Environ Health Perspect

DOI: 10.1289/EHP5184

Note to readers with disabilities: *EHP* strives to ensure that all journal content is accessible to all readers. However, some figures and Supplemental Material published in *EHP* articles may not conform to 508 standards due to the complexity of the information being presented. If you need assistance accessing journal content, please contact ehp508@niehs.nih.gov. Our staff will work with you to assess and meet your accessibility needs within 3 working days.

Supplemental Material

Prenatal Exposures to Perfluoroalkyl Acids and Associations with Markers of Adiposity and Plasma Lipids in Infancy: An Odense Child Cohort Study

Richard Christian Jensen, Marianne S. Andersen, Pia Veldt Larsen, Dorte Glintborg, Christine Dalgård, Clara Amalie Gade Timmermann, Flemming Nielsen, Maria Boysen Sandberg, Helle Raun Andersen, Henrik Thybo Christesen, Philippe Grandjean, and Tina Kold Jensen

Table of Contents

Table S1. Summarizing previously published literature on associations between PFAA and markers of adiposity in infancy.

Table S2. Distribution of mothers and children in the entire Odense Child Cohort and in respective included subsets of participants.

Table S3. Offspring markers of adiposity and lipid metabolism.

Table S4. Prenatal maternal serum PFAA concentrations.

Table S5. Spearman correlation coefficients between five serum PFAA concentrations in pregnant women (n=613).

Table S6. Adjusted difference (β) in lipid outcome in offspring at ages three and 18 months for one unit (ng/mL) increase in maternal pregnancy serum-PFAA concentration obtained from linear regression models.

Table S7. Adjusted difference (β) in lipid concentration in offspring at three and 18 months of age for one unit (ng/mL) increase in maternal pregnancy serum-PFAA concentration stratified according to sex, obtained from linear regression models.

Figure S1. Directed acyclic graph illustrating the causal pathway between maternal pregnancy serum-PFAA concentration (green node) and children's markers of adiposity and lipid metabolism (blue node with I). Red lines represent biasing paths and green lines depict causal paths.

References

Table S1. Summarizing previously published literature on associations between PFAA and markers of adiposity in infancy

Study	Location/setting	Design	Sample size	PFAA	Outcome	Conclusion
(Alkhalawi et al. 2016)	Duisburg Birth Cohort Study, Germany. 2010	Prospective	*n*=156	PFHxS, PFOS, PFOA (From late pregnancy maternal plasma and cord blood)	Birth, and from 1, 4, 6 and 12 months of age: Length, weight, ponderal index (kg/m^3) from examination booklets	PFAA were not significantly associated with longitudinal ponderal index during the child's first year of life assessed by generalized estimating equations.
(Andersen et al. 2010)	Danish National Birth Cohort, Denmark. 1996-2002	Prospective	*n*=1,154	PFOS, PFOA (Maternal plasma from 1st trimester)	At 5 and 12 months of age: Weight and length. Self-reported from the child's book measured by the general practitioner.	PFOA was associated with reduced weight and BMI at five months in boys only. In both sexes, PFOS was significantly associated with decreased body mass index at 12 months of age.
(Braun et al. 2016)	HOME study, America, Cincinnati, Ohio. 2003-2006	Prospective	*n*=285	PFHxS, PFOS, PFOA, PFNA (Maternal serum from gestational week 16 and 26.)	At 2, 3, 4, 5, and 8 years: Weight, length, BMI z score (adj. for sex and age), body fat from clinical examinations at the HOME-study.	Between 2 and 8 years of age, BMI z-scores increased at a greater rate among children in the 2nd and 3rd PFOA tercile compared to children in the 1st tertile. Higher PFOA were associated with increasing BMI z-score, waist circumference, and body fat in a non-monotonic fashion in 8-year-old boys and girls.
(Gyllenhammar et al. 2018)	POPUP study, Uppsala County, Sweden. 1996-2011	Prospective	*n*=381 at birth. *n*=200 at follow-up.	PFHxS, PFOS, PFBS, PFOA, PFNA, PFDA, PFUnDA (Maternal serum three weeks postpartum)	Weight, length, and head circumference at birth from Swedish medical Birth Register. During infancy and childhood (3, 6, 12 and 18 months, and 3, 4, 5 years), measurements of weight, length/height and head circumference from health records. Measures were standardized (SDS).	No significant associations between PFAA and childhood weight SDS from 3 months to 5 years, but tendency of positive associations for PFOA, PFNA, PFHxS, and PFOS already at 3 months. PFOA, PFNA, and PFHxS had a similar pattern with positive associations for BMI SDS at age 3 and 4, however, less strong and not significant at age 5 years

