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Determinants and Health Impacts of PFAS Exposures in Humans

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Disclaimers

- I have no financial conflicts of interest

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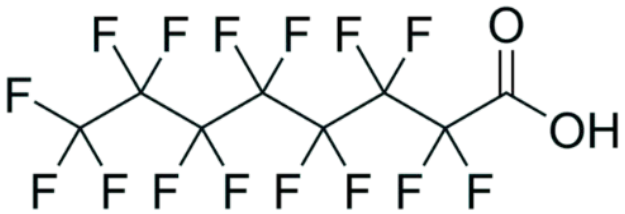
Outline

- Source of PFAS Exposure
  - Relative contributions
  - Water
  - Food
  - Other media
- Health Effects of PFAS Exposure in Humans
  - Fetal growth
  - Child/adult adiposity
  - Breastfeeding

Perfluoroalkyl Substances (PFAS)

- Persistent chemical compound used in commercial products and industrial applications
  - Carpet, textiles, leather, paper, cardboard, food packaging, electronics, cleaning agents, cosmetics, firefighting foams
- Perfluorooctanoate (PFOA) & perfluorooctane sulfonate (PFOS) commonly detected in serum
  - Half-life of 3-7 years
- Concern over effects on fetal, infant, and child health
- 2016 EPA drinking water advisory level set to 70 ppt (ng/L)
  - Cumulative



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Sources of PFAS Exposure

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PFAS Exposure in Adults

- General population primarily exposed by ingesting contaminated food, water, or dust
- Diet is predominant route of exposure for adults

	Daily Intake (pg/kg b.w.)	
	Mean	High
PFOA		
Indoor Air	0.9	0.9
Outdoor Air	1.3	12.0
House Dust	16.4	1028.3
Diet	2816.7	11483.3
Drinking water	21.7	86.7
Overall intake	**2857.0**	**12611.2**
PFOS		
Indoor Air	4.7	4.7
Outdoor Air	.01	1.0
House Dust	31.7	4216.7
Diet	1500.0	4483.3
Drinking water	23.2	130.0
Overall intake	**1559.8**	**8835.7**

Table adapted from Fromme et al. 2009.

Fromme et al. 2009, Mogensen et al. 2015.

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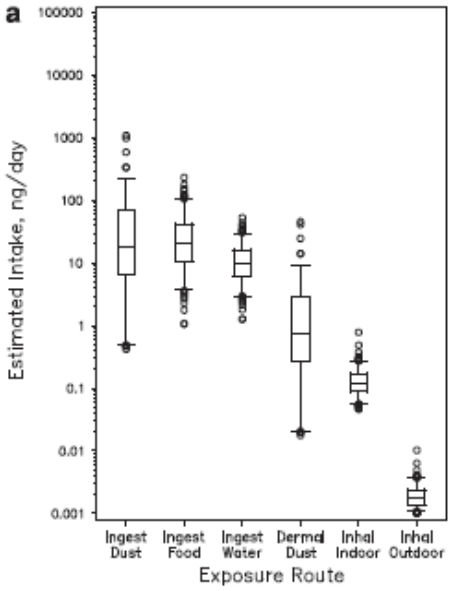
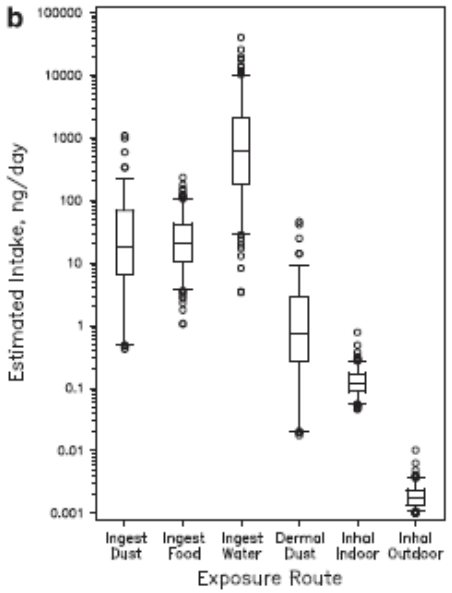
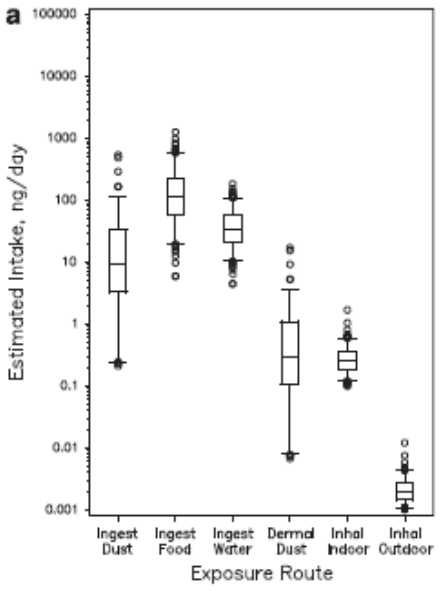
PFOS Exposures in Children

