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Supplemental Material

Urinary Concentrations of Organophosphate Flame Retardant Metabolites and Pregnancy Outcomes among Women Undergoing in Vitro Fertilization

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Table of Contents

Table S1. Unadjusted mean (95% CI) proportion of cycles resulting in implantation, live birth and clinical pregnancy by quartile of urinary organophosphate flame retardant metabolite concentrations among 211 women undergoing 297 IVF cycles.

	ΣPFRs	BDCIPP	DPHP	ip-DPHP
Implantation				
Q1	0.70 (0.58, 0.80)	0.71 (0.59, 0.81)	0.67 (0.55, 0.77)	0.74 (0.62, 0.83)
Q2	0.60 (0.48, 0.71)	0.59 (0.47, 0.7)	0.63 (0.51, 0.74)	0.49 (0.38, 0.61)
Q3	0.57 (0.45, 0.68)	0.53 (0.41, 0.64)	0.56 (0.44, 0.68)	0.61 (0.49, 0.71)
Q4	0.50 (0.38, 0.62)*	0.55 (0.43, 0.66)	0.51 (0.39, 0.62)	0.53 (0.41, 0.65)*
p-trend	0.02	0.05	0.04	0.06
Pregnancy				
Q1	0.63 (0.51, 0.74)	0.61 (0.49, 0.72)	0.60 (0.48, 0.71)	0.63 (0.51, 0.73)
Q2	0.52 (0.40, 0.64)	0.51 (0.39, 0.62)	0.54 (0.42, 0.65)	0.41 (0.30, 0.53)
Q3	0.49 (0.37, 0.61)	0.46 (0.34, 0.58)	0.48 (0.37, 0.60)	0.51 (0.39, 0.63)
Q4	0.39 (0.28, 0.51)*	0.45 (0.34, 0.57)	0.41 (0.30, 0.53)*	0.48 (0.36, 0.59)
p-trend	0.007	0.05	0.02	0.17
Live birth				
Q1	0.49 (0.37, 0.61)	0.50 (0.38, 0.62)	0.46 (0.34, 0.58)	0.52 (0.40, 0.64)
Q2	0.40 (0.29, 0.53)	0.37 (0.26, 0.50)	0.42 (0.31, 0.54)	0.36 (0.25, 0.48)
Q3	0.38 (0.27, 0.50)	0.37 (0.26, 0.49)	0.39 (0.28, 0.52)	0.37 (0.26, 0.49)
Q4	0.34 (0.24, 0.46)	0.37 (0.26, 0.49)	0.34 (0.24, 0.46)	0.36 (0.25, 0.48)
p-trend	0.09	0.16	0.17	0.07

*Significantly different from Q1 at the p=0.05 level

Table S2: Adjusted mean (95% CI) proportion of cycles resulting in implantation, live birth and clinical pregnancy by quartile of the molar sum of the urinary organophosphate flame retardant metabolite concentrations (ΣPFRs).

	Restricted to Cycles with Successful Oocyte Retrieval[a]	Restricted to First IVF Cycle[b]	Restricted to Nulliparous Women[c]	Controlling for maternal year of birth[d]
Implantation				
Q1	0.75 (0.62, 0.84)	0.71 (0.39, 0.91)	0.77 (0.61, 0.87)	0.71 (0.59, 0.81)
Q2	0.66 (0.53, 0.77)	0.66 (0.35, 0.88)	0.62 (0.46, 0.76)	0.61 (0.49, 0.73)
Q3	0.55 (0.42, 0.67)	0.57 (0.27, 0.83)	0.53 (0.38, 0.68)	0.57 (0.45, 0.69)
Q4	0.59 (0.46, 0.71)	0.56 (0.26, 0.81)	0.45 (0.31, 0.61)*	0.50 (0.37, 0.62)*
p-trend	0.04	0.16	0.006	0.02
Pregnancy				
Q1	0.63 (0.51, 0.74)	0.63 (0.31, 0.86)	0.64 (0.48, 0.78)	0.63 (0.50, 0.74)
Q2	0.54 (0.42, 0.67)	0.60 (0.29, 0.84)	0.56 (0.40, 0.71)	0.54 (0.41, 0.66)
Q3	0.49 (0.37, 0.61)	0.51 (0.22, 0.78)	0.53 (0.37, 0.68)	0.50 (0.38, 0.62)
Q4	0.47 (0.35, 0.60)	0.41 (0.16, 0.72)	0.31 (0.19, 0.47)*	0.37 (0.26, 0.50)*
p-trend	0.06	0.09	0.006	0.004
Live birth				
Q1	0.50 (0.37, 0.63)	0.51 (0.22, 0.79)	0.43 (0.27, 0.60)	0.48 (0.35, 0.60)
Q2	0.39 (0.27, 0.53)	0.44 (0.18, 0.74)	0.50 (0.34, 0.67)	0.41 (0.30, 0.54)
Q3	0.39 (0.27, 0.52)	0.41 (0.16, 0.72)	0.48 (0.32, 0.64)	0.38 (0.27, 0.51)
Q4	0.38 (0.26, 0.51)	0.34 (0.12, 0.66)	0.26 (0.15, 0.43)	0.31 (0.20, 0.43)*
p-trend	0.20	0.17	0.13	0.05