Study	Location/setting	Design	Sample size	PFAA	Outcome	Conclusion
(Halldorsson et al. 2012)	Birth cohort in Aarhus, Denmark, 1988-1989	Prospective	*n*=665	PFOS, PFOA, PFOSA, PFNA (Maternal serum from gestational week 30)	Follow-up 20 years later (2008-2009), height and weight, waist circumference, BMI. Data from clinical examination were used when available (n=423), and the rest (n=242) was self-reported.	Increased concentrations of maternal pregnancy PFOA was associated with increased BMI, waist circumference, and risk of overweight in female offspring at 20 years of age, but not in men.
(Hoyer et al. 2015)	Ukraine and Greenland, 2002-2004	Prospective	*n*=1,023	PFOS, PFOA (Maternal plasma from gestational week 24)	Weight, height, waist circumference, waist-to-height ratio, BMI BMI was standardized according to WHO 2007.	Higher prenatal exposure to PFOS was associated with child obesity (waist-to-height ratio > 0.5) in pooled analysis of Greenlandic and Ukrainian children aged 5-9 years, particularly in girls.
(Karlsen et al. 2017)	Faroe Islands, 2007-2009	Prospective	*n*=444	PFOS, PFOA, PFHxS, PFNA, PFDA (Maternal serum 2 weeks postpartum)	Weight, height, BMI from clinical examinations at ages 18 months and 5 years. BMI was standardized according to WHO.	Increased maternal serum PFOS was associated with increased BMI z-scores and overweight risk at age 18 months, but no association was observed at age 5 years. Same trends were observed for PFOA and PFHxS concentrations in regard to the child's BMI z-scores at age 18 months.
(Maisonet et al. 2012)	The ALSPAC study, Avon, Great Britain. 1991-1992	Prospective	*n*=447	PFOS, PFOA, PFHxS (Maternal serum sample, gestational week 15)	Weight, length, and ponderal index obtained from birth records and from clinical examinations at 2, 9, and 20 months of age. Weight standardized according to British Growth reference curves for girls.	Infant girls with higher prenatal serum concentrations of PFOS, PFOA, and PFHxS during pregnancy tend to be smaller at birth and heavier at 20 months.

Study	Location/setting	Design	Sample size	PFAA	Outcome	Conclusion
(Manzano-Salgado et al. 2017)	INMA birth cohort, Spain 2003-2008	Prospective	*n*=1,243	PFHxS, PFOS, PFOA, PFNA (Maternal plasma from first trimester.)	Weight, height at birth and 6 months of age from medical records. From clinical examinations at 4 and 7 years, waist circumference, weight and height were measured, and BMI was calculated. Weight and BMI were standardized according to WHO.	In boys, a doubling in prenatal PFOA concentrations were positively associated with weight gain z-scores at 6 months of age, but not in girls. At 4 and 7 years, no significant association between PFAA and anthropometric measurements. But a tendency of positive associations between PFHxS and BMI and waist circumference z-scores in girls, while a tendency of inverse association in boys.
(Mora et al. 2017)	Project VIVA, Boston, Massachusetts, America. 1999-2002	Prospective	*n*=1,006	PFHxS, PFOS, PFOA, PFNA (Maternal plasma from 1st trimester)	Weight, height, BMI, hip and waist circumference, and skinfold thickness from clinical examinations in early (3 years) and mid-childhood (7 years). BMI standardized according to US reference data.	In mid-childhood, positive associations were found between prenatal exposure to PFAA and with overall and central adiposity measurements and risk of obesity in girls, but not boys. Null association in early-childhood.
(Shoaff et al. 2018)	HOME study, America, Cincinnati, Ohio. 2003-2006	Prospective	*n*=345	PFHxS, PFOS, PFOA, PFNA (Maternal serum from gestational week 16 and 26.)	Weight-for-age, length-for-age, body mass index (BMI) from clinical examinations at 4 weeks, 1 year, and 2 years old Standardized according to WHO reference data.	Prenatal PFOA tended to be inversely associated with longitudinal measures of infant anthropometry from four weeks to two years of age. No association between PFAA and risk of rapid growth between four weeks and two years of age.
(Starling et al. 2019)	The Healthy Start Study, America, Colorado, 2009-1014	Prospective	*n*=415	PFHxS, PFOS, PFOA, PFNA, PFDA (Maternal serum samples from gestational week 27)	Weight, length, and adiposity (fat mass as percentage of total body mass) from clinical examinations at five months of age. Weight score standardized according to WHO reference data.	In male infants at five months of age, maternal PFNA and PFOA were associated with increased fat mass, whereas PFHxS and PFOS were associated with reduced weight for age in female infants.

