SUPPORTING DOCUMENT FOR EPIDEMIOLOGICAL STUDIES FOR PERFLUOROALKYLS

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

March 2020

TABLE OF CONTENTS

EPIDEMIOLOGICAL STUDIES

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Barry et al. 2014 Cross-sectional study of 8,764 20–40-year-old adults participating in the C8 Health Project; height and weight data self-reported; early life exposure and obesity in adults	**Exposure:** Average early life (first 3 years) PFOA blood levels based on environmental levels of PFOA (based on lifetime residential history) and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life; maternal serum levels were factored into early life estimates for years 1 and 2. Estimated serum PFOA levels above background were used for the analysis. **Logistic regression model adjustments:** Age, cigarette smoking, education, average walking pace	No significant association between early life PFOA exposure and overweight or obesity risks at age 20–40 years; OR 0.9 (95% CI 0.7–1.1) and OR 0.9 (95% CI 0.7–1.1) in women and men, respectively, with estimated above-background serum PFOA levels in the 6th quintile (medians of 194.3 and 164.6 ng/mL in women and men).
Alkhalawi et al. 2016 Retrospective study of 156 mother-child pairs participating in the Duisburg Birth Cohort study in Germany; weight and length recorded at birth and at 1, 4, 6, and 12 months of age	**Exposure:** Geometric mean maternal serum PFOA 2.43 ng/mL; 1st quartile: <0.4–1.97 ng/mL, 2nd quartile: 1.99–2.73 ng/mL, 3rd quartile: 2.75–3.48 ng/mL, 4th quartile: 3.52–9.20 ng/mL **Statistical adjustments:** Pregnancy duration, maternal BMI before pregnancy, maternal height, maternal blood lead levels, infant sex, mode of delivery, mother place of birth, smoking during pregnancy	No association (p>0.05) between maternal PFOA and infant body weight or length at specific measurement times or in longitudinal analysis.
Andersen et al. 2010 Cross-sectional study of 1,010 infants (follow-up to Fei et al. 2007); infant data obtained from questionnaire completed by the mother	**Exposure:** Median maternal serum PFOA levels (measured during first trimester) 5.21 ng/mL (range: 0.5–21.9 ng/mL) **Linear regression model adjustments:** Maternal age, parity, prepregnancy BMI, smoking during pregnancy, socioeconomic status, gestational week at blood draw, duration of breastfeeding, child's exact age at measurements	Significant inverse association (p<0.05) between maternal serum PFOA and body weight and BMI in boys at 5 and 12 months of age. No association (p>0.05) with height in boys at 12 months of age. No significant association (p>0.05) between maternal serum PFOA and body weight and BMI at 5 and 12 months of age in girls or in boys and girls combined.

EPIDEMIOLOGICAL STUDIES

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Andersen et al. 2013 Cross-sectional study of 811 7-year-old children (follow-up to Fei et al. 2007); data regarding size obtained from the mothers	**Exposure:** Median maternal serum PFOA levels (measured during first trimester) 5.25 ng/mL (range: 0.5–21.9 ng/mL) **Linear regression model adjustments:** Maternal age, parity, prepregnancy BMI, smoking during pregnancy, socioeconomic status, gestational week at blood draw, duration of breastfeeding, child's exact age at measurements	No significant association (p>0.05) between maternal PFOA levels and child BMI or waist circumference at 7 years of age.
Braun et al. 2016a, 2016b Prospective study of 204 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; height, weight, waist circumference, and body fat were measured when the children were 8 years of age; height and weight were also measured at ages 2, 3, 4, and 5 years	**Exposure:** Median maternal serum PFOA levels (measured at 16 weeks of gestation): 5.3 ng/mL **Statistical adjustments:** Maternal age, race, education, marital status, employment, household income, maternal depressive symptoms, maternal BMI at 16 weeks of gestation, parity, maternal serum cotinine, frequency of fruit/vegetable and fish consumption during pregnancy, prenatal vitamin use	A positive association between maternal PFOA levels and adiposity scores (BMI, waist circumference, and body fat) was observed at maternal serum PFOA levels in the 15th and 50th percentiles. At the 90th and 95th percentile, there were inverse associations between PFOA and adiposity scores. Between ages 2 and 8 years, BMI scores increased at a greater rate in children with maternal serum PFOA levels in the 2nd and 3rd tertiles, as compared to children in the 1st tertile (p=0.03). No significant increases in the risk of overweight/obesity at age 8 years were observed; the relative risks for serum PFOA levels in the 2nd and 3rd tertiles were RR 1.84 (95% CI 0.97–3.50) and RR 1.54 (95% CI 0.77–3.07).
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age.	**Exposure:** Mean umbilical cord serum PFOA 1.59 ng/mL; 1st tertile <0.99 ng/mL, 2nd tertile 0.99–1.59 ng/mL, 3rd tertile >1.59 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFOA and postnatal body weight (p=0.57), postnatal length (p=0.16), or postnatal head circumference (p=0.94).

EPIDEMIOLOGICAL STUDIES

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
de Cock et al. 2014 Cross-sectional study of 89 mother-infant pairs in the Netherlands; weight, height, and head circumference were measured at 1, 2, 4, 6, 9, and 11 months of age	**Exposure:** Mean and median cord blood plasma PFOA levels were 0.9402 and 0.870 ng/mL **Statistical adjustments:** Maternal/paternal BMI, height, birth weight, gestational age, parity, alcohol, smoking, education, breastfeeding duration	Significant association between cord blood plasma PFOA and infant height (p=0.045). No significant association between cord blood plasma PFOA and infant BMI (p=0.813), weight (p=0.350), or head circumference (p=0.774).
Halldorsson et al. 2012 Prospective cohort study of 665 offspring of women participating in a birth cohort study in Denmark; the offspring were examined at 20 years of age	**Exposure:** Median maternal serum PFOA level (measured at gestation week 30) 3.7 ng/mL **Statistical adjustments:** Maternal age, maternal education, maternal prepregnancy BMI, smoking during pregnancy, parity, infant birth weight, and offspring age at follow-up	Significant positive associations between BMI (p=0.001) and waist circumference (p=0.006) in female offspring and maternal serum PFOA levels. Increased risk of being overweight (BMI ≥25 kg/m^2) (RR 3.1, 95% CI 1.4–6.9) or having a high waist circumference (RR 3.0, 95% CI 1.3–6.8) were also observed in female offspring of mothers with serum PFOA levels in the 4th quartile (median 5.8, range 4.8–19.8). No statistically significant association between maternal PFOA and BMI (p=0.30) or waist circumference (p=0.48) was observed in male offspring. Biomarkers of adiposity—insulin (p=0.001), leptin (p=0.03), and leptin-adiponectin ratio (p=0.004)—were positively associated with maternal serum PFOA levels in female offspring and adiponectin levels were negatively associated (p=0.03) with serum PFOA levels.

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Hartman et al. 2017 Prospective cohort study of 359 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data were obtained from medical records; weight and height at age 9 years were measured	**Exposure:** Median maternal serum PFOA (measured at gestation week 15) 3.7 ng/mL **Linear regression model adjustments:** Sampling design, maternal prepregnancy BMI, maternal education	No association between maternal serum PFOA and total body fatness (evaluated using dual-energy x-ray absorptiometry) in girls (β -0.30, 95% CI -0.76–0.16, p=0.20) or trunk fatness (β -0.27, 95% CI -0.55–0.00, p=0.05). No association for BMI (β -0.16, 95% CI -0.32–0.00, p=0.05). When stratified based on maternal education, an association was found for total body fatness in the medium education (β 1.41, 95% CI 0.28–2.54, p=0.01) or high education (β -0.58, 95% CI -1.12 to -0.04, p=0.03).
Høyer et al. 2015b Prospective study of 1,022 children of mothers participating in the INUENDO cohort in Greenland (n=531) and Ukraine (n=491); weight and height were measured when the children were between 5 and 9 years of age	**Exposure:** Median maternal serum PFOA (measured at any time during pregnancy): 1.8 ng/mL for Greenland cohort and 1.0 ng/mL for Ukraine cohort **Statistical adjustments:** Maternal age at birth, prepregnancy BMI, smoking during pregnancy, education, parity	No significant associations between maternal PFOA levels and risk of children being overweight were found; RR 1.23 (95% CI 0.87–1.74) for Greenland children with maternal PFOA levels in the 3rd tertile (2.2–5.1 ng/mL) and RR 0.78 (95% CI 0.47–1.29) for Ukraine children with maternal PFOA levels in the 3rd tertile (1.1–9.8 ng/mL). No significant association between maternal PFOA levels and risk of children having a waist-to-height ratio of >0.5 was observed for the combined cohort (RR 1.30, 95% CI 0.97–1.74 for continuous PFOA). The associations were not significant for children with maternal PFOA levels in the 3rd tertile: RR 1.18 (95% CI 0.80–1.74) for Greenland and RR 1.11 (95% CI 0.48–2.57) for Ukraine cohorts.

EPIDEMIOLOGICAL STUDIES

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Karlsen et al. 2017 Prospective study of 444 mother-child pairs in the Faroe Islands; children's height and weight measurements were taken at ages 18 months and 5 years	**Exposure:** Maternal geometric mean serum PFOA (measured 2 weeks after childbirth) 1.37 ng/mL (range of 0.25–6.49 ng/mL) and child geometric mean serum PFOA (measured at age 5 years) 2.22 ng/mL (range of 0.68–13.3 ng/mL) **Statistical adjustments:** Maternal nationality, age at delivery, prepregnancy BMI, gestational weight gain, parity, smoking during pregnancy, maternal fish intake during pregnancy, type of delivery, child sex and birth weight	No association between maternal serum PFOA and child's BMI z-score at 18 months (β 0.14, 95% CI -0.03–0.31, p>0.05) or 5 years of age (β 0.16, 95% CI -0.01–0.33, p>0.05). Association between maternal serum PFOA and child's risk of child being overweight at 5 years of age (RR 1.50, 95% CI 1.01–2.24, p<0.05), but no association at 18 months (RR 1.14, 95% CI 0.92–1.40). Inverse association between child serum PFOA and BMI score at age 5 years (β -0.27, 95% CI -0.52 to -0.02). No association with risk of being overweight (RR 0.68, 95% CI 0.38–1.22).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOA 1.81 ng/mL (WTCHR group) and 1.39 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFOA and risk of being overweight (OR 0.98, 95% CI 0.90–1.13, p=0.97).
Liu et al. 2018a Prospective study of 624 adults participating in the POUNDS Lost randomized 2-year clinical weight loss trial in Boston, Massachusetts and Baton Rouge, Louisiana	**Exposure:** Median serum PFOA 4.5 ng/mL (range 3.3–6.3 ng/mL) **Statistical adjustments:** Smoking status, physical activity, baseline BMI, dietary intervention group	No association between serum PFOA and weight loss during first 6 months of study (p=0.73, trend). No association between PFOA and weight regain between study months 6 and 24 (p=0.16, trend). Dividing the subjects by sex resulted in significant associations in weight regain in females (p=0.007, trend), but not in males (p=0.78, trend). PFOA was not associated with greater decline in resting metabolic rate during weight loss period (p=0.48, trend), but associated with lower increase in resting metabolic rate during weight regain period (p=0.03, trend).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFOA 2.32 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFOA and weight gain until 6 months of age (β 0.04, 95% CI -0.04–0.12). No association between maternal serum PFOA and BMI score at 4 years of age (β 0.04, 95% CI -0.04–0.13) or 7 years of age (β 0.03, 95% CI -0.08–0.13). No association between maternal serum PFOA and waist circumference score at 4 years of age (β 0.00, 95% CI -0.09–0.10) or 7 years of age (β -0.02, 95% CI -0.11–0.06).
Mora et al. 2017 Prospective study of children (n=1,006 at median age of 3.2 years and n=876 at median age of 7.7 years) participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFOA 5.6 ng/mL in early childhood group and 5.6 ng/mL in late childhood group (measured during first trimester) **Statistical adjustments:** Maternal age, race/ethnicity, education, parity prepregnancy BMI, timing of blood draw, household income, child sex and age at outcome assessment	Association between maternal PFOA and early childhood waist circumference (β 0.31, 95% CI 0.04–0.57) in boys and girls combined and in boys only (β 0.50, 95% CI 0.06–0.93), but not in girls only (β 0.14, 95% CI -0.18–0.47). No associations (boys and girls combined) between maternal PFOA and early childhood BMI (β 0.09, 95% CI -0.02–0.19), subscapular and triceps skinfold thickness (β 0.19, 95% CI -0.12–0.49), waist-to-hip circumference (β 0.18, 95% CI -0.24–0.59), or subscapular to triceps skinfold thickness ratio (β 0.55, 95% CI -0.58–1.68). No associations (boys and girls combined) between maternal PFOA and mid childhood BMI (β 0.13, 95% CI -0.10–0.35), subscapular and triceps skinfold thickness (β 0.49, 95% CI -0.23–1.20), total fat mass index (β 0.13, 95% CI -0.02–0.29), total fat-free mass index (β 0.06, 95% CI -0.05–0.17), waist circumference (β 0.20, 95% CI -0.39–0.80), waist-to-hip circumference (β 0.11, 95% CI -0.36–0.59), subscapular to triceps skinfold thickness ratio (β 1.02, 95% CI -0.41–1.52), or trunk fat mass index (β 0.06, 95% CI -0.01–0.13).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		No associations (boys and girls combined) between maternal PFOA and risk of being overweight in early childhood (RRR 1.05, 95% CI 0.87–1.26) or mid childhood (RRR 1.02, 95% CI 0.88–1.29) or being obese in early childhood (RRR 1.03, 95% CI 0.80–1.32) or mid childhood (RRR 1.10, 95% CI 0.88–1.37).
Timmermann et al. 2014 Cross-sectional study of 499 Danish children (8–10 years of age) participants of the European Youth Heart Study; insulin, HOMA-β, HOMA-IR, glucose, and triglyceride levels were used as markers of glycemic control, and BMI, skinfold thickness, waist circumference, adiponectin, and leptin levels were used as markers of adiposity	**Exposure:** Median plasma concentration of PFOA 9.3 ng/mL (range: 0.8–35.2 ng/mL) **Linear regression model adjustments:** Sex, age, ethnicity, paternal income, fast food consumption, and fitness; model adjusted for height when using waist circumference as outcome measured	Increases of 10 ng/mL plasma PFOA were not associated with significant (p>0.05) alterations in markers of adiposity. No significant associations (p>0.05) between PFOA and markers of glycemic control among normal-weight children. Among overweight children, an increase of 10 ng/mL plasma PFOA was associated with 71.6% (95% CI 2.4–187.5) increase in insulin levels (p=0.04), 67.5% (95% CI 5.5–166.0) increase in HOMA-β levels (p=0.03), 73.9% (95% CI 0.2–202.0), increase in HOMA-IR levels (p=0.05), and 76.2% (95% CI 22.8–153.0) increase in triglyceride levels (p=0.002). No significant association (p=0.71) between plasma PFOA and glucose levels.
Wang et al. 2016 Prospective cohort study of 223 children (117 boys and 106 girls) whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at birth and at 2 (n=82 males, 80 females), 5 (n=51 males, 50 females), 8 (n=48 males, 47 females), and 11 (n=48 males, 46 females) years of age	**Exposure:** Median maternal serum PFOA (measured during third trimester) 2.37 ng/mL for male children and 2.34 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	No significant association (p>0.05) between maternal PFOA levels and growth (weight and height) during childhood.

EPIDEMIOLOGICAL STUDIES

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Alkhalawi et al. 2016 Retrospective study of 156 mother-child pairs participating in the Duisburg Birth Cohort study in Germany; weight and length recorded at birth and at 1, 4, 6, and 12 months of age	**Exposure:** Geometric mean maternal serum PFOS 9.04 ng/mL; 1st quartile: 1.70–6.98 ng/mL, 2nd quartile: 7.02–9.31 ng/mL, 3rd quartile: 9.33–11.80 ng/mL, 4th quartile: 11.86–21.93 ng/mL **Statistical adjustments:** Pregnancy duration, maternal BMI before pregnancy, maternal height, maternal blood lead levels, infant sex, mode of delivery, mother place of birth, smoking during pregnancy	No association (p>0.05) between maternal PFOS and infant body weight or length at specific measurement times or in longitudinal analysis.
Andersen et al. 2010 Cross-sectional study of 1,010 infants (follow-up to Fei et al. 2007); infant data obtained from questionnaire completed by the mother	**Exposure:** Median maternal serum PFOS levels (measured during first trimester) 33.8 ng/mL (range: 6.4–106.7 ng/mL) **Linear regression model adjustments:** Maternal age, parity, prepregnancy BMI, smoking during pregnancy, socioeconomic status, gestational week at blood draw, duration of breastfeeding, child's exact age at measurements	Inverse association between maternal serum PFOS and body weight (β -9 g, 95% CI -15.9 to -2.2 g per 1 ng/mL PFOS, p<0.05) and BMI (β -0.17, 95% CI -0.028 to -0.005 per 1 ng/mL PFOS, p<0.01) in boys at 12 months of age. No association (p>0.05) with height in boys at 12 months of age. No significant association (p>0.05) between maternal serum PFOA and body weight and BMI at 5 months of age in boys or girls or at 12 months of age in girls.
Andersen et al. 2013 Cross-sectional study of 811 7-year-old children (follow-up to Fei et al. 2007); data regarding size obtained from the mothers	**Exposure:** Median maternal serum PFOS levels (measured during first trimester) 33.8 ng/mL (range: 6.4–106.7 ng/mL) **Linear regression model adjustments:** Maternal age, parity, prepregnancy BMI, smoking during pregnancy, socioeconomic status, gestational week at blood draw, duration of breastfeeding, child's exact age at measurements	No significant association (p>0.05) between maternal PFOS levels and child BMI or waist circumference at 7 years of age.

