Recent Epidemiologic studies of Benzophenone, 4-OH-nydroxypenzophenone and related derivatives

Urinary Concentrations of Benzophenone-type UV Filters in US Women and Their Association with Endometriosis https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3352028/			
The association of urinary concentrations of BP derivatives with an increase in the odds of a diagnosis of endometriosis was examined in 600 women who underwent laparoscopy/laparotomy (n = 473: operative cohort) or pelvic magnetic resonance imaging (n = 127: population cohort), during 2007-2009	Urine samples were collected from 431 and 63 currently-menstruating women, aged 18-44 years, who were scheduled to undergo a diagnostic and/or therapeutic laparoscopy or laparotomy (referred to as "operative or surgical cohort"). Urine samples were collected from 131 currently-menstruating women who were matched to the operative cohort on age and residence (referred to as "population or unexposed cohort"). The intent of the population cohort was to identify women at risk for endometriosis (*i.e*., currently menstruating) who did not seek medical care; this group served as a comparison cohort for the operative cohort and for the assessment of consistency of findings across cohorts. 4OH-BP was detected in 83.8% of the urine samples analyzed.	The strength of correlation between BP derivative concentrations was evaluated by simple regression analysis. The relation between BP derivative concentrations and odds of an incident endometriosis diagnosis was explored using multivariable logistic regression. Given the uncertain timing of endometriosis onset, we estimated the odds ratios (ORs) for diagnosis along with corresponding 95% confidence intervals (CIs) for each BP derivative, rather than estimating incident disease, *per se*.	The unadjusted and adjusted ORs were elevated for 2OH-4MeO-BP and 2,4OH-BP, particularly at the higher quartiles, but not for 4OH-BP. A significant trend was observed between 2,4OH-BP and the odds of an endometriosis diagnosis, but only in the operative cohort (OR = 1.19; 95% CI = 1.01, 1.41). A similar pattern was observed in the population cohort, but the CIs for all BP derivatives included one, denoting the absence of significance, possibly indicative of the limited number (*n* = 14) of women in the population cohort with endometriosis. CONCLUSION: No association between 4OH-BP and endometriosis. **NOTE: study distinguishes between BP UV filter type**.

Odds of an endometriosis diagnosis by urinary concentrations of BP derivatives and cohort (ENDO Study)

BP analyte	**Operative cohort (*n*=473)**		**Population cohort (*n*=127)**	
(quarter ng/mL)	**OR [c] (95% CI)**	**OR [d] (95% CI)**	**OR [c] (95% CI)**	**OR [d] (95% CI)**
4OH-BP				
1st quartile (<0.082-0.17)	reference	reference	reference	reference
2nd quartile (0.18-0.35)	0.87 (0.52, 1.45)	0.92 (0.55, 1.54)	1.08 (0.20, 5.85)	1.51 (0.25, 9.20)
3rd quartile (0.36-0.71)	1.02 (0.61, 1.71)	1.03 (0.62, 1.73)	1.24 (0.25, 6.06)	2.20 (0.38, 12.7)
4th quartile (0.71-22.40)	0.84 (0.49, 1.42)	0.87 (0.51, 1.48)	1.16 (0.24, 5.66)	1.69 (0.31, 9.21)
Trend test [a]	0.97 (0.82, 1.14)	0.97 (0.82, 1.15)	1.06 (0.65, 1.73)	1.19 (0.71, 1.98)
>Q3 versus <Q3 [b]	0.87 (0.56, 1.36)	0.89 (0.57, 1.38)	1.05 (0.31, 3.58)	1.12 (0.31, 4.01)

[a]Trend test assessed linear trends of BP derivatives across the four intervals defined by the 25th, 50th, and 75th percentiles.
[b]Women in the highest quartile for each BP derivative were compared with women in the combined first three quartiles.
[c]Odds ratios from unadjusted logistic regressions
[d]Odds ratios from multivariable logistic regressions adjusting for site (Utah, California) and hair color (red, blonde, brown/black)