Table S2. Distribution of mothers and children in the entire Odense Child Cohort and in respective included subsets of participants

Variables	Odense Child Cohort	Included in anthropometric analyses	Included in lipid analyses (both 3 and 18 months)
Age, years	(*n*=2,608)	(*n*=613)	(*n*=84)
Mean (±standard deviation), years	30.2 (±4.5)	30.2 (±4.5)	30.4 (±4.5)
Pre-pregnancy BMI	(*n*=2,558)	(*n*=613)	(*n*=84)
Median (Interquartile range) (kg/m^2)	23.3 (18.9; 33.3)	23.8 (19.3; 32.6)	24.3 (19.0; 37.0)
Parity	(*n*=2,873)	(*n*=613)	(*n*=84)
Nulliparous (%)	49.2	57.9	56.0
Primi+Multiparous (%)	50.8	42.1	44.0
Smoking	(*n*=2,548)	(*n*=613)	(*n*=84)
Yes (%)	5.7	3.4	3.6
No (%)	94.3	96.6	96.4
Educational level	(*n*=2,778)	(*n*=605)	(*n*=83)
High school or less (%)	31.7	30.4	32.5
High school +1-4 years (%)	48.6	50.9	42.2
High school +>4 years (%)	19.7	18.7	25.3
Ethnicity	(*n*=2,827)	(*n*=613)	(*n*=81)
European	95.8	97.7	98.8
Non-European	4.2	2.3	1.2
Offspring sex	(*n*=2,552)	(*n*=613)	(*n*=84)
Girls	46.9	47.0	48.8
Boys	53.1	53.0	51.2
Gestational age	(*n*=2,553)	(*n*=613)	(*n*=84)
Median (Interquartile range), weeks	40.1 (37.4; 41.9)	40.3 (38.0; 41.9)	40.1 (37.7, 42.0)

