136 (16.7)	94 (17.3)
<\$40K	141 (15.8)	76 (9.4)	56 (10.3)
Employment			
No	141 (15.8)	93 (11.4)	61 (11.2)
Yes	754 (84.2)	719 (88.5)	483 (88.8)
Parity			
0	390 (43.6)	357 (44.0)	241 (44.3)
1	359 (40.1)	332 (40.9)	218 (40.1)
2+	146 (16.3)	123 (15.1)	85 (15.6)
Smoking During Pregnancy			
No	832 (93.0)	783 (96.4)	527 (96.9)
Yes	63 (7.4)	29 (3.3)	17 (3.1)
Alcohol Use During Pregnancy			
No	516 (57.7)	448 (55.2)	309 (56.8)
Yes	379 (42.3)	364 (44.8)	235 (43.2)
Folic Acid Supplement During Pregnancy			
No	101 (11.3)	534 (65.8)	368 (67.6)
Yes	794 (88.7)	278 (34.2)	176 (32.4)

Table S3: Covariate adjusted mean child BASC-2 and BRIEF-P scores by specific gravity standardized maternal urinary BPA quintile: MIREC Study (n=806-812)^a

Outcome/BPA Quintile	Boys		Girls	
	Mean	Difference (95% CI)	Mean	Difference (95% CI)
Internalizing				
1 st (0.1-<0.4 ng/mL)	50	Ref	52	Ref
2 nd (0.4-<0.7 ng/mL)	50	-0.5 (-3.1, 2.1)	53	0.7 (-1.8, 3.2)
3 rd (0.7-<1.0 ng/mL)	52	1.4 (-1.2, 3.9)	53	0.5 (-2.0, 3.0)
4 th (1.0-<1.7 ng/mL)	53	2.4 (-0.1, 4.9)	50	-2.1 (-4.7, 0.5)
5 th (1.7-79 ng/mL)	51	0.9 (-1.7, 3.5)	52	0.1 (-2.4, 2.6)
Somatization				
1 st (0.1-<0.4 ng/mL)	49	Ref	52	Ref
2 nd (0.4-<0.7 ng/mL)	49	0.6 (-2.0, 3.2)	50	-1.9 (-4.4, 0.6)
3 rd (0.7-<1.0 ng/mL)	50	1.2 (-1.3, 3.8)	51	-0.7 (-3.2, 1.9)
4 th (1.0-<1.7 ng/mL)	50	1.6 (-0.9, 4.1)	49	-2.1 (-4.7, 0.5)
5 th (1.7-79 ng/mL)	51	2.6 (0, 5.2)	49	-2.5 (-5.0, 0)
Working Memory				
1 st (0.1-<0.4 ng/mL)	52	Ref	55	Ref
2 nd (0.4-<0.7 ng/mL)	51	-1.0 (-3.9, 1.9)	55	-0.4 (-3.2, 2.5)
3 rd (0.7-<1.0 ng/mL)	52	0.2 (-2.7, 3.0)	56	0.8 (-2.1, 3.6)
4 th (1.0-<1.7 ng/mL)	56	4.1 (1.2, 6.9)	53	-1.7 (-4.6, 1.2)
5 th (1.7-79 ng/mL)	55	3.9 (0.9, 6.8)	52	-2.6 (-5.4, 0.2)
Plan/Organize				
1 st (0.1-<0.4 ng/mL)	49	Ref	52	Ref
2 nd (0.4-<0.7 ng/mL)	49	0.1 (-2.8, 2.9)	52	-0.2 (-3.0, 2.6)
3 rd (0.7-<1.0 ng/mL)	47	-1.7 (-4.5, 1.2)	53	0.3 (-2.5, 3.1)
4 th (1.0-<1.7 ng/mL)	52	3.3 (0.5, 6.1)	52	-0.3 (-3.2, 2.6)
5 th (1.7-79 ng/mL)	51	1.9 (-1.0, 4.8)	50	-2.6 (-5.4, 0.2)

a-Adjusted for maternal race, education, age, marital status, employment, smoking during pregnancy, alcohol use during pregnancy, folic acid supplement use, parity, months of exclusive breastfeeding, parental stress, and depressive symptoms

*-N's are 806, 805, 810, and 812 for internalizing, somatization, plan/organize, and working memory, respectively.