Urinary Concentrations of Benzophenone-Type Ultraviolet Radiation Filters and Couples' Fecundity https://www.ncbi.nlm.nih.gov/pubmed/25395025			
501 couples who were discontinuing use of contraceptives in order to become pregnant recruited for the Longitudinal Investigation of Fertility and the Environment (LIFE) Study. Couples provided urine specimens and completed daily journals until they either achieved pregnancy or had tried for 12 months. Multiple BP derivatives measured in urnine including 4OH-BP.	Fecundability odds ratios (FORs) and 95% confidence intervals were estimated for each UV filter, modeling each partner's concentrations individually and then modeling both partners' concentrations. UV filter concentrations were dichotomized at the 75th percentile to assess more-exposed persons versus less-exposed persons relative to couple fecundity. FOR estimates the odds of becoming pregnant for partners/couples above the 75th exposure percentile relative to those below the 75th percentile.	When FORs were estimated for each partner separately, 2 UV filters were significantly associated with FORs below 1, indicative of diminished fecundity or a longer time to pregnancy Specifically, BP-2 was associated with an approximately 31% reduction in fecundity (FOR = 0.69, 95% confidence interval (CI): 0.50, 0.95), and 4-OH-BP was associated with a 26% reduction (FOR = 0.74, 95% CI: 0.54, 1.00). None of the UV filters measured in females were associated with fecundability, with the exception of BP-8, but only in the creatinine- and age-adjusted model (FOR = 1.34, 95% CI: 1.02, 1.78)	The strongest signal was for males' concentrations of BP-2, which reflected a consistent reduction in fecundability when partners' concentrations were modeled individually or jointly. In addition, when only males' 4-OH-BP concentrations were modeled, 4-OH-BP was negatively associated with fecundability. CONCLUSION: 4-OH-BP was associated with a 26% reduction **(FOR = 0.74, 95% CI: 0.54, 1.00).**

Table 3. Fecundability Odds Ratios According to Urinary Concentrations of Benzophenone-Type Ultraviolet Radiation Filters, by Partner Sex and Model, LIFE Study, 2005–2009[a]

UV Filter	Female Partners ($n = 454$)						Male Partners ($n = 439$)					
	Unadjusted Model[b]		Adjusted Model 1[c]		Adjusted Model 2[d]		Unadjusted Model[b]		Adjusted Model 1[c]		Adjusted Model 2[d]	
	FOR	95% CI	FOR	95% CI	FOR	95% CI	FOR	95% CI	FOR	95% CI	FOR	95% CI
BP-1 (2,4-OH-BP)	1.06	0.80, 1.40	1.13	0.85, 1.49	1.02	0.76, 1.37	1.06	0.79, 1.42	1.06	0.79, 1.43	0.97	0.71, 1.32
BP-2 (2,2′4,4′-OH-BP)	0.77	0.57, 1.04	0.81	0.60, 1.10	0.82	0.60, 1.12	0.66[e]	0.48, 0.90	0.70[f]	0.51, 0.95	0.69[f]	0.50, 0.95
BP-3 (2-OH-4-MeO-BP)	1.11	0.83, 1.47	1.21	0.91, 1.62	1.12	0.83, 1.53	1.20	0.90, 1.59	1.20	0.90, 1.59	1.10	0.81, 1.49
BP-8 (2,2′-OH-4-MeO-BP)	1.25	0.95, 1.65	1.34[f]	1.02, 1.78	1.20	0.89, 1.63	1.39[f]	1.04, 1.86	1.43[f]	1.07, 1.91	1.34	0.98, 1.83
4-OH-BP	0.83	0.61, 1.12	0.86	0.63, 1.16	0.77	0.56, 1.06	0.84	0.64, 1.11	0.85	0.65, 1.12	0.74[f]	0.54, 1.00

Abbreviations: CI, confidence interval; FOR, fecundability odds ratio; LIFE, Longitudinal Investigation of Fertility and the Environment; 4-OH-BP, 4-hydroxybenzophenone; 2,4-OH-BP, 2,4-dihydroxybenzophenone; 2,2′4,4′-OH-BP, 2,2′,4,4′-tetrahydroxybenzophenone; 2-OH-4-MeO-BP, 2-hydroxy-4-methoxybenzophenone; 2,2′-OH-4-MeO-BP, 2,2′-dihydroxy-4-methoxybenzophenone; UV, ultraviolet.