Table S3. Offspring markers of adiposity and lipid metabolism

	All children		Girls		Boys	
	n		*n*		*n*	
Birth						
BMI (kg/m^2)	609	13.11 (±1.24)	286	13.05 (±1.20)	323	13.16 (±1.27)
BMI SDS	609	0.02 (±1.01)	286	0.002 (±0.97)	323	0.03 (±1.04)
Ponderal index (kg/m^3)	609	25.12 (±2.35)	286	25.17 (±2.29)	323	25.07 (±2.41)
Ponderal index SDS	609	0.003 (±0.97)	286	-0.01 (±0.93)	323	0.02 (±1.01)
Waist circumference (cm)	606	33.59 (±2.11)	285	33.46 (±2.12)	321	33.70 (±2.10)
Waist circumference SDS	606	0.80 (±1.02)	285	0.66 (±1.01)	321	0.93 (±1.02)
At 3 months						
BMI (kg/m^2)	600	16.84 (±1.46)	281	16.50 (±1.48)	319	17.14 (±1.37)
BMI SDS	600	0.07 (±0.97)	281	0.04 (±0.99)	319	0.09 (±0.94)
Ponderal index (kg/m^3)	600	26.84 (±2.39)	281	26.70 (±2.44)	319	26.97 (±2.35)
Ponderal index SDS	600	-0.03 (±1.00)	281	-0.03 (±1.04)	319	-0.04 (±0.96)
Waist circumference (cm)	599	41.33 (±2.66)	280	40.64 (±2.67)	319	41.92 (±2.50)
Waist circumference SDS	599	-0.13 (±1.00)	280	-0.07 (±1.03)	319	-0.19 (±0.98)
Body fat%	592	16.51 (±2.30)	277	16.22 (±2.21)	315	16.76 (±2.35)
Body fat% SDS	592	0.48 (±0.74)	277	0.46 (±0.70)	315	0.51 (±0.77)
Cholesterol (mmol/L)	262	4.01 (±0.69)	128	4.10 (±0.73)	134	3.91 (±0.62)
Cholesterol SDS	262	-0.01 (±0.97)	128	-0.002 (±0.98)	134	-0.02 (±0.96)
LDL-C (mmol/L)	260	1.97 (±0.67)	127	2.06 (±0.67)	133	1.89 (±0.66)
LDL-C SDS	260	-0.03 (±0.98)	127	-0.01 (±0.98)	133	-0.06 (±0.99)
HDL-C (mmol/L)	262	1.14 (±0.28)	128	1.15 (±0.28)	134	1.13 (±0.27)
HDL-C SDS	262	0.03 (±0.99)	128	-0.03 (±0.96)	134	0.08 (±1.02)
Triglycerides (mmol/L) [§]	262	1.91 (1.20; 3.05)	128	1.88 (1.10; 3.20)	134	1.94 (1.30; 2.89)
Triglycerides SDS	262	-0.03 (±0.96)	128	-0.004 (±1.08)	134	-0.06 (±0.85)
At 18 months						
BMI (kg/m^2)	496	16.41 (±1.22)	230	16.32 (±1.25)	266	16.50 (±1.20)
BMI SDS	496	-0.20 (±1.46)	230	-0.16 (±1.00)	266	-0.23 (±1.03)
Ponderal index (kg/m^3)	496	19.48 (±1.53)	230	19.56 (±1.53)	266	19.42 (±1.53)
Ponderal index SDS	496	-0.10 (±0.99)	230	-0.07 (±1.01)	266	-0.13 (±0.98)
Waist circumference (cm)	486	46.39 (±2.53)	224	46.16 (±2.63)	262	46.59 (±2.43)
Waist circumference SDS	486	-0.41 (±0.87)	224	-0.32 (±0.86)	262	-0.49 (±0.87)
Body fat%	488	15.55 (±2.51)	225	15.67 (±2.55)	263	15.43 (±2.48)
Body fat% SDS	488	0.28 (±0.84)	225	0.22 (±0.83)	263	0.33 (±0.85)
Cholesterol (mmol/L)	199	3.90 (±0.75)	91	4.98 (±0.87)	108	3.84 (±0.63)
Cholesterol SDS	199	-0.02 (±0.99)	91	-0.03 (±1.03)	108	-0.01 (±0.97)
LDL-C (mmol/L)	198	2.27 (±0.69)	90	2.32 (±0.80)	108	2.22 (±0.57)
LDL-C SDS	198	-0.04 (±1.01)	90	-0.07 (±1.08)	108	-0.02 (±0.95)
HDL-C (mmol/L)	198	1.03 (±0.24)	90	1.05 (±0.23)	108	1.01 (±0.25)
HDL-C SDS	198	-0.02 (±0.96)	90	-0.05 (±0.99)	108	0.01 (±0.94)
Triglycerides (mmol/L) [§]	198	1.21 (0.76; 1.94)	90	1.22 (0.82; 1.83)	108	1.20 (0.71; 2.02)
Triglycerides SDS	198	0.02 (±0.93)	90	-0.01 (±0.68)	108	0.04 (±1.10)

Note: Data are presented as mean (±SD). [§]Triglyceride was ln-transformed and reported as geometric mean (mean – SD; mean + SD).

Table S4. Prenatal maternal serum PFAA concentrations

	Included (*n*=613)		
Perfluorinated compound	***n* (%) < LOQ[a]**	**Median (5th; 95th percentile)**	**Geometric Mean (mean-SD; mean+SD)**
Serum PFHxS (ng/mL)	7 (1.1 %)	0.30 (0.08; 0.66)	0.28 (0.14; 0.54)
Serum PFOS (ng/mL)	0 (0 %)	8.04 (3.82; 15.46)	7.93 (5.15; 12.20)
Serum PFOA (ng/mL)	0 (0 %)	1.62 (0.67; 4.03)	1.60 (0.90; 2.83)
Serum PFNA (ng/mL)	0 (0 %)	0.66 (0.33; 1.52)	0.67 (0.42; 1.07)
Serum PFDA (ng/mL)	0 (0 %)	0.26 (0.15; 0.53)	0.27 (0.18; 0.41)

[a] Values below limit of quantification (LOQ) were substituted by LOQ/2.

n: Number, LOQ: Limit of Quantification, SD: Standard deviation

Table S5. Spearman correlation coefficients between five serum PFAA concentrations in pregnant women (*n*=613).