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Braun et al. 2016a, 2016b Prospective study of 204 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; height, weight, waist circumference, and body fat were measured when the children were 8 years of age; height and weight were also measured at ages 2, 3, 4, and 5 years	**Exposure:** Median maternal serum PFOS levels (measured at 16 weeks of gestation): 13 ng/mL **Statistical adjustments:** Maternal age, race, education, marital status, employment, household income, maternal depressive symptoms, maternal BMI at 16 weeks of gestation, parity, maternal serum cotinine, frequency of fruit/vegetable and fish consumption during pregnancy, prenatal vitamin use	No association between maternal serum PFOS levels and child adiposity scores or changes in BMI scores between 2 and 8 years of age ($p>0.23$). No significant increases in the risk of overweight/obesity at age 8 years were observed; the relative risks for serum PFOS levels in the 2nd and 3rd tertiles were RR 0.87 (95% CI 0.48–1.56) and RR 1.08 (95% CI 0.59–1.95).
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFOS 1.43 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFOS and postnatal body weight ($p=0.72$), postnatal length ($p=0.91$), or postnatal head circumference ($p=0.63$) at 19 months of age.
Halldorsson et al. 2012 Prospective cohort study of 665 offspring of women participating in a birth cohort study in Denmark; the offspring were examined at 20 years of age	**Exposure:** Median maternal serum PFOS level (measured at gestation week 30) 21.5 ng/mL **Statistical adjustments:** Maternal age, maternal education, maternal prepregnancy BMI, smoking during pregnancy, parity, infant birth weight, offspring age at follow-up	No significant associations ($p>0.56$) between maternal serum PFOS and offspring BMI and waist circumference were found.
Hartman et al. 2017 Prospective cohort study of 359 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data were obtained from medical records; weight and height at age 9 years were measured	**Exposure:** Median maternal serum PFOS (measured at gestation week 15) 19.7 ng/mL **Linear regression model adjustments:** Sampling design, maternal prepregnancy BMI, maternal education	Inverse association between maternal serum PFOS and trunk body fatness (evaluated using dual-energy x-ray absorptiometry) in girls (β -0.06 95% CI -0.12 to -0.01, $p=0.02$) and with BMI (β -0.04, 95% CI -0.07–0.00, $p=0.03$). No association between maternal serum PFOS and total body fatness (β -0.07, 95% -0.16–0.02, $p=0.12$). When stratified based on maternal education, an inverse association was found for total body

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		fatness in the high education group (β -0.07, 95% CI -0.11 to -0.03, p=0.001).
Høyer et al. 2015b Prospective study of 1,022 children of mothers participating in the INUENDO cohort in Greenland (n=531) and Ukraine (n=491); weight and height were measured when the children were between 5 and 9 years of age	**Exposure:** Median maternal serum PFOS (measured at any time during pregnancy): 20.2 ng/mL for Greenland cohort and 5.0 ng/mL for Ukraine cohort **Statistical adjustments:** Maternal age at birth, prepregnancy BMI, smoking during pregnancy, education, parity	No significant association between maternal PFOS levels and risk of children being overweight were found; RR 0.84 (95% CI 0.61–1.14) for Greenland children with maternal PFOS levels in the 3rd tertile (23.9–87.3 ng/mL) and RR 0.89 (95% CI 0.57–1.37) for Ukraine children with maternal PFOS levels in the 3rd tertile (5.9–18.1 ng/mL). Significant association between maternal PFOS levels and risk of children having a waist-to-height ratio of >0.5 was observed for the combined cohort (RR 1.38, 95% CI 1.05–1.82, continuous PFOS). When segregated by sex, a significant association was found in girls (RR 1.54, 95% CI 1.06–2.23), but not in boys (RR 1.24, 95% CI 0.82–1.87). The associations were not significant for children with maternal PFOS levels in the 3rd tertile: RR 1.22 (95% CI 0.86–1.74) for Greenland and RR 1.44 (95% CI 0.62–3.31) for Ukraine.
Karlsen et al. 2017 Prospective study of 444 mother-child pairs in the Faroe Islands; children's height and weight measurements were taken at ages 18 months and 5 years	**Exposure:** Maternal geometric mean serum PFOS (measured 2 weeks after childbirth) 8.04 ng/mL (range of 1.89–24.6 ng/mL) and child geometric mean serum PFOA (measured at age 5 years) 4.68 ng/mL (range of 0.68–16.3 ng/mL) **Statistical adjustments:** Maternal nationality, age at delivery, prepregnancy BMI, gestational weight gain, parity, smoking during pregnancy, maternal fish intake during pregnancy, type of delivery, child sex and birth weight	Association between maternal serum PFOS and child's BMI z-score at 18 months (β 0.23, 95% CI 0.04–0.42 p<0.05), but no association at 5 years of age (β 0.04, 95% CI -0.15–0.22, p>0.05). Association between maternal serum PFOS and child's risk of child being overweight at 18 months of age (RR 1.29, 95% CI 1.01–1.64, p<0.05), but no association at 5 years (RR 1.01, 95% CI 0.58–1.75). No associations between child serum PFOS and BMI score at age 5 years (β -0.21, 95% CI -0.44–0.02) or risk of being overweight (RR 0.68, 95% CI 0.36–1.29).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOS 3.72 ng/mL (WTCHR group) and 2.78 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFOS and risk of being overweight (OR 1.00, 95% CI 0.90–1.07, p=0.66).
Liu et al. 2018a Prospective study of 624 adults participating in the POUNDS Lost randomized 2-year clinical trial in Boston, Massachusetts and Baton Rouge, Louisiana	**Exposure:** Median serum PFOS 24.5 ng/mL (range 16.2–37.0 ng/mL) **Statistical adjustments:** Smoking status, physical activity, baseline BMI, dietary intervention group	No association between serum PFOS and weight loss during first 6 months of study (p=0.27, trend). PFOS associated with greater weight regain between study months 6 and 24 (p=0.009, trend). Dividing the subjects by sex resulted in significant associations in weight regain in females (p=0.001, trend), but not in males (p=0.34, trend). PFOS associated with greater decline in resting metabolic rate during weight loss period (p<0.001, trend) and lower increase in resting metabolic rate during weight regain period (p<0.001, trend).
Maisonet et al. 2012 Prospective cohort study of 447 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data were obtained from medical records; weight and height at age 2 and 20 months were measured	**Exposure:** Median maternal serum PFOS (measured at gestation week 15) 19.6 ng/mL (range: 3.8–112.0 ng/mL) **Linear regression model adjustments:** Maternal smoking during pregnancy (birth weight and length only), maternal prepregnancy BMI, previous live births, gestational age, maternal education (birth length only)	No significant trend with unadjusted weight at 20 months (p=0.0598). Significant trend when weight at 20 months was adjusted by birth weight (p=0.0195), adjusted for height (p=0.0008) and when adjusted by height and weight (p<0.0001).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFOS 5.80 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFOS and weight gain from birth to 6 months of age (β -0.02, 95% CI -0.11–0.07). No association between maternal serum PFOS and BMI score at 4 years of age (β 0.04, 95% CI -0.05–0.13) or 7 years of age (β 0.03, 95% CI -0.08–0.14). No association between maternal serum PFOS and waist circumference score at 4 years of age (β -0.03, 95% CI -0.13–0.07) or 7 years of age (β 0.00, 95% CI -0.09–0.09).
Mora et al. 2017 Prospective study of children (n=1,006 at median age of 3.2 years and n=876 at median age of 7.7 years) participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFOS 24.8 ng/mL in early childhood group and 24.7 ng/mL in late childhood group (measured during first trimester) **Statistical adjustments:** Maternal age, race/ethnicity, education, parity prepregnancy BMI, timing of blood draw, household income, child sex and age at outcome assessment	Association between maternal PFOS and early childhood BMI (β 0.04, 95% CI 0.05–0.12) in boys and girls combined, but not sex-stratified analyses of boys only (β 0.02, 95% CI -0.11–0.15) or girls only (β 0.04, 95% CI -0.08–0.16). No associations (boys and girls combined) between maternal PFOS and early childhood subscapular and triceps skinfold thickness (β -0.10, 95% CI -0.36–0.16), waist circumference (β 0.05, 95% CI -0.17–0.27), waist-to-hip circumference (β 0.00, 95% CI -0.35–0.34), or subscapular to triceps skinfold thickness ratio (β 0.25, 95% CI -0.70–1.20). No associations (boys and girls combined) between maternal PFOS and mid childhood BMI (β 0.16, 95% CI -0.04–0.36), subscapular and triceps skinfold thickness (β 0.47, 95% CI -0.16–1.10), total fat mass index (β 0.11, 95% CI -0.03–0.25), total fat-free mass index (β 0.08, 95% CI -0.01–0.18), waist circumference (β 0.34, 95% CI -0.19–0.87), waist-to-hip circumference (β 0.38, 95% CI -0.04–0.80), subscapular to triceps skinfold thickness ratio

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		(β 0.96, 95% CI -0.31–2.23), or trunk fat mass index (β 0.05, 95% CI -0.02–0.11). No association (boys and girls combined) between maternal PFOS and risk of being overweight in early childhood (RRR 1.07, 95% CI 0.92–1.24) or mid childhood (RRR 1.15, 95% CI 0.95–1.40) or being obese in early childhood (RRR 0.97, 95% CI 0.76–1.23) or mid childhood (RRR 1.12, 95% CI 0.99–1.47)
Timmermann et al. 2014 Cross-sectional study of 499 Danish children (8–10 years of age) participants of the European Youth Heart Study; insulin, HOMA-β, HOMA-IR, glucose, and triglyceride levels were used as markers of glycemic control, and BMI, skinfold thickness, waist circumference, adiponectin, and leptin levels were used as markers of adiposity	**Exposure:** Median plasma concentration of PFOS 41.5 ng/mL (range: 6.2–132.5 ng/mL) **Linear regression model adjustments:** Sex, age, ethnicity, paternal income, fast food consumption, and fitness; model adjusted for height when using waist circumference as outcome measured	Increases of 10 ng/mL plasma PFOS were not associated with significant (p>0.05) alterations in markers of adiposity. No significant associations (p>0.05) between PFOS and markers of glycemic control among normal-weight children. Among overweight children, an increase of 10 ng/mL plasma PFOS was associated with 16.2% (95% CI 5.2–28.3) increase in insulin levels (p=0.003), 12.0% (95% CI 2.4–22.4) increase in HOMA-β levels (p=0.01), 17.6% (95% CI 5.8–30.8) increase in HOMA-IR levels (p=0.003), and 8.6% (95% CI 1.2–16.5) increase in triglyceride levels (p=0. 02). No significant association (p=0.09) between plasma PFOS and glucose levels.

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHxS		
Alkhalawi et al. 2016 Retrospective study of 156 mother-child pairs participating in the Duisburg Birth Cohort study in Germany; weight and length recorded at birth and at 1, 4, 6, and 12 months of age	**Exposure:** Geometric mean maternal serum PFHxS 0.62 ng/mL; 1st quartile: <0.2–0.54 ng/mL, 2nd quartile: 0.55–0.76 ng/mL, 3rd quartile: 0.79–0.97 ng/mL, 4th quartile: 0.97–1.72 ng/mL **Statistical adjustments:** Pregnancy duration, maternal BMI before pregnancy, maternal height, maternal blood lead levels, infant sex, mode of delivery, mother place of birth, smoking during pregnancy	No association (p>0.05) between maternal PFHxS and infant body weight or length at specific measurement times. In longitudinal analysis, an inverse association between maternal PFHxS and infant body weight (β -5.270, 95% CI -9.591 to -0.950) and an association with length (β 4.516, 95% CI 1.368–7.664).
Braun et al. 2016a, 2016b Prospective study of 204 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; height, weight, waist circumference, and body fat were measured when the children were 8 years of age; height and weight were also measured at ages 2, 3, 4, and 5 years	**Exposure:** Median maternal serum PFHxS levels (measured at 16 weeks of gestation): 1.4 ng/mL **Statistical adjustments:** Maternal age, race, education, marital status, employment, household income, maternal depressive symptoms, maternal BMI at 16 weeks of gestation, parity, maternal serum cotinine, frequency of fruit/vegetable and fish consumption during pregnancy, prenatal vitamin use	No association between maternal serum PFHxS levels and child adiposity scores or changes in BMI scores between 2 and 8 years of age (p>0.23). No significant increases in the risk of overweight/obesity at age 8 years were observed; the relative risks for serum PFHxS levels in the 2nd and 3rd tertiles were RR 1.33 (95% CI 0.72–2.48) and RR 1.48 (95% CI 0.75–2.96), respectively.
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFHxS 0.16 ng/mL; 1st tertile <0.06 ng/mL, 2nd tertile 0.06–0.139 ng/mL, 3rd tertile >0.13 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFHxS and postnatal body weight (p=0.96) or postnatal length (p=0.31) at 19 months of age.

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Hartman et al. 2017 Prospective cohort study of 359 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data were obtained from medical records; weight and height at age 9 years were measured	**Exposure:** Median maternal serum PFHxS (measured at gestation week 15) 1.6 ng/mL **Linear regression model adjustments:** Sampling design, maternal prepregnancy BMI, maternal education	No association between maternal serum PFHxS and total body fatness (evaluated using dual-energy X-ray absorptiometry) in girls (β -0.01, 95% -0.21–0.09, p=0.47) or trunk fatness (β -0.11, 95% CI -0.55–0.08, p=0.77). No association for BMI (β -0.02, 95% CI -0.08–0.03, p=0.37). When stratified based on maternal education, an inverse association was found for BMI in the low education group (β -1.22, 95% CI -2.29 to -0.15, p=0.03).
Karlsen et al. 2017 Prospective study of 444 mother-child pairs in the Faroe Islands; children's height and weight measurements were taken at ages 18 months and 5 years	**Exposure:** Maternal geometric mean serum PFHxS (measured 2 weeks after childbirth) 0.19 ng/mL (range of 0.02–1.49 ng/mL) and child geometric mean serum PFOS (measured at age 5 years) 0.34 ng/mL (range of 0.08–3.30 ng/mL) **Statistical adjustments:** Maternal nationality, age at delivery, prepregnancy BMI, gestational weight gain, parity, smoking during pregnancy, maternal fish intake during pregnancy, type of delivery, child sex and birth weight	No association between maternal serum PFHxS and child's BMI z-score at 18 months (β 0.10, 95% CI -0.01–0.21, p>0.05) or 5 years of age (β 0.04, 95% CI -0.07–0.15, p>0.05). No association between maternal serum PFHxS and child's risk of child being overweight at 18 months (RR 1.12, 95% CI 0.97–1.30) or 5 years (RR 1.11, 95% CI 0.77–1.59). No associations between child serum PFHxS and BMI score at age 5 years (β -0.15, 95% CI -0.34–0.04) or risk of being overweight (RR 0.73, 95% CI 0.44–1.23).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFHxS 0.67 ng/mL (WTCHR group) and 0.53 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFHxS and risk of being overweight (OR 1.04, 95% CI 0.97–1.11, p=0.30).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Liu et al. 2018a Prospective study of 624 adults participating in the POUNDS Lost randomized 2-year clinical trial in Boston, Massachusetts and Baton Rouge, Louisiana	**Exposure:** Median serum PFHxS 2.4 ng/mL (range 1.5–3.6 ng/mL) **Statistical adjustments:** Smoking status, physical activity, baseline BMI, dietary intervention group	No association between serum PFHxS and weight loss during first 6 months of study (p=0.45, trend). No association between PFHxS and weight regain between study months 6 and 24 (p=0.49, trend). Dividing the subjects by sex resulted in significant associations in weight regain in females (p=0.009, trend), but not in males (p=0.17, trend). PFHxS associated with greater decline in resting metabolic rate during weight loss period (p=0.04, trend) and lower increase in resting metabolic rate during weight regain period (p=0.02, trend).
Maisonet et al. 2012 Prospective cohort study of 447 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data were obtained from medical records; weight and height at age 2 and 20 months were measured	**Exposure:** Median maternal serum PFHxS (measured at gestation week 15) 1.6 ng/mL (range: 0.2–54.8 ng/mL). **Linear regression model adjustments:** Maternal smoking during pregnancy (birth weight and length only), maternal prepregnancy BMI, previous live births, gestational age, maternal education (birth length only)	No significant association between maternal serum PFHxS adjusted by height at 20 months and birth weight (p=0.4375).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFHxS 0.61 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFHxS and weight gain from birth to 6 months of age (β -0.06, 95% CI -0.15–0.02). No association between maternal serum PFHxS and BMI score at 4 years of age (β -0.02, 95% CI -0.10–0.07) or 7 years of age (β -0.04, 95% CI -0.14–0.06). No association between maternal serum PFHxS and waist circumference score at 4 years of age (β -0.04, 95% CI -0.14–0.15) or 7 years of age (β -0.04, 95% CI -0.12–0.04).
Mora et al. 2017 Prospective study of children (n=1,006 at median age of 3.2 years and n=876 at median age of 7.7 years) participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFHxS 2.4 ng/mL in early childhood group and 2.3 ng/mL in late childhood group (measured during first trimester) **Statistical adjustments:** Maternal age, race/ethnicity, education, parity, prepregnancy BMI, timing of blood draw, household income, child sex and age at outcome assessment	Association between maternal PFHxS and early childhood subscapular and triceps skinfold thickness (β 0.16, 95% CI 0.01–0.31) in boys and girls combined, but not sex-stratified analyses of boys only (β 0.15, 95% CI -0.09–0.38) or girls only (β 0.18, 95% CI -0.03–0.38). No associations (boys and girls combined) between maternal PFHxS and early childhood (median age 3.2 years) BMI (β 0.01, 95% CI -0.05–0.06), waist circumference (β 0.03, 95% CI -0.10–0.16), waist-to-hip circumference (β -0.01, 95% CI -0.22–0.20), or subscapular to triceps skinfold thickness ratio (β -0.12, 95% CI -0.69–0.45). Association between maternal PFHxS and mid childhood (median age 7.7 years) subscapular to triceps skinfold thickness ratio in girls only (β 1.61, 95% CI 0.58–2.65), but not in boys and girls combined (β 0.02, 95% CI -0.02–0.06) or boys only (β -0.50, 95% CI -1.70–0.71). No associations (boys and girls combined) between maternal PFHxS and mid childhood (median age 7.7 years) BMI (β 0.04, 95% CI -0.08–0.17, subscapular and triceps skinfold

