CHE Fertility call: Effects of BPA on *in vitro* Fertilization

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Study of metals & assisted reproductive technologies (SMART)

- In an effort to respond to the knowledge gap concerning environmental contaminants & periconceptual events, we initiated a prospective cohort of couples undergoing treatment at the Center for Reproductive Health at the University of California at San Francisco:
  - The aim of this pilot study is to generate specific testable hypotheses concerning associations between background exposures to environmental toxicants suspected to interfere with human reproduction & proximal IVF endpoints

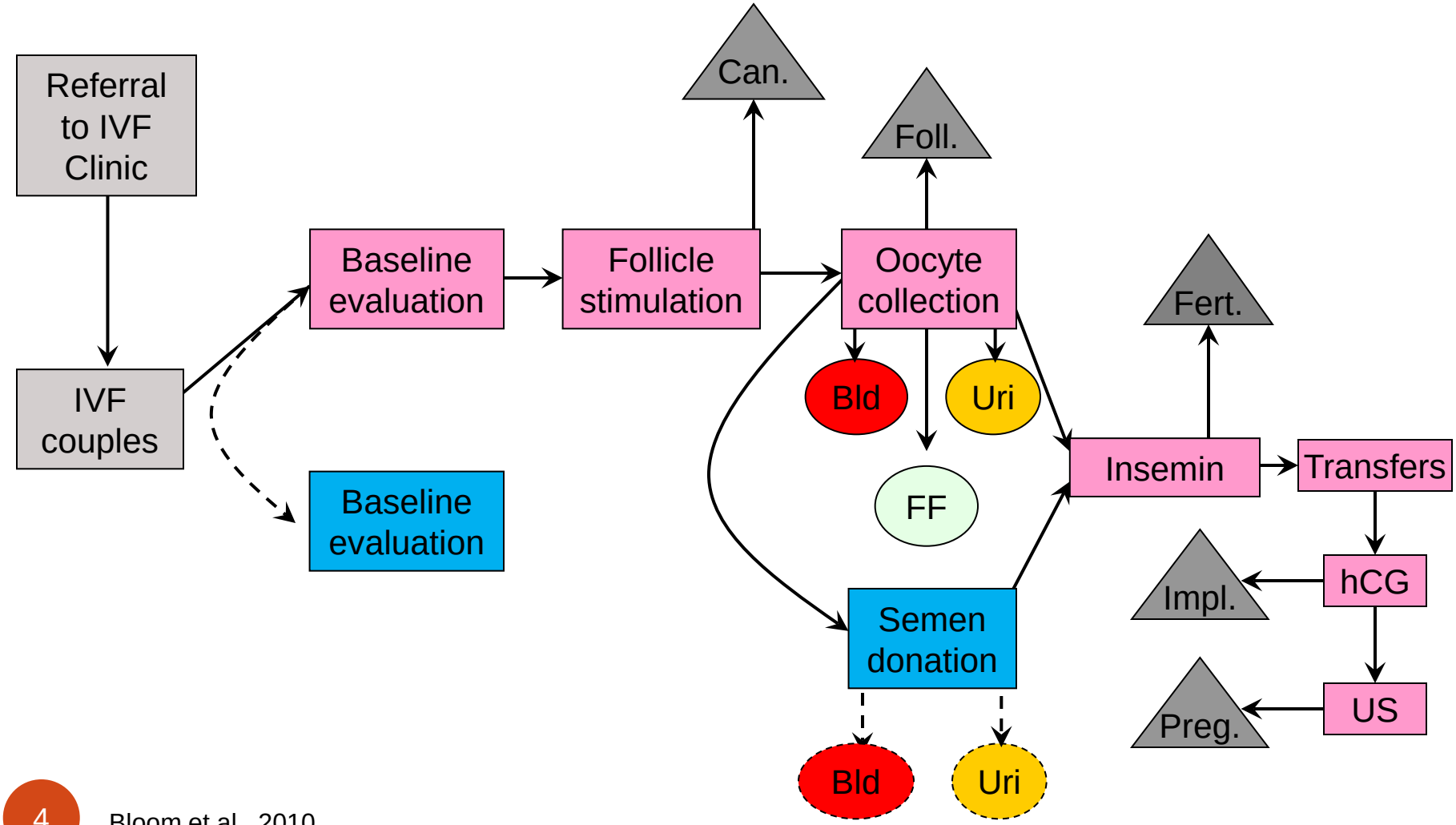
Bloom et al., 2010

Approach

- Collection of biologic specimens for assessment of environmental exposures at the time of oocyte retrieval from female patients & their male partners:
  - Laboratory analysis for serum unconjugated BPA concentrations using HPLC with Coularray Detection
- Biomarkers of internal dose correlated with endpoints at the:
  - Follicle level
  - Oocyte level
  - Embryo level
- Analysis conducted using the person unit of measurement & using the oocyte/embryo unit of measurement