[a] Separate models were fitted for each UV filter and partner. Concentrations of UV filters were dichotomized at the 75th percentile, with the group corresponding to lower values serving as the referent. All models accounted for left-truncation or time off contraception.

[b] Adjusted for each partner's UV filter concentration (ng/mL; dichotomized) and urinary creatinine concentration (mg/dL; continuous).

[c] Adjusted for each partner's UV filter concentration (ng/mL; dichotomized), urinary creatinine concentration (mg/dL; continuous), and age (years; continuous).

[d] Adjusted for each partner's UV filter concentration (ng/mL; dichotomized), urinary creatinine concentration (mg/dL; continuous), age (years; continuous), body mass index (categorical; see Table 1), smoking status as defined by serum cotinine level (active exposure, passive exposure, or no exposure; see Table 1), season (winter, spring, summer, or fall), and research site (Michigan or Texas).

[e] $P < 0.01$ (*t* test).

[f] $P < 0.05$.

Bisphenol A, benzophenone-type ultraviolet filters, and phthalates in relation to uterine leiomyoma. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4355097/			
Utilized the Endometriosis, Natural history, Diagnosis, and Outcomes (ENDO) Study in which all women underwent either a diagnostic and/or therapeutic laparoscopy or laparotomy allowing for the detection of uterine fibroids. 5 benzophenone-type ultraviolet (UV) filter metabolites were measured 2OH-4MeO-BP, 2,4OH-BP, 2,2'4,4'OH-BP, and 4OH-BP in spot urine samples.	Women with and without fibroids were compared by various characteristics using the Chi-square statistics or nonparametric Wilcoxon rank sum test for categorical and continuous, respectively. Geometric mean urinary concentrations and accompanying 95% confidence intervals (CIs) for all chemicals were compared by fibroid status using the Wilcoxon test for assessing significance. Logistic regression was used to estimate the odds of fibroids along with 95% CIs. Separate models were run for each chemical generating both unadjusted and adjusted odds ratios (OR) and corresponding 95% confidence interval (CI).	Significantly higher geometric mean creatinine-corrected concentrations of BPA, 2,4OH-BP, and 2OH-4MeO-BP were observed in women with than without fibroids [BPA: 2.09 µg/g vs. 1.46 µg/g p=0.004; 2,4OH-BP:11.10 µg/g vs. 6.71 µg/g p=0.01; 2OH-4MeO-BP: 11.31 µg/g vs. 6.10 µg/g p=0.01]. .	CONCLUSION: No association between urinary 4OH-BP levels and presence of fibroids

Geometric mean (95% confidence interval) comparison of chemicals by fibroid status (n=473)

Chemicals (µg/g)	Fibroids (n=99) Geometric Mean (95% CI)	No Fibroids (n=374) Geometric Mean (95% CI)	LOQ value (ng/mL)	% above LOQ/L OD	% of negative & zero values
Benzophenone derivatives					
2,4OH-BP	11.1 (7.1, 17.4)	6.7 (5.4, 8.3) [a]	0.08	99	0
4OH-BP	0.2 (0.2, 0.3)	0.3 (0.2, 0.3)	0.08	83	0
2OH-4MeO-BP	11.3 (6.4, 20.1)	6.1 (4.6, 8.0) [a]	0.28	91	0

[a] $p<0.05$

[b] $p<0.005$

NOTE: All chemicals were creatinine (mg/dL) standardized using the following formula: 100 × chemical (ng/ml)/creatinine (mg/dL). Nonparametric Wilcoxon rank sum test was used to compare chemical concentrations between those with and without fibroids.