*Significantly different from Q1 at the p=0.05 level

[a]205 women and 281 cycles

[b]201 women and 210 cycles

[c]140 women and 187 cycles

[d]211 women and 297 cycles, Adjusted model controls for maternal year of birth (continuous, mean=1974).

Adjusted models control for maternal age (continuous), body mass index (continuous), race/ethnicity (black/Asian/other, white/Caucasian), year of IVF treatment cycle (continuous), and primary SART infertility diagnosis at study entry (female, male, unknown). Adjusted means are presented for the mean maternal age (35.2), body mass index (23.9), race/ethnicity (white), year of IVF treatment cycle (2010), and primary SART infertility diagnosis at study entry (female=1, male=0, unexplained=0).

Table S3. Unadjusted means (95% CI) for early developmental outcomes by quartile of urinary organophosphate flame retardant metabolite concentrations among 205 women undergoing 281 IVF cycles that had oocyte retrieval.

	ΣPFRs	BDCIPP	DPHP	ip-PPP
E2 trigger levels, pmol/L				
Q1	1944 (1771, 2118)	2011 (1835, 2187)	1998 (1821, 2174)	2051 (1878, 2225)
Q2	2173 (2001, 2345)	2065 (1892, 2238)	2095 (1919, 2270)	2122 (1952, 2293)
Q3	2007 (1839, 2176)	2031 (1856, 2206)	2148 (1972, 2323)	2147 (1979, 2315)
Q4	2142 (1966, 2318)	2156 (1979, 2333)	2022 (1843, 2202)	1944 (1766, 2121)
p-trend	0.22	0.29	0.88	0.49
Total oocytes, count				
Q1	10.8 (9.7, 12.0)	9.9 (8.8, 11.0)	11.0 (9.9, 12.3)	10.9 (9.7, 12.1)
Q2	11.1 (10.0, 12.3)	11.5 (10.3, 12.7)	11.1 (9.9, 12.3)	11.0 (9.9, 12.2)
Q3	10.7 (9.6, 11.9)	11.2 (10.1, 12.5)	11.5 (10.3, 12.7)	12.0 (10.8, 13.2)
Q4	11.9 (10.7, 13.3)	12.0 (10.8, 13.3)*	10.9 (9.8, 12.2)	10.7 (9.5, 11.9)
p-trend	0.21	0.02	0.94	0.81
Total MII oocytes, count				
Q1	9.3 (8.4, 10.4)	8.5 (7.6, 9.5)	9.3 (8.3, 10.4)	9.0 (8.0, 10.1)
Q2	9.4 (8.4, 10.5)	9.4 (8.4, 10.5)	9.4 (8.4, 10.5)	9.4 (8.4, 10.5)
Q3	8.7 (7.7, 9.7)	9.4 (8.4, 10.5)	9.5 (8.5, 10.6)	10.1 (9.1, 11.2)
Q4	9.9 (8.9, 11.0)	9.9 (8.9, 11.1)*	9.0 (8.0, 10.0)	8.7 (7.7, 9.8)
p-trend	0.57	0.06	0.61	0.98
Fertilization, proportion				
Q1	0.77 (0.72, 0.81)	0.75 (0.70, 0.79)	0.75 (0.70, 0.79)	0.77 (0.72, 0.81)
Q2	0.72 (0.67, 0.76)	0.73 (0.68, 0.77)	0.68 (0.63, 0.73)*	0.75 (0.71, 0.79)
Q3	0.71 (0.66, 0.75)*	0.71 (0.66, 0.76)	0.77 (0.73, 0.81)	0.71 (0.67, 0.75)
Q4	0.70 (0.65, 0.74)*	0.71 (0.66, 0.75)	0.68 (0.63, 0.73)*	0.65 (0.60, 0.70)*
p-trend	0.03	0.21	0.19	0.0004
Best quality embryos, count				
Q1	1.7 (1.3, 2.1)	1.5 (1.1, 2.0)	1.6 (1.2, 2.1)	1.5 (1.1, 1.9)
Q2	1.5 (1.2, 2.0)	1.3 (1.0, 1.7)	1.4 (1.1, 1.9)	1.8 (1.5, 2.3)
Q3	1.4 (1.1, 1.8)	1.7 (1.3, 2.2)	1.7 (1.3, 2.2)	1.6 (1.2, 2.0)
Q4	1.6 (1.2, 2.0)	1.6 (1.2, 2.1)	1.4 (1.1, 1.8)	1.2 (0.9, 1.6)
p-trend	0.70	0.45	0.69	0.30
Endometrial wall thickness, mm				
Q1	10.3 (9.83, 10.8)	10.2 (9.7, 10.7)	10.3 (9.8, 10.8)	10.2 (9.7, 10.7)
Q2	10.3 (9.76, 10.8)	10.1 (9.6, 10.6)	10.2 (9.7, 10.7)	10.1 (9.6, 10.6)
Q3	9.80 (9.32, 10.3)	9.9 (9.4, 10.4)	10.1 (9.6, 10.6)	9.7 (9.3, 10.2)
Q4	9.97 (9.46, 10.5)	10.0 (9.5, 10.5)	9.8 (9.3, 10.3)	10.3 (9.8, 10.8)
p-trend	0.19	0.47	0.15	0.97