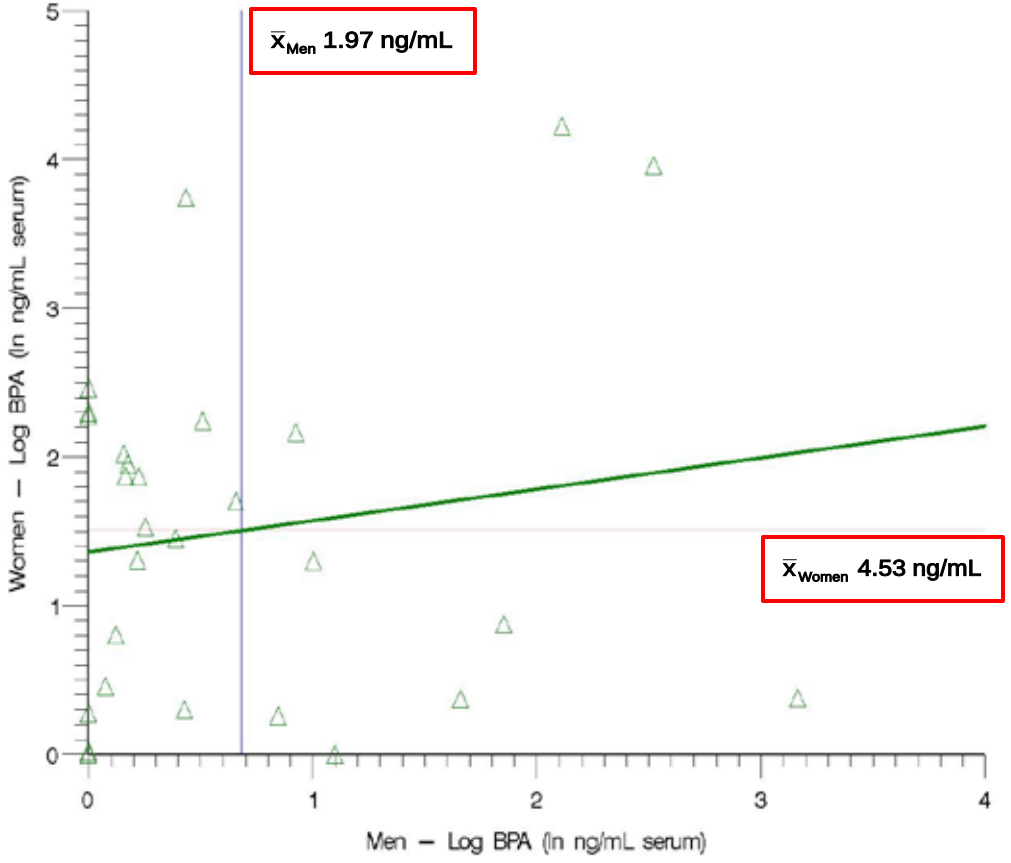
Bloom et al., 2010

Study protocol



Bloom et al., 2010

No association between BPA in women & BPA in men, comprising 28 couples

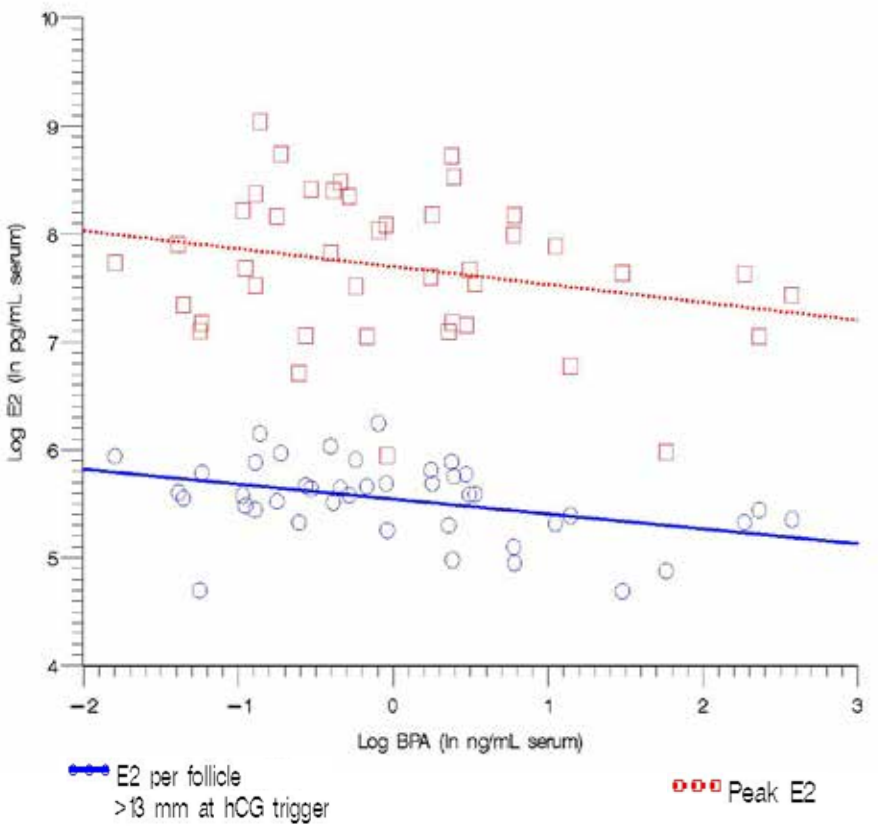


- Linear correlation for BPA in women & men:
  - 0.15 (95% CI -0.24, 0.49)
  - No substantial change when adjusted for age, race / ethnicity, or cigarette smoking
- Fasting vs. non-fasting specimens?

Unpublished observations

Increased BPA is associated with decreased peak estradiol (E_2) in 42 women

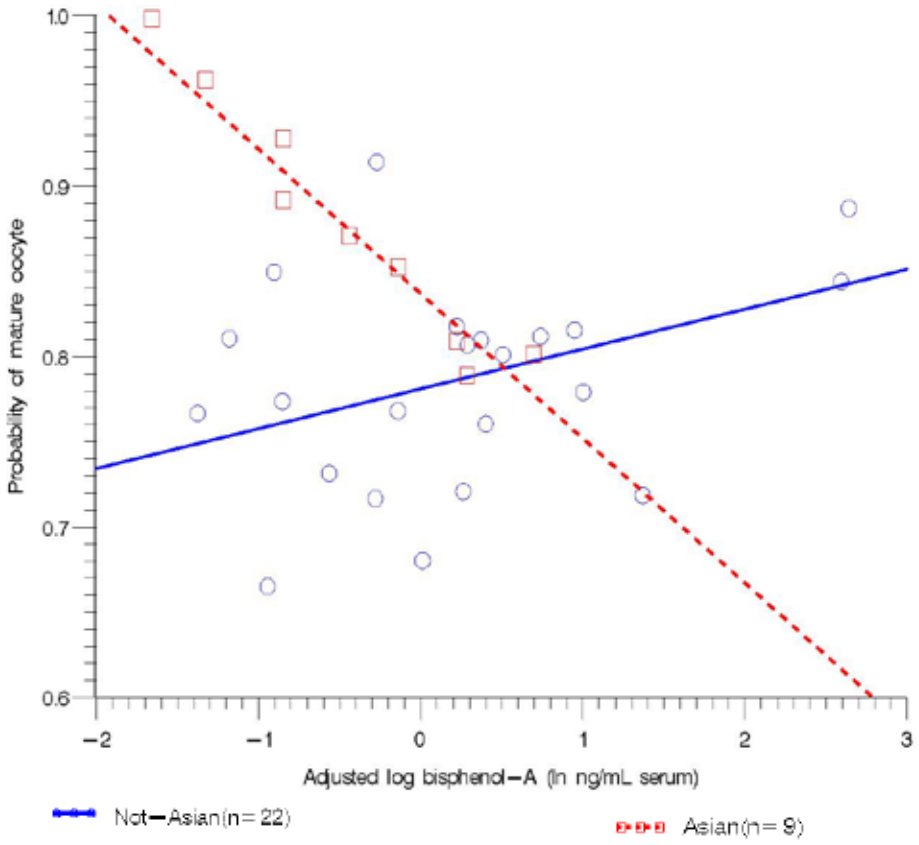
Note log scale ↓



- Doubling of BPA:
  - Reduction in peak E_2
    - -11% (95% CI -89%, 27%)
  - Reduction in peak E_2 per mature-sized follicle
    - -9% (95% CI -15%, -2%)
- Adjusted for AFC, cigarette smoking, & race/ethnicity
- BPA interfere with E_2 synthesis?

Bloom et al., submitted-1

Increase in female BPA associated with decreased oocyte maturity in ICSI cases



- Doubling of BPA:
  - A reduction in probability for a mature oocyte among Asian women
    - -9% (95% CI -17%, 0%)
  - No effect on probability for mature oocyte among not-Asian women
    - 3% (95% CI -4%, 10%)
- Adjusted for age & cigarette smoking
- BPA interfere with 1st meiotic division?