	PFHxS			
PFOS	0.59*	PFOS		
PFOA	0.37*	0.55*	PFOA	
PFNA	0.50*	0.57*	0.59*	PFNA
PFDA	0.33*	0.52*	0.52*	0.74*

*p< 0.05

Table S6. Adjusted difference (β) in lipid outcome in offspring at ages three and 18 months for one unit (ng/mL) increase in maternal pregnancy serum-PFAA concentration obtained from linear regression models.

Compound (ng/mL)	Total cholesterol SDS		LDL SDS		HDL SDS		Triglyceride SDS	
	β (95 % CI)	*p*	β (95 % CI)	*p*	β (95 % CI)	*p*	β (95 % CI)	*p*
PFHxS								
3 months [a]	-0.08 (-0.34, 0.17)	0.51	0.01 (-0.25, 0.25)	0.99	-0.09 (-0.35, 0.17)	0.52	0.18 (-0.08, 0.43)	0.17
18 months [b]	-0.06 (-0.32, 0.21)	0.68	-0.07 (-0.35, 0.22)	0.65	0.01 (-0.24, 0.26)	0.92	-0.23 (-0.51, 0.05)	0.10
PFOS								
3 months [a]	0.01 (-0.03, 0.04)	0.68	0.01 (-0.02, 0.05)	0.44	0.002 (-0.04, 0.04)	0.91	-0.01 (-0.05, 0.02)	0.52
18 months [b]	0.02 (-0.04, 0.08)	0.57	0.04 (-0.03, 0.10)	0.28	-0.03 (-0.09, 0.02)	0.25	0.003 (-0.06, 0.07)	0.94
PFOA								
3 months [a]	-0.08 (-0.18, 0.02)	0.13	-0.03 (-0.13, 0.08)	0.59	-0.07 (-0.18, 0.04)	0.21	-0.03 (-0.14, 0.08)	0.59
18 months [b]	0.07 (-0.08, 0.22)	0.39	0.03 (-0.13, 0.20)	0.69	-0.07 (-0.21, 0.08)	0.36	0.11 (-0.05, 0.27)	0.17
PFNA								
3 months [a]	-0.15 (-0.44, 0.13)	0.30	-0.07 (-0.36, 0.22)	0.63	-0.04 (-0.34, 0.26)	0.79	-0.10 (-0.39, 0.20)	0.52
18 months [b]	0.35 (-0.08, 0.78)	0.11	0.23 (-0.23, 0.70)	0.32	-0.04 (-0.45, 0.38)	0.86	0.18 (-0.27, 0.64)	0.42
PFDA								
3 months [a]	-0.24 (0.91, 0.43)	0.48	-0.08 (-0.75, 0.59)	0.82	-0.01 (-0.70, 0.69)	0.98	-0.21 (-0.89, 0.47)	0.54
18 months [b]	1.01 (0.02, 2.00)	0.04	0.61 (-0.48, 1.69)	0.27	-0.23 (-1.19, 0.74)	0.64	0.94 (-0.10, 1.98)	0.08

Note: CI, Confidence interval; HDL, High-density lipoprotein cholesterol; LDL, Low-density lipoprotein cholesterol; PFDA, Perfluorodecanoic acid; PFHxS, Perfluorohexane sulfonic acid; PFOA, Perfluorooctanoic acid; PFOS, Perfluorooctane sulfonic acid; PFNA, Perfluorononanoic acid; SDS, Standard deviation scores.

[a] Adjusted for maternal age, parity, pre-pregnancy BMI, pre-pregnancy BMI^2, educational level, smoking, sex, and infant BMI at three months. (*n*=259 for total cholesterol SDS, HDL SDS, and triglyceride SDS, and *n*=257 for LDL SDS)

[b] Adjusted for maternal age, parity, pre-pregnancy BMI, pre-pregnancy BMI^2, educational level, smoking, sex, lipid outcome at age three months, and infant BMI at 18 months. (*n*=82 for all markers of lipid metabolism)

Table S7. Adjusted difference (β) in lipid concentration in offspring at three and 18 months of age for one unit (ng/mL) increase in maternal pregnancy serum-PFAA concentration stratified according to sex, obtained from linear regression models.

