

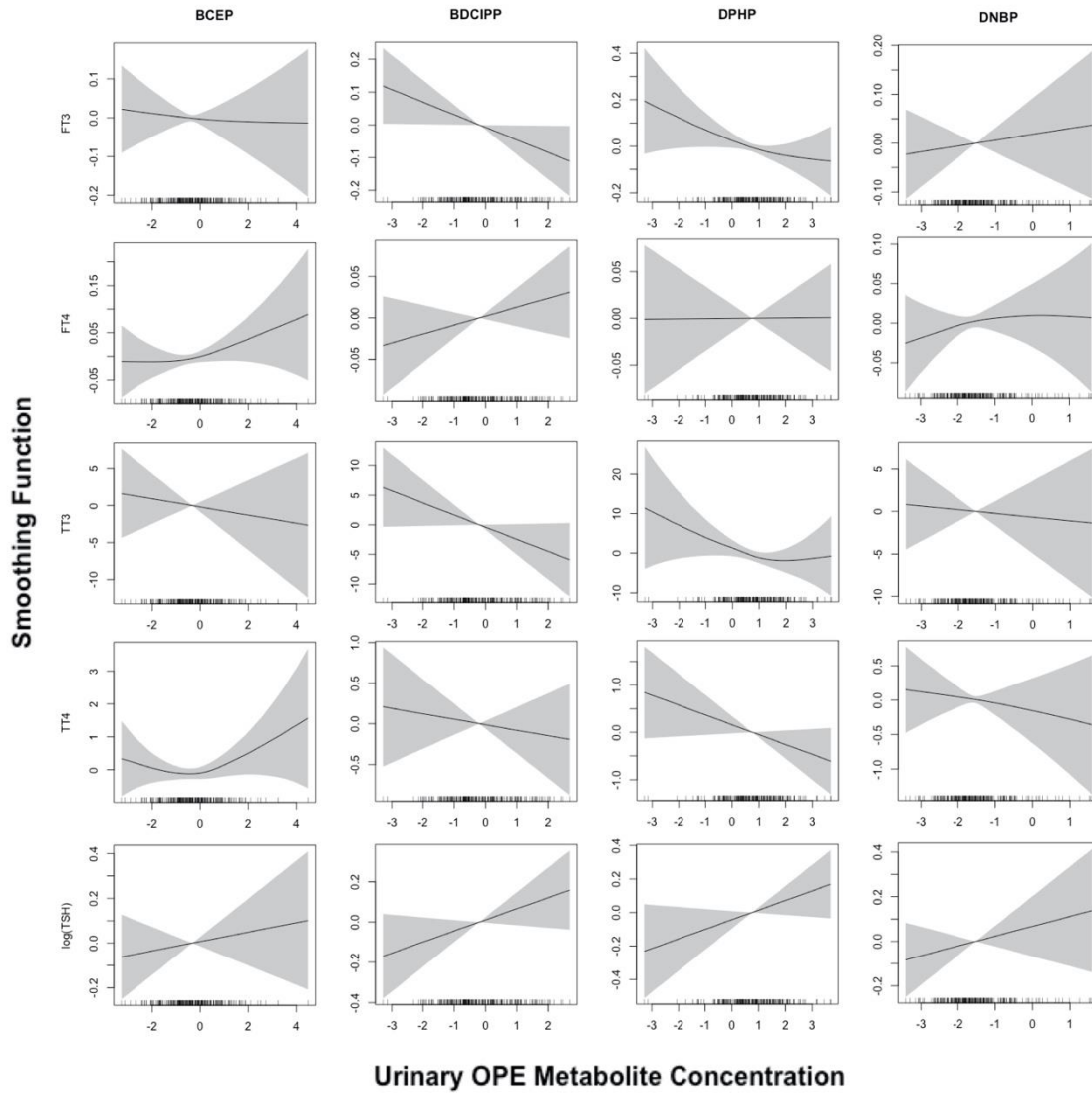
**Maternal Urinary Organophosphate Esters and Alterations in Maternal and Neonatal
Thyroid Hormones**

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Web Figure 1: Smoothing functions derived from generalized additive models of urinary OPE metabolites associated with thyroid hormones at birth in the HOME Study, 2003-2006.^a



Abbreviations: OPE, organophosphate ester; FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyroid stimulating hormone; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate. ^aOPE metabolites are creatinine-standardized and ln-transformed. Models are adjusted for mother's age at delivery, mother's education, race, year of birth, and infant sex.