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		thickness (β 0.25, 95% CI -0.14–0.64), total fat mass index (β 0.04, 95% CI -0.04–0.13), total fat-free mass index (β 0.00, 95% CI -0.05–0.06), waist circumference (β 0.11, 95% CI -0.22–0.43), waist-to-hip circumference (β 0.19, 95% CI -0.07–0.45), or trunk fat mass index (β 0.02, 95% CI -0.02–0.06). No associations (boys and girls combined) between maternal PFHxS and risk of being overweight in early childhood (RRR 1.03, 95% CI 0.94–1.13) or mid childhood (RRR 1.04, 95% CI 0.92–1.17) or being obese in early childhood (RRR 1.02, 95% CI 0.89–1.17) or mid childhood (RRR 1.07, 95% CI 0.94–1.22).
PFNA		
Braun et al. 2016a, 2016b Prospective study of 204 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; height, weight, waist circumference, and body fat were measured when the children were 8 years of age; height and weight were also measured at ages 2, 3, 4, and 5 years	**Exposure:** Median maternal serum PFNA levels (measured at 16 weeks of gestation): 0.9 ng/mL **Statistical adjustments:** Maternal age, race, education, marital status, employment, household income, maternal depressive symptoms, maternal BMI at 16 weeks of gestation, parity, maternal serum cotinine, frequency of fruit/vegetable and fish consumption during pregnancy, prenatal vitamin use	No association between maternal serum PFNA levels and child adiposity scores or changes in BMI scores between 2 and 8 years of age (p>0.23). No significant increases in the risk of overweight/obesity at age 8 years were observed; the relative risks for serum PFNA levels in the 2nd and 3rd tertiles were RR 1.18 (95% CI 0.63–2.22) and RR 1.26 (95% CI 0.64–2.48), respectively.
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFNA 0.13 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFNA and postnatal body weight (p=0.88), postnatal length (p=0.15), or postnatal head circumference (p=0.62) at 19 months of age.

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Halldorsson et al. 2012 Prospective cohort study of 665 offspring of women participating in a birth cohort study in Denmark; the offspring were examined at 20 years of age	**Exposure:** Median maternal serum PFNA level (measured at gestation week 30) 0.3 ng/mL **Statistical adjustments:** Maternal age, maternal education, maternal prepregnancy BMI, smoking during pregnancy, parity, infant birth weight, and offspring age at follow-up	No significant associations (p>0.56) between maternal serum PFNA and offspring BMI and waist circumference were found.
Hartman et al. 2017 Prospective cohort study of 359 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data were obtained from medical records; weight and height at age 9 years were measured	**Exposure:** Median maternal serum PFNA (measured at gestation week 15) 0.5 ng/mL **Linear regression model adjustments:** Sampling design, maternal prepregnancy BMI, maternal education	No association between maternal serum PFNA and total body fatness (evaluated using dual-energy X-ray absorptiometry) in girls (β 1.71, 95% -1.29–4.71, p=0.26) or trunk fatness (β -0.03, 95% CI -1.83–1.77, p=0.97). No association for BMI (β 0.22, 95% CI -0.83–1.27, p=0.68). When stratified based on maternal education, an association was found for total fatness in the low education group (β 12.73, 95% CI 0.11 to -25.36, p=0.04).
Karlsen et al. 2017 Prospective study of 444 mother-child pairs in the Faroe Islands; children's height and weight measurements were taken at ages 18 months and 5 years	**Exposure:** Maternal geometric mean serum PFNA (measured 2 weeks after childbirth) 0.67 ng/mL (range of 0.18–4.30 ng/mL) and child geometric mean serum PFNA (measured at age 5 years) 1.12 ng/mL (range of 0.12–5.75 ng/mL) **Statistical adjustments:** Maternal nationality, age at delivery, prepregnancy BMI, gestational weight gain, parity, smoking during pregnancy, maternal fish intake during pregnancy, type of delivery, child sex and birth weight	No association between maternal serum PFNA and child's BMI z-score at 18 months (β 0.01, 95% CI -0.19–0.21, p>0.05) or 5 years of age (β -0.00, 95% CI -0.21–0.20, p>0.05). No association between maternal serum PFNA and child's risk of child being overweight at 18 months (RR 1.02, 95% CI 0.79–1.31) or 5 years (RR 1.15, 95% CI 0.67–1.98). Inverse association between child serum PFNA and BMI score at age 5 years (β -0.18, 95% CI -0.34 to -0.02, p<0.05). No association with risk of being overweight (RR 0.67, 95% CI 0.45–1.00).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFNA 0.61 ng/mL (WTCHR group) and 0.49 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFNA and risk of being overweight (OR 1.01, 95% CI 0.92–1.13, p=0.72).
Liu et al. 2018a Prospective study of 624 adults participating in the POUNDS Lost randomized 2-year clinical trial in Boston, Massachusetts and Baton Rouge, Louisiana	**Exposure:** Median serum PFNA 1.5 ng/mL (range 1.0–2.4 ng/mL) **Statistical adjustments:** Smoking status, physical activity, baseline BMI, dietary intervention group	No association between serum PFNA and weight loss during first 6 months of study (p=0.28, trend). PFNA associated with greater weight regain between study months 6 and 24 (p=0.01, trend). Dividing the subjects by sex resulted in significant associations in weight regain in females (p=0.006, trend), but not in males (p=0.48, trend). PFNA associated with greater decline in resting metabolic rate during weight loss period (p<0.001, trend) and lower increase in resting metabolic rate during weight regain period (p=0.03, trend).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFNA 0.66 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFNA and weight gain until 6 months of age (β 0.0, 95% CI -0.07–0.09). No association between maternal serum PFNA and BMI score at 4 years of age (β 0.05, 95% CI -0.03–0.13) or 7 years of age (β 0.06, 95% CI -0.04–0.16). No association between maternal serum PFNA and waist circumference score at 4 years of age (β 0.02, 95% CI -0.07–0.10) or 7 years of age (β -0.02, 95% CI -0.07–0.10).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Mora et al. 2017 Prospective study of children (n=1,006 at median age of 3.2 years (early childhood) and n=876 at median age of 7.7 years (mid-childhood)) participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFNA 0.6 ng/mL in early childhood group and 0.6 ng/mL in late childhood group (measured during first trimester) **Statistical adjustments:** Maternal age, race/ethnicity, education, parity prepregnancy BMI, timing of blood draw, household income, child sex and age at outcome assessment	No associations (boys and girls combined) between maternal PFNA and early childhood BMI (β 0.02, 95% CI -0.07–0.12), subscapular and triceps skinfold thickness (β -0.01, 95% CI -0.28–0.25), waist circumference (β 0.01, 95% CI -0.23–0.22), waist-to-hip circumference (β 0.19, 95% CI -0.17–0.54), or subscapular to triceps skinfold thickness ratio (β 0.50, 95% CI -0.48–1.47). Association between maternal PFNA and mid childhood subscapular and triceps skinfold thickness for boys and girls combined (β 0.62, 95% CI 0.01–1.22) and in girls only (β 1.01, 95% CI 0.16–1.86), but not in boys only (β 0.13, 95% CI -0.74–1.01). Association between maternal PFNA and mid childhood subscapular to triceps skinfold thickness ratio in boys and girls combined (β 1.78, 95% CI 0.57–2.98) and in girls only (β 2.17, 95% CI 0.52–3.83), but not boys only (β 1.23, 95% CI -0.58–3.03). No associations (boys and girls combined) between maternal PFNA and mid childhood BMI (β 0.17, 95% CI -0.03–0.36), total fat mass index (β 0.08, 95% CI -0.07–0.23), total fat-free mass index (β 0.08, 95% CI -0.02–0.18), waist circumference (β 0.31, 95% CI -0.19–0.82), waist-to-hip circumference (β 0.37, 95% CI -0.03–0.77), or trunk fat mass index (β 0.04, 95% CI -0.03–0.11). No associations (boys and girls combined) between maternal PFNA and risk of being overweight in early childhood (RRR 1.12, 95% CI 0.96–1.30) or mid childhood (RRR 1.06, 95% CI 0.85–1.32) or being obese in early childhood (RRR 0.97, 95% CI 0.75–1.27) or mid childhood (RRR 1.21, 95% CI 0.99–1.47).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age	**Exposure:** Median maternal serum PFNA (measured during third trimester) 1.55 ng/mL for male children and 1.58 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	No significant association (p>0.05) between maternal PFNA levels and growth (weight and height) during childhood.
PFDA		
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFDA 0.12 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFDA and postnatal body weight (p=0.57), postnatal length (p=0.18), or postnatal head circumference (p=0.94) at 19 months of age.
Karlsen et al. 2017 Prospective study of 444 mother-child pairs in the Faroe Islands; children's height and weight measurements were taken at ages 18 months and 5 years	**Exposure:** Maternal geometric mean serum PFDA (measured 2 weeks after childbirth) 0.26 ng/mL (range of 0.07–1.00 ng/mL) and child geometric mean serum PFDA (measured at age 5 years) 0.33 ng/mL (range of 0.02–1.72 ng/mL) **Statistical adjustments:** Maternal nationality, age at delivery, prepregnancy BMI, gestational weight gain, parity, smoking during pregnancy, maternal fish intake during pregnancy, type of delivery, child sex and birth weight	No association between maternal serum PFDA and child's BMI z-score at 18 months (β 0.09, 95% CI -0.10–0.21, p>0.05) or 5 years of age (β -0.044, 95% CI -0.23–0.14, p>0.05). No association between maternal serum PFNA and child's risk of child being overweight at 18 months (RR 1.14, 95% CI 0.91–1.43) or 5 years (RR 1.02, 95% CI 0.61–1.70). Inverse associations between child serum PFDA and BMI score at age 5 years (β -0.18, 95% CI -0.33 to -0.02, p<0.05) and risk of being overweight (RR 0.64, 95% CI 0.46–0.90).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFDA 0.14 ng/mL (WTCHR group) and 0.11 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFDA and risk of being overweight (OR 0.98, 95% CI 0.93–1.03, p=0.49).

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Liu et al. 2018a Prospective study of 624 adults participating in the POUNDS Lost randomized 2-year clinical trial in Boston, Massachusetts and Baton Rouge, Louisiana	**Exposure:** Median serum PFDA 0.37 ng/mL (range 0.27–0.52 ng/mL) **Statistical adjustments:** Smoking status, physical activity, baseline BMI, dietary intervention group	No association between serum PFDA and weight loss during first 6 months of study (p=0.45, trend). No association between PFDA and weight regain between study months 6 and 24 (p=0.16, trend). Dividing the subjects by sex resulted in significant associations in weight regain in females (p=0.03, trend), but not in males (p=0.75, trend). PFDA associated with greater decline in resting metabolic rate during weight loss period (p=0.01, trend) and lower increase in resting metabolic rate during weight regain period (p=0.05, trend).
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age	**Exposure:** Median maternal serum PFDA (measured during third trimester) 0.46 ng/mL for male children and 0.43 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	Significant inverse association between maternal PFDA levels and childhood weight in girls (β -0.32, 95% CI -0.63 to -0.00; p<0.05) and height in girls (β -0.52, 95% CI -0.80 to -0.24; p<0.01). No associations (p>0.05) for height or weight in boys.
PFUnA		
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFUnA 0.10 ng/mL; 1st tertile <0.06 ng/mL, 2nd tertile 0.06–0.11 ng/mL, 3rd tertile >0.11 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	Association between cord PFUnA and postnatal length at 19 months of age (β, 95% CI): 2nd tertile: 1.19 (-0.68–3.07) (p<0.05) 3rd tertile: 1.67 (-0.24–3.58) (p<0.05) No association between cord PFUnA and postnatal body weight (p=0.88) or postnatal head circumference (p=0.60) at 19 months of age.

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFUnA 0.12 ng/mL (WTCHR group) and 0.04 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Inverse association between serum PFUnA and risk of being overweight (OR 0.95, 95% CI 0.91–0.99, p=0.02).
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age	**Exposure:** Median maternal serum PFUnA (measured during third trimester) 3.52 ng/mL for male children and 3.31 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	Significant inverse association between maternal PFUnA levels and childhood weight in girls (β -0.15, 95% CI -0.28 to -0.02; p<0.05) and height in girls (β -0.14, 95% CI -0.27 to -0.01; p<0.05). No associations (p>0.05) for height or weight in boys.
PFDoDA		
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFDoDA 0.04 ng/mL; 1st tertile <0.02 ng/mL, 2nd tertile 0.02–0.04 ng/mL, 3rd tertile >0.04 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFDoDA and postnatal body weight (p=0.74) or postnatal head circumference (p=0.97) at 19 months of age.
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age	**Exposure:** Median maternal serum PFDoDA (measured during third trimester) 0.37 ng/mL for male children and 0.37 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	Significant inverse association between maternal PFDoDA levels and childhood weight in girls (β -0.30, 95% CI -0.55 to -0.06; p<0.05) and height in girls (β -0.25, 95% CI -0.49 to -0.00; p<0.05). No associations (p>0.05) for height or weight in boys.

Table 1. Body Weight Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
FOSA		
Halldorsson et al. 2012 Prospective cohort study of 665 offspring of women participating in a birth cohort study in Denmark; the offspring were examined at 20 years of age	**Exposure:** Median maternal serum FOSA level (measured at gestation week 30) 1.1 ng/mL **Statistical adjustments:** Maternal age, maternal education, maternal prepregnancy BMI, smoking during pregnancy, parity, infant birth weight, and offspring age at follow-up	No significant associations (p>0.56) between maternal serum FOSA and offspring BMI and waist circumference were found.

BMI = body mass index; CI = confidence interval; FOSA = perfluorooctane sulfonamide; HOMA = homeostatic model assessment; INMA = INfancia y Medio Ambiente; IR = insulin resistance; OR = odds ratio; PBPK = physiologically based pharmacokinetic; PFDoDA = perfluorododecanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; RR = relative risk

Table 2. Respiratory Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Sakr et al. 2007b Cross-sectional study of 1,025 male (76%) and female (24%) workers at a fluoropolymers production plant (Washington Works)	**Exposure:** Median serum PFOA concentrations were 490 (range: 17.4–9,550), 176 (8.1–2,070), 195 (8.6–2,590), and 114 ng/mL (4.6–963) among current workers (n=259), current workers with intermittent exposure (n=160), past occupational exposure to PFOA (n=264), or never assigned to APFO area (n=342), respectively. The mean and median concentrations in all workers were 428 ppm and 189 ng/mL, respectively. **Linear regression model adjustments:** Age, sex, BMI, alcohol consumption, heart attack in a parent (lipid models only)	The investigators noted that pulmonary function tests and chest roentgenogram were within normal limits; no additional information was provided.
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was calculated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum levels PFOA in 2005–2006 were 325 and 113 ng/mL in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant association between estimated cumulative serum PFOA and risk of COPD (p=0.86 and 0.97 for trend with no lag or 10-year lag).

