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Supplemental Material

Identifying Vulnerable Periods of Neurotoxicity to Triclosan Exposure in Children

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Table S1: Distribution of HOME Study Participant's Age (in months) at Child Urine Sample Collections from Ages 12 through 96 months.

Exposure Period	N	Mean (Range)
12 months	174	13 (11, 19)
24 months	155	25 (22, 28)
36 months	159	37 (35, 43)
48 months	128	50 (47,56)
60 months	156	62 (57, 72)
96 months	198	98 (90, 120)

Table S2: Average, standard deviation, and coefficients of variation of low and high concentration quality control samples included in analytic runs at the Centers for Disease Control and Prevention from 2005-2014.

Year	QC Concentration	N	Start date	End date	Mean TCS	STD of TCS	% CV	Website with details on QC methods
2013-2014	High	67	6/19/14	11/3/15	49.3	2.6	5.2	https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/labmethods/EPHPP_H_MET.pdf
2013-2014	low	67	6/19/14	11/3/15	16.6	1.5	9.0	
2011-2012	high	66	4/4/12	3/27/13	67.9	2.9	4.2	http://www.cdc.gov/nchs/data/nhanes/nhanes_11_12/EPH_G_met.pdf
2011-2012	low	66	4/4/12	3/27/13	22.7	1.2	5.2	
2009-2010	high	73	7/19/10	6/27/11	25.2	2.4	9.3	http://www.cdc.gov/nchs/data/nhanes/nhanes_09_10/EPH_F_met_phenols_parabens.pdf
2009-2010	low	73	7/19/10	6/27/11	65.4	3.9	5.9	
2007-2008	high	62	5/7/08	2/9/09	25.3	1.2	6.9	http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/eph_e_met_phenols_parabens.pdf
2007-2008	low	61	5/7/08	2/9/09	65.8	3.4	5.2	
2005-2006	high	66	6/20/06	2/8/07	26.1	2.5	9.6	http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/eph_d_met_phenols_parabens.pdf
	low	66	6/20/06	2/8/07	63.5	5.4	8.4	

Table S3: Baseline Characteristics of HOME Study Participants and Those Included in the Present Analysis.

	Full Cohort [n=389] N (%)	Analysis Cohort [n=198] N (%)
Child Sex		
Female	205 (53)	110 (56)
Male	179 (47)	88 (44)
Missing	5 (1.3)	
Race/Ethnicity		
White	233 (61)	124 (62)
Black	121 (32)	64 (34)
Other	25 (7)	10 (4)
Missing	5 (1.3)	
Maternal Education		
College Graduate or More	187 (49)	95 (48)
Some College	97 (26)	57 (29)
High School or less	95 (25)	46 (23)
Missing	10 (2.6)	
Household Income		
>$80K	100 (26)	53 (27)
$40-80K	126 (33)	65 (33)
$20-40K	65 (17)	31 (15)
<$20K	88 (23)	49 (24)
Missing	10 (2.6)	
Marital Status		
Married	240 (63)	126 (64)
Unmarried	144 (38)	72 (36)
Missing	10 (2.6)	
Caregiving Environment[a]		
<35	60 (18)	40 (20)
35 - 40	79 (24)	53 (27)
>40	190 (58)	105 (53)
Missing	49 (13)	
Maternal FSIQ		
<96	89 (26)	58 (29)
96-109	89 (26)	47 (24)
<109-117	80 (23)	42 (21)
> 117	82 (24)	51 (26)
Missing	49 (13)	
NICU		
Yes	17 (4)	9 (5)
No	367 (96)	189 (95)
Missing	5 (1.3)	
Serum Cotinine (ng/mL)[b]		
< LOD (Unexposed)	149 (39)	88 (44)
LOD-3.0 (SHS)	192 (50)	92 (47)
> 3.0 (Active)	43 (11)	18 (9)
Missing	5 (1.3)	

Abbreviations: NICU-neonatal intensive care unit, SHS-secondhand smoke, LOD-limit of detection.

a- Administered at age 1, higher scores indicate greater quality and quantity of caregiving.

b- LOD= 0.015 ng/mL. Threshold of 3 ng/mL for active smoking was chosen based on results from the 1999-2004 National Health and Nutrition Examination Survey which compared self-reported smoking status and serum cotinine levels among a representative sample of the US population (Benowitz et al. 2009).