Web Table 1: Summary statistics for creatinine-standardized maternal urinary OPE metabolites by sample collection time point in the HOME Study, 2003-2006.^a

	% <LOD	Q1	Median	GM	Q3	N
BCEP						
16 weeks	11.83	0.31	0.58	0.59	1.00	262
26 weeks	16.81	0.30	0.69	0.67	1.20	254
Birth	14.37	0.36	0.90	0.72	1.37	250
BDCIPP						
16 weeks	5.35	0.41	0.71	0.75	1.26	262
26 weeks	10.72	0.35	0.64	0.74	1.33	254
Birth	10.94	0.42	0.97	0.81	1.46	250
DPHP						
16 weeks	0.91	0.92	1.44	1.74	2.65	262
26 weeks	2.90	0.86	1.42	1.73	2.53	254
Birth	2.50	1.19	1.98	2.10	4.08	250
DNBP						
16 weeks	17.46	0.15	0.24	0.25	0.36	262
26 weeks	26.38	0.16	0.24	0.26	0.40	254
Birth	43.13	0.12	0.19	0.21	0.31	250

Abbreviations: OPE, organophosphate ester; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate; LOD, limit of detection; Q1, first quartile; GM, geometric mean; Q3, third quartile.

^aConcentrations <LOD were replaced by $\text{LOD}/\sqrt{2}$. All urinary OPE metabolite concentrations are divided by creatinine concentration with units of $\mu\text{g}/\text{g}$ creatinine.

Web Table 2: Pearson correlations among creatinine-standardized and ln-transformed urinary OPE metabolites at 16 and 26 weeks pregnancy and at birth in the HOME Study, 2003-2006.

16 Weeks (n=304)				
	BCEP	BDCIPP	DPHP	DNBP
BCEP	1	0.13*	0.03	0.04
BDCIPP		1	0.03	-0.02
DPHP			1	0.06
DNBP				1
26 Weeks (n=296)				
	BCEP	BDCIPP	DPHP	DNBP
BCEP	1	0.00	0.10	0.03
BDCIPP		1	0.29**	0.02
DPHP			1	0.07
DNBP				1
Birth (n=279)				
	BCEP	BDCIPP	DPHP	DNBP
BCEP	1	0.18*	0.09	0.03
BDCIPP		1	0.25**	-0.05
DPHP			1	0.03
DNBP				1

Abbreviations: OPE, organophosphate ester; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate.

*P<0.05, **P<0.001.

Web Table 3: Pearson correlations among maternal thyroid hormones at 16 weeks pregnancy and infant cord serum thyroid hormones at birth in the HOME Study, 2003-2006.

16 weeks (n=196)					
	FT3	FT4	TT3	TT4	Log-TSH
FT3	1	0.11	0.68**	0.32**	0.07
FT4		1	-0.02	0.45**	-0.16*
TT3			1	0.46**	0.00
TT4				1	-0.17*
Log-TSH					1
Birth (n=254)					
	FT3	FT4	TT3	TT4	Log-TSH
FT3	1	0.23**	0.71**	0.28**	0.08
FT4		1	0.17**	0.60**	-0.09
TT3			1	0.33**	0.19*
TT4				1	-0.03
Log-TSH					1

Abbreviations: FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyrod stimulating hormone. *P<0.05, **P<0.001.

Web Table 4: Cross-sectional associations between creatinine-standardized and ln-transformed Σ mOPEs and thyroid hormones at 16 weeks pregnancy and birth in the HOME Study, 2003-2006.^a

Time point	FT3 (pg/mL)		FT4 (ng/dL)		TT3 (ng/dL)		TT4 (μ g/dL)		TSH (μ IU/mL)	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
16 weeks	-0.01	-0.06, 0.05	-0.01	-0.03, 0.01	-0.14	-4.85, 4.58	-0.10	-0.47, 0.27	0.98	0.84, 1.14
Birth	-0.04	-0.08, 0.01	0.01	-0.02, 0.03	-2.35	-4.96, 0.26	-0.16	-0.05, 0.13	1.08	0.99, 1.17

Abbreviations: Σ mOPEs, arithmetic sum of organophosphate ester metabolites; FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyroid stimulating hormone. ^a Models adjusted for mother's age at delivery, mother's education, race, year of birth, and infant sex.