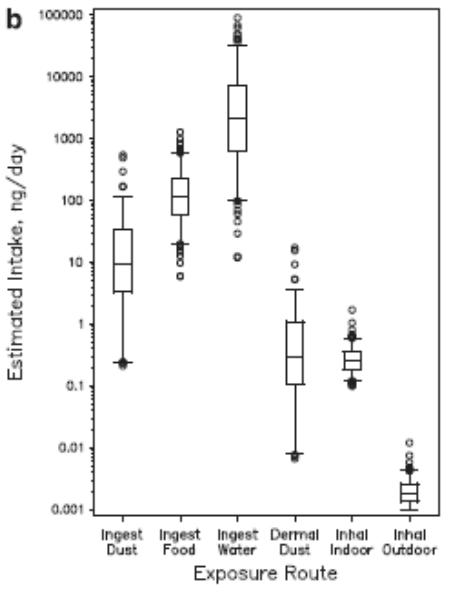
2-Year Old Children





Adult





- After weaning, PFAS sources likely to be similar to that of adults
- However, breast milk is a major source of exposure in infants . . .

Egeghy and Lorber 2011

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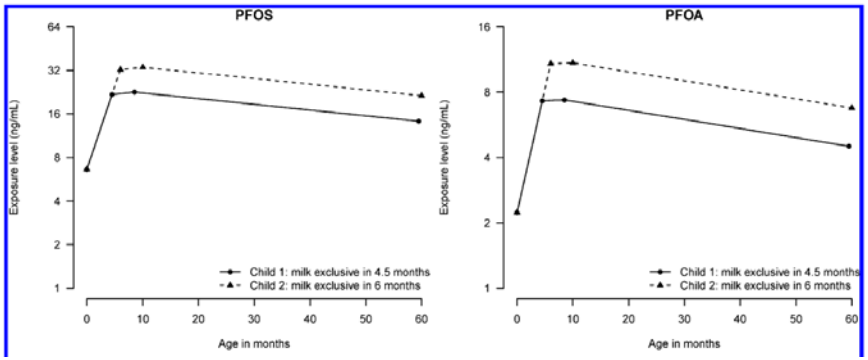
Breastfeeding and PFAS

- Haug et al. (Envr Int, 2011) estimates that breastmilk represents majority of PFOA (83%) and PFOS (94%) exposure in infants
  - Infant intakes were 13 to 16-fold greater than adults
- Mogensen et al. (ES&T, 2015):
  - Exclusively breastfed infants had 30% greater PFOA/PFOS concentrations compared to non-breastfed infants

Person	PFOA (ng/kg/d)	PFOS (ng/kg/d)
Infant	4.3	8.7
Adult	0.26	0.62



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Water PFAS

- Drinking water could be a major source in communities with contaminated water supplies

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Comparing Water-Serum PFOA

Study	N	Location	Water Source	Median
Emmett et al. 2006	291	Parkersburg, WV	Public/Private	105
Hoffman et al. 2011	108	Parkersburg, WV	Private	142
Hoffman et al. 2011	N/A	PK model	N/A	114
Hurley et al. 2016	1,566	California	Public	145