Table S4: Univariate Statistics of Repeated Maternal and Child Urinary Triclosan Concentrations (ng/mL) for HOME Study Participants.

Exposure Period	N	Min	5th	25th	Median	75th	95th	Max
16 Weeks	198	< LOD	< LOD	6.5	23	72	576	1784
26 Weeks	192	< LOD	< LOD	4.6	16	41	365	1657
Delivery	179	< LOD	< LOD	3.5	13	44	229	2013
Gestational GM[a]	198	< LOD	3.0	6.6	17	37	197	638
1 Year	174	< LOD	< LOD	< LOD	5	10	46	118
2 Year	155	< LOD	< LOD	2.5	9	19	119	7487
3 Year	159	< LOD	< LOD	5.6	17	45	301	1194
4 Year	128	< LOD	< LOD	6.0	19	57	301	751
5 Year	156	< LOD	< LOD	7.0	16	39	155	515
8 Year	198	< LOD	< LOD	3.7	12	38	227	1610
Childhood GM[a]	198	1.4	2.8	4.2	13	22	51	911

Abbreviations: GM-geometric mean, LOD-limit of detection, min-minimum, and max- maximum.

a-Gestational and childhood geometric mean urinary triclosan concentrations were calculated by averaging $\log_{10}$-transformed maternal (16 and 26 week and delivery) and child (age 1-8 years) urinary triclosan concentrations.

LOD= 0.015 ng/mL. Threshold of 3 ng/mL for active smoking was chosen based on results from the 1999-2004 National Health and Nutrition Examination Survey which compared self-reported smoking status and serum cotinine levels among a representative sample of the US population (Benowitz et al. 2009).

Table S5: Unadjusted and Adjusted Differences (95% CI) in FSIQ and Subscale Scores at Age 8-Years per 10-Fold Increase in Gestational and Childhood Urinary Triclosan Concentrations.[a]