Urinary Concentrations of Benzophenone-Type Ultra Violet Light Filters and Semen Quality https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4592813/			
413 men provided semen and urine samples, 2005–2009. Five UV filters were quantified in urine: BP-1, BP-2, BP-3, and 4-OH-BP.	Using linear regression, beta coefficients (β) and 95% Cis for each chemical dichoto-mized at the 75th percentile and Box-Cox transformed semen endpoint were esti-mated, after adjusting for age, BMI, cotinine, season, and site.	BP-2 associated with diminished sperm concen-tration (β=−0.74; CI −1.41, −0.08), straight (β=−4.57; 95% CI −8.95, −0.18) and linear move-ment (β=−3.15; CI −6.01, −0.30), more immature (β=0.38; CI 0.15, 0.62) sperm, and a decreased percentage of other tail abnormalities (β=−0.16; CI −0.31, −0.01). No associations were observed for BP-1, BP-3 or 4OH-BP.	CONCLUSION: No association between 4OH-BP and semen quality

Semen Quality Endpoint	BP-1		BP-2		BP-3		BP-8		4OH-BP	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
General Characteristics										
Volume (mL)	0.13	−0.04, 0.29	0.04	−0.13, 0.22	0.12	−0.04, 0.28	0.09	−0.08, 0.26	0.04	−0.13, 0.21
Sperm concentration (×10^6/mL)	−0.05	−0.69, 0.59	**−0.74**	**−1.41, −0.08**	0.11	−0.53, 0.74	−0.03	−0.68, 0.61	−0.49	−1.16, 0.18
Total sperm count (x10^6/ejaculate)	0.41	−0.55, 1.36	−0.91	−1.91, 0.09	0.59	−0.36, 1.55	0.22	−0.75, 1.18	−0.40	−1.40, 0.61
Hypo-osmotic swollen (%)	0.22	−2.05, 2.50	−1.75	−4.14, 0.63	−0.13	−2.40, 2.14	**−2.57**	**−4.86, −0.29**	−0.34	−2.73, 2.05
Straw distance (mm)	0.01	−0.13, 0.15	0.02	−0.13, 0.17	0.00	−0.13, 0.14	−0.06	−0.20, 0.08	−0.01	−0.15, 0.14
Sperm Motility (24 hour)										
Average path velocity (μm/sec)	0.72	−2.05, 3.49	−0.62	−3.53, 2.30	0.33	−2.44, 3.10	−0.63	−3.43, 2.16	1.29	−1.63, 4.20
Straight line velocity (μm/sec)	0.12	−2.15, 2.40	−0.71	−3.10, 1.69	−0.37	−2.64, 1.91	−1.00	−3.30, 1.30	0.78	−1.61, 3.18
Curvilinear velocity (μm/sec)	1.92	−2.91, 6.75	−0.27	−5.35, 4.80	1.10	−3.73, 5.93	−1.18	−6.06, 3.70	3.83	−1.24, 8.90
Amplitude head displacement (μm)	0.01	−0.29, 0.32	0.03	−0.29, 0.35	0.04	1.29, −1.63	−0.02	−0.33, 0.29	0.29	−0.03, 0.61
Beat cross frequency (Hz)	1.01	−0.52, 2.54	−0.47	−2.08, 1.14	0.67	−0.86, 2.20	−0.98	−2.52, 0.56	0.50	−1.11, 2.11
Straightness (%)	0.30	−3.89, 4.50	**−4.57**	**−8.95, −0.18**	−0.19	1.29, −1.63	−3.51	−7.72, 0.71	−0.89	−5.29, 3.52
Linearity (%)	0.05	−2.68, 2.78	**−3.15**	**−6.01, −0.30**	−0.19	−2.92, 2.54	−2.25	−4.99, 0.49	−1.56	−4.42, 1.30
Percent motility (%)	−0.23	−0.87, 0.40	−0.31	−0.98, 0.36	−0.36	−1.00, 0.27	−0.37	−1.01, 0.27	−0.30	−0.97, 0.37
Sperm Head Measurements										
Length (μm)	−0.01	−0.02, 0.01	0.01	−0.01, 0.02	−0.01	−0.02, 0.00	0.00	−0.01, 0.02	0.00	−0.02, 0.01
Area (μm^2)	−0.12	−0.32, 0.08	−0.07	−0.28, 0.14	−0.13	−0.33, 0.07	−0.04	−0.24, 0.16	−0.06	−0.27, 0.15
Width (μm)	−0.02	−0.06, 0.02	−0.04	−0.08, 0.00	−0.01	−0.05, 0.03	−0.03	−0.08, 0.01	0.00	−0.05, 0.04
Elongation factor (%)	−0.02	−1.27, 1.23	−1.29	−2.60, 0.01	0.41	−0.84, 1.66	−1.13	−2.39, 0.14	0.00	−1.32, 1.32
Perimeter (μm)	−0.07	−0.19, 0.05	0.02	−0.10, 0.15	−0.08	−0.20, 0.03	0.01	−0.10, 0.13	−0.04	−0.16, 0.08
Acrosome area of head (%)	0.59	−0.53, 1.70	−0.82	−1.99, 0.35	0.88	−0.24, 1.99	**1.14**	**0.01, 2.26**	−0.01	−1.19, 1.17
Morphology										
Strict criteria (%)[a]	0.59	−0.47, 1.64	−0.85	−1.99, 0.30	0.40	−0.66, 1.45	−0.08	−1.16, 1.00	0.72	−0.41, 1.86