*Significantly different from Q1 at the p=0.05 level

Table S4. Comparison of GM (95% CI) concentrations of urinary organophosphate flame retardant metabolites (μg/L).

Region (sample size)	Year	BDCIPP	DPHP	ip-PPP	Reference
Massachusetts (n=211)	2005-2015	0.70 (0.63, 0.77)	0.81 (0.75, 0.89)	0.24 (0.22, 0.26)	This study
California (n=28)	2015	3.3 (2.5, 4.2)	1.2 (0.97, 1.5)	2.0 (1.5, 2.5)	Butt et al. (2016)
New Jersey (n=22)	2013-2014	2.4 (1.5, 3.7)	1.9 (1.1, 3.4)	0.85 (0.67, 1.1)	Butt et al. (2014)
North Carolina (n=53)	2012	0.63 (0.49, 0.81)[a]	1.7 (1.36, 2.18)[a]	NR	Hoffman et al. (2015)
United States (n=9)	2011	0.41 (NR)	3.0 (NR)	NR	Cooper et al. (2011)
Massachusetts (n=29)	2009	0.41 (0.28-0.59)	1.9 (1.2-3.0)[b]	NR	Carignan et al. (2013)
Massachusetts (n=45)	2002-2007	0.13 (NR)	0.31 (NR)	NR	Meeker et al. (2013)
California (n=14)	2011	0.09[c] (NR)	0.44[c] (NR)	NR	Dodson et al. (2014)
Norway (n=48)[d]	2012	0.12[d] (NR)	0.51[d] (NR)	NR	Cequier et al. (2015)
Australia (n=3224, pooled)[e]	2010-2013	1.00, 0.66[e]	24.4, 64.4[e]	NR	Van den Eede et al. (2015)

Normalized using a mean specific gravity of 1.024 unless otherwise indicated
NR=Not reported
[a]Confidence interval obtained from study authors, n=52 for TBBA
[b]Previously unpublished data obtained from the authors
[c]Not SG normalized, median concentrations
[d]Normalized using a mean specific gravity of 1.015, 244 urine samples total
[e]Not SG normalized, GMs for two sampling campaigns (2010-2011 and 2012-2013)

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