Exp/ Pd	Full Scale IQ		Verbal Comprehension		Perceptual Reasoning		Processing Speed		Working Memory	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
16 W	1.1(-2.1,4.3)	-0.5(-3.2,2.2)	2.0(-1.1,5.0)	0.3(-2.4,3.0)	1.5(-1.7,4.6)	-0.1(-2.8,2.5)	1.2(-1.9,4.3)	0.7(-2.3,3.6)	-1.6(-4.8,1.7)	-2.5(-5.5,0.4)
26 W	1.3(-1.8,4.4)	-0.4(-3.1,2.4)	3.6(0.7,6.4)	2.1(-0.3,4.5)	1.1(-2.1,4.4)	-0.6(-3.5,2.4)	-0.3(-3.5,2.9)	-1.1(-4.3,2.1)	-1.6(-4.9,1.7)	-2.5(-5.4,0.3)
Del	-1.1(-4.3,1.9)	-4.5(-7.0,-2.0)	-0.8(-4.0,2.5)	-3.6(-6.0,-1.1)	-0.9(-4.1,2.3)	-4.2(-7.0,-1.4)	1.1(-1.7,3.8)	-0.4(-3.2,2.4)	-3.3(-6.5,-0.1)	-5.5(-8.4,-2.6)
1 Y	3.4(-1.3,8.1)	-1.0(-5.2,3.2)	3.6(-1.0,8.2)	-0.5(-4.6,3.5)	2.8(-1.7,7.4)	-0.9(-4.9,3.0)	1.9(-3.0,6.8)	0.1(-4.5,4.7)	2.0(-3.0,6.9)	-1.2(-5.8,3.4)
2 Y	-1.3(-5.0,2.5)	-1.3(-4.3,1.6)	2.6(-1.2,6.4)	2.6(-0.5,5.7)	-4.0(-8.0,0.0)	-3.8(-6.9,-0.7)	-0.7(-4.2,2.9)	-0.8(-4.1,2.6)	-2.6(-6.3,1.1)	-2.9(-6.2,0.5)
3 Y	3.1(-0.9,7.0)	0.8(-2.3,3.9)	3.4(-0.7,7.5)	1.2(-2.1,4.5)	3.9(-0.8,8.5)	1.5(-2.4,5.4)	-0.3(-3.6,3.1)	-1.3(-4.6,1.9)	1.4(-2.6,5.3)	0.1(-3.5,3.8)
4 Y	3.8(-0.4,7.9)	1.0(-2.3,4.2)	2.9(-1.1,6.9)	0.4(-2.9,3.7)	5.1(1.2,9.0)	2.4(-0.7,5.4)	0.5(-3.6,4.5)	-0.8(-4.5,3.0)	2.9(-1.4,7.2)	1.1(-2.5,4.8)
5 Y	3.8(-0.7,8.3)	0.7(-2.8,4.2)	3.5(-0.9,8.0)	0.2(-3.4,3.8)	4.1(-0.4,8.5)	1.4(-1.8,4.5)	0.1(-4.0,4.2)	-1.0(-4.7,2.6)	3.0(-1.7,7.6)	1.1(-3.0,5.3)
8 Y	3.1(-0.2,6.4)	0.7(-2.1,3.4)	3.3(-0.2,6.8)	1.1(-1.8,4.0)	3.5(0.4,6.6)	1.1(-1.4,3.7)	-0.4(-3.1,2.4)	-1.3(-3.9,1.3)	1.9(-1.1,4.9)	0.3(-2.5,3.1)

Beta's and 95% CI derived from a multiple informants regression model.

Abbreviations: CI-confidence interval, FSIQ-full scale intelligence quotient, Exp/Pd- Exposure Period, W-weeks, Del-delivery, Y-year

a-Adjusted for $\log_{10}$ urinary creatinine and serum cotinine concentrations, child sex, child race/ethnicity, household income, marital status, maternal education, caregiving environment scores, and maternal FSIQ.

Table S6. Adjusted Differences in FSIQ (95% CI) and Subscale Scores at Age 8-Years per 10-Fold Increase in Gestational and Childhood Urinary Triclosan Concentrations.[a]