Table S4: Covariate adjusted mean child SRS-2 scores by specific gravity standardized maternal urinary BPA quintile: MIREC Study (n=537).^a

Scale and BPA Quintile	Mean T-Score	Difference (95% CI)
Total		
1 st (0.1-<0.4 ng/mL)	45	Ref
2 nd (0.4-<0.7 ng/mL)	46	0.9 (-0.4, 2.3)
3 rd (0.7-<1.0 ng/mL)	45	-0.1 (-1.4, 1.3)
4 th (1.0-<1.7 ng/mL)	46	1.2 (-0.2, 2.6)
5 th (1.7-79 ng/mL)	47	1.6 (0.2, 2.9)
Awareness		
1 st (0.1-<0.4 ng/mL)	45	Ref
2 nd (0.4-<0.7 ng/mL)	46	0.4 (-1.5, 2.4)
3 rd (0.7-<1.0 ng/mL)	45	-0.1 (-2.1, 1.9)
4 th (1.0-<1.7 ng/mL)	45	0.2 (-1.8, 2.1)
5 th (1.7-79 ng/mL)	47	1.6 (-0.4, 3.6)
Cognition		
1 st (0.1-<0.4 ng/mL)	44	Ref
2 nd (0.4-<0.7 ng/mL)	45	1.4 (0, 2.9)
3 rd (0.7-<1.0 ng/mL)	44	0.2 (-1.3, 1.7)
4 th (1.0-<1.7 ng/mL)	45	1.0 (-0.5, 2.5)
5 th (1.7-79 ng/mL)	45	1.8 (0.3, 3.3)
Communication		
1 st (0.1-<0.4 ng/mL)	45	Ref
2 nd (0.4-<0.7 ng/mL)	46	1.0 (-0.4, 2.4)
3 rd (0.7-<1.0 ng/mL)	45	0.1 (-1.3, 1.5)
4 th (1.0-<1.7 ng/mL)	46	1.2 (-0.2, 2.6)
5 th (1.7-79 ng/mL)	46	1.7 (0.3, 3.1)
Motivation		
1 st (0.1-<0.4 ng/mL)	48	Ref
2 nd (0.4-<0.7 ng/mL)	48	0.2 (-1.6, 2)
3 rd (0.7-<1.0 ng/mL)	48	-0.5 (-2.3, 1.3)
4 th (1.0-<1.7 ng/mL)	50	1.8 (0, 3.6)
5 th (1.7-79 ng/mL)	49	0.4 (-1.4, 2.2)
RI/RB		
1 st (0.1-<0.4 ng/mL)	48	Ref
2 nd (0.4-<0.7 ng/mL)	49	0.7 (-0.9, 2.3)
3 rd (0.7-<1.0 ng/mL)	48	-0.1 (-1.7, 1.6)
4 th (1.0-<1.7 ng/mL)	49	0.7 (-0.9, 2.2)
5 th (1.7-79 ng/mL)	49	1.4 (-0.3, 3)
DSM-V Social		
1 st (0.1-<0.4 ng/mL)	45	Ref
2 nd (0.4-<0.7 ng/mL)	46	0.8 (-0.5, 2.2)
3 rd (0.7-<1.0 ng/mL)	45	0 (-1.4, 1.3)
4 th (1.0-<1.7 ng/mL)	46	1.2 (-0.1, 2.6)
5 th (1.7-79 ng/mL)	46	1.5 (0.1, 2.9)
DSM-RI/RB		
1 st (0.1-<0.4 ng/mL)	48	Ref
2 nd (0.4-<0.7 ng/mL)	49	0.7 (-0.9, 2.3)
3 rd (0.7-<1.0 ng/mL)	48	-0.1 (-1.7, 1.6)
4 th (1.0-<1.7 ng/mL)	49	0.7 (-0.9, 2.3)
5 th (1.7-79 ng/mL)	49	1.4 (-0.3, 3)

a-Adjusted for maternal race, education, age, marital status, employment, smoking during pregnancy, alcohol use during pregnancy, folic acid supplement use, parity, months of exclusive breastfeeding, parental stress, and depressive symptoms

*-n's are 107, 110, 105, 108, and 107 for the 1st, 2nd, 3rd, 4th, and 5th quintiles, respectively

Figure S1: Directed acyclic graph describing the relations between prenatal urinary BPA concentrations, child neurobehavior at 3 years of age, and covariates.