Web Table 5: Associations between creatinine-standardized and ln-transformed urinary OPE metabolites at 16 weeks by quartile and cord blood thyroid hormones in the HOME Study, 2003-2006.^a

Parameter	FT3 (pg/mL)		FT4 (ng/dL)		TT3 (ng/dL)		TT4 (µg/dL)		TSH (µIU/mL)	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
BCEP	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q1	-0.03	-0.14, 0.08	-0.04	-0.09, 0.01	0.25	-6.46, 6.96	-0.04	-0.70, 0.63	0.91	0.74, 1.12
Q2	0.04	-0.07, 0.15	-0.04	-0.09, 0.02	1.60	-5.25, 8.45	-0.17	-0.85, 0.51	1.03	0.84, 1.26
Q3	-0.01	-0.12, 0.10	-0.02	-0.08, 0.03	2.39	-4.40, 9.17	-0.26	-0.94, 0.41	0.91	0.74, 1.10
Q4										
<i>P</i> for trend	0.99		0.73		0.47		0.42		0.43	
BDCIPP										
Q1	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q2	0.02	-0.09, 0.13	-0.02	-0.07, 0.04	0.84	-5.94, 7.61	-0.23	-0.90, 0.43	0.94	0.77, 1.15
Q3	-0.06	-0.17, 0.06	-0.03	-0.08, 0.03	-1.32	-8.28, 5.64	0.00	-0.69, 0.69	1.17	0.95, 1.45
Q4	-0.06	-0.17, 0.05	-0.05	-0.10, 0.01	1.51	-5.28, 8.30	-0.59	-1.26, 0.08	0.97	0.79, 1.19
<i>P</i> for trend	0.20		0.07		0.66		0.08		0.83	
DPHP										
Q1	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q2	-0.03	-0.15, 0.08	0.01	-0.05, 0.06	1.85	-5.05, 8.74	0.06	-0.63, 0.74	1.07	0.87, 1.32
Q3	-0.03	-0.14, 0.09	0.03	-0.02, 0.09	1.19	-5.69, 8.06	0.33	-0.36, 1.01	1.09	0.88, 1.34
Q4	0.03	-0.08, 0.14	0.03	-0.02, 0.09	3.32	-3.47, 10.01	0.05	-0.63, 0.73	1.04	0.85, 1.28
<i>P</i> for trend	0.34		0.25		0.38		0.98		0.96	
DNBP										
Q1	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q2	-0.05	-0.16, 0.06	-0.00	-0.06, 0.05	-2.82	-9.77, 4.13	-0.12	-0.81, 0.58	1.13	0.92, 1.39
Q3	-0.06	-0.17, 0.06	-0.00	-0.06, 0.0	-1.64	-8.59, 5.31	-0.23	-0.93, 0.46	1.30	1.06, 1.60
Q4	-0.08	-0.20, 0.03	0.01	-0.04, 0.07	-1.86	-9.03, 5.31	-0.06	-0.77, 0.65	1.33	1.07, 1.65
<i>P</i> for trend	0.33		0.96		0.69		0.52		0.01	

Abbreviations: OPE, organophosphate ester; FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyroid stimulating hormone; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate. ^aModels adjusted for mother's age at delivery, mother's education, race, year of birth, and infant sex.

Web Table 6: Associations between creatinine-standardized and ln-transformed urinary OPE metabolites at 26 weeks by quartile and cord blood thyroid hormones in the HOME Study, 2003-2006.^a