Exp/ Pd	Full Scale IQ		Verbal Comprehension		Perceptual Reasoning		Processing Speed		Working Memory	
	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
16 W	-0.5(-4.2,3.3)	-0.5(-3.6,2.6)	-0.3(-3.7,3.1)	1.3(-2.2,4.8)	-0.5(-4.4,3.4)	0.5(-2.4,3.5)	2.0(-1.6,5.7)	-1.4(-5.3,2.5)	-2.5(-6.7,1.6)	-2.4(-5.8,1.1)
26 W	1.6(-2.7,5.9)	-2.1(-5.3,-1.2)	3.1(-0.2,6.5)	0.7(-3.0,4.5)	1.2(-3.0,5.5)	-1.2(-4.7,2.3)	1.5(-3.7,6.6)	-4.0(-7.7,0.3)	-2.4(-6.6,1.8)	-2.5(-6.1,1.1)
Del	-3.6(-6.6,-0.6)	-4.5(-8.0,-1.0)	-4.9(-7.9,-1.9)	-1.5(-5.0,2.1)	-3.2(-6.8,0.3)	-4.7(-8.2,-1.1)	3.3(-0.1,6.8)	-3.2(-6.8,0.5)	-5.3(-8.9,-1.7)	-4.8(-8.7,-0.8)
1 Y	3.8(-1.0,8.5)	-5.9(-12,-0.4)	2.7(-2.2,7.6)	-5.8(-12,0.1)	1.0(-3.9,6.0)	-3.8(-9.2,1.5)	5.9(0.0,11.9)	-4.4(-11,1.7)	3.3(-2.1,8.6)	-3.5(-9.5,2.4)
2 Y	-0.1(-3.4,3.1)	-2.2(-7.2,2.8)	2.4(-1.1,5.9)	2.3(-2.9,7.4)	-2.1(-5.5,1.2)	-3.3(-7.8,-1.3)	0.3(-3.7,4.4)	-3.8(-9.8,2.1)	-2.0(-5.2,1.3)	-2.7(-8.6,3.2)
3 Y	0.0(-3.8,3.8)	1.4(-3.0,5.9)	0.0(-4.6,4.6)	2.6(-1.6,6.8)	-1.0(-5.7,3.7)	3.6(-1.4,8.6)	0.8(-3.8,5.3)	-3.5(-7.7,0.7)	-0.4(-4.7,3.8)	0.3(-5.4,6.0)
4 Y	1.5(-2.6,5.5)	0.0(-4.6,4.6)	0.0(-4.9,4.9)	-0.3(-4.5,3.9)	1.2(-2.3,4.8)	3.1(-1.4,7.6)	1.8(-3.1,6.7)	-3.2(-7.9,1.5)	2.2(-1.5,5.9)	0.5(-5.1,5.9)
5 Y	2.4(-1.8,6.5)	-2.0(-7.4,3.4)	-0.3(-5.1,4.4)	-0.5(-5.5,4.4)	2.0(-1.6,5.6)	-0.1(-5.6,5.4)	2.4(-2.1,6.9)	-5.7(-13,1.3)	3.1(-1.4,7.8)	-0.9(-7.3,5.5)
8 Y	0.4(-3.7,4.6)	0.5(-2.6,3.7)	-1.3(-5.2,2.6)	2.4(-1.4,6.2)	1.1(-2.9,5.1)	1.1(-2.2,4.3)	-0.6(-4.4,3.2)	-1.4(-4.7,1.8)	1.5(-2.3,5.2)	-0.9(-4.5,2.6)

Beta's and 95% CI derived from a multiple informants regression model.

Abbreviations: FSIQ-full scale intelligence quotient, CI-confidence interval, Exp/Pd- Exposure Period, W-weeks, Del-delivery, Y-year.

a-Adjusted for $\log_{10}$ urinary creatinine and serum cotinine concentrations, child race/ethnicity, household income, marital status, maternal education, caregiving environment scores, and maternal FSIQ.

Sex x triclosan x exposure period p-values = 0.4 (FSIQ), 0.2 (Verbal Comprehension), 0.8 (Perceptual Reasoning), 0.7 (Processing Speed), and 0.6 (Working Memory).