Semen Quality Endpoint	BP-1		BP-2		BP-3		BP-8		4OH-BP	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Traditional normal (%)[a]	1.92	−1.18, 5.02	−2.64	−6.00, 0.71	1.46	−1.63, 4.56	−0.14	−3.31, 3.03	1.35	−1.98, 4.68
Amorphous (%)	−0.13	−0.37, 0.12	0.23	−0.04, 0.50	−0.15	−0.40, 0.09	−0.06	−0.32, 0.19	0.02	−0.25, 0.28
Round (%)	−0.02	−0.15, 0.11	0.09	−0.05, 0.23	0.02	−0.11, 0.15	−0.01	−0.15, 0.12	−0.04	−0.18, 0.10
Pyriform (%)	0.03	−0.17, 0.22	0.11	−0.10, 0.32	−0.02	−0.22, 0.17	0.15	−0.05, 0.35	−0.01	−0.23, 0.20
Bicephalic (%)	−0.04	−0.17, 0.10	0.12	−0.03, 0.27	−0.04	−0.17, 0.10	0.00	−0.14, 0.13	−0.03	−0.18, 0.11
Taper (%)	−0.06	−0.22, 0.11	0.09	−0.09, 0.26	−0.09	−0.25, 0.07	0.05	−0.11, 0.22	−0.01	−0.18, 0.17
Megalo head (%)	0.02	−0.10, 0.14	0.11	−0.02, 0.24	−0.02	−0.14, 0.10	0.03	−0.09, 0.15	0.07	−0.06, 0.19
Micro head (%)	−0.02	−0.13, 0.09	0.00	−0.12, 0.12	−0.03	−0.14, 0.08	0.05	−0.06, 0.17	−0.04	−0.16, 0.08
Neck/mid-piece abnormalities (%)	−0.05	−0.14, 0.04	0.05	−0.04, 0.15	−0.02	−0.11, 0.06	0.00	−0.09, 0.09	−0.05	−0.15, 0.05
Coiled tail (%)	0.05	−0.06, 0.15	−0.01	−0.12, 0.11	0.02	−0.09, 0.13	−0.01	−0.12, 0.10	−0.02	−0.13, 0.10
Other tail abnormalities (%)	−0.11	−0.24, 0.03	**−0.16**	**−0.31, −0.01**	−0.08	−0.22, 0.06	−0.03	−0.17, 0.11	−0.07	−0.21, 0.08
Cytoplasmic droplet (%)	0.09	−0.17, 0.35	0.09	−0.19, 0.37	0.07	−0.19, 0.33	−0.03	−0.29, 0.24	0.10	−0.18, 0.38
Immature sperm (#)	0.08	−0.14, 0.30	**0.38**	**0.15, 0.62**	0.05	−0.17, 0.27	0.01	−0.21, 0.24	0.16	−0.08, 0.40
Sperm Chromatin Stability Assay										
DNA fragmentation index (%)	−0.02	−0.15, 0.11	−0.01	−0.14, 0.13	0.00	−0.13, 0.12	0.09	−0.04, 0.22	−0.04	−0.18, 0.09
High DNA stainability (%)	−0.08	−0.21, 0.06	0.13	−0.01, 0.27	−0.09	−0.22, 0.04	−0.09	−0.23, 0.04	0.01	−0.13, 0.15