- Rule of thumb:
  - Serum PFOA (μg/L) = 125 x Water PFOA (μg/L)
- Note, there are a range of values, and individuals could be higher or lower
- Ratio for PFOS is ~ 175

Comparing Water-Serum PFAS

- 1 μg/L increase in water PFOA associated with 142 μg/L increase in serum PFOA

Water PFOA (μg/L)	Serum PFOA (μg/L)	NHANES Percentile (2011-12)	NHANES Percentile Preg ♀ 2003-08
0.015	2.1	~50th	~25th
0.03	4.2	~90th	~75th
0.07	9.9	>95th	>95th

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Dietary PFAS

- Detected in many foods (milk, butter, meats, fish, & vegetables)
  - PFOA less bio-accumulative in fish than PFOS
  - For some PFAS, precursors may be important (e.g., PFHxS)
- NHANES study did not report expected relations between diet and serum PFAS
  - Reasons?

Jain 2014, Post et al. 2012, Gebbink et al. 2015 Conder 2008, Holzer 2011

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Dietary PFAS: Packaging

- PFAS used in paper and paperboard as water and oil repellants
  - Fast food wrappers, microwave popcorn, and pizza box liners
- Breakdown of precursors in food packaging (Fromme et al., 2009)
  - FDA banned PFAS from food contact in 2016 (81 CFR 5)

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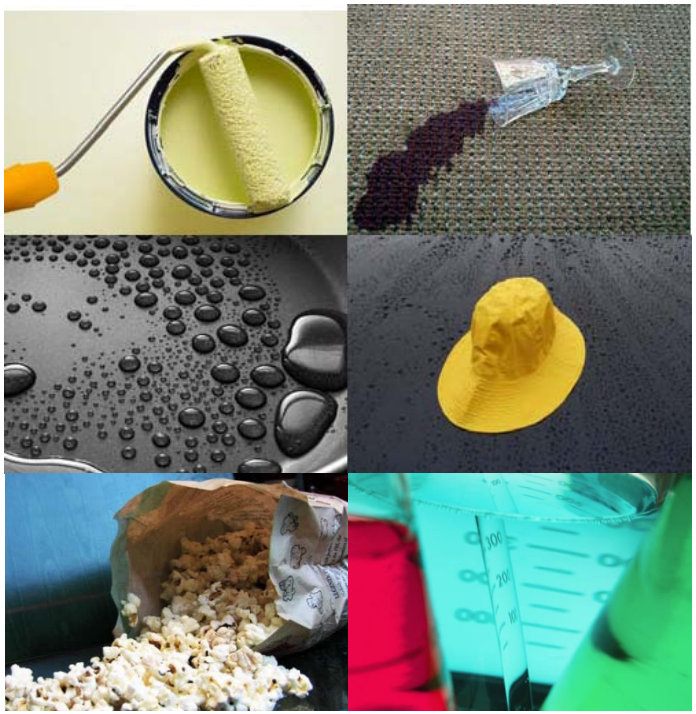
Other Potential PFAS Exposures

- Washburn et al. 2005 evaluated PFOA in:
  - Treated/milled carpets, treated apparel, PTFE tape, cookware, and woven medical garments
- Low potential for exposure
- Assuming aggregate exposures, <0.5 ng/mL increase in serum PFOA



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Conclusions about Sources of PFAS

- Relative contribution of different media will vary by many factors
  - Age: Infants > adults
  - Geography: Water contamination vs. none
  - Relative contributions vary: Dust
- Public health messaging:
  - Balanced diet (i.e., hedging)
  - GAC water filtration
  - Wet mopping, remove PFAS containing textiles