Figure S1. Directed Acyclic Graph
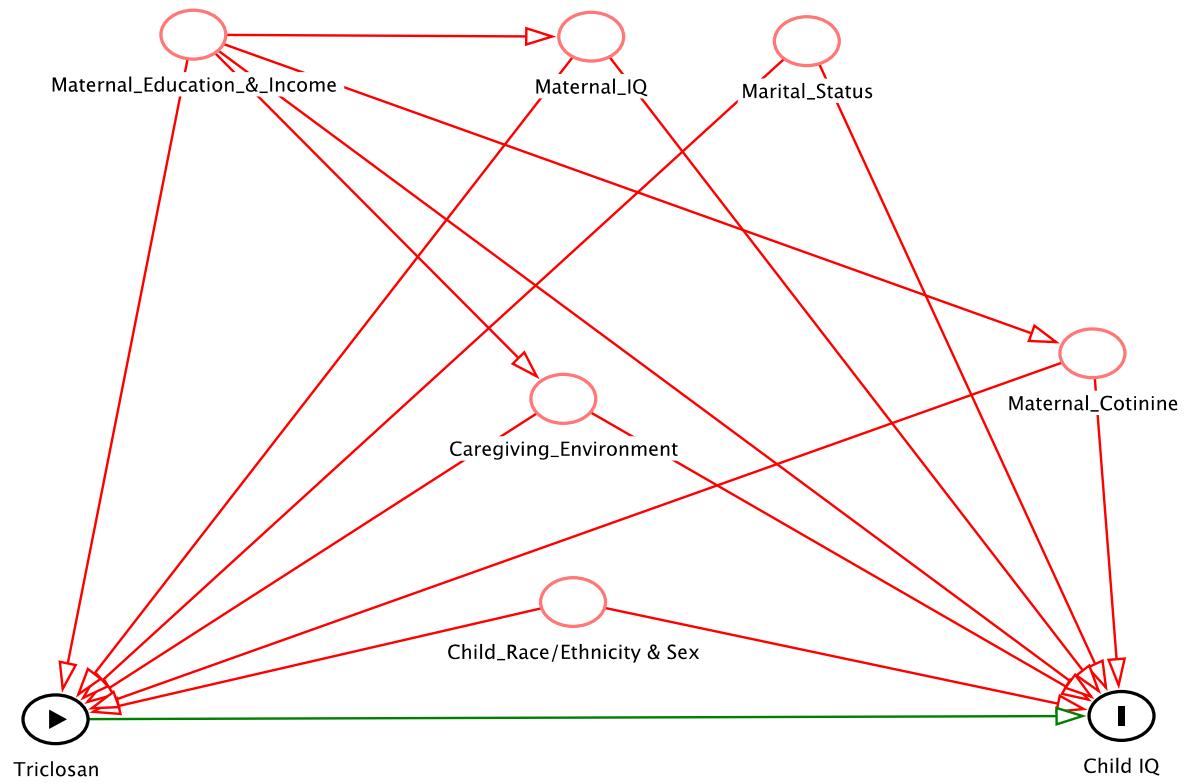
Figure S2. Adjusted Differences in Child FSIQ Scores at Age 8-Years per 10-Fold Increase in Gestational and Childhood Urinary Triclosan Concentrations after Adjusting for (A) NICU Admission and (B) Delivery Hospital.[a,b,c]

A

NICU

	Beta [95%CI]
16W (n=198)	−0.0 [−2.6, 2.6]
26W (n=192)	−0.0 [−2.9, 2.9]
Delivery (n=179)	−4.8 [−7.4, −2.2]
1Y (n=174)	−1.2 [−5.4, 2.9]
2Y (n=155)	−1.4 [−4.4, 1.6]
3Y (n=159)	0.5 [−2.6, 3.6]
4Y (n=128)	1.1 [−2.1, 4.2]
5Y (n=156)	0.4 [−3.1, 3.8]
8Y (n=198)	0.9 [−1.7, 3.6]

Beta (95%CI)