Table 2. Respiratory Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Anderson-Mahoney et al. 2008 Cross-sectional study of 566 adult residents (mean age of 49.9 years) living near a Teflon manufacturing facility in West Virginia for at least 1 year; most subjects were exposed to PFOA in drinking water provided by Lubeck Public Service District (37%) or Little Hocking water district (27%); some subjects also worked at the facility	**Exposure:** Individual biomonitoring data were not provided; reported PFOA levels in the Lubeck and Little Hocking water districts were 0.4–3.9 and 1.7–4.3 µg/L, respectively. **Reference population:** SPRs were estimated using NHANES data; statistical analyses were adjusted for age and sex	Incidence data were based on the results of participant-completed health surveys. Significantly increased risks of respiratory diseases were found; the SPRs (95% CI) were: • Chronic bronchitis 3.60 (2.92–4.44) • Shortness of breath 2.05 (1.70–2.46)

APFO = ammonium perfluorooctanoate; CI = confidence interval; COPD = chronic obstructive pulmonary disease; NHANES = National Health and Nutrition Examination Survey; PFOA = perfluorooctanoic acid; SPR = standard prevalence ratio; WTCHR = World Trade Center Health Registry

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Leonard 2006 Retrospective cohort mortality study of 6,027 (80% males) (806 deaths) workers at a fluoropolymers production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between January 1, 1948 (plant start-up) and December 31, 2002	**Exposure:** Based on the results of a cross-sectional study (Sakr et al. 2007b), serum PFOA levels ranged from 5 to 9,550 ng/mL Workers divided into three exposure categories: • no APFO use jobs (serum PFOA levels 250 ng/mL) • APFO-use jobs with median serum level between >250 and ≤750 ng/mL • APFO jobs with median serum levels >750 ng/mL Cumulative exposure was calculated for each worker by multiplying time in various jobs categories by an intensity factor (210, 430, or 1,690 ng/mL, respectively) **Reference populations:** Three comparisons groups were used: U.S. general population, West Virginia population, and population of DuPont workers residing in West Virginia and seven neighboring states (excluding workers at Washington Works)	For males, no significant increases in deaths from all heart disease (SMR 110, 95% CI 98–123), cerebrovascular disease (SMR 86, 95% CI 60–120), or ischemic heart disease (SMR 109, 95% CI 96–124) were found when the DuPont worker population was used as a reference. In females, the SMR for all heart disease was 143 (95% CI 46–333); SMRs were not calculated for other cardiovascular endpoints because three or less deaths occurred. The SMRs in males and females were lower when the United States and West Virginia populations were used as references. Cox proportional hazard modeling for ischemic heart disease in white males (n=235 cases and 4,225 controls). No significant increases in MRRs were found when analyzed by exposure category, case calendar year, or if hired before 1954, with lags (5, 10, 15, or 20 years) or without lags. The highest MRRs were found among workers hired before 1954; the MRRs and 95% CIs were: 1.001 (0.738–1.360), 1.042 (0.764–1.421), 1.089 (0.791–1.501), 1.087 (0.780–1.513), and 1.053 (0.744–1.492) with 0-, 5-, 10-, 15-, or 20-year lags, respectively.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lundin et al. 2009 Cohort mortality study of 3,993 (80% male) workers at an APFO manufacturing facility (Cottage Grove); 807 workers died during the follow-up period; cohort consisted of workers employed for at least 365 days prior to December 31, 1997	**Exposure:** Workers were divided into three exposure classifications: • definite occupational exposure; workers exposed on a regular basis with potential high exposure (group 1) • probable occupational exposure; jobs in other chemical division where APFO exposure was possible, but likely lower or transient (group 2) • no or minimal occupational exposure (group 3) Serum PFOA levels collected in 2000 from 131 current workers ranged from 2,600 to 5,200 ng/mL in definite exposure jobs and from 300 to 1,500 ng/mL in the probable exposure jobs; no data were available for the no exposure jobs **Reference population and adjustments:** Mortality rates were compared to rates from Minnesota general population; statistical models were adjusted for sex, year of birth, age at entry into the cohort, smoking status, and wage type; Cox regression analyses were done with an internal referent population	No significant increases in deaths from all heart disease, cerebrovascular disease, or ischemic heart disease; the SMRs (95% CI) were: • Group 1: 0.7 (0.5–1.3), 1.6 (0.5–3.7), 0.8 (0.5–1.4) • Group 2: 0.8 (0.6–0.9), 0.7 (0.4–1.1), 0.8 (0.7–1.0) • Group 3: 0.8 (0.7–0.9), 0.5 (0.3–0.8), 0.7 (0.6–0.9). In time-dependent Cox regression analysis, there was a significant increase in cerebrovascular disease among workers with high exposure (defined as definite exposure for ≥6 months), HR 4.6 (95% CI 1.3–17.0) and in workers exposed for ≥5 years, HR 2.1 (95% CI 1.0–4.6).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Raleigh et al. 2014 Retrospective cohort mortality study of 9,027 workers (84% male) at two 3M facilities in Minnesota; 4,668 workers at an APFO facility in Cottage Grove (3,993 of these workers were included in the Lundin et al. 2009 cohort) and 4,359 workers at a non-APFO facility in St. Paul; cohort consisted of workers employed for at least 1 year; the Cottage Grove cohort included workers in a non-chemical division without exposure to APFO	**Exposure:** Work history and industrial monitoring were used to estimate PFOA exposure; cumulative exposure in the Cottage Grove workers was divided into quartiles: • 1st quartile: >2.9x10^{-5} µg/m^3 • 2nd quartile: ≤1.5x10^{-4} µg/m^3 • 3rd quartile: ≤7.9x10^{-4} µg/m^3 • 4th quartile: >7.9x10^{-4} µg/m^3 **Reference population:** Mortality rates were compared to rates from Minnesota general population; Cottage Grove cohort was also compared to the St. Paul cohort	As compared to the Minnesota population, significantly lower deaths from ischemic heart disease (SMR 0.84, 95% CI 0.74–0.95) and no significant alteration in risk of death from cerebrovascular disease (SMR 0.81, 95% CI 0.61–1.05) were found in the Cottage Grove cohort. As compared to the St. Paul cohort, no significant alterations in the risk of death from ischemic heart disease (HR 0.89, 95% CI 0.66–1.21) or cerebrovascular disease (HR 0.98, 95% CI 0.53–1.81) in Cottage Grove workers in the 4th quartile.
Sakr et al. 2007b Cross-sectional study of 1,025 male (76%) and female (24%) workers at a fluoropolymer production plant (Washington Works)	**Exposure:** Median serum PFOA concentrations were 490 (range: 17.4–9,550), 176 (8.1–2,070), 195 (8.6–2,590), and 114 ng/mL (4.6–963) among current workers (n=259), current workers with intermittent exposure (n=160), past occupational exposure to PFOA (n=264), or never assigned to APFO area (n=342), respectively; the mean and median concentrations in all workers were 428 ppm and 189 ng/mL, respectively **Linear regression model adjustments:** Age, sex, BMI, alcohol consumption, heart attack in a parent (lipid models only)	Investigators noted that electrocardiogram readings were within normal limits.
Sakr et al. 2009 Case-control study of 4,747 (98% males) workers at a fluoropolymers production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between January 1, 1948 (plant start-up) and December 31, 2002; these are workers from the same cohort as Leonard (2006)	**Exposure:** Typical exposure for each job title was estimated using serum PFOA levels for current workers; exposure categories were assigned intensity factors that corresponded to the mean serum levels of all jobs in a particular category	No significant increases in RR of ischemic heart disease was found when analyzed by exposure category with or without 5-, 10-, 15-, or 20-year lags. The highest RR were found in the 10-year lag; the RRs (95% CI) were 1.5 (0.9–2.4) and 1.4 (0.9–2.3) in the two highest exposure categories. The trend for increasing risk with increasing exposure was not statistically significant (p=0.16).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was calculated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum PFOA levels in 2005–2006 were 325 and 113 ng/mL in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant associations between estimated cumulative serum PFOA and risk of coronary heart disease (p=0.78 and 0.75 for trend with no lag or 10-year lag), medicated hypertension (p=0.95 and 0.54 for trend with no lag or 10-year lag), or stroke (p=0.35 and 0.64 for trend with no lag or 10-year lag).
Steenland and Woskie 2012 Retrospective cohort mortality study of 1,084 deceased workers at a fluoropolymer production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between 1948 and 2002; deaths were obtained through 2008; extension of the Leonard (2006) study	**Exposure:** Cumulative exposure was estimated using serum PFOA levels of workers collected between 1979 and 2004 (median of 580 ng/mL with a range of 160–2,880 ng/mL). Exposures over time were estimated for eight job categories. The mean estimated cumulative exposure was 7,800 ng/mL-years (median of 4,300 ng/mL-years) and an estimated average annual serum PFOA concentration of 350 (median 230 ng/mL). **Reference population:** Population, of DuPont workers residing in West Virginia and seven neighboring states (excluding workers at Washington Works)	No significant increase in deaths from ischemic heart disease was observed; the SMRs (95% CI) for the 4th exposure quartile were 0.93 (0.72–1.19) and 0.97 (0.86–1.09) for all quartiles combined. Analyzing with a 10- or 20-year lag did not alter the findings (SMR 0.93, 95% CI 0.71–1.20 for 10-year lag and SMR 0.89, 95% CI 0.65–1.18 for 20-year lag) for the 4th quartile exposure group.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Anderson-Mahoney et al. 2008 Cross-sectional study of 566 adult residents (mean age of 49.9 years) living near a Teflon manufacturing facility in West Virginia for at least 1 year; most subjects were exposed to PFOA in drinking water provided by Lubeck Public Service District (37%) or Little Hocking water district (27%); some subjects also worked at the facility (15%)	**Exposure:** Individual biomonitoring data were not provided; reported PFOA levels in the Lubeck and Little Hocking water districts were 0.4–3.9 and 1.7–4.3 µg/L, respectively **Reference population:** SPRs were estimated using NHANES data; statistical analyses were adjusted for age and sex	Incidence data were based on the results of participant-completed health surveys. Significantly increased risks of cardiovascular problems and specific cardiovascular outcomes were found; the SPRs (95% CIs) were: • Cardiovascular 4.29 (3.47–5.29) • Angina 8.07 (6.54–9.95) • Myocardial infarction 1.91 (1.40–2.62) • Stroke 2.17 (1.47–3.21). No significant increase in the risk of hypertension (SPR 1.18, 95% CI 0.97–1.43) was found.
Darrow et al. 2013 Cross-sectional study of 1,330 women participating in the C8 Health Project and giving birth between 2005 and 2010; maternal blood samples collected in 2005–2006; birth outcome data self-reported and taken from Ohio and West Virginia health departments; 74% of pregnancies occurred after blood sampling	**Exposure:** Mean and geometric mean serum PFOA were 31.0 and 16.2 ng/mL (range:0.6–459.5 ng/mL) • 1st quintile: 0–<6.9 ng/mL • 2nd quintile: 6.9–<11.1 ng/mL • 3rd quintile: 11.1–<18.9 ng/mL • 4th quintile: 18.9–<37.2 ng/mL • 5th quintile: ≥37.2 ng/mL **Logistic regression model adjustments:** Maternal age, educational level, smoking, parity, BMI, self-reported diabetes, time between conception, serum measurement	Increased odds of self-reported pregnancy-induced hypertension in women with PFOA levels in the 2nd, 3rd, 4th, or 5th quintiles; the linear trend across quintiles was also significant (p=0.005). The ORs (95% CI) were: • 2nd quintile: 2.39 (1.05–5.46) • 3rd quintile: 3.42 (1.50–7.82) • 4th quintile: 3.12 (1.35–7.18) • 5th quintile: 3.16 (1.35–7.38).
Nolan et al. 2010 Cross-sectional study of exposed to PFOA-contaminated residential drinking water; 1,548 pregnant women, 11% in exclusive LHWA; 13% partial LHWA, and 76% no LHWA (see Nolan et al. 2009)	**Exposure:** No biomonitoring performed **Logistic regression model adjustments:** Race, parity, preterm birth, maternal age, maternal education, diabetic status, tobacco and alcohol use during pregnancy	No significant associations between residence area and pregnancy-induced hypertension (as reported on birth certificates) in women living in LHWA area (unadjusted OR 1.2, 95% CI 0.7–2.0) or the partial LHWA area (unadjusted OR 0.8, 0.5–1.4).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Savitz et al. 2012a Cross-sectional study of 11,737 singleton infants born to mothers living in an area of the Mid-Ohio Valley with known PFOA contamination from 1990 to 2006 and with birth records linked to the C8 Health Project; birth outcome data taken from Ohio and West Virginia health departments	**Exposure:** Maternal PFOA blood levels based on environmental levels of PFOA (based on maternal lifetime residential history) and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life; used a Bayesian time-dependent calibration that used measured serum concentrations (2005–2006) to update estimates Median maternal serum PFOA: 6.0, 10.7, and 15.9 ng/mL in the 1990–1994, 1995–1999, and 2000–2005 time periods • 1st quartile: 3.9–<6.8 ng/mL • 2nd quartile: 6.8–<16.6 ng/mL • 3rd quartile: 16.6–<63.1 ng/mL • 4th quartile: 63.1–934.3 ng/mL **Regression model adjustments:** Maternal age, parity, education, smoking status	An increased risk of self-reported pre-eclampsia was observed; the ORs (95% CIs) for each quartile were: • 2nd quartile: 1.2 (1.0–1.5) • 3rd quartile: 1.1 (0.9–1.4) • 4th quartile: 1.2 (1.0–1.6).
Savitz et al. 2012b Case-control study of singleton pregnancy of women living in Mid-Ohio Valley with known PFOA contamination from 1990 to 2004; birth outcome data taken from Ohio and West Virginia health departments; 224 cases of pregnancy-induced hypertension were compared to controls with term births and without pregnancy-induced hypertension	**Exposure:** Maternal PFOA levels based on estimated environmental levels of PFOA (based on maternal address on birth certificate and assumption that mother lived at address for 6 years) and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life Median maternal serum PFOA: 7.7 ng/mL (range: 1.0–717.6 ng/mL) **Logistic regression model adjustments:** Maternal age, education, tobacco use, exposure year, state of residence	No significant association between pregnancy-induced hypertension and estimated serum PFOA levels was found. The OR for women with estimated serum PFOA levels in the 5th quintile (21.0–717.6 ng/mL) was 1.0 (95% CI 0.7–1.3).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Savitz et al. 2012b Case-control study of 4,547 singleton infants born to mothers living in an area of the Mid-Ohio Valley with known PFOA contamination from 1990 to 2004 and with birth records linked to the C8 Health Project; birth outcome data taken from Ohio and West Virginia health departments; cases of pregnancy-induced hypertension (n=250) were compared to controls with term births	**Exposure:** Serum PFOA levels from the mother estimated for the early pregnancy period. Serum levels were estimated based on plant operations and chemical releases, address, and age- and sex-specific PBPK modeling with standards for water intake, body weights, and PFOA half-life. Bayesian time-dependent calibration that used measured serum concentrations (2005–2006) to update estimates. Median maternal serum PFOA: 13.4 ng/mL (range: 3.9–921.3 ng/mL) **Logistic regression model adjustments:** Maternal age, education, tobacco use, exposure year, state of residence, gestational age	No significant association between pregnancy-induced hypertension and estimated serum PFOA levels was found. The OR for women with estimated serum PFOA levels in the 5th quartile (21.0–717.6 ng/mL) was 1.1 (95% CI 0.8–1.5).
Simpson et al. 2013 Retrospective and prospective study of 28,541 participants in the C8 Health Project and a cohort of 3,713 workers at a DuPont Washington Works facility who worked at the plant between 1948 and 2002	**Exposure:** Serum PFOA levels based on estimated environmental levels on a fate and transport model to estimate PFOA levels in in water and air per year since production began in 1951 and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life. Exposures of workers were estimated using a job history matrix. Mean and median serum PFOA levels of the combined cohort were 86.6 and 26.1 ng/mL, respectively. PFOA levels were categorized into quintiles: • 2nd quintile: >178–319 ng/mL • 3rd quintile: >319–912 ng/mL • 4th quintile: >912–4,490 ng/mL • 5th quintile: >4,490 ng/mL **Cox proportional hazards model adjustments:** Hypertension, self-reported	Significant association between estimated cumulative serum PFOA and stroke in retrospective analysis; HRs (95% CI): • 2nd quintile: 1.39 (95% CI 1.11–1.76) • 3rd quintile: 1.36 (95% CI 1.08–1.71) • 4th quintile: 1.45 (95% CI 1.15–1.82) • 5th quintile: 1.13 (95% CI 0.90–1.44) When categorized by different study end dates, significant associations were found for stroke risk in 1996 (p=0.02), 1993 (p=0.001), and 1990 (p=0.001), but not at later dates (p>0.05 for 1998, 2002, 2005, 2008, and present). No significant association between estimated cumulative serum PFOA and risk of stroke in prospective analysis; HR 0.99 (95% CI 0.97–1.01, p=0.28) for continuous variable.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	diabetes, sex, education, race, smoking, alcohol consumption	
Stein et al. 2009 Cross-sectional study of 1,845 pregnancies (1,589 live births) in Mid-Ohio Valley residents that occurred within the 5 years preceding blood sample collections for the C8 Health Project; self-reported birth outcome	**Exposure:** Mean and median serum PFOA: 48.8 and 21.2 ng/mL (range: 0.25–894.4 ng/mL) • 1st quartile: 0.25–<21.3 ng/mL • 2nd quartile: 21.3–<50.0 ng/mL • 3rd quartile: 50.0–<120.6 ng/mL • 4th quartile: 120.6–894.4 ng/mL **Logistic linear regression model adjustments:** Maternal age, parity, education, smoking status	No association between PFOA levels and odds of self-reported pre-eclampsia were found; OR 0.9 (95% CI 0.5–1.8) for the 4th quartile.
Winquist and Steenland 2014a Retrospective and prospective study of 28,541 participants in the C8 Health Project and a cohort of 3,713 workers at a DuPont Washington Works facility who worked at the plant between 1948 and 2002	**Exposure:** Serum PFOA levels based on estimated environmental levels on a fate and transport model to estimate PFOA levels in water and air per year since production began in 1951 and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life. Exposures of workers were estimated using a job history matrix. The mean serum PFOA level of the combined cohort was 86.6 ng/mL. PFOA levels were categorized into quintiles: • 2nd quintile: 142–<234 ng/mL • 3rd quintile: 234–<630 ng/mL • 4th quintile: 630–<3,579 ng/mL • 5th quintile: ≥3,579 ng/mL **Cox proportional hazards model adjustments:** Education, race, smoking, BMI, self-reported diabetes, alcohol consumption	No significant association between estimated cumulative serum PFOA and hypertension, HR 0.98 (95% CI 0.91–1.06) for the 5th quintile in retrospective analysis. No association was found in the prospective analysis with HR <1. No significant association between estimated cumulative serum PFOA and coronary artery disease; HR 1.07 (95% CI 0.93–1.23) for the 5th quintile in retrospective analysis. No association was found in the prospective analysis with HR <1.
Bao et al. 2017	**Exposure:** Median serum PFOA 6.19 ng/mL (range of 4.08–9.31 ng/mL); median serum concentration in males and	No association between serum PFOA and risk of hypertension (OR 1.12, 95% CI 0.97–1.30).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	females 6.59 ng/mL (4.08–9.31 ng/mL) and 5.08 ng/mL (3.17–7.73 ng/mL), respectively **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	Association between serum PFOA and change in systolic blood pressure (per 1 ln increase in PFOA) in males and females combined (1.69 mm Hg, 95% CI 0.25–3.13) and in females only (2.91 mm Hg, 95% CI 0.10–5.72), but not in males only (-0.06 mm Hg, 95% CI -1.70–1.59). Association between serum PFOA and change in diastolic blood pressure (per 1 ln increase in PFOA) in males and females combined (2.12 mm Hg, 95% CI 1.33–2.90) and in males only (1.48 mm Hg, 95% CI 0.60–2.35), but not in females only 1.34 mm Hg, 95% CI -0.14–3.05).
Geiger et al. 2014a Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,655 children 12–18 years of age; Hypertension was defined as age, height, and sex specific systolic and/or diastolic blood pressure level at the 95th percentile	**Exposure:** Mean serum PFOA level 4.4 ng/mL; perfluorochemical levels were categorized into quartiles **Linear regression model adjustments:** Age, sex, race/ethnicity, BMI, annual household income, moderate activity, total serum cholesterol, serum cotinine	No significant association between serum PFOA and hypertension; OR 0.69 (95% CI 0.41–1.17) for 4th quartile (>5.4 ng/mL).
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFOA 3.17 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	No association between serum PFOA and risk of cardiovascular disease (p=0.0926, for trend) 2nd quartile: OR 1.04 (0.79–1.38) 3rd quartile: OR 1.24 (0.92–1.67) 4th quartile: OR 1.25 (0.91–1.70)
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOA 1.81 ng/mL (WTCHR group) and 1.39 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFOA and arterial wall stiffness of the brachial artery (β 0.45, 95% CI 0.04–0.87, p=0.03); no association with pulse wave velocity (β -1.41, 95% CI -4.59–1.78, p=0.39) or augmentation index (β 0.05, 95% CI -0.17–0.28, p=0.64).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lin et al. 2013a, 2013b Cross-sectional study of 644 adolescents and young adults from the Taiwanese general population	**Exposure:** Median serum level of PFOA 3.49 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, smoking status, systolic blood pressure, BMI, LDL cholesterol, triglycerides, high-sensitivity C-reactive protein, HOMA-IR	No significant association (p=0.285 for trend) between CIMT and serum PFOA.
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	No association between serum PFOA and intima media thickness in the common carotid artery (β 0.007, 95% CI -0.017–0.03, p=0.58). No association between serum PFOA and echogenicity of intima media complex in males (β -0.582, 95% CI -4.974–3.81, p=0.80) or females (β 2.72, 95% CI -1.875–7.315, p=0.25).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFOA 2.32 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFOA and blood pressure score at 4 years of age (β -0.06, 95% CI -0.16–0.04) or 7 years of age (β -0.02, 95% CI -0.11–0.07).
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFOA 4.2 ng/mL in cases and 4.0 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	No significant association between serum PFOA and risk of coronary artery disease; OR 0.88 (95% CI 0.50–1.55) for participants with serum PFOA levels in the 4th quartile.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Melzer et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,966 adults (≥20 years of age)	**Exposure:** Mean serum PFOA levels were 5.23 ng/mL (0.1–45.9 ng/mL) in men and 4.25 ng/mL (0.1–123.0 ng/mL) in women Mean levels in each quartile: • 1st quartile: M 2.47 ng/mL; F 1.71 ng/mL • 2nd quartile: M 4.42 ng/mL; F 3.32 ng/mL • 3rd quartile: M 6.12 ng/mL; F 4.79 ng/mL • 4th quartile: M 10.39 ng/mL; F 9.47 ng/mL **Logistic regression model adjustments:** Age, ethnicity, study year, BMI, smoking status, alcohol consumption	No associations between serum PFOA levels and any physician-diagnosed report of coronary heart disease, angina, and/or heart attack: • 4th quartile: 1.08 (0.70–1.69), p=0.715
Min et al. 2012 Cross-sectional study utilizing 2003–2004 and 2005–2006 NHANES data for 2,208 adults (>20 years of age)	**Exposure:** Geometric mean serum PFOA levels was 4.00 ng/mL **Linear regression model adjustments:** Serum PFOS levels, age, sex, race/ethnicity, education, annual household income, cigarette smoking, alcohol consumption, exercise, total fatty acid intake, obesity status, total cholesterol, poor kidney function (assessed by estimated GFR), serum folate and vitamin B12 levels (only for homocysteine analyses) Hypertension defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg or as self-reported medical diagnosis of hypertension	Systolic blood pressure (p=0.0004) and homocysteine levels (p=0.039) were significantly correlated with log-transformed serum PFOA levels. A significant association between serum PFOA levels and risk of hypertension was found; the ORs were 2.62 (95% CI 2.09–3.14) when comparing participants with serum PFOA levels in the 80th percentile to those in the 20th percentile and 1.71 (95% CI 1.23–2.36) when comparing 4th quartile to the 1st quartile.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Shankar et al. 2012 Cross-sectional study utilizing 1999–2003 NHANES data for 1,216 adults (>20 years of age)	**Exposure:** Serum PFOA levels: • Q1 F: <2.9 ng/mL, M: <3.0 ng/mL • Q2 F: 2.9–3.9 ng/mL, M: 3.0–4.3 ng/mL • Q3 F:4.0–5.6 ng/mL, M: 4.4–6.1 ng/mL • Q4 F: >5.6 ng/mL; M: >6.1 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, race/ethnicity, educational level, smoking status, alcohol consumption, BMI, diabetes mellitus, hypertension, total cholesterol Examined relationship between serum PFOA levels and self-reported CVD and measured peripheral arterial disease (defined as ankle-brachial blood pressure index of <0.9)	Significant increases in the risk of CVD (Q3 and Q4) and peripheral arterial disease (Q4) were observed. The ORs (95% CI) were: CVD: • Q3: 1.77 (1.04–3.02) • Q4: 2.01 (1.12–3.60). Peripheral arterial disease: • Q3: 1.18 (0.47–2.96) • Q4: 1.78 (1.03–3.08). Significant increases in specific CVD were also found for participants with serum PFOA levels in the 4th quartile: CHD: 2.24 (1.02–4.94) Stroke: 4.26 (1.84–9.89).
Starling et al. 2014b Case-control study of pre-eclampsia among 976 pregnant women (466 cases, 510 non-cases) participating in the Norwegian Mother and Child Cohort Study; Diagnosis of pre-eclampsia was independently validated	**Exposure:** Median plasma PFOA level (collected at mid-pregnancy) 2.78 ng/mL levels **Weighed Cox proportional hazards models adjustments:** Maternal age at delivery, maternal education, prepregnancy BMI, smoking at mid-pregnancy	No significant associations between plasma PFOA and risk of pre-eclampsia; HR 0.89 (95% CI 0.65–1.22) per ln-unit.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Darrow et al. 2013 Cross-sectional study of 1,330 women participating in the C8 Health Project and giving birth between 2005 and 2010; maternal blood samples collected in 2005–2006; birth outcome data self-reported and taken from Ohio and West Virginia health departments	**Exposure:** Mean and geometric mean serum PFOS were 15.6 and 13.2 ng/mL (range: LOD [0.25]–92.9 ng/mL) • 1st quintile: 0–<8.6 ng/mL • 2nd quintile: 8.6–<12.1 ng/mL • 3rd quintile: 12.1–<15.9 ng/mL • 4th quintile: 15.9–<21.4 ng/mL • 5th quintile: ≥21.4 ng/mL **Logistic regression model adjustments:** Maternal age, educational level, smoking, parity, BMI, self-reported diabetes, time between conception, serum measurement	Serum PFOS levels were also associated with increased risk of pregnancy-induced hypertension for serum PFOS levels in the 3rd and 4th quintiles, but not the 5th quintile. The trend across quintiles was not statistically significant (p=0.107): • 3rd quintile: 2.71 (1.33–5.52) • 4th quintile: 2.21 (1.07–4.54) • 5th quintile: 1.56 (0.72–3.38)
Stein et al. 2009 Cross-sectional study of 5,262 pregnancies in Mid-Ohio Valley residents that occurred within the 5 years preceding blood sample collections for the C8 Health Project; self-reported birth outcome	**Exposure:** Mean and median serum PFOS: 14.1 and 12.8 ng/mL (range: 0.25–83.4 ng/mL) • 1st quartile: 0.25–<12.7 ng/mL • 2nd quartile:12.7–<17.7 ng/mL • 3rd quartile:17.7–<23.2 ng/mL • 4th quartile: 23.2–83.4 ng/mL **Logistic linear regression model adjustments:** Maternal age, parity, education, smoking status	Increased odds of pre-eclampsia in women with PFOS levels in the 4th quartile (OR 1.6, 95% CI 1.2–2.3).
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFOS 24.22 ng/mL (range of 14.62–37.19 ng/mL); median serum concentration in males and females 27.39 ng/mL (18.05–40.62 ng/mL) and 14.05 ng/mL (8.02–24.41 ng/mL), respectively **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	Association between serum PFOS and risk of hypertension (OR 1.24, 95% CI 1.08–1.44). When categorized by sex, the association was significant in females (OR 1.63, 95% CI 1.24–2.13), but not in males (OR 1.08, 95% CI 0.90–1.29) Association between serum PFOS and change in systolic blood pressure (per 1 ln increase in PFOS) in males and females combined (4.84 mm Hg, 95% CI 3.55–6.12) and in females only (6.65 mm Hg, 95% CI 4.32–8.99),