PFAS and Human Health

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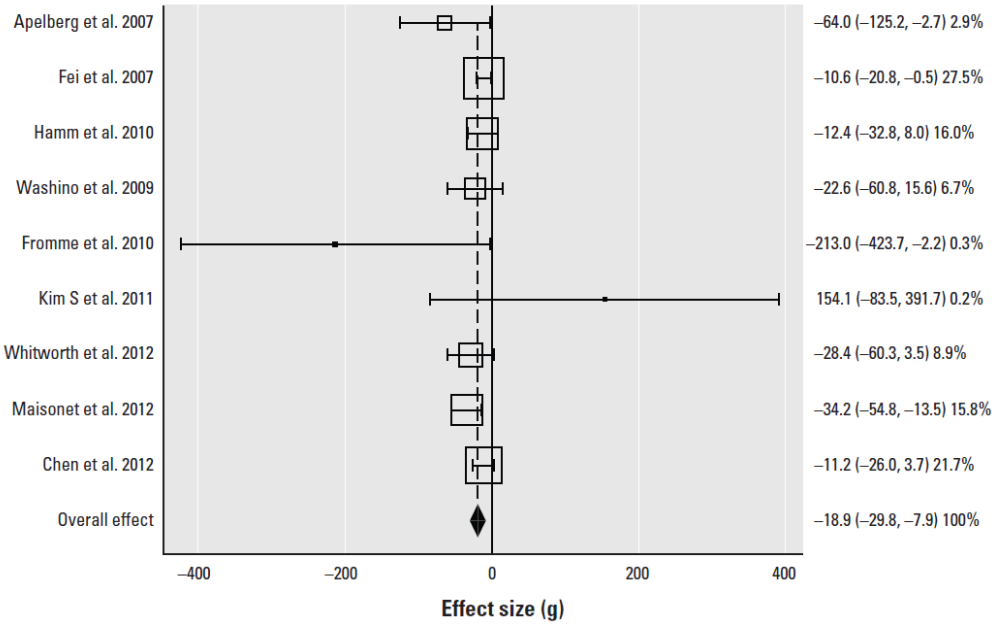
PFOA/PFOS and Fetal Growth

- Consistent animal & human evidence that PFOA (maybe PFOS) exposure associated with reduced birth weight
  - 19 gram decrease in BW per 1 ng/mL increase in serum PFOA (95% CI: -30, -7)
  - 23 mg decrease in pup birth weight (95% CI: -29, -16) for each 1 mg/kg/d increase in PFOA exposure



Koustas et al., EHP, 2014; Johnson et al., EHP 2014

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PFAS and Child/Adult Adiposity

- Prenatal PFOA/PFOS associated with excess adiposity in some, but not all studies
- Cohort of 700+ US mom-child pairs:
  - Prenatal PFOA/PFOS associated with multiple measures of adiposity at 8, but not 3 years of age
- Cohort of 664 Danish mom-adult pairs
  - Prenatal PFOA associated with higher BMI/WC at 20 years of age
  - Stronger associations in females

Table 4. Associations[a] between *in utero* exposure to PFOA and the offspring BMI and waist circumference at 20 years of age for females ($n = 345$) and males ($n = 320$).

PFOA in quartiles [median (range)][b]	ΔBMI [mean (95% CI)]		ΔWaist circumference [mean (95% CI)]	
	Crude	Adjusted[c]	Crude	Adjusted[c]
Females				
1 2.3 (0.1–2.8)	Referent	Referent	Referent	Referent
2 3.2 (2.8–3.7)	0.2 (–0.7, 1.2)	0.4 (–0.6, 1.3)	1.0 (–1.7, 3.7)	1.4 (–1.4, 4.2)
3 4.2 (3.7–4.8)	0.8 (–0.2, 1.8)	0.9 (–0.1, 1.9)	0.9 (–1.9, 3.6)	1.2 (–1.7, 4.0)
4 5.8 (4.8–19.8)	1.6 (0.6, 2.5)	1.6 (0.6, 2.6)	4.2 (1.5, 6.9)	4.3 (1.4, 7.3)
p-Value for trend[d]	0.0007	0.001	0.005	0.006
Males[e]				
1 2.4 (1.2–2.8)	Referent	Referent	Referent	Referent
2 3.3 (2.8–3.7)	0.5 (–0.4, 1.4)	0.6 (–0.3, 1.5)	1.3 (–1.7, 4.3)	1.3 (–1.5, 4.1)
3 4.2 (3.7–4.8)	0.3 (–0.7, 1.2)	0.2 (–0.7, 1.1)	1.0 (–2.0, 4.0)	1.0 (–1.9, 3.8)
4 5.8 (4.8–16.6)	0.4 (–0.5, 1.3)	0.6 (–0.3, 1.5)	0.7 (–2.2, 3.6)	1.3 (–1.6, 4.1)
p-Value for trend[d]	0.47	0.30	0.72	0.48