B

Hospital

	Beta [95%CI]
16W (n=198)	−0.4 [−3.2, 2.3]
26W (n=192)	−0.4 [−3.2, 2.4]
Delivery (n=179)	−4.6 [−7.1, −2.0]
1Y (n=174)	−1.0 [−5.2, 3.3]
2Y (n=155)	−1.3 [−4.4, 1.7]
3Y (n=159)	0.9 [−2.3, 4.0]
4Y (n=128)	1.1 [−2.2, 4.3]
5Y (n=156)	0.7 [−2.8, 4.2]
8Y (n=198)	0.8 [−1.9, 3.6]
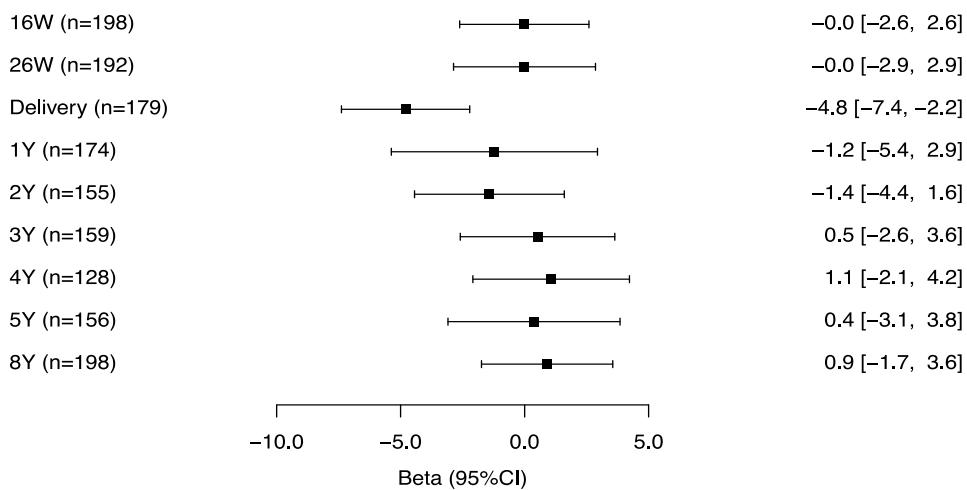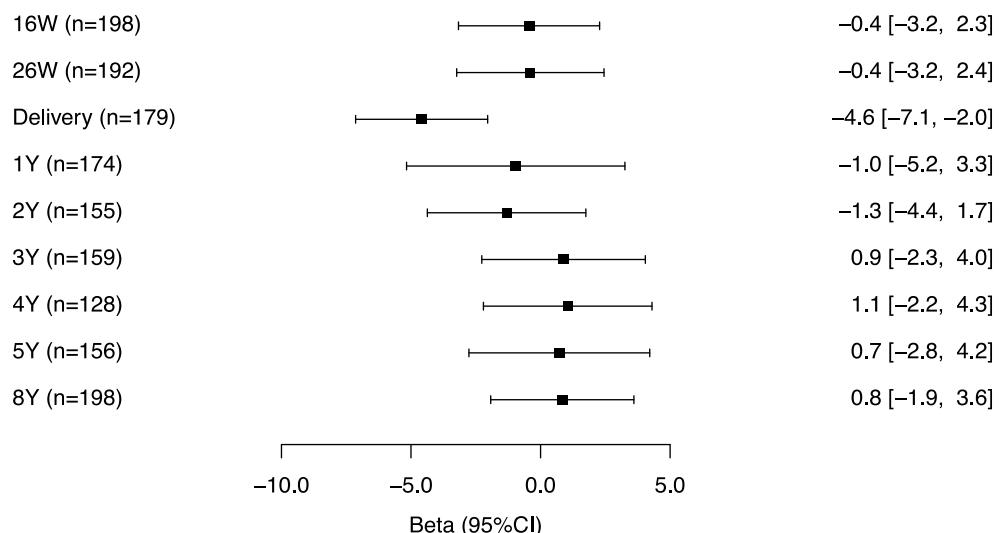
Beta (95%CI)

Betas and 95% confidence intervals derived from a multiple informants model.
Abbreviations: W-weeks of gestation, Y-age in years, FSIQ-full-scale intelligence quotient, CI-confidence interval, NICU-neonatal intensive care unit.
a-Multiple Informant regression model adjusted for $\log_{10}$-transformed urinary creatinine concentrations and serum cotinine concentrations (continuous), child sex (male vs. female), child race/ethnicity (White-non-Hispanic, Black-non, Hispanic, and other), household income (continuous), marital status (married vs. unmarried), maternal education (high school or less, some college, and college graduate or more), caregiving environment scores (continuous), and maternal FSIQ (continuous).
b-Error bars are 95% confidence intervals.
c-Urinary triclosan concentration by exposure period interaction term p-value = 0.01(NICU) and 0.03 (Delivery Hospital).