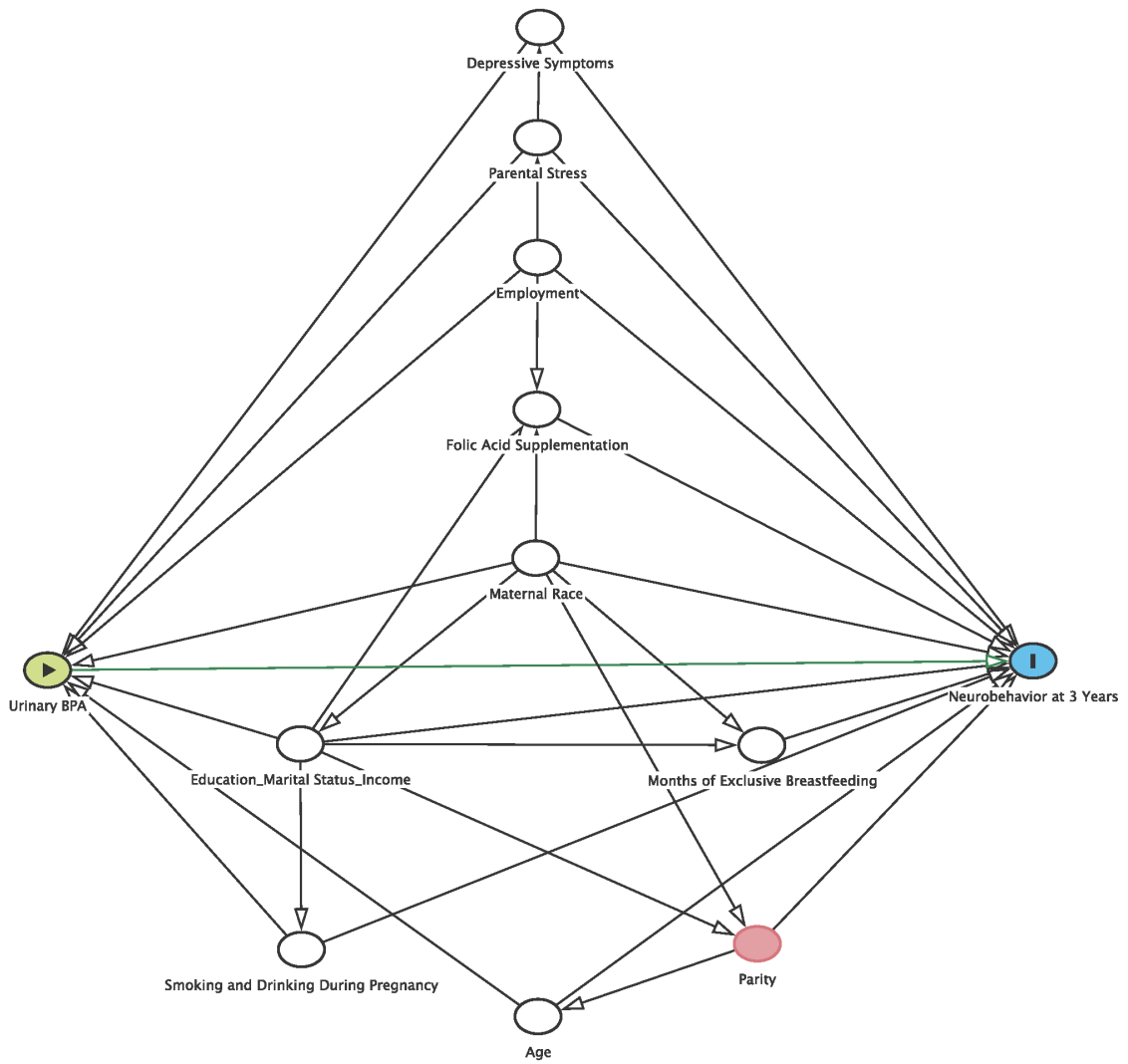