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		but not in males only (1.50 mm Hg, 95% CI -0.17–3.18). Association between serum PFOS and change in diastolic blood pressure (per 1 ln increase in PFOS) in males and females combined (2.70 mm Hg, 95% CI 1.98–3.42) and in females only (2.86 mm Hg, 95% CI 1.51–4.20), but not in males only (0.45 mm Hg, 95% CI -0.47–4.36).
Geiger et al. 2014a Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,655 children 12–18 years of age; Hypertension was defined as age, height, and sex specific systolic and/or diastolic blood pressure level at the 95th percentile	**Exposure:** Mean serum PFOS level 18.4 ng/mL; perfluorochemical levels were categorized into quartiles **Linear regression model adjustments:** Age, sex, race/ethnicity, BMI, annual household income, moderate activity, total serum cholesterol, serum cotinine	No significant association between serum PFOS and hypertension; OR 0.77 (95% CI 0.37–1.61) for 4th quartile (>25.5 ng/mL).
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFOS 12.40 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	No association between serum PFOS and risk of cardiovascular disease (p=0.0681, for trend) 2nd quartile: OR 1.04 (0.78–1.40) 3rd quartile: OR 1.36 (1.07–1.74) 4th quartile: OR 1.25 (0.92–1.69).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOS 3.72 ng/mL (WTCHR group) and 2.78 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFOS and arterial wall stiffness of the brachial artery (β 0.30, 95% CI -0.01–0.62, p=0.06), pulse wave velocity (β -0.06, 95% CI -0.23–0.11, p=0.51), or augmentation index (β -0.24, 95% CI -2.02–2.41, p=0.85).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lin et al. 2013a, 2013b Cross-sectional study of 644 adolescents and young adults from the Taiwanese general population	**Exposure:** Median serum levels of PFOS 8.65 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, smoking status, systolic blood pressure, BMI, LDL cholesterol, triglycerides, high-sensitivity C-reactive protein, HOMA-IR	Significant increases (p for trend <0.001) in CIMT across PFOS quartiles. Subpopulation analyses showed a stronger association between PFOS and CIMT in females, nonsmokers, subjects 12–19 years old, those with BMIs <24, and those with APOE genotype of E2 carrier and E3/E3.
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	No association between serum PFOS and intima media thickness in the common carotid artery (β 0.003, 95% CI -0.015–0.022, p=0.72). No association between serum PFOS and echogenicity of intima media complex in males (β 1.366, 95% CI -1.814–4.545, p=0.40) or females (β 1.068, 95% CI -2.51–4.647, p=0.56).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFOS 5.80 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFOS and blood pressure score at 4 years of age (β 0.00, 95% CI -0.09–0.10) or 7 years of age (β -0.05, 95% CI -0.15–0.06).
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFOS 22.8 ng/mL in cases and 22.0 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	No significant association between serum PFOS and risk of coronary artery disease; OR 1.07 (95% CI 0.60–1.92) for participants with serum PFOS levels in the 4th quartile.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Melzer et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,966 adults (≥20 years of age)	**Exposure:** Mean serum PFOS levels were 29.57 ng/mL (0.3–435.0 ng/mL) in men and 23.24 ng/mL (0.14–406.0 ng/mL) in women Mean levels in each quartile: • 1st quartile: M 12.29 ng/mL; F 8.13 ng/mL • 2nd quartile: M 21.82 ng/mL; F 15.75 ng/mL • 3rd quartile: M 30.81 ng/mL; F 24.21 ng/mL • 4th quartile: M 57.73 ng/mL; F 50.96 ng/mL **Logistic regression model adjustments:** Age, ethnicity, study year, BMI, smoking status, alcohol consumption	There were no significant associations between serum PFOS levels and participants ever reporting physician-diagnosed CHD, angina, and/or heart attack; OR 0.91 (95% CI 0.50–1.64, p=0.745) for the 4th quartile.
Starling et al. 2014b Case-control study of pre-eclampsia among 976 pregnant women (466 cases, 510 non-cases) participating in the Norwegian Mother and Child Cohort Study; Diagnosis of pre-eclampsia was independently validated	**Exposure:** Median plasma PFOS level (collected at mid-pregnancy) 12.87 ng/mL levels **Weighed Cox proportional hazards models adjustments:** Maternal age at delivery, maternal education, prepregnancy BMI, smoking at mid-pregnancy	No significant associations between plasma PFOS and risk of pre-eclampsia; HR 1.13 (95% CI 0.84–1.52) per ln-unit.
PFHxS		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFHxS 0.71 ng/mL (range of 0.01–2.68 ng/mL) **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	No association between serum PFHxS and risk of hypertension (OR 0.99, 95% CI 0.95–1.03). No association between serum PFHxS and change in systolic blood pressure (per 1 ln increase in PFHxS) in males and females combined (0.10 mm Hg, 95% CI -0.30–0.51). No association between serum PFHxS and change in diastolic blood pressure (per 1 ln increase in PFHxS) in males and females combined (0.12 mm Hg, 95% CI -0.11–0.35).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFHxS 1.60 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	No association between serum PFHxS and risk of cardiovascular disease (p=0.07031, for trend): 2nd quartile: OR 1.05 (0.76–1.44) 3rd quartile: OR 0.99 (074–1.34) 4th quartile: OR 0.96 (0.68–1.37).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFHxS 0.67 ng/mL (WTCHR group) and 0.53 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFHxS and arterial wall stiffness of the brachial artery (β 0.15, 95% CI -0.07–0.38, p=0.69), pulse wave velocity (β -0.05, 95% CI -0.16–0.07, p=0.43), or augmentation index (β -0.48, 95% CI -2.20–1.25, p=0.89).
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	No association between serum PFHxS and intima media thickness in the common carotid artery (β 0.001, 95% CI -0.004–0.016, p=0.90). No association between serum PFHxS and echogenicity of intima media complex in males (β -1.298, 95% CI -4.339–1.742, p=0.40) or females (β -0.085, 95% CI -2.737–2.567, p=0.95).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFHxS 0.61 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFHxS and blood pressure score at 4 years of age (β -0.01, 95% CI -0.10–0.09) or 7 years of age (β 0.04, 95% CI -0.04–0.13).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFHxS 1.6 ng/mL in cases and 1.6 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	No significant association between serum PFHxS and risk of coronary artery disease; OR 0.95 (95% CI 0.54–1.67) for participants with serum PFHxS levels in the 4th quartile.
Starling et al. 2014b Case-control study of pre-eclampsia among 976 pregnant women (466 cases, 510 non-cases) participating in the Norwegian Mother and Child Cohort Study; Diagnosis of pre-eclampsia was independently validated	**Exposure:** Median plasma PFHxS level (collected at mid-pregnancy) 0.69 ng/mL levels **Weighed Cox proportional hazards models adjustments:** Maternal age at delivery, maternal education, prepregnancy BMI, smoking at mid-pregnancy	No significant associations between plasma PFHxS and risk of pre-eclampsia; HR 0.91 (95% CI 0.72–1.14) per ln-unit.
PFNA		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFNA 1.96 ng/mL (range of 1.11–3.07); median serum concentration in males and females 2.19 ng/mL (1.33–14.62 ng/mL) and 1.31 ng/mL (0.68–2.23 ng/mL), respectively. **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	Association between serum PFNA and risk of hypertension (OR 1.19, 95% CI 1.04–1.36). When categorized by sex, the association was significant in females (OR 1.49, 95% CI 1.16–1.92), but not in males (OR 1.08, 95% CI 0.92–1.26). Association between serum PFNA and change in systolic blood pressure (per 1 ln increase in PFNA) in males and females combined (3.01 mm Hg, 95% CI 1.79–4.23) and in females only (5.70 mm Hg, 95% CI 3.55–7.85), but not in males only (-0.12 mm Hg, 95% CI -1.62–1.39). Association between serum PFNA and change in diastolic blood pressure (per 1 ln increase in PFNA) in males and females combined (2.48 mm Hg, 95% CI 1.80–3.16) and in males only (0.94 mm Hg, 95% CI 0.12–1.76) and in females only 2.74 mm Hg, 95% CI 1.51–3.97).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFNA 0.98 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	No association between serum PFNA and risk of cardiovascular disease (p=0.0480, for trend): 2nd quartile: OR 1.00 (0.75–1.33) 3rd quartile: OR 1.02 (0.78–1.34) 4th quartile: OR 1.30 (0.99–1.72). Adjusting for serum total proteins and estimated GFR resulted in an association between serum PFNA and cardiovascular disease (p=0.0136 for trend): 2nd quartile: OR 1.08 (0.81–1.44) 3rd quartile: OR 1.10 (0.83–1.44) 4th quartile: OR 1.42 (1.07–1.88). For individual types of cardiovascular disease, association between serum PFNA and coronary heart disease (p=0.0101, for trend): 2nd quartile: OR 1.63 (1.07–2.51) 3rd quartile: OR 1.12 (0.79–1.57) 4th quartile: OR 1.89 (1.29–2.76). Heart attack (p=0.0240): 2nd quartile: OR 1.32 (0.88–1.99) 3rd quartile: OR 1.51 (1.02–2.23) 4th quartile: OR 1.62 (1.07–2.43).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFNA 0.61 ng/mL (WTCHR group) and 0.49 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFNA and arterial wall stiffness of the brachial artery (β 0.34, 95% CI 0.02–0.67, p=0.04); no association with pulse wave velocity (β -0.13, 95% CI -0.30–0.04, p=0.14) or augmentation index (β -0.51, 95% CI -2.51–2.53, p=0.70).
Lin et al. 2013a, 2013b Cross-sectional study of 644 adolescents and young adults from the Taiwanese general population	**Exposure:** Median serum levels of PFNA 0.38 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, smoking status, systolic blood pressure, BMI, LDL cholesterol, triglycerides, high-sensitivity C-reactive protein, HOMA-IR	Significant inverse association (p=0.014 for trend) between serum PFNA and CIMT when serum PFOA, PFOS, and PFUnA were included in analysis.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	No association between serum PFNA and intima media thickness in the common carotid artery (β 0.003, 95% CI -0.008–0.025, p=0.76). Association between serum PFNA and echogenicity of intima media complex in females (β 5.268, 95% CI 1.048–9.489, p=0.01), but not in males (β -0.902, 95% CI -4.98–3.176, p=0.66).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFNA 0.66 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No association between maternal serum PFNA and blood pressure score at 4 years of age (β -0.01, 95% CI -0.10–0.08) or 7 years of age (β 0.00, 95% CI -0.08–0.09).
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFNA 0.5 ng/mL in cases and 0.5 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	No significant association between serum PFNA and risk of coronary artery disease; OR 0.68 (95% CI 0.39–1.20) for participants with serum PFNA levels in the 4th quartile.
Starling et al. 2014b Case-control study of pre-eclampsia among 976 pregnant women (466 cases, 510 non-cases) participating in the Norwegian Mother and Child Cohort Study; Diagnosis of preeclampsia was independently validated	**Exposure:** Median plasma PFNA level (collected at mid-pregnancy) 0.54 ng/mL levels **Weighed Cox proportional hazards models adjustments:** Maternal age at delivery, maternal education, prepregnancy BMI, smoking at mid-pregnancy	No significant associations between plasma PFNA and risk of pre-eclampsia; HR 0.90 (95% CI 0.70–1.16) per ln-unit.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFDA		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFDA 0.86 ng/mL (range of 0.51–1.45 ng/mL) **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	No association between serum PFDA and risk of hypertension (OR 0.96, 95% CI 0.85–1.09). No association between serum PFDA and change in systolic blood pressure (per 1 ln increase in PFDA) in males and females combined (-0.19 mm Hg, 95% CI -1.39–1.02). Association between serum PFDA and change in diastolic blood pressure (per 1 ln increase in PFDA) in males and females combined (1.19 mm Hg, 95% CI 0.52–1.37) and in males only (0.81 mm Hg, 95% CI 0.08–1.54), but not in females only 0.61 mm Hg, 95% CI -0.81–2.04).
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFDA 0.20 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	No association between serum PFDA and risk of cardiovascular disease (p=0.1409, for trend): 2nd quartile OR 1.22 (0.94–1.58) 3rd quartile OR 1.06 (0.80–1.39) 4th quartile OR 1.32 (0.99–1.78). Adjusting for serum total proteins and estimated GFR resulted in an association between serum PFDA and cardiovascular disease (p=0.0136 for trend): 2nd quartile OR 1.30 (1.00–1.70) 3rd quartile OR 1.10 (0.86–1.49) 4th quartile OR 1.43(1.06–1.92).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFDA 0.14 ng/mL (WTCHR group) and 0.11 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFDA and arterial wall stiffness of the brachial artery (β 0.11, 95% CI -0.06–0.28, p=0.10), pulse wave velocity (β -0.04, 95% CI -0.13–0.05, p=0.39), or augmentation index (β 0.08, 95% CI -1.23–1.39, p=0.14).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	No association between serum PFDA and intima media thickness in the common carotid artery (β 0.003, 95% CI -0.025–0.03, p=0.85). No association between serum PFDA and echogenicity of intima media complex in males (β -3.303, 95% CI -8.672–2.067, p=0.84) or females (β 4.09, 95% CI -1.353–9.533, p=0.14).
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFDA 0.2 ng/mL in cases and 0.2 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	No significant association between serum PFDA and risk of coronary artery disease; OR 0.92 (95% CI 0.53–1.60) for participants with serum PFDA levels in the 4th quartile.
Starling et al. 2014b Case-control study of pre-eclampsia among 976 pregnant women (466 cases, 510 non-cases) participating in the Norwegian Mother and Child Cohort Study; Diagnosis of pre-eclampsia was independently validated	**Exposure:** Median plasma PFDA level (collected at mid-pregnancy) 0.10 ng/mL levels **Weighed Cox proportional hazards models adjustments:** Maternal age at delivery, maternal education, prepregnancy BMI, smoking at mid-pregnancy	No significant association between plasma PFDA and risk of pre-eclampsia; HR 0.88 (95% CI 0.75–1.04) per ln-unit.
PFUnA		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFUnA 0.5 ng/mL (range of 0.01–0.95 ng/mL) **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	No association between serum PFUnA and risk of hypertension (OR 0.95, 95% CI 0.90–1.01). No association between serum PFUnA and change in systolic blood pressure (per 1 ln increase in PFUnA) in males and females combined (-0.49 mm Hg, 95% CI -1.04–0.05). No association between serum PFUnA and change in diastolic blood pressure (per 1 ln increase in PFUnA) in males and females combined (-0.11 mm Hg, 95% CI -0.41–0.20).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFUnA 0.20 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	Association between serum PFUnA and risk of cardiovascular disease (p=0.0111, for trend): 2nd quartile OR 1.58 (1.17–2.12) 3rd quartile OR 1.63 (1.25–2.11) 4th quartile OR 1.47 (1.07–2.04). Adjusting for serum total proteins and estimated GFR resulted in an association between serum PFUnA and cardiovascular disease (p=0.0043 for trend): 2nd quartile OR 1.57 (1.17–2.10) 3rd quartile OR 1.68 (1.29–2.18) 4th quartile OR 1.56 (1.11–2.16). For individual types of cardiovascular disease, association between serum PFUnA and coronary heart disease (p=0.0008, for trend): 2nd quartile OR 1.57 (1.00–2.46) 3rd quartile OR 1.72 (1.11–267) 4th quartile OR 2.02 (1.36–3.00). Angina pectoris (p=0.0408): 2nd quartile OR 1.64 (0.99–2.71) 3rd quartile OR 1.97 (1.09–3.55) 4th quartile OR 1.71 (0.98–2.97).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFUnA 0.12 ng/mL (WTCHR group) and 0.04 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFUnA and arterial wall stiffness of the brachial artery (β 0.11, 95% CI -0.04–0.26, p=0.97), pulse wave velocity (β -0.03, 95% CI -0.11–0.05, p=0.41), or augmentation index (β 0.37, 95% CI -0.79–1.52, p=0.35).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lin et al. 2013a, 2013b Cross-sectional study of 644 adolescents and young adults from the Taiwanese general population	**Exposure:** Median serum level of PFUnA 6.59 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, smoking status, systolic blood pressure, BMI, LDL cholesterol, triglycerides, high-sensitivity C-reactive protein, HOMA-IR	No significant association (p=0.953 for trend) between CIMT and serum PFUnA.
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	No association between serum PFUnA and intima media thickness in the common carotid artery (β -0.001, 95% CI -0.027–0.026, p=0.96). No association between serum PFUnA and echogenicity of intima media complex in males (β -4.405, 95% CI -9.52–0.71, p=0.09) or females (β 3.948, 95% CI -1.23–9.126, p=0.14).
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFUnA 0.2 ng/mL in cases and 0.2 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	No significant association between serum PFUnA and risk of coronary artery disease; OR 0.88 (95% CI 0.51–1.51) for participants with serum PFUnA levels in the 4th quartile.
Starling et al. 2014b Case-control study of pre-eclampsia among 976 pregnant women (466 cases, 510 non-cases) participating in the Norwegian Mother and Child Cohort Study; Diagnosis of pre-eclampsia was independently validated	**Exposure:** Median plasma PFUnA level (collected at mid-pregnancy) 0.17 ng/mL levels **Weighed Cox proportional hazards models adjustments:** Maternal age at delivery, maternal education, prepregnancy BMI, smoking at mid-pregnancy	Significant inverse association between plasma PFUnA and risk of pre-eclampsia; HR 0.78 (95% CI 0.66–0.92) per ln-unit. The association was significant for all quartiles: • 2nd quartile: 0.51 (0.35–0.76) • 3rd quartile: 0.60 (0.41–0.88) • 4th quartile: 0.55 (0.38–0.81).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHpA		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFHpA 0.01 ng/mL (range of 0.01–0.01 ng/mL); median serum concentration in males and females 0.01 ng/mL (range of 0.01–0.01 ng/mL) and 0.01 ng/mL (range of 0.01–0.01 ng/mL), respectively **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	No association between serum PFHpA and risk of hypertension (OR 1.02, 95% CI 0.89–1.16). Association between serum PFHpA and change in systolic blood pressure (per 1 ln increase in PFHpA) in males and females combined (1.50 mm Hg, 95% CI 0.21–2.80) and in males only (1.84 mm Hg, 95% CI 0.43–3.25), but not in females only (0.34 mm Hg, 95% CI -2.47–3.15). No association between serum PFHpA and change in diastolic blood pressure (per 1 ln increase in PFHpA) in males and females combined (0.66 mm Hg, 95% CI -0.05–1.40). An association in males only (0.79 mm Hg, 95% CI 0.02–1.55), but not in females only (0.14 mm Hg, 95% CI -1.45–1.73).
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFHpA 0.20 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	No association between serum PFHpA and risk of cardiovascular disease (p=0.0821, for trend) 2nd quartile OR 0.91 (0.56–1.46) 3rd quartile OR 1.20 (0.98–1.48) 4th quartile OR 1.16 (0.71–1.91).
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	No association between serum PFHpA and intima media thickness in the common carotid artery (β 0.002, 95% CI -0.012–0.016, p=0.78). No association between serum PFHpA and echogenicity of intima media complex in males (β -0.859, 95% CI -3.648–1.93, p=0.553) or females (β 2.18, 95% CI -0.608–4.967, p=0.13).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFHpA 0.06 ng/mL in cases and 0.04 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	A significant association between serum PFHpA and risk of coronary artery disease was observed in participants with serum PFHpA levels in the 3rd quartile (OR 2.58, 95% CI 1.39–4.78), but not for the 4th quartile (OR 1.73, 95% CI 0.94–3.16).
PFBS		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFBS 0.01 ng/mL (range of 0.01–0.01 ng/mL) **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	No association between serum PFBS and risk of hypertension (OR 0.94, 95% CI 0.78–1.12). No association between serum PFBS and change in systolic blood pressure (per 1 ln increase in PFBS) in males and females combined (-0.69 mm Hg, 95% CI -2.49–1.11). No association between serum PFBS and change in diastolic blood pressure (per 1 ln increase in PFBS) in males and females combined (-0.41 mm Hg, 95% CI -1.42–0.60).
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFBS 0.07 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	Association between serum PFBS and risk of cardiovascular disease (p=0.0193, for trend): 2nd quartile OR 1.34 (1.05–1.723). Adjusting for serum total proteins and estimated GFR resulted in an association between serum PFBS and cardiovascular disease (p=0.0162 for trend): 2nd quartile OR 1.16 (1.03–1.31).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFBA		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFBA 0.15 ng/mL (range of 0.01–0.51 ng/mL); median serum concentration in males and females 0.17 ng/mL (0.01–0.12 ng/mL) and 0.12 ng/mL (0.01–0.38 ng/mL), respectively **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	Association between serum PFBA and risk of hypertension (OR 1.10, 95% CI 1.04–1.17). When categorized by sex, the association was significant in males (OR 1.09, 95% CI 1.02–1.16) and in females (OR 1.16, 95% CI 1.04–1.29). Association between serum PFBA and change in systolic blood pressure (per 1 ln increase in PFBA) in males and females combined (0.80 mm Hg, 95% CI 0.25–1.34) and in males only (0.66 mm Hg, 95% CI 0.03–1.28), but not in females only (0.77 mm Hg, 95% CI -0.27–1.80). No association between serum PFBA and change in diastolic blood pressure (per 1 ln increase in PFBA) in males and females combined (0.09 mm Hg, 95% CI -0.22–0.40).
PFDoDA		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFDoDA 0.12 ng/mL (range of 0.05–0.19); median serum concentration in males and females 0.17 ng/mL (0.01–0.12 ng/mL) and 0.12 ng/mL (0.01–0.38 ng/mL), respectively **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	No association between serum PFDoDA and risk of hypertension (OR 1.02, 95% CI 0.93–1.11). No association between serum PFDoA and change in systolic blood pressure (per 1 ln increase in PFDoA) in males and females combined (0.30 mm Hg, 95% CI -0.56–1.16). An association in females only (1.89 mm Hg, 95% CI 0.21–3.56), but not in males only (-0.74, 95% CI -1.71–0.22). Association between serum PFDoDA and change in diastolic blood pressure (per 1 ln increase in PFDoDA) in males and females combined (0.59 mm Hg, 95% CI 0.12–1.07) and in females only (1.02 mm Hg, 95% CI 0.07–