Fujimoto et al., in press

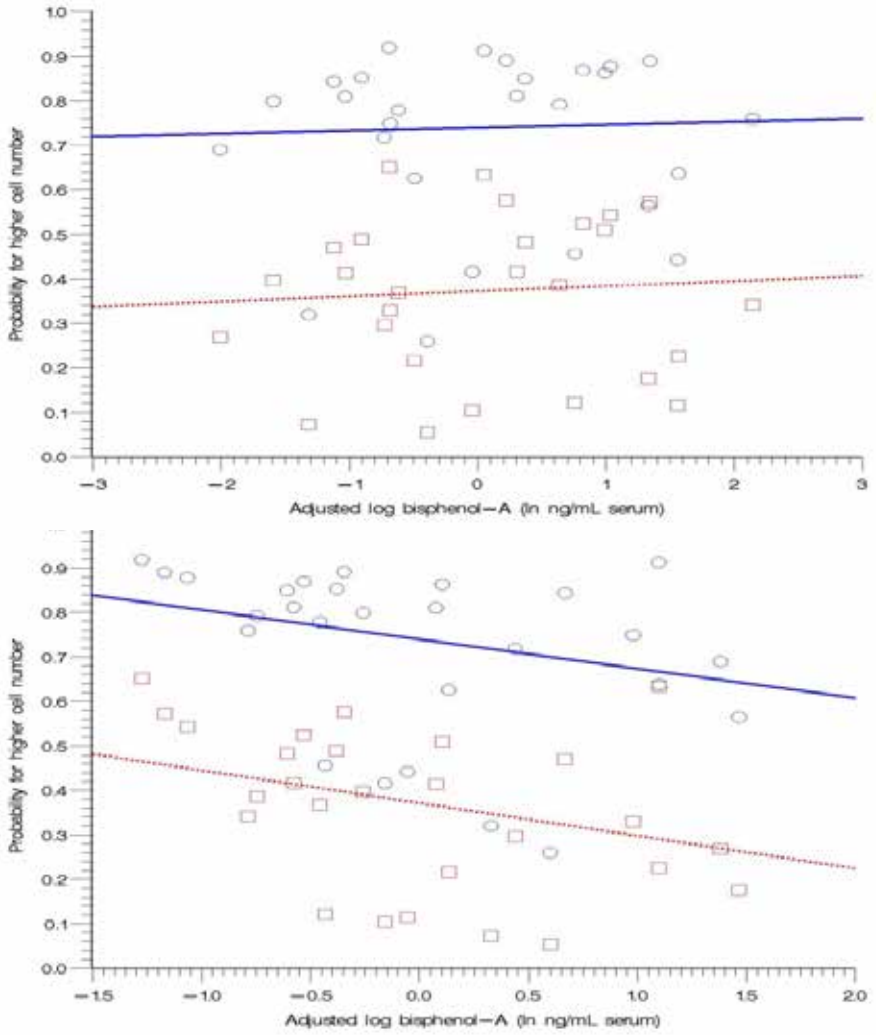
Increase in female BPA associated with decreased oocyte fertilization

	Model for oocyte fertilization			
Predictor variable	aRR	Low 95% CL	High 95% CL	*P* value
BPA-female (ng/mL serum)	0.45	0.31	0.66	<.0001
BPA-male (ng/mL serum)	0.96	0.88	1.04	.308
Age-female (y)	0.98	0.95	1.02	.261
Age-male (y)	0.96	0.94	0.99	.008
Race-female (not Asian/Asian)	1.17	0.70	1.97	.547
Race-male (not Asian/Asian)	1.25	0.75	2.08	.386
Smoking-female (never/ever)	1.15	1.03	1.28	.014
Smoking-male (never/ever)	0.82	0.69	0.98	.028
BPA-female × race-female	–	–	–	–
BPA-female × age-female	1.02	1.01	1.03	<.0001
BPA-female × BPA-male	1.06	1.02	1.10	.001
BPA-male × race-male	0.88	0.79	0.98	.022

- Doubling of BPA:
  - Reduced probability for normal fertilization for women
    - 55% (95% CI -69%, 34%)
    - Affected by age & race / ethnicity
  - Reduced probability for normal fertilization for Asian men only
    - 12% (95% CI -21%, -2%)

Fujimoto et al., in press

Increased male BPA associated with decreased embryo cleavage rate



- Doubling BPA:
  - No effect for women
    - 4% (95% CI -19%, 33%)
  - Reduced odds for men
    - -71% (95% CI -40%, 2%)
- Adjusted for partner BPA, age & race/ethnicity
- BPA in male partner interfere with early embryo cleavage?

Bloom et al., submitted - 2

Summary of BPA findings from the SMART Study

- Male BPA exposure may influence embryo quality in couples undergoing IVF
- A doubling of female BPA exposure is associated with a 50% reduction in normally fertilized oocytes with IVF
- There may be a race / ethnicity-specific association between female BPA exposure & reduction in mature oocytes retrieved during IVF
- Increasing female BPA exposure alters the E_2 response during gonadotropin stimulation during IVF
- Non-dietary sources of BPA exposure may be important