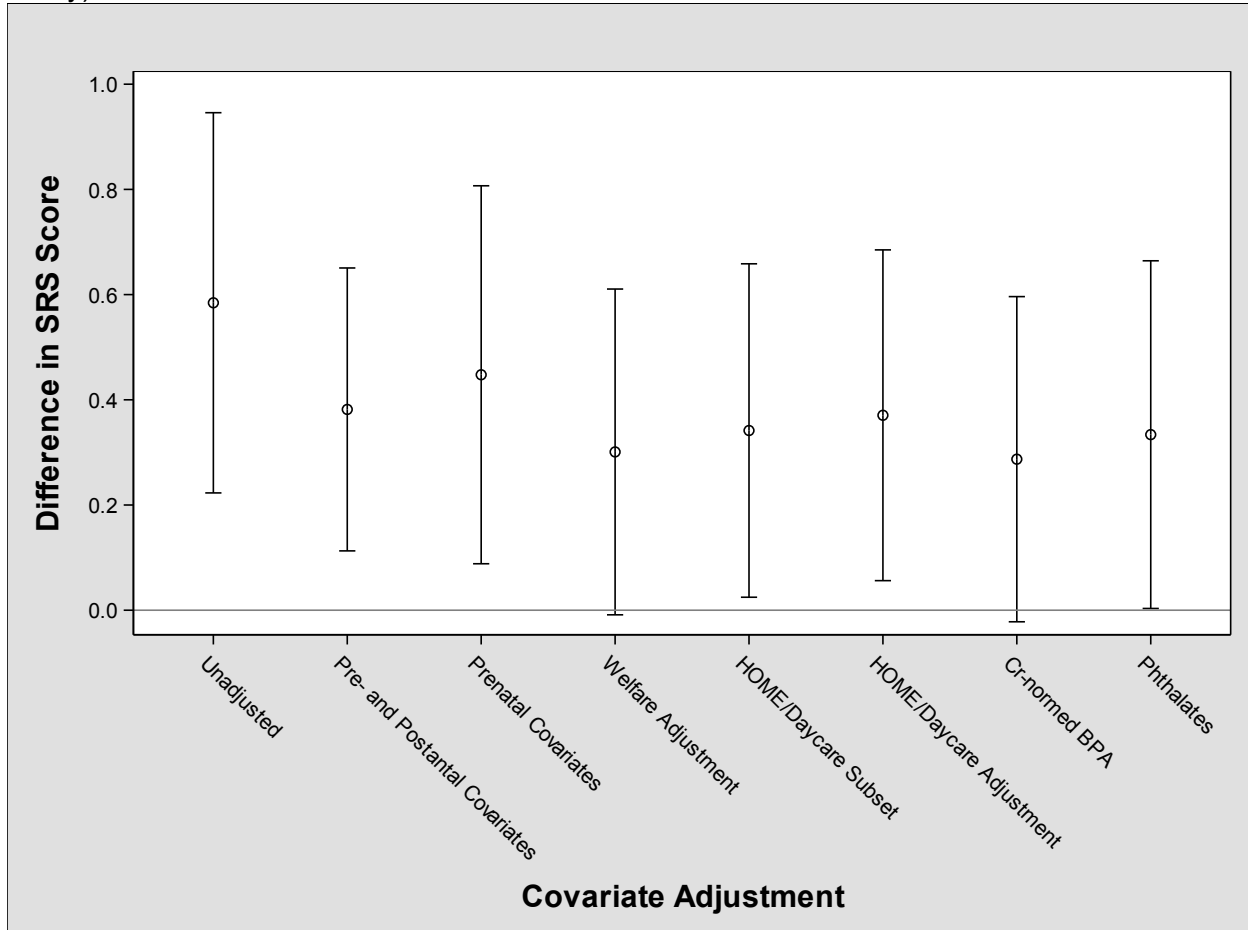