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		1.97), but not in males only (0.13 mm Hg, 95% CI -0.40–0.66).
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum PFDoDA 0.14 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	Association between serum PFDoDA and risk of cardiovascular disease (p=0.0075, for trend): 2nd quartile OR 1.02 (0.57–1.81 3rd quartile OR 1.15 (0.89–1.47) 4th quartile OR 1.53 (1.14–2.04). Adjusting for serum total proteins and estimated GFR resulted in an association between serum PFDoDA and cardiovascular disease (p=0.0079 for trend): 2nd quartile OR 1.05 (0.58–1.88) 3rd quartile OR 1.13 (0.88–1.44) 4th quartile OR 1.57 (1.17–2.10). For individual types of cardiovascular disease, association between serum PFDoDA and congestive heart failure (p=0.0162, for trend): 2nd quartile OR 0.62 (0.19–2.00) 3rd quartile OR 1.55 (1.07–2.25) 4th quartile OR 1.60 (1.01–2.54) Angina pectoris (p=0.0138) 2nd quartile OR 1.07 (0.39–2.96) 3rd quartile OR 1.42 (0.97–2.09) 4th quartile OR 1.64 (1.06–2.54).
Mattsson et al. 2015 Population-based prospective cohort study of 231 male farmers and rural residents from Sweden diagnosed with CHD between 1992 and 2009 and 231 controls	**Exposure:** Median serum PFDoDA 0.02 ng/mL in cases and 0.02 ng/mL in controls **Conditional logistic regression model adjustments:** BMI, systolic blood pressure, HDL, total cholesterol, tobacco use (cotinine levels)	No significant association between serum PFDoDA and risk of coronary artery disease; OR 0.63 (95% CI 0.35–1.11) for participants with serum PFDoDA levels in the 4th quartile.

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHxA		
Bao et al. 2017 Cross-sectional study of 1,612 adults (mean age of 55.1 years) living in an area of China	**Exposure:** Median serum PFHxA 0.03 ng/mL (range of 0.01–1.55); median serum concentration in males and females 0.03 ng/mL (0.01–1.70 ng/mL) and 0.03 ng/mL (0.01–1.22 ng/mL), respectively. **Statistical adjustments:** Age, sex, BMI, education, income, exercise, smoking, drinking, family history of hypertension	No association between serum PFHxA and risk of hypertension (OR 1.03, 95% CI 0.99–1.08). When categorized by sex, an association was significant in females (OR 1.10, 95% CI 1.00–1.21, but not in males (OR 1.02, 95% CI 0.97–1.07). No association between serum PFHxA and change in systolic blood pressure (per 1 ln increase in PFHxA) in males and females combined (0.41 mm Hg, 95% CI -0.02–0.84). No association between serum PFHxA and change in diastolic blood pressure (per 1 ln increase in PFHxA) in males and females combined (0.21 mm Hg, 95% CI -0.03–0.45).
FOSA		
Huang et al. 2018 Cross-sectional study utilizing 1999–2000, 2003–2004, 2005–2006, 2007–2008, 2009–2010, 2011–2013, and 2013–2014 NHANES data for 10,859 adults (≥20 years of age)	**Exposure:** Median serum FOSA 0.07 ng/mL **Statistical adjustments:** Age, sex, race/ethnicity, family poverty income ratio, education, physical activity, alcohol consumption, smoking, BMI, diabetes, hypertension, family history of cardiovascular disease, total energy intake, serum cotinine, serum total cholesterol	Association between serum FOSA and risk of cardiovascular disease (p=0.0404, for trend) 2nd quartile OR 1.29 (1.01–1.65) Adjusting for serum total proteins and estimated GFR resulted in an association between serum FOSA and cardiovascular disease (p=0.0062 for trend) 2nd quartile OR 1.13 (1.01–1.28).