Parameter	FT3 (pg/mL)		FT4 (ng/dL)		TT3 (ng/dL)		TT4 (µg/dL)		TSH (µIU/mL)	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
BCEP										
Q1	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q2	0.01	-0.11, 0.12	-0.01	-0.06, 0.05	-1.23	-8.11, 5.65	0.21	-0.47, 0.89	0.90	0.74, 1.10
Q3	0.04	-0.08, 0.15	0.00	-0.05, 0.06	1.13	-5.88, 8.14	0.03	-0.67, 0.73	0.77	0.63, 0.95
Q4	-0.01	-0.12, 0.11	-0.01	-0.06, 0.05	0.52	-76.57, 7.61	-0.10	-0.79, 0.60	1.04	0.85, 1.28
<i>P</i> for trend	0.86		0.88		0.74		0.53		0.29	
BDCIPP										
Q1	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q2	-0.06	-0.18, 0.05	-0.00	-0.06, 0.05	-3.52	-10.39, 3.38	-0.09	-0.77, 0.59	1.10	0.90, 1.35
Q3	-0.03	-0.14, 0.09	0.01	-0.05, 0.07	-0.97	-7.97, 6.09	0.03	-0.66, 0.72	0.95	0.77, 1.17
Q4	-0.13	-0.24, -0.02	-0.03	-0.08, 0.03	-6.47	-13.47, 0.52	-0.75	-1.44, -0.07	1.12	0.91, 1.30
<i>P</i> for trend	0.03		0.29		0.09		0.01		0.35	
DPHP										
Q1	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q2	0.14	0.03, 0.25	0.05	-0.01, 0.10	4.21	-2.86, 11.28	0.72	0.03, 1.41	1.03	0.84, 1.27
Q3	0.09	-0.03, 0.20	0.02	-0.04, 0.07	5.02	-2.16, 12.19	0.09	-0.62, 0.80	0.94	0.76, 1.16
Q4	0.07	-0.04, 0.19	0.03	-0.04, 0.07	3.39	-3.91, 10.69	0.05	-0.66, 0.76	1.08	0.87, 1.34
<i>P</i> for trend	0.73		0.76		0.59		0.44		0.54	
DNBP										
Q1	0	Referent	0	Referent	0	Referent	0	Referent	1	Referent
Q2	-0.05	-0.17, 0.07	0.04	-0.02, 0.09	-4.60	-11.84, 2.64	0.12	-0.61, 0.85	0.90	0.72, 1.12
Q3	-0.06	-0.17, 0.06	0.03	-0.03, 0.09	-4.53	-11.73, 2.67	-0.17	-0.89, 0.55	0.92	0.74, 1.14
Q4	-0.15	-0.27, -0.03	0.03	-0.03, 0.09	-8.34	-15.92, -0.77	-0.37	-1.12, 0.39	0.99	0.79, 1.24
<i>P</i> for trend	0.01		0.52		0.05		0.21		0.76	

Abbreviations: OPE, organophosphate ester; FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyroid stimulating hormone; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate. ^a Models adjusted for mother's age at delivery, mother's education, race, year of birth, and infant sex.

Web Table 7: Multiple informant models for the association between creatinine-standardized and ln-transformed urinary OPE metabolites at three time points and cord blood thyroid hormones in the HOME Study, 2003-2006.^a

Parameter	FT3 (pg/mL)		FT4 (ng/dL)		TT3 (ng/dL)		TT4 (µg/dL)		TSH (µIU/mL)	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
BCEP										
16 weeks	0.01	-0.03, 0.04	-0.01	-0.02, 0.01	0.90	-0.79, 2.58	-0.09	-0.25, 0.08	0.97	0.91, 1.02
26 weeks	-0.00	-0.03, 0.03	0.00	-0.02, 0.02	-0.36	-2.78, 2.06	-0.05	-0.27, 0.17	1.02	0.96, 1.08
Birth	-0.01	-0.04, 0.02	0.01	-0.00, 0.03	-0.84	-2.58, 0.89	0.09	-0.11, 0.29	1.03	0.97, 1.10
BDCIPP										
16 weeks	-0.02	-0.07, 0.03	-0.03	-0.04, -0.01	0.85	-2.68, 4.37	-0.24	-0.45, -0.03	0.97	0.89, 1.06
26 weeks	-0.04	-0.08, 0.00	-0.00	-0.02, 0.02	-2.32	-5.44, 0.79	-0.24	-0.41, -0.06	1.06	0.99, 1.13
Birth	-0.04	-0.08, -0.01	0.01	-0.01, 0.03	-2.29	-4.15, -0.43	-0.07	-0.30, 0.16	1.06	0.99, 1.12
DPHP										
16 weeks	0.02	-0.02, 0.06	0.01	-0.01, 0.03	1.60	-1.29, 4.49	0.11	-0.12, 0.34	1.00	0.93, 1.08
26 weeks	-0.02	-0.08, 0.04	0.01	-0.01, 0.03	-1.53	-6.82, 3.76	-0.06	-0.31, 0.20	1.04	0.95, 1.15
Birth	-0.04	-0.07, -0.00	0.00	-0.02, 0.02	-2.03	-4.15, 0.07	-0.21	-0.41, 0.00	1.07	1.00, 1.15
DNBP										
16 weeks	-0.02	-0.07, 0.03	0.01	-0.02, 0.04	-0.23	-3.82, 3.37	0.05	-0.23, 0.32	1.10	0.98, 1.23
26 weeks	-0.06	-0.12, -0.00	0.01	-0.02, 0.03	-4.28	-8.39, -0.16	-0.24	-0.50, 0.03	1.03	0.93, 1.13
Birth	0.00	-0.05, 0.05	0.01	-0.01, 0.03	-1.46	-4.81, 1.89	-0.09	-0.09, 0.18	1.07	0.98, 1.16