Figure S2: Adjusted difference in child SRS-2 total scores with 2-fold increase in maternal urinary BPA concentrations during pregnancy: Impact of various covariate adjustments (MIREC Study).^{a,b,c}



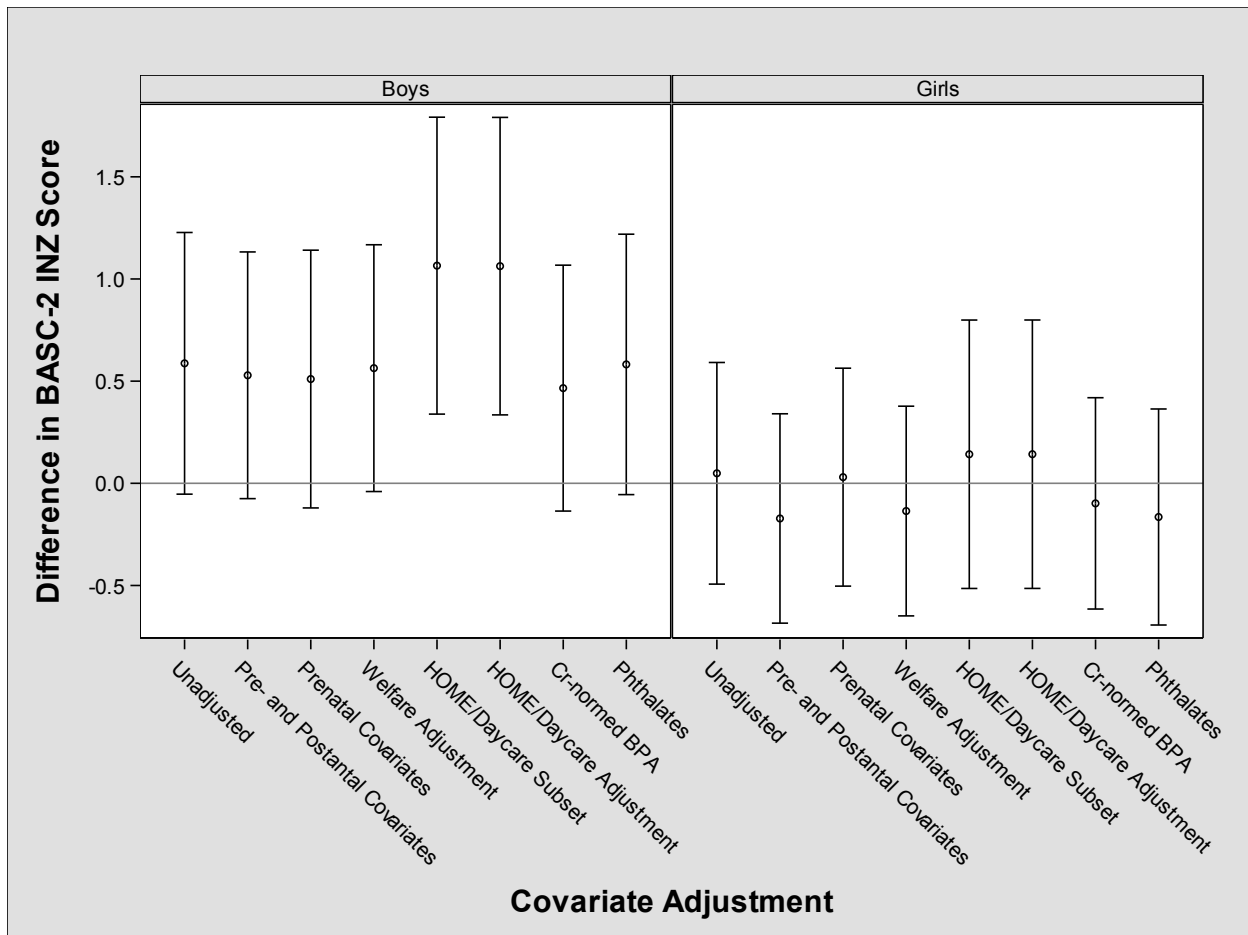
a-Prenatal covariates adjustment includes adjustment for maternal race, education, age, marital status, employment, smoking during pregnancy, alcohol use during pregnancy, folic acid supplement use, and parity.

b-Postnatal covariates include breastfeeding duration, parenting stress, maternal depressive symptoms, and maternal delinquency.

c-HOME and day care subset includes children whose parents completed in-person follow-up when the child was ~3 years of age. We compared the magnitude and precision of this association with and without adjustment for HOME scores and day care attendance among this subset to avoid potential selection bias.

d-Phthalate adjustment model included pre- and postnatal covariates, as well as log₂-transformed, specific gravity normalized urinary di-2-ethylhexyl phthalate metabolite, mono-ethyl phthalate, mono-benzyl phthalate, and mono-n-butyl phthalate concentrations.

Figure S3: Difference in child BASC-2 internalizing scores with 2-fold increase in maternal urinary BPA concentrations during pregnancy: Impact of various covariate adjustments (MIREC Study).^{a,b,c}



a-Prenatal covariates adjustment includes adjustment for maternal race, education, age, marital status, employment, smoking during pregnancy, alcohol use during pregnancy, folic acid supplement use, and parity.

b-Postnatal covariates include breastfeeding duration, parenting stress, maternal depressive symptoms, and maternal delinquency.

c-HOME and day care subset includes children whose parents completed in-person follow-up when the child was ~3 years of age. We compared the magnitude and precision of this association with and without adjustment for HOME scores and day care attendance among this subset to avoid potential selection bias.

d-Phthalate adjustment model included pre- and postnatal covariates, as well as log₂-transformed, specific gravity normalized urinary di-2-ethylhexyl phthalate metabolite, mono-ethyl phthalate, mono-benzyl phthalate, and mono-n-butyl phthalate concentrations.