[a]Linear regression with continuous outcome variables (BMI or waist circumference) and PFOA divided into quartiles. [b]Nanograms per milliliter serum. [c]Adjusted for maternal age, maternal education, maternal preprepregnancy BMI, smoking during pregnancy, parity, infant birth weight, and offspring age at follow-up. [d]Student's *t*-test with PFOA included in the regression model as an ordinal variable. [e]Waist circumference was missing for two male offspring ($n = 318$).

Mora et al. 2016, Halldorsson et al. 2012, Maisonet et al. 2012, Andersen et al. 2013, Barry et al. 2014, Johnson et al. 2014, Braun et al., 2015

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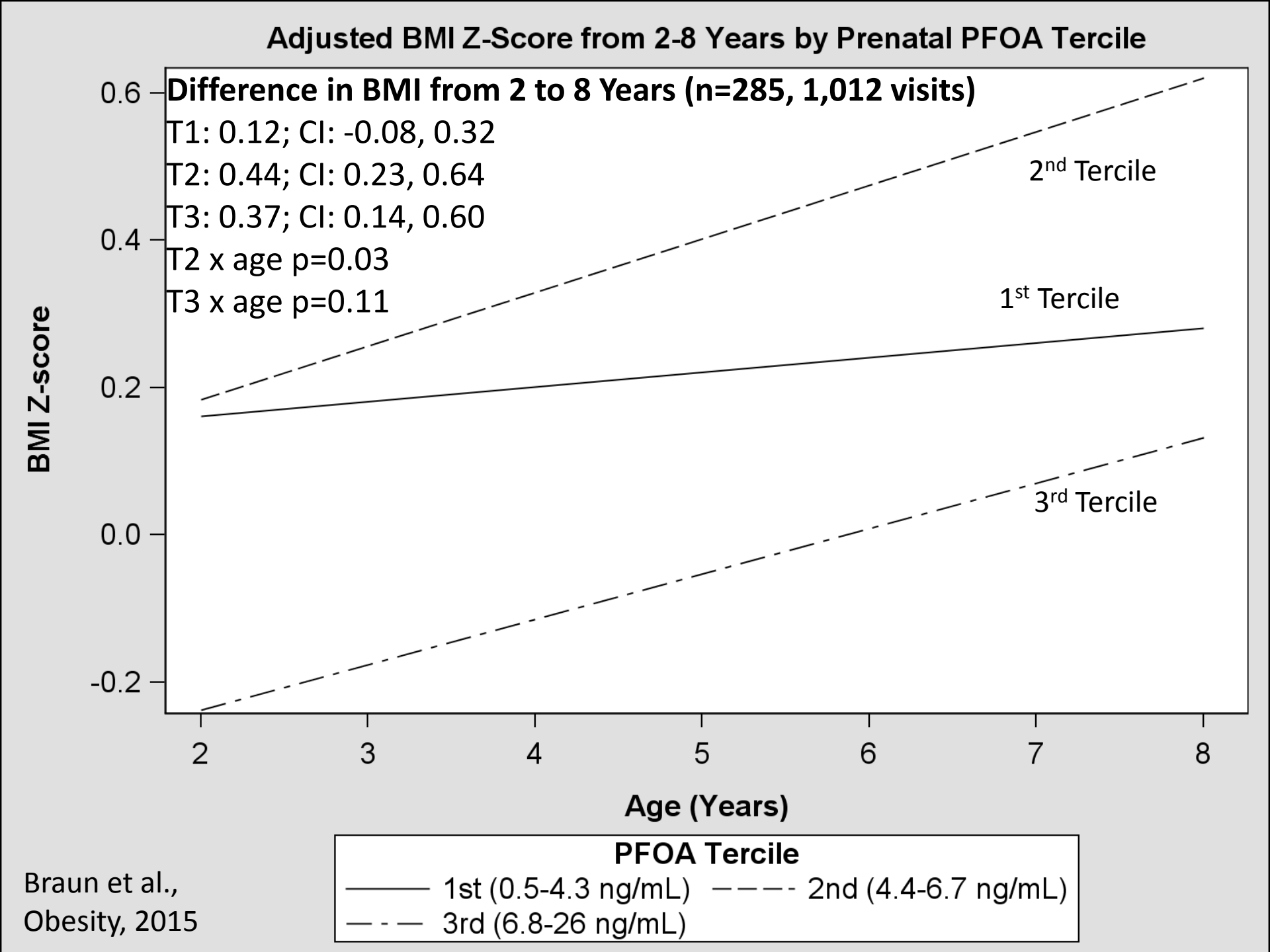
Prenatal PFAS and Child Growth