Abbreviations: OPE, organophosphate ester; FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyroid stimulating hormone; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate.^a Models adjusted for mother's age at delivery, mother's education, race, year of birth, and infant sex.

Web Table 8: ANOVA table p-values computed for multiple linear regression models of creatinine-standardized and ln-transformed urinary OPE metabolites and thyroid hormones with a full set of covariates or a full set of covariates plus maternal iodine status in the HOME Study, 2003-2006.^a

Model independent and dependent variables	p-value for difference
BCEP & FT3	0.56
BCEP & FT4	0.20
BCEP & TT3	0.12
BCEP & TT4	0.42
BCEP & log-TSH	0.99
BDCIPP & FT3	0.45
BDCIPP & FT4	0.17
BDCIPP & TT3	0.11
BDCIPP & TT4	0.32
BDCIPP & log-TSH	0.97
DPHP & FT3	0.54
DPHP & FT4	0.21
DPHP & TT3	0.11
DPHP & TT4	0.38
DPHP & log-TSH	0.98
DNBP & FT3	0.56
DNBP & FT4	0.19
DNBP & TT3	0.12
DNBP & TT4	0.40
DNBP & log-TSH	0.99

Abbreviations: OPE, organophosphate ester; FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyroid stimulating hormone; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate. ^aModels were considered significantly different if $P < 0.1$.

Web Table 9: Beta estimates and confidence intervals for creatinine-standardized and ln-transformed urinary OPE metabolites by infant sex interaction term in generalized estimating equation models in the HOME Study, 2003-2006.^a

Parameter	FT3 (pg/mL)		FT4 (ng/dL)		TT3 (ng/dL)		TT4 (µg/dL)		TSH (µIU/mL)	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
BCEP * Sex	0.03	-0.01, 0.08	-0.00	-0.03, 0.02	1.02	-1.53, 3.57	-0.10	-0.39, 0.18	1.04	0.95, 1.29
BDCIPP * Sex	0.01	-0.04, 0.06	-0.00	-0.03, 0.02	0.35	-2.40, 3.09	-0.09	-0.39, 0.20	1.00	0.91, 1.11
DPHP * Sex	-0.00	-0.05, 0.05	-0.00	-0.03, 0.02	0.82	-1.88, 3.52	0.06	-0.23, 0.34	1.02	0.92, 1.12
DNBP * Sex	0.04	-0.04, 0.11	0.02	-0.01, 0.05	1.99	-3.78, 7.75	0.05	-0.29, 0.39	0.96	0.85, 1.09

Abbreviations: OPE, organophosphate ester; FT3, free triiodothyronine; FT4, free thyroxine; TT3, total triiodothyronine; TT4, total thyroxine; TSH, thyroid stimulating hormone; BCEP, bis-2-chloroethyl phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DPHP, diphenyl phosphate; DNBP, di-n-butyl phosphate. ^a TSH estimates are expressed in as exponentiated betas and confidence intervals. Models are generalized estimating equations additionally adjusted for mother's age at delivery, mother's education, race, year of birth.