Compound (ng/mL)	Total cholesterol SDS			LDL SDS			HDL SDS		
	Girls	Boys		Girls	Boys		Girls	Boys	
	β (95 % CI)	β (95 % CI)	$p_{interaction}$ [a]	β (95 % CI)	β (95 % CI)	$p_{interaction}$ [a]	β (95 % CI)	β (95 % CI)	$p_{interaction}$ [a]
PFHxS									
3 months [b]	-0.11 (-0.38, 0.15)	0.08 (-0.63, 0.80)	0.61	0.04 (-0.23, 0.31)	-0.31 (-1.03, 0.41)	0.36	-0.19 (-0.47, 0.08)	0.69 (-0.05, 1.42)	0.03
18 months [c]	-0.05 (-0.32, 0.21)	-0.09 (-1.46, 1.28)	0.96	-0.08 (-0.37, 0.21)	0.36 (-1.10, 1.82)	0.55	0.01 (-0.25, 0.27)	0.13 (-1.21, 1.47)	0.86
PFOS									
3 months [b]	0.01 (-0.04, 0.06)	0.01 (-0.04, 0.06)	0.95	0.04 (-0.01, 0.09)	-0.01 (-0.06, 0.04)	0.22	-0.03 (-0.09, 0.02)	0.03 (-0.02, 0.09)	0.07
18 months [c]	0.01 (-0.07, 0.09)	0.03 (-0.06, 0.12)	0.63	0.04 (-0.04, 0.13)	0.03 (-0.07, 0.12)	0.77	-0.07 (-0.14, 0.01)	0.01 (-0.08, 0.09)	0.19
PFOA									
3 months [b]	-0.07 (-0.22, 0.08)	-0.09 (-0.23, 0.05)	0.83	-0.03 (-0.18, 0.12)	-0.03 (-0.17, 0.11)	0.99	-0.10 (-0.26, 0.05)	-0.04 (-0.19, 0.11)	0.55
18 months [c]	0.14 (-0.04, 0.31)	-0.12 (-0.39, 0.15)	0.11	0.16 (-0.02, 0.34)	-0.29 (-0.57, -0.003)	0.01	-0.07 (-0.24, 0.11)	-0.07 (-0.33, 0.19)	0.99
PFNA									
3 months [b]	-0.07 (-0.48, 0.34)	-0.23 (-0.63, 0.17)	0.59	0.06 (-0.35, 0.48)	-0.20 (-0.60, 0.21)	0.38	-0.33 (-0.75, 0.10)	0.24 (-0.18, 0.65)	0.06
18 months [c]	0.38 (-0.10, 0.87)	0.21 (-0.73, 1.15)	0.75	0.45 (-0.06, 0.97)	-0.60 (-1.61, 0.41)	0.07	-0.14 (-0.62, 0.35)	0.31 (-0.62, 1.23)	0.41
PFDA									
3 months [b]	-0.39 (-1.45, 0.66)	-0.16 (-1.03, 0.72)	0.74	-0.05 (-1.11, 1.01)	-0.10 (-0.99, 0.78)	0.94	-0.82 (-1.95, 0.31)	0.58 (-0.62, 1.79)	0.10
18 months [c]	1.26 (0.11, 2.41)	0.11 (-2.02, 2.24)	0.36	1.53 (0.34, 2.72)	-2.39 (-4.62, -0.17)	<0.01	-0.43 (-1.58, 0.71)	0.41 (-1.68, 2.51)	0.50

Compound (ng/mL)	Triglyceride SDS		
	Girls	Boys	
	β (95 % CI)	β (95 % CI)	$p_{interaction}$ [a]
PFHxS			
3 months [b]	0.20 (-0.07, 0.48)	-0.02 (-0.75, 0.70)	0.56
18 months [c]	-0.22 (-0.50, 0.06)	-0.56 (-1.96, 0.84)	0.63
PFOS			
3 months [b]	-0.01 (-0.06, 0.04)	-0.02 (-0.07, 0.04)	0.85
18 months [c]	-0.04 (-0.12, 0.05)	0.05 (-0.04, 0.14)	0.16
PFOA			
3 months [b]	0.004 (-0.15, 0.16)	-0.06 (-0.20, 0.09)	0.55
18 months [c]	-0.02 (-0.20, 0.15)	0.44 (0.16, 0.71)	<0.01
PFNA			
3 months [b]	0.09 (-0.33, 0.51)	-0.27 (-0.68, 0.14)	0.23
18 months [c]	-0.13 (-0.61, 0.36)	1.40 (0.44, 2.37)	<0.01
PFDA			
3 months [b]	0.12 (-0.95, 1.20)	-0.44 (-1.34, 0.45)	0.43
18 months [c]	-0.13 (-1.24, 0.98)	4.47 (2.39, 6.55)	<0.01

Note: Confidence interval; HDL, High-density lipoprotein cholesterol; LDL, Low-density lipoprotein cholesterol; PFDA, Perfluorodecanoic acid; PFHxS, Perfluorohexane sulfonic acid; PFOA, Perfluorooctanoic acid; PFOS, Perfluorooctane sulfonic acid; PFNA, Perfluorononanoic acid; SDS, Standard deviation scores.