Preconception seminal plasma concentrations of endocrine disrupting chemicals in relation to semen quality parameters among male partners planning for pregnancy			
5 UV filters (BP-1, BP-2, BP-3, BP-8, and 4-OH-BP) were quantified in seminal plasma from 339 male partners who participated in a prospective pregnancy study. Semen samples underwent next day analysis using a standardized protocol for the quantification of 35 endpoints.	Linear mixed-effects models of EDCs that were log transformed and rescaled by their standard deviations or dichotomized at the 75th percentile for each exposure and outcomes with covariate adjustment were performed. EDCs in seminal plasma were also assessed relative to clinical reference values of semen quality endpoints using logistic regression or generalized estimating equations.	BP-2 was associated with a 5% reduction in straightness and a 3% reduction in linearity, when measured in both urine and seminal plasma. No association between semen quality and 4OH-BP	CONCLUSION: No association between 4OH-BP and semen quality

Odds Ratios (95% CI) for seminal plasma chemicals and semen quality parameters [a].

	Volume (mL)[c] OR (95% CI)	FDR p-value	Sperm Concentration (x 10^6/m)[c] OR (95% CI)	FDR p-value	Total Count (per ejaculate)[c] OR (95% CI)	FDR p-value	Sperm Viability (%)[c] OR (95% CI)	FDR p-value	WHO Normal (%)[b] OR (95% CI)	FDR p-value	Strict Normal (%)[b] OR (95% CI)	FDR p-value	DNA Fragmentation (%)[c] OR (95% CI)	FDR p-value
Bisphenols														
BPA	0.71 (0.51, 0.99)	0.33	0.97 (0.73, 1.27)	0.95	0.75 (0.61, 0.91)	0.07	0.91 (0.75, 1.10)	0.67	0.94 (0.74, 1.19)	0.94	**6.29 (1.12, 35.5)**	0.76	0.85 (0.46, 1.57)	0.80
BPF	0.77 (0.53, 1.10)	0.47	1.32 (0.83, 2.09)	0.63	1.23 (0.83, 1.84)	0.67	1.01 (0.81, 1.25)	0.99	0.89 (0.70, 1.13)	0.80	2.60 (0.78, 8.68)	0.76	0.99 (0.63, 1.56)	0.99
BPS	0.80 (0.60, 1.07)	0.47	1.16 (0.73, 1.83)	0.78	1.03 (0.61, 1.75)	0.99	1.11 (0.89, 1.38)	0.67	0.77 (0.60, 0.98)	0.76	1.85 (0.78, 4.35)	0.76	0.89 (0.59, 1.34)	0.79
UV Filters														
BP – 1	0.63 (0.24, 1.65)	0.60	0.70 (0.28, 1.75)	0.55	1.01 (0.41, 2.51)	0.81	1.08 (0.63, 1.86)	0.97	1.19 (0.70, 2.03)	0.88	3.21 (0.39, 26.1)	0.69	0.63 (0.25, 1.56)	0.55
BP – 2	2.89 (1.29, 6.49)	0.37	1.12 (0.49, 2.54)	0.97	1.19 (0.50, 2.82)	0.97	1.62 (0.98, 2.66)	0.37	0.95 (0.55, 1.64)	0.95	– [e]	–	1.28 (0.42, 3.88)	0.84
BP – 3	0.55 (0.21, 1.48)	0.55	0.71 (0.29, 1.76)	0.55	0.88 (0.35, 2.24)	0.72	1.13 (0.66, 1.94)	0.91	1.23 (0.72, 2.10)	0.88	3.27 (0.40, 26.6)	0.69	0.63 (0.26, 1.56)	0.55
BP – 8[f]														
4-OH-BP	1.36 (0.59, 3.15)	0.72	1.53 (0.67, 3.49)	0.60	1.96 (0.84, 4.58)	0.55	1.77 (1.05, 2.99)	0.37	1.60 (0.92, 2.78)	0.69	3.66 (0.45, 29.8)	0.69	1.26 (0.42, 3.74)	0.91