- Could exposure-related reductions in BW be responsible for excess adiposity later in life?
- Rapid growth in 1st 3 years of life associated with increased adiposity at 6-10 years of age
- Rapid growth also associated with risk of cardiometabolic disease
  - Increased blood pressure, triglycerides, LDL, insulin resistance, and central adiposity

Perng et al., J. Pediatr, 2016, Kelishadi et al., Paediatr Int Child Health, 2015



Braun et al.,
Obesity, 2015

PFAS and Breastfeeding

- PFOA/PFOS exposure during pregnancy associated with decreased breastfeeding duration
  - Doubling in PFOA associated with 0.5 month (95% CI: 0.3, 0.7) reduction in exclusive breastfeeding duration
- Animal studies show that PFAS can influence breast development and lactation hormones

Fei et al., 2010, Romano et al., 2016, and Timmerman et al. 2016, Tucker et al. 2015, White et al. 2007, Yang et al. 2009

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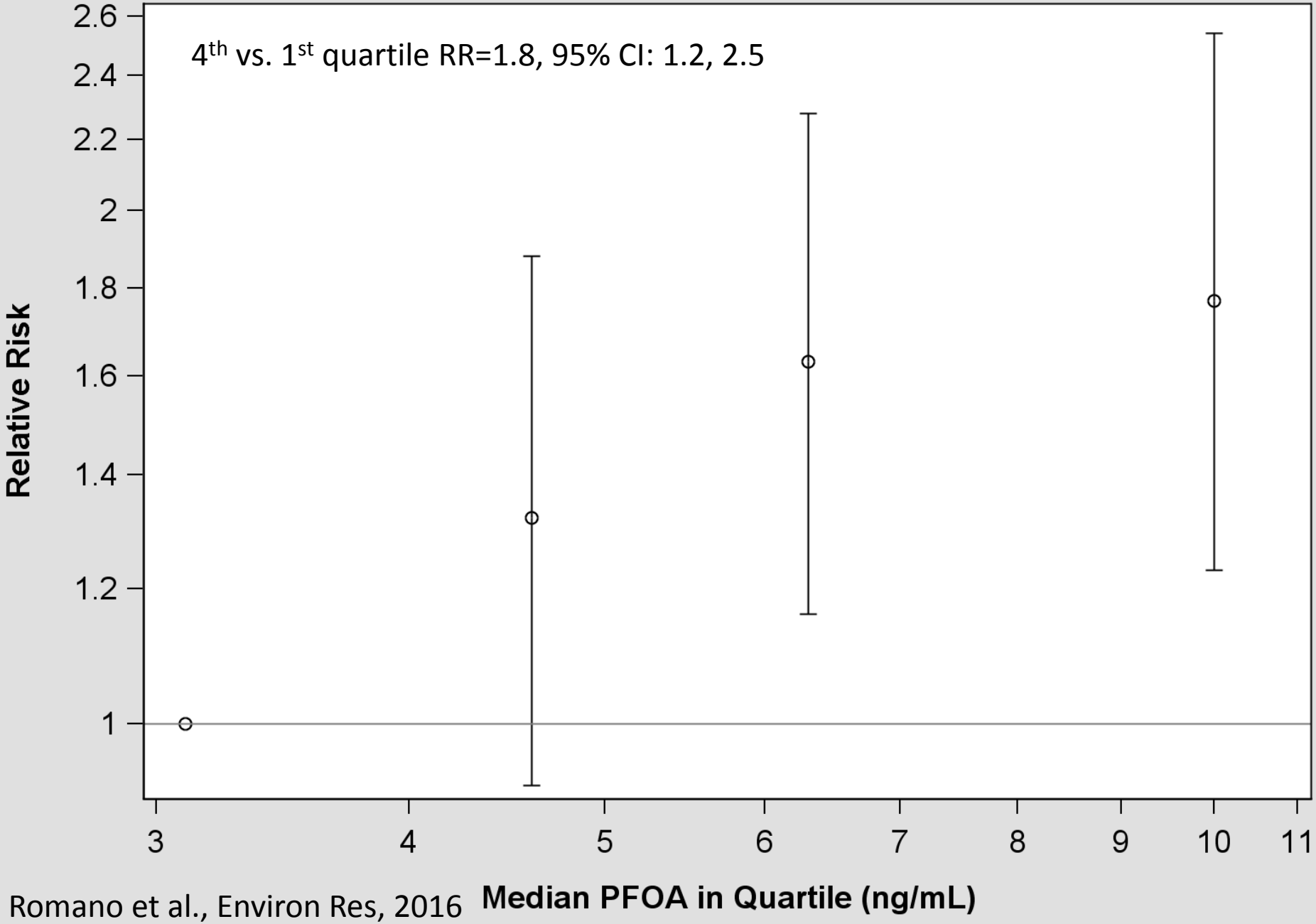
Risk of Quitting Breastfeeding at 3 Months by Prenatal PFOA



Romano et al., Environ Res, 2016

PFAS and Breastfeeding

- Important for mother and infant
- Weanlings dilemma: Does human milk contamination limit the advantage of extended breastfeeding?
- Public health messaging
  - Continue breastfeeding
  - Reduce or minimize exposure