[a] Interaction between the compound and sex on marker of lipid metabolism, adjusted as described under [b] or [c], tested with the Wald test.

[b] Adjusted for maternal age, parity, pre-pregnancy BMI, pre-pregnancy BMI^2, educational level, smoking, and infant BMI at three months. (For total cholesterol SDS, HDL SDS, and triglyceride SDS *n*=125 girls and *n*=134 boys; and for LDL SDS *n*=124 girls and *n*=133 boys.)

[c] Adjusted for maternal age, parity, pre-pregnancy BMI, pre-pregnancy BMI^2, educational level, smoking, lipid outcome at age three months, and infant BMI at 18 months**.** **(**For all lipid outcomes *n*=40 girls and *n*=42 boys.)

Figure S1. Directed acyclic graph illustrating the causal pathway between maternal pregnancy serum-PFAA concentration (green node) and children's markers of adiposity and lipid metabolism (blue node with I). Red lines represent biasing paths and green lines depict causal paths.

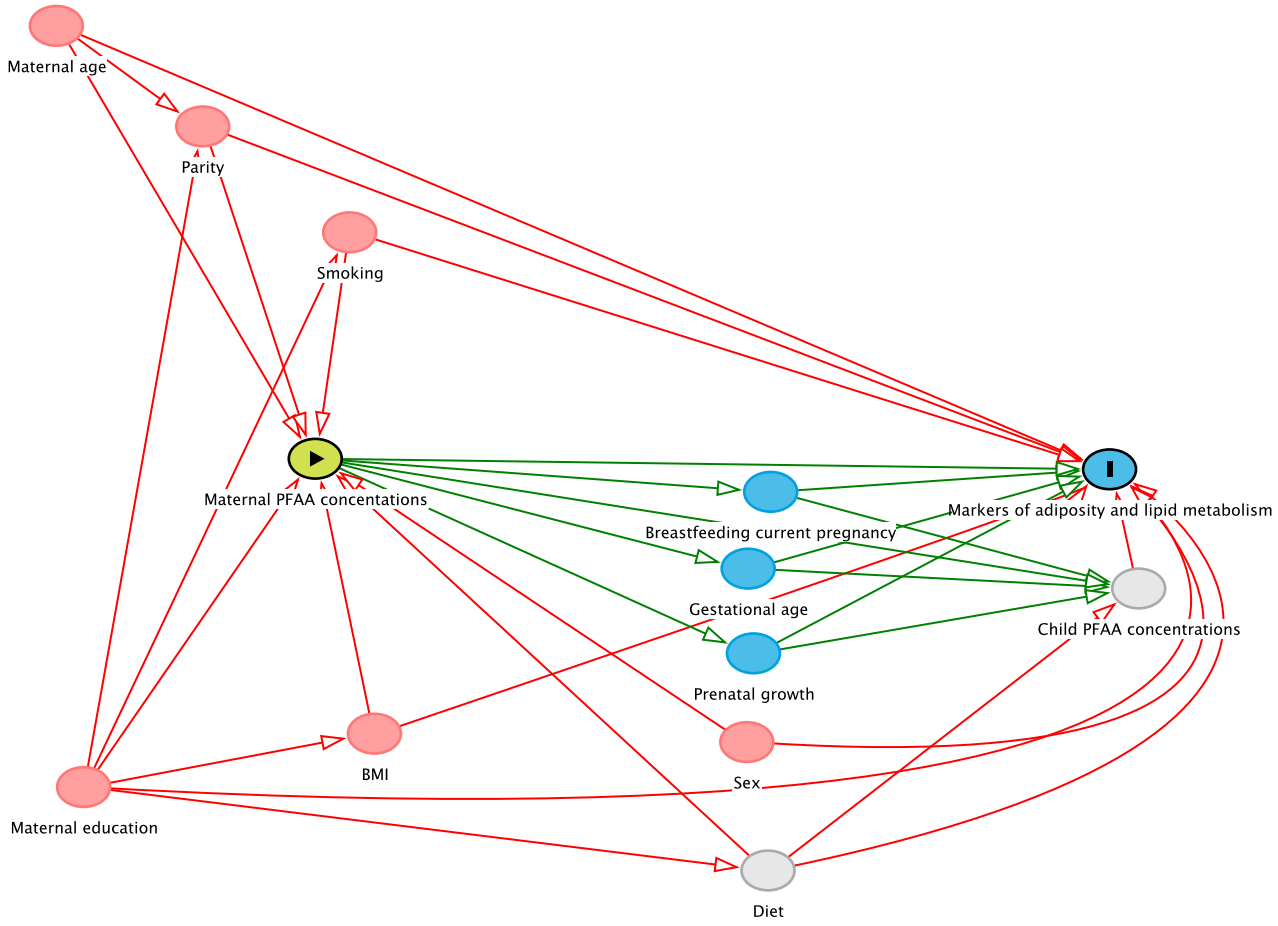

Figure made by use of daggity.net

Reference list

Alkhalawi E, Kasper-Sonnenberg M, Wilhelm M, Volkel W, Wittsiepe J. 2016. Perfluoroalkyl acids (pfaas) and anthropometric measures in the first year of life: Results from the duisburg birth cohort. J Toxicol Environ Health A 79:1041-1049.

Andersen CS, Fei C, Gamborg M, Nohr EA, Sorensen TI, Olsen J. 2010. Prenatal exposures to perfluorinated chemicals and anthropometric measures in infancy. Am J Epidemiol 172:1230-1237.

Braun JM, Chen A, Romano ME, Calafat AM, Webster GM, Yolton K, et al. 2016. Prenatal perfluoroalkyl substance exposure and child adiposity at 8 years of age: The home study. Obesity (Silver Spring, Md) 24:231-237.

Gyllenhammar I, Diderholm B, Gustafsson J, Berger U, Ridefelt P, Benskin JP, et al. 2018. Perfluoroalkyl acid levels in first-time mothers in relation to offspring weight gain and growth. Environ Int 111:191-199.