Maternal urinary benzophenones and infant birth size: Identifying critical windows of exposure			
BP-1, BP-3 and 4-OH-BP were measured in maternal urine from first, second, and third trimester (847). Birth weight and length were measured at time of delivery. Information on maternal age, parity, weight at delivery, birth date, infant sex, and gestational age at delivery were collected. Information on maternal demographic characteristics (age, educational levels, and ethnicity), socioeconomic factors (annual family income) and lifestyle (consumption of tobacco and alcohol) was collected.	Birth weight and length were continuous variables in the generalized estimating equation (GEE) models with a linear function. In the final multiple linear regression model, the following potential confounders were included: gestational age, pregnancy weight gain (kg), prepregnancy body mass index, parity (primiparous and multiparous), maternal education, passive smoking, paternal height (cm), and infant sex (except in models stratified by sex). In the stratified analysis by infant sex, the interaction term between infant sex and exposure to BPs was added into the model to assess the potential modification effects of infant sex.	No significant association was found between between maternal urinary levels of BPs with birth weight in all newborns, and also in boys after stratification by infant sex. In girls, each log unit increase in maternal urinary BP-1 and BP-3 concentrations in the 3rd trimester were associated with decreases in birth weight by 27.99 g (95% CI: -50.66, -5.31), and 19.75 g (95% CI: -37.31, -2.19), respectively.	CONCLUSION: No association between 4OH-BP urinary levels and birth weight and length.

Table 3
Regression coefficients [β (95% CI)] for associations of ln-transformed SG-adjusted concentrations of benzophenones (ng/mL) in three trimesters with birth weight.

Birth Weight	All (n = 847)	Boys (n = 445)	Girls (n = 402)	p^{c}-value
	Adjusted β^{a} (95% CI)	Adjusted β^{b} (95% CI)	Adjusted β^{b} (95% CI)	
lnBP-1				
1st trimester	−13.19 (−26.58, 0.20)	−16.82 (−36.99, 3.35)	−10.88 (−28.71, 6.95)	0.64
2nd trimester	−6.77 (−21.44, 7.90)	−3.34 (−23.94, 17.26)	−10.15 (−31.00, 10.70)	0.72
3rd trimester	−11.37 (−26.46, 3.71)	1.40 (−18.82, 21.62)	−27.99 (−50.66, −5.31)*	0.07
p^{d}-value	0.81	0.43	0.43	
lnBP-3				
1st trimester	−7.79 (−19.23, 3.66)	−8.77 (−25.45, 7.91)	−7.37 (−23.06, 8.33)	0.91
2nd trimester	−4.98 (−16.86, 6.91)	−5.92 (−22.52, 10.68)	−4.84 (−21.86, 12.18)	0.78
3rd trimester	−9.48 (−21.48, 2.52)	−2.18 (−18.64, 14.28)	−19.75 (−37.31, −2.19)*	0.17
p^{d}-value	0.87	0.86	0.52	
ln4-OH-BP				
1st trimester	−13.97 (−32.94, 5.00)	−9.90 (−37.05, 17.24)	−17.84 (−44.32, 8.64)	0.68
2nd trimester	−17.85 (−37.14, 1.44)	−12.70 (−39.72, 14.33)	−22.22 (−49.74, 5.30)	0.71
3rd trimester	−14.14 (−33.18, 4.89)	−2.76 (−29.59, 24.07)	−26.16 (−53.12, 0.79)	0.31
p^{d}-value	0.95	0.87	0.91	
lnBP sum				
1st trimester	−7.19 (−24.80, 10.42)	−12.58 (−39.03, 13.86)	−7.25 (−30.85, 16.35)	0.90
2nd trimester	−5.70 (−34.31, 22.91)	−11.43 (−61.77, 38.91)	−4.23 (−38.76, 30.29)	0.90
3rd trimester	14.95 (−21.00, 50.90)	46.95 (−30.93, 124.83)	5.98 (−34.16, 46.11)	0.37
p^{d}-value	0.55	0.36	0.86	