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Summary of PFAS Associations with Growth, Adiposity, and Breastfeeding

- High quality epidemiological data suggest that prenatal PFAS exposure associated with
  - Reduced birth weight
  - Increased risk of obesity/overweight and excess adiposity
    - Possibly through alterations in child growth
  - Decreased duration of lactation

Summary of Other Health Effects

- Neurodevelopment: "Insufficient" evidence to conclude whether PFAS exposures have adverse effects on child neurodevelopment
  - Vrijheid et al. Int J Hyg Environ Health., 2015
  - Braun, Nature Reviews Endocrinology, 2016
- Immune Function: NTP monograph has tentative conclusion that PFOA/PFOS are presumed to be immune hazards to humans
  - http://ntp.niehs.nih.gov/pubhealth/hat/noms/pfoa/index.html

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Implications of Elevated Water PFOA for Human Health

- Using data from Romano et al. 2016 and Hoffman et al. 2011
- Assuming only water exposure, increased risk of quitting breastfeeding at or below current health advisory level

Quartile	Serum PFOA (ng/mL)	Water PFOA (ng/L)	RR of Quitting BF at 3M
1st	3.1	22	Ref
2nd	4.6	33	1.32
3rd	6.3	45	1.63
4th	10	71	1.77

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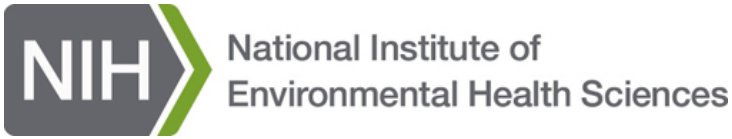

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