Table 3. Cardiovascular Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lind et al. 2017b Cross-sectional study of 1,016 males and females in Sweden (70 years of age)	**Exposure:** Not reported **Statistical adjustments:** Sex, HDL and LDL cholesterol, serum triglycerides, BMI, blood pressure, smoking, exercise, calorie intake, alcohol intake, diabetes, education	Association between serum FOSA and intima media thickness in the common carotid artery (β 0.024, 95% CI 0.006–0.042, p=0.01). Categorizing by sex, the association with intima media thickness in the common carotid artery was found in females (β 0.039, 95% CI 0.012–0.035, p=0.004), but not in males (β 0.013, 95% CI -0.014–0.039, p=0.35). No association between serum FOSA and echogenicity of intima media complex in males (β 0.329, 95% CI -2.875–3.532, p=0.84) or females (β 0.438, 95% CI -2.646–3.522, p=0.78).

APFO = ammonium perfluorooctanoate; BMI = body mass index; CHD = coronary heart disease; CI = confidence interval; CIMT = carotid intima media thickness; CVD = cardiovascular disease; F = female; FOSA = perfluorooctane sulfonamide; GFR = glomerular filtration rate; HDL = high density lipoprotein; HOMA = homeostatic model assessment; HR = hazard ratio; INMA = INfancia y Medio Ambiente; IR = insulin resistance; LDL = low density lipoprotein; LHWA = Little Hocking Water Authority; LOD = limit of detection; M = male; MRR = mortality risk ratio; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PBPK = physiologically based pharmacokinetic; PFBA = perfluorobutanoic acid; PFBS = perfluorobutane sulfonic acid; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHpA = perfluoroheptanoic acid; PFHxA = perfluorohexanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; RR = relative risk; SMR = standardized mortality ratio; SPR = standardized prevalence ratio; WTCHR = World Trade Center Health Registry

Table 4. Gastrointestinal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Grice et al. 2007 A cohort study of 1,400 (81% males) current, retired, or former workers employed for at least 1 year at a PFOS-based fluorochemical manufacturing facility in Decatur, Alabama	**Exposure:** Workers were assigned to an exposure category based on job history; geometric serum PFOS levels were assigned to each category based on monitoring data conducted in 1998 on 186 workers • Group 1: no direct workplace exposure (serum PFOS 110–290 ng/mL) • Group 2: low potential workplace exposure (serum PFOS 390–890 ng/mL) • Group 3: high potential workplace exposure (serum PFOS 1,300–1,970 ng/mL) **Logistic regression model adjustments:** Group 1 was used as a comparison group; ORs were adjusted for age and sex	Health conditions were self-reported. No significant associations between exposure to PFOS and colon polyps or gastric ulcer were found. The ORs (95% CI) in the ever-exposed group (groups 2 and 3) and the high-exposure group (group 3) were: Colon polyps: • all ORs <1.0 Gastric ulcer: • Groups 2 or 3: 1.07 (0.78–1.47) • Group 3: 1.09 (0.78–1.54).
Olsen et al. 2004a Cross-sectional study examining episodes of care among current or retired workers employed for at least 1 year between 1993 and 1998 at a PFOS-based fluorochemical manufacturing facility in Decatur, Alabama	**Exposure:** Workers working at the chemical plant (n=652) were considered exposed to PFOS; these workers were divided into low and high potential subgroups; workers at the film plant (n=659) were not considered exposed to PFOS and served as the comparison group **Statistical analysis:** The ratio of two indirect standardization methods was used to calculate RRE_pC, which was adjusted for age and sex	An increased RRE_pC was calculated for benign colonic polyps (1.4, 95% CI 0.9–2.1); among long-term workers (>10 years) with high potential for exposure, the RRE_pC was 2.4 (95% CI 1.3–4.5).

CI = confidence interval; OR = odds ratio; PFOS = perfluorooctane sulfonic acid; RRE_pC = risk ratio episode of care

Table 5. Hematological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Emmett et al. 2006b Cross-sectional study of 371 residents (aged 2.5–89 years) who had resided in the Little Hocking Water Association district for ≥2 years; includes 18 residents with occupational exposure to PFOA	**Exposure:** Median serum PFOA level was 354 ng/mL	A significant correlation between serum PFOA and absolute monocytes (p=0.01) was found; however, the slope was very low (0.000005). No significant correlations (p>0.05) between serum PFOA and total and differential WBC, RBC, hemoglobin, hematocrit, MCV, MCH, MCHC, or platelets were found. There were no significant (p>0.05) differences in the serum PFOA levels between residents with abnormal or normal hematological parameter levels with the exception of percent neutrophils (p=0.02) and percent lymphocytes (p=0.01) in which residents with abnormal values had lower serum PFOA levels.
PFOS		
Olsen et al. 1998a Cross-sectional study of workers at two PFOS-based fluorochemical manufacturing facility in Decatur, Alabama or Antwerp, Belgium; workers were examined in 1995 (n=178) and 1997 (n=149); 61 workers participated in both years; this is the same cohort of workers as Olsen et al. (1999)	**Exposure:** 20–22% of the workers in Decatur and 14–24% in Antwerp had serum PFOS levels of >3,000 ng/mL; the mean PFOS levels in 1995 and 1997 were 2,440 and 1,960 ng/mL in Decatur and 1,930 and 1,480 ng/mL in Antwerp **Multivariable regression model adjustments:** Age, BMI, alcohol consumption, smoking	Significant negative correlations between serum PFOS levels and hematocrit (p<0.05) in 1997 for all workers and with platelets for all workers and with workers at Antwerp and Decatur facilities in 1995. Significant positive correlations (p<0.05) were found between serum PFOS with MCH and MCV in the Antwerp cohort in 1995, but not in 1997, and with WBC in 1995 in both facilities and in the Antwerp cohort. These associations were not found at the other monitoring period. No significant correlations were found for hemoglobin, RBC, or MCHC levels. No significant associations between serum PFOS and hematological parameters were found.

Table 5. Hematological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Gilliland 1992 Cross-sectional study of 115 (79% male) current workers employed at a PFOA production facility in Cottage Grove, Minnesota between 1985 and1989; this is same cohort examined by Gilliland and Mandell (1996)	**Exposure:** Serum fluorine levels were used as surrogate for serum PFOA; workers were categorized into five exposure groups based on serum fluorine levels: <1, 1–3, >3–10, >10–15, and >15–26 ppm **Regression model adjustments:** Age, BMI, alcohol use, tobacco use	Inverse association between serum fluorine levels and hemoglobin (β -0.002, p=0.02) and lymphocyte count (β -342.7, p=0.007). Association between serum fluorine levels and monocyte count (β 110.4, p=0.005) and platelet count (β 29.8, p=0.02). No association between serum fluorine levels and mean corpuscular hemoglobin (β 0.15, p=0.10), mean corpuscular volume (β -0.04, p=0.52), or WBC (β 0.07, p=0.49).
Olsen et al. 2003a Cohort study of workers at two fluorochemical manufacturing facility in Decatur, Alabama (n=263, 82% male) or Antwerp, Belgium (n=255, 81% male) with potential exposure to PFOA and PFOS; workers were examined in 2000; 174 workers participated in at least one other medical survey conducted in 1994/5 or 1997	**Exposure:** Mean serum PFOS levels were 1,320 ng/mL (range: 60–10,060 ng/mL) in Decatur and 800 ng/mL (range: 40–6,240 ng/mL) in Antwerp Median PFOS levels in the 1st, 2nd, 3rd, and 4th quartiles were 290, 590, 1,170, and 2,460 ng/mL, respectively, for males and 80, 130, 370, and 1,340 ng/mL in females Mean serum PFOA levels were 1,780 ng/mL (range: 40–12,700 ng/mL) in Decatur and 840 ng/mL (range: 10–7,040 ng/mL) in Antwerp **Regression model adjustments:** Age, BMI, current alcohol consumption, cigarette use, employment duration	The investigators noted that there were no significant differences between serum PFOS or PFOA quartiles for hematological indices (hematocrit, hemoglobin, RBC WBC, platelet count).

BMI = body mass index; CI = confidence interval; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; MCV = mean corpuscular volume; OR = odds ratio; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; RBC = red blood cells; WBC = white blood cells

Table 6. Musculoskeletal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was estimated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum PFOA levels in 2005–2006 were 325 and 113 ng/mL, respectively, in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant associations between estimated cumulative serum PFOA and risk of osteoarthritis (p=0.92 and 0.13 for trend with no lag or 10-year lag, respectively).
Innes et al. 2011 Cross-sectional study of 49,432 male and female adult (3,731 subjects reporting physician-diagnosed osteoarthritis) participants in the C8 Health Project	**Exposure:** Mean serum PFOA level was 87.4 ng/mL (range: <0.5–22,412 ng/mL) • 1st quartile: 0.25–13.5 ng/mL • 2nd quartile: 13.6–28.0 ng/mL • 3rd quartile: 28.1–71.9 ng/mL • 4th quartile: ≥72.0 ng/mL **Logistic regression model adjustments:** Age, sex, race/ethnicity, marital status, socioeconomic status, exercise, vegetarian diet, smoking, alcohol use, menopausal status, use of hormone replacement therapy (women), BMI, medical comorbidity, military service and associated chemical exposures, recent memory loss, mood and sleep impairment, and serum estradiol, cholesterol, uric acid, and C-reactive protein levels	Increased risk of physician diagnosed osteoarthritis; the OR (95% CI) were: • 2nd quartile: 1.16 (1.03–1.31) • 3rd quartile: 1.21 (1.07–1.36) • 4th quartile: 1.42 (1.26–1.59). Segregating by age, the association was only significant in participants under 55 years old: • 2nd quartile: 1.22 (1.02–1.45) • 3rd quartile: 1.26 (1.05–1.51) • 4th quartile: 1.53 (1.27–1.83). The OR for the 4th quartile in participants ≥55 years was 1.12 (95% CI 0.97–1.32). When segregated by BMI, the association was only significant in nonobese (BMI <30) subjects: • 2nd quartile: 1.02 (0.88–1.22) • 3rd quartile: 1.18 (1.01–1.37) • 4th quartile: 1.38 (1.19–1.61).

Table 6. Musculoskeletal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		The OR for the 4th quartile in obese participants was 1.12 (95% CI 0.94–1.36). The investigators noted that when analysis was restricted to participants with serum PFOA levels of ≤20 ng/mL (17,885 adults, 1,167 with osteoarthritis), serum PFOA was not associated with osteoarthritis.
Khalil et al. 2016 Cross-sectional study utilizing 2009–2010 NHANES data for 1,914 participants (956 males, 958 females) ≥12 years of age	**Exposure:** Mean serum concentrations of PFOA 3.7 ng/mL **Multivariate logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, smoking status, daily milk intake, physical activity, menopause, blood lead concentration	An inverse association between serum PFOA and total femur neck mineral density in women (β -0.017, 95% CI -0.033 to -0.001), but not in men (β 0.001, 95% CI -0.025–0.022). No associations between serum PFOA and total femur bone mineral density or lumbar spine bone mineral density in men and women. An association between serum PFOA and risk of osteoporosis in women OR 1.84 (95% CI 1.17–2.90; p=0.008) per ln-PFOA increase.
Khalil et al. 2018 Cross-sectional study of 48 obese children (ages 8–12) in Ohio	**Exposure:** Mean serum PFOA 0.99 ng/mL **Statistical adjustments:** Age, sex, race	No associations between serum PFOA and bone mineral density measurements.
Lin et al. 2014 Cross-sectional study utilizing 2005–2008 NHANES data for 2,339 adults (1,192 males and 1,147 females) ≥20 years of age	**Exposure:** Geometric mean serum PFOA 4.70 and 3.31 ng/mL in males and females **Multivariate logistic regression model adjustments:** Age, race/ethnicity, BMI, smoking status, alcohol use, treatment for osteoarthritis, daily use of prednisone or cortisone	No association (p>0.01) between serum PFOA and total lumbar spine bone mineral density or total hip bone mineral density in men, premenopausal women, and postmenopausal women. No associations between self-reported bone fractures were observed; OR (95% CI) per ln unit increase: All fracture types • Premenopausal women: 0.98 (0.75–1.28) • Postmenopausal women: 1.53 (0.63–3.74) • Men: 0.84 (0.67–1.07)

Table 6. Musculoskeletal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		Hip, wrist, and spine fracture • Premenopausal women: 1.09 (0.66–1.79) • Postmenopausal women: 1.12 (0.38–3.29) • Men: 1.04 (0.71–1.54) Hip fracture • Premenopausal women: 1.59 (0.57–4.46) • Postmenopausal women: 0.48 (0.06–4.16) • Men: 0.64 (0.39–1.06) Wrist fracture • Premenopausal women: 1.07 (0.65–1.77) • Postmenopausal women: 1.21 (0.46–3.13) • Men: 1.12 (0.75–1.70) Spine fracture • Premenopausal women: 1.83 (0.59–5.61) • Postmenopausal women: 0.84 (0.46–1.53) • Men: 1.54 (0.85–2.79).
Uhl et al. 2013 Cross-sectional study utilizing 2003–2008 NHANES data for 1,888 male and 1,921 female adults (20–84 years of age); 365 participants self-reported having osteoarthritis	**Exposure:** Weighted mean serum PFOA level was 4.83 ng/mL (range: 0.07–104 ng/mL) • 1st quartile: ≤2.95 ng/mL • 2nd quartile: >2.95–4.22 ng/mL • 3rd quartile: >4.22–5.89 ng/mL • 4th quartile: >5.89 ng/mL **Logistic regression model adjustments:** Age, poverty:income ratio, race/ethnicity, sex, smoking, BMI, vigorous recreational activity, and prior hip, wrist, or spine facture	Associations ($p<0.01$) between serum PFOA levels and self-reported osteoarthritis were found in women with serum PFOA levels in the 4th quartile (OR 1.98, 95% CI 1.24–3.19). The associations were not significant in males (4th quartile OR 0.82 [0.40–1.70]) or in males and females combined (4th quartile OR 1.55 [95% CI 0.99–2.43]). When women were stratified by age, a significant association was found in young women (20–49 years of age) (4th quartile OR 4.95 [1.27–19.4]), but not in older women (50–84 years) (4th quartile OR 1.33 [0.82–1.16]).

Table 6. Musculoskeletal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Innes et al. 2011 Cross-sectional study of 49,432 male and female adult (3,731 subjects reporting physician-diagnosed osteoarthritis) participants in the C8 Health Project	**Exposure:** Mean serum PFOS level was 23.5 ng/mL (range: <0.5–729.2 ng/mL • 1st quartile: 0.25–13.6 ng/mL • 2nd quartile: 13.7–20.2 ng/mL • 3rd quartile: 20.3–29.3 ng/mL • 4th quartile: ≥29.4 ng/mL **Logistic regression model adjustments:** Age, sex, race/ethnicity, marital status, socioeconomic status, exercise, vegetarian diet, smoking, alcohol use, menopausal status, use of hormone replacement therapy (women), BMI, medical comorbidity, military service and associated chemical exposures, recent memory loss, mood and sleep impairment, and serum estradiol, cholesterol, uric acid, C-reactive protein levels	An inverse association between serum PFOS levels and the odds of physician diagnosed osteoarthritis was in the 4th quartile; OR 0.76 (95% CI 0.68–0.85). When analyzed by serum PFOS percentiles, the risk of osteoarthritis declined with increasing serum PFOS concentrations.
Khalil et al. 2016 Cross-sectional study utilizing 2009–2010 NHANES data for 1,914 participants (956 males, 958 females) ≥12 years of age; study examined association between serum perfluorinated chemicals and bone health (femur and lumbar spine mineral density and physician diagnosed osteoporosis)	**Exposure:** Mean serum concentrations of PFOS 12.7 ng/mL **Multivariate logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, smoking status, daily milk intake, physical activity, menopause, blood lead concentration	Inverse association between serum PFOS and total femur neck mineral density in women (β -0.016, 95% CI -0.029 to -0.002) and men (β -0.013, 95% CI -0.024 to -0.002). No associations between serum PFOS and total femur bone mineral density or lumbar spine bone mineral density in men and women. No association between serum PFOS and risk of osteoporosis in women; OR 1.14 (95% CI 0.68–1.94; p=0.619) per ln-PFOS increase.
Khalil et al. 2018 Cross-sectional study of 48 obese children (ages 8–12) in Ohio	**Exposure:** Mean serum PFOS 2.79 ng/mL **Statistical adjustments:** Age, sex, race	No associations between serum PFOS and bone mineral density measurements.