Halldorsson TI, Rytter D, Haug LS, Bech BH, Danielsen I, Becher G, et al. 2012. Prenatal exposure to perfluorooctanoate and risk of overweight at 20 years of age: A prospective cohort study. Environ Health Perspect 120:668-673.

Hoyer BB, Ramlau-Hansen CH, Vrijheid M, Valvi D, Pedersen HS, Zviezdai V, et al. 2015. Anthropometry in 5- to 9-year-old greenlandic and ukrainian children in relation to prenatal exposure to perfluorinated alkyl substances. Environ Health Perspect 123:841-846.

Karlsen M, Grandjean P, Weihe P, Steuerwald U, Oulhote Y, Valvi D. 2017. Early-life exposures to persistent organic pollutants in relation to overweight in preschool children. Reprod Toxicol 68:145-153.

Maisonet M, Terrell ML, McGeehin MA, Christensen KY, Holmes A, Calafat AM, et al. 2012. Maternal concentrations of polyfluoroalkyl compounds during pregnancy and fetal and postnatal growth in british girls. Environ Health Perspect 120:1432-1437.

Manzano-Salgado CB, Casas M, Lopez-Espinosa MJ, Ballester F, Iniguez C, Martinez D, et al. 2017. Prenatal exposure to perfluoroalkyl substances and cardiometabolic risk in children from the spanish inma birth cohort study. Environ Health Perspect 125:097018.

Mora AM, Oken E, Rifas-Shiman SL, Webster TF, Gillman MW, Calafat AM, et al. 2017. Prenatal exposure to perfluoroalkyl substances and adiposity in early and mid-childhood. Environ Health Perspect 125:467-473.

Shoaff J, Papandonatos GD, Calafat AM, Chen A, Lanphear BP, Ehrlich S, et al. 2018. Prenatal exposure to perfluoroalkyl substances: Infant birth weight and early life growth. Environmental epidemiology (Philadelphia, Pa) 2.

Starling AP, Adgate JL, Hamman RF, Kechris K, Calafat AM, Dabelea D. 2019. Prenatal exposure to per- and polyfluoroalkyl substances and infant growth and adiposity: The healthy start study. Environ Int 131:104983.