Table 4
Regression coefficients [β (95% CI)] for associations of ln-transformed SG-adjusted concentrations of benzophenones (ng/mL) in three trimesters with birth length.

Birth length	All (n = 847)	Boys (n = 445)	Girls (n = 402)	p^{c}-value
	Adjusted β^{a} (95% CI)	Adjusted β^{b} (95% CI)	Adjusted β^{b} (95% CI)	
lnBP-1				
1st trimester	−0.06 (−0.11, −0.01)*	−0.10 (−0.17, −0.03)**	−0.03 (−0.09, 0.04)	0.11
2nd trimester	−0.01 (−0.07, 0.04)	−0.02 (−0.10, 0.06)	0.00 (−0.07, 0.08)	0.67
3rd trimester	−0.04 (−0.10, 0.01)	0.00 (−0.08, 0.07)	−0.08 (−0.17, 0.00)*	0.20
p^{d}-value	0.42	0.13	0.38	
lnBP-3				
1st trimester	−0.03 (−0.08, 0.01)	−0.05 (−0.11, 0.01)	−0.02 (−0.07, 0.04)	0.35
2nd trimester	−0.02 (−0.06, 0.02)	−0.01 (−0.07, 0.05)	−0.03 (−0.09, 0.03)	0.76
3rd trimester	−0.03 (−0.08, 0.01)	0.02 (−0.05, 0.08)	−0.08 (−0.15, −0.02)*	0.04
p^{d}-value	0.93	0.29	0.50	
ln4-OH-BP				
1st trimester	−0.08 (−0.15, −0.01)*	−0.09 (−0.19, 0.01)	−0.05 (−0.15, 0.05)	0.51
2nd trimester	−0.06 (−0.13, 0.01)	−0.09 (−0.19, 0.01)	−0.03 (−0.13, 0.07)	0.50
3rd trimester	−0.05 (−0.12, 0.02)	−0.02 (−0.12, 0.08)	−0.07 (−0.16, 0.03)	0.59
p^{d}-value	0.83	0.53	0.85	
lnBP sum				
1st trimester	0.02 (−0.04, 0.09)	0.02 (−0.08, 0.12)	0.02 (−0.07, 0.10)	0.84
2nd trimester	0.03 (−0.07, 0.14)	0.01 (−0.17, 0.20)	0.03 (−0.09, 0.16)	0.96
3rd trimester	0.08 (−0.06, 0.21)	0.13 (−0.16, 0.41)	0.07 (−0.08, 0.21)	0.75
p^{d}-value	0.74	0.76	0.84	

Abbreviation: CI, confidence interval.
*p-value < 0.05, **p-value < 0.01.
[a] Adjusted for pre-pregnancy body mass index, pregnancy weight gain, gestational age, parity, maternal education, paternal height, passive smoking, and infant sex.
[b] Adjusted as model A expect for infant sex.
[c] p values for interaction between ln-transformed specific gravity adjusted urinary benzophenones concentrations and infant sex.
[d] Score test of homogeneity of estimates in three trimesters.

Summary of Epidemiologic Data: A limited number of epidemioligc studies have been conducted with benzophenone (BP), predominantly by one group. These are population studies in which UV filters 1 (BP and 4-OH-BP) and 2 (all others) in the urine from women and urine and seminal fluid were compared with multiple reproduction and developmental endpoints. Only one association between BP and an effect (fecundability) was detected. The data suggests no reproductive or developmental effects of BP and 4-OH-BP in humans.