Table 6. Musculoskeletal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lin et al. 2014 Cross-sectional study utilizing 2005–2008 NHANES data for 2,339 adults (1,192 males and 1,147 females) ≥20 years of age	**Exposure:** Geometric mean serum PFOS 19.23 and 12.09 ng/mL in males and females **Multivariate logistic regression model adjustments:** Age, race/ethnicity, BMI, smoking status, alcohol use, treatment for osteoarthritis, daily use of prednisone or cortisone	Inverse association ($p<0.01$) between serum PFOS and total lumbar spine bone mineral density in premenopausal women (β -0.022 (95% CI -0.038 to -0.007). When categorized by serum PFOS levels, the mean bone mineral density decreased ($p<0.001$ for trend) with increasing serum PFOS quartile. No association for total hip bone mineral density. No associations ($p>0.01$) between serum PFOS and total lumbar spine bone mineral density or total hip bone mineral density in men and postmenopausal women. No associations between self-reported bone fractures were observed; OR (95% CI) per ln unit increase: All fracture types • Premenopausal women: 0.97 (0.75–1.24) • Postmenopausal women: 1.59 (0.88–2.86) • Men: 0.92 (0.73–1.16) Hip, wrist, and spine fracture • Premenopausal women: 1.05 (0.64–1.73) • Postmenopausal women: 1.21 (0.61–2.38) • Men: 1.04 (0.74–1.47) Hip fracture • Premenopausal women: 1.12 (0.62–2.03) • Postmenopausal women: 0.83 (0.23–3.00) • Men: 1.07 (0.76–1.52) Wrist fracture • Premenopausal women: 1.04 (0.63–1.72) • Postmenopausal women: 1.22 (0.61–2.45) • Men: 1.09 (0.72–1.66)

Table 6. Musculoskeletal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		Spine fracture • Premenopausal women: 0.52 (0.15–1.86) • Postmenopausal women: 1.12 (0.26–4.78) • Men: 1.27 (0.67–2.42).
Uhl et al. 2013 Cross-sectional study utilizing 2003–2008 NHANES data for 1,888 male and 1,921 female adults (20–84 years of age); 365 participants self-reported having osteoarthritis	**Exposure:** Weighted mean serum PFOS level was 21.23 ng/mL (range: 0.14–435 ng/mL) • 1st quartile: ≤8.56 ng/mL • 2nd quartile: >8.56–13.59 ng/mL • 3rd quartile: >13.59–20.97 ng/mL • 4th quartile: >20.97 ng/mL **Logistic regression model adjustments:** Age, poverty:income ratio, race/ethnicity, sex, smoking, BMI, vigorous recreational activity, and prior hip, wrist, or spine facture	An association ($p<0.05$) between serum PFOS levels and self-reported osteoarthritis was found in males and females (4th quartile OR 1.77 [1.05–2.96]). The associations were not significant for females only (4th quartile OR 1.73 [95% CI 0.97–3.10]) or males only (4th quartile OR 0.95 [95% CI 0.73–1.23]). When women were stratified by age, a significant association was found in young women (20–49 years of age) (4th quartile OR 4.99 [1.61–15.4]), but not in older women (50–84 years of age) (4th quartile OR 1.30 [0.65–2.60]).
PFHxS		
Khalil et al. 2016 Cross-sectional study utilizing 2009–2010 NHANES data for 1,914 participants (956 males, 958 females) ≥12 years of age; study examined association between serum perfluorinated chemicals and bone health (femur and lumbar spine mineral density and physician diagnosed osteoporosis)	**Exposure:** Mean serum concentrations of PFHxS 2.5 ng/mL **Multivariate logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, smoking status, daily milk intake, physical activity, menopause, blood lead concentration	Inverse association between serum PFHxS (4th quartile) and total femur bone mineral density in women (β -0.014, 95% CI -0.074 to -0.014), but not in men (β -0.026, 95% CI -0.065–0.013). No significant associations between serum PFHxS and total femur neck mineral density or lumbar spine bone mineral density in men and women. Significant association between serum PFHxS and risk of osteoporosis in women; OR 1.64 (95% CI 1.14–2.38; p=0.008) per ln-PFHxS increase.

Table 6. Musculoskeletal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Khalil et al. 2018 Cross-sectional study of 48 obese children (ages 8–12) in Ohio	**Exposure:** Mean serum PFHxS 1.09 ng/m **Statistical adjustments:** Age, sex, race	No associations between serum PFHxS and bone mineral density measurements.
PFNA		
Khalil et al. 2016 Cross-sectional study utilizing 2009–2010 NHANES data for 1,914 participants (956 males, 958 females) ≥12 years of age; study examined association between serum perfluorinated chemicals and bone health (femur and lumbar spine mineral density and physician diagnosed osteoporosis)	**Exposure:** Mean serum concentrations of PFNA 1.9 ng/mL **Multivariate logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, smoking status, daily milk intake, physical activity, menopause, blood lead concentration.	Inverse association between serum PFNA (4th quartile) and total femur bone mineral density in women (β -0.040, 95% CI -0.077 to -0.003), but not in men (β 0.007, 95% CI -0.031–0.045). No significant associations between serum PFNA and total femur bone mineral density, total femur neck mineral density or lumbar spine bone mineral density in men and women. Significant association between serum PFNA and risk of osteoporosis in women; OR 1.45 (95% CI 1.02–2.05; p=0.001) per ln-PFNA increase.
Khalil et al. 2018 Cross-sectional study of 48 obese children (ages 8–12) in Ohio	**Exposure:** Mean serum PFNA 0.24 ng/mL **Statistical adjustments:** Age, sex, race	Inverse association between serum PFNA and one measure of bone mineral density (p<0.05); however, after adjustment for multiple testing, the association was no longer significant.

BMI = body mass index; CI = confidence interval; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Costa 2004 Cohort study of 35 workers at a perfluoroalkyl manufacturing facility in Italy	**Exposure:** Serum PFOA levels were measured, but values were not reported	Significantly higher serum total cholesterol (p=0.03) and non-HDL cholesterol (p=0.03) were found in comparisons between PFOA and non-PFOA workers. No significant differences were observed for HDL, LDL, or total triglyceride levels.
Costa et al. 2009 Cohort study of 53 current (n=37) and former (n=16) male workers at a perfluoroalkyl manufacturing facility in Italy undergoing annual health examinations from 1978–2007; a control group of 107 male workers with no exposure to PFOA was also examined	**Exposure:** Mean and median serum PFOA levels measured in 2007 were 12,930 and 5,710 ng/mL (range: 200–47,040 ng/mL) in current workers and 6,810 and 4,430 ng/mL (range: 530–18,660 ng/mL) in former workers. Mean and median serum PFOA levels decreased over time; the mean levels were 18,800 ng/mL in 2000 and 11,600 ng/mL in 2007; the median levels were 11,920 and 3,890 ng/mL during those same times. **Regression model adjustments:** Age, years of exposure, year of PFOA sampling, BMI, smoking, alcohol consumption	Significant differences (p=0.003) in total cholesterol levels between 34 current PFOA workers and 34 matched controls. No significant differences in HDL, triglycerides, total bilirubin, AST, ALT, or GGT were found. A statistically significant difference was found in total cholesterol (p=0.005) when the levels in the 34 current workers were compared to all non-exposed workers. When evaluating all workers (current, former, and non-exposed) who had concurrent measurements of serum PFOA and liver biomarkers (n=56), significant associations were found between serum PFOA and total cholesterol (p<0.05), total bilirubin (negative association, p<0.01), ALT (p<0.01), and GGT (p<0.01).
Gilliland 1992; Gilliland and Mandel 1996 Cross-sectional study of 115 (79% male) current workers employed at a PFOA production facility in Cottage Grove, Minnesota between 1985 and1989	**Exposure:** Serum fluorine levels were used as surrogate for serum PFOA; workers were categorized into five exposure groups based on serum fluorine levels: <1, 1–3, >3–10, >10–15, and >15–26 ppm **Regression model adjustments:** Age, BMI, alcohol use, tobacco use	No significant differences in total cholesterol (p=0.62), total LDL (p=0.87), or total HDL (p=0.66) were found between the different exposure groups, and there were no significant correlations with total fluorine levels. No significant differences in serum ALT (p=0.32), AST (p=0.80), or GGT (p=0.81) levels were found between the different exposure groups. Serum fluorine levels were negatively correlated with ALT and AST levels in all workers; however, among obese workers, there were positive significant associations.

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Olsen et al. 2000 Cross-sectional study of male workers employed at a PFOA production facility in Cottage Grove, Minnesota; workers were examined in 1993 (n=111), 1995 (n=80), and 1997 (n=74); 68 workers were examined in 1993 and 1995, 21 in 1995 and 1997, and 17 in 1993, 1995, and 1997	**Exposure:** Mean and median serum PFOA levels were 5,000 and 1,100 ng/mL (range: 0.0–80,000 ng/mL) in 1993, 6,400 and 1,300 ng/mL (0–114,100 ng/mL) in 1995, and 6,400 and 1,300 ng/mL (100–81,300 ng/mL) in 1997; workers were divided into three exposure groups: 0–<1,000, 1,000–<10,000, and ≥10,000 ng/mL	No significant differences (p≥0.08) in ALT, AST, GGT, total bilirubin, cholesterol, LDL, HDL, or triglyceride levels were found between the three exposure groups at each measurement period. Cholecystokinin levels decreased with increasing serum PFOA levels in 1997 (only year examined) (p=0.03), although all but two levels were within the reference range. No significant interactions between and PFOA and BMI on serum ALT levels were found.
Olsen and Zobel 2007 Cross-sectional study of workers at three fluorochemical manufacturing facility in Decatur, Alabama (n=215), Cottage Grove, Minnesota (n=131), or Antwerp, Belgium (n=206) with potential exposure to PFOA and PFOS; workers were examined in 2000; 92% of the workers reported that they did not take cholesterol-lowering medication	**Exposure:** Mean, median, and range of PFOA levels were 2,210, 1,100, and 10–92,030 ng/mL, and mean, median, and range of PFOS levels were 1,050, 720, and 20–6,240 ng/mL Serum PFOA levels were categorized into deciles (ranges); the mean levels were: • D1: 60 ng/mL (7–130) • D2: 200 ng/mL (130–290) • D3: 360 ng/mL (300–440) • D4: 550 ng/mL (440–710) • D5: 910 ng/mL (720–1,100) • D6: 1,260 ng/mL (1,110–1,400) • D7: 1,640 ng/mL (1,420–1,850) • D8: 2,170 ng/mL (1,860–2,500) • D9: 3,000 ng/mL (2,510–3,690) • D10: 12,150 ng/mL (3,710–92,030) **Logistic and multiple regression adjustments:** Age, BMI, alcohol use, location	Serum PFOA was significantly associated with HDL cholesterol (p=0.01) and triglyceride levels (p=0.0001). No significant associations were found between serum PFOA levels and the risks of decreased HDL levels (≤40 mg/dL and elevated triglyceride levels (≥150 mg/dL) after adjustment for age, BMI, alcohol use, and location; the ORs (95% CI) for the 10th decile were 1.8 (0.7–4.8) and 1.8 (0.8–4.4), respectively. Serum PFOA levels were not significantly associated with total cholesterol (p=0.20) or LDL cholesterol (p=0.81) levels. There were no increases in the risk of elevated cholesterol (≥200 mg/dL) or LDL (≥130 mg/dL) levels. The ORs (95% CI) for workers with serum PFOA levels in the 10th decile were 1.1 (0.5–2.6) and 1.2 (0.5–2.8), respectively. Significant correlations (after adjustment for age, BMI, and alcohol) were found between serum PFOA and serum GGT (p=0.05) and total bilirubin (negative correlation, p=0.001); for ALT, the correlation was marginally significant (p=0.06). No significant correlation was found for AST (p=0.55). No significant associations between elevated ALT (≥40 IU/L) or GGT

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		(≥40 IU/L) and serum PFOA were found; the ORs (95% CI) for the 10th decile were 1.2 (0.5–3.4) and 1.0 (0.3–2.9), respectively.
Olsen et al. 2012 Longitudinal study of 179 workers (95% male, none taking lipid-lowering medication) involved in the demolition of perfluoroalkyl manufacturing facilities in Cottage Grove, Minnesota involved in the production of APFO and Decatur, Alabama involved in the production of PFOS; 14 subjects were 3M workers with significantly higher serum PFOA and PFOS levels than other workers and were involved in the project longer than other workers (306 days compared to 152 days); clinical assessments made at the end of the project were compared to baseline values	**Exposure:** Comparison of baseline and end of project mean serum PFOA and PFOS levels showed a decrease in levels in the 3M workers (-218.3 and -101.3 ng/mL, respectively) and increase in other workers (+32.1 and +1.0 ng/mL, respectively) **Linear regression model adjustments:** Sex, age, BMI, alcohol consumption, time intervals between assessments	In comparisons between baseline and end of project, significant increases in HDL and decreases in cholesterol/HDL ratio were found in workers who had increases in serum PFOA levels, and a significant increase in AST levels was found in workers who had decreases in serum PFOA levels.
Sakr et al. 2007a Longitudinal study of 454 workers at a fluoropolymers production plant (Washington Works) who had ≥2 serum PFOA measurements between 1979 and 2004; the average number of tests was 3.7, with an average of 10.8 years between the first and last test	**Exposure:** The mean serum PFOA level was 1,130 ng/mL (range: 0–22,660 ng/mL); average serum PFOA levels decreased over time **Linear mixed effects model:** Age, BMI, sex, decade of hire	Serum PFOA was significantly associated with total cholesterol; an increase of 1.06 mg/dL cholesterol for each 1,000 ng/mL increase in serum PFOA (p=0.011). There were no significant associations between serum PFOA and triglyceride, LDL, or HDL levels (p>0.05). Serum PFOA was significantly associated with total bilirubin and AST, with a 0.01 mg/dL decrease in total bilirubin (0.006) and a 0.35 IU/L increase in AST (p=0.009) with a 1,000 ng/mL increase in serum PFOA. There were no significant associations with GGT or ALT.

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Sakr et al. 2007b Cross-sectional study of 1,025 male (76%) and female (24%) workers at a fluoropolymers production plant (Washington Works)	**Exposure:** Median serum PFOA concentrations were 490 ng/mL (range: 17.4–9,550 ng/mL), 176 (8.1–2,070 ng/mL), 195 ng/mL (8.6–2,590 ng/mL), and 114 ng/mL (4.6–963 ng/mL) among current workers (n=259), current workers with intermittent exposure (n=160), past occupational exposure to PFOA (n=264), or never assigned to APFO area (n=342), respectively. The mean and median concentrations in all workers were 428 and 189 ng/mL, respectively. **Linear regression model adjustments:** Age, sex, BMI, alcohol consumption, heart attack in a parent (lipid models only)	Significant correlation between serum PFOA level and total cholesterol (p=0.002), LDL cholesterol (p=0.008), and VLDL cholesterol (p=0.031); not significant for HDL cholesterol (p=0.680) or triglycerides p=0.384). When analyses were restricted to workers not taking lipid-lowering medication (n=840), correlations were still significant for cholesterol, LDL, and VLDL levels. The regression model predicted that a 1 ppm increase in serum PFOA would result in increases of 5.519 mg/dL total cholesterol, 3.561 mg/dL LDL cholesterol, and 0.055 mg/dL VLDL cholesterol. Significant correlation between serum PFOA level and GGT levels (p=0.016); no significant correlations for AST (p=0.317), ALT (p=0.124), or bilirubin (p=0.590). Restricting the analyses to workers not on lipid-lowering medication did not alter results.
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was estimated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum PFOA levels in 2005–2006 were 325 and 113 ng/mL, respectively, in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant associations between estimated cumulative serum PFOA and risk of non-hepatitis liver disease (p=0.86 and 0.40 for trend with no lag or 10-year lag) or medicated high cholesterol (p=0.56 and 0.62 for trend with no lag or 10-year lag).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wang et al. 2012 Cross-sectional study of 55 workers at a fluorochemical plant in China for at least 5 years	**Exposure:** The mean and median serum PFOA levels were 2,157.74 and 1,635.96 ng/mL (range: 84.98–7,737.13 ng/mL) **Linear regression model adjustments:** Age, BMI	No significant correlations were found between serum PFOA and cholesterol (p=0.36), LDL cholesterol 0.43), triglycerides (p=0.37), or ALT (p=0.38). Significant negative associations between serum PFOA levels and HDL cholesterol (p=0.01) and ratio of HDL to LDL cholesterol (p=0.01) and a significant positive correlation between serum PFOA and AST (p=0.02) were found.
Anderson-Mahoney et al. 2008 Cross-sectional study of 566 adult residents (mean age of 49.9 years) living near a Teflon manufacturing facility in West Virginia for at least 1 year; most subjects were exposed to PFOA in drinking water provided by Lubeck Public Service District (37%) or Little Hocking water district (27%); some subjects also worked at the facility	**Exposure:** Individual biomonitoring data were not provided; reported PFOA levels in the Lubeck and Little Hocking water districts were 0.4–3.9 and 1.7–4.3 µg/L, respectively **Reference population:** SPRs estimated using NHANES data; statistical analyses adjusted for age and sex	Incidence data were based on the results of participant completed health surveys. No significant increase in the risk of liver problems (SPR 1.01, 95% CI 0.64–1.59) was found.
Darrow et al. 2016 Retrospective and prospective study of 28,831 participants in the C8 Health Project and a cohort of 1,892 workers at a DuPont Washington Works facility who worked at the plant between 1948 and 2002	**Exposure:** Serum PFOA levels based on estimated environmental levels on a fate and transport model to estimate PFOA levels in in water and air per year since production began in 1951 and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life. Exposures of workers were estimated using a job history matrix. The median estimated PFOA level in 2005–2006 was 16.5 ng/mL (range: 2.6–3,559 ng/mL). **Cox proportional hazards models adjustments:** Sex, race, education, smoking, BMI, birth year **Multivariate linear regression adjustments:** Age, sex, BMI, alcohol consumption, regular exercise, smoking,	Significant association between ALT levels and estimated cumulative serum PFOA (p<0.0001 for trend) and 2005/2006 serum PFOA levels (p<0.0001 for trend); the increase in ALT levels from 1st quartile to 5th quartile was approximately 5–6%. Significant inverse association between direct bilirubin levels and estimated cumulative serum PFOA (p=0.0029 for trend) and 2005/2006 serum PFOA levels p=0.0036 for trend); the decrease in bilirubin levels from 1st quartile to 5th quartile was 1.3–1.7%. No significant association between GGT levels and estimated cumulative PFOA (p=0.1021) or 2005–2006 PFOA (p=0.1552). No significant association between estimated cumulative serum PFOA levels and risk of any

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	education, insulin resistance, fasting status, history of working at DuPont facility, race	liver disease (HR 0.97, 95% CI 0.92–1.03 with no lag and HR 0.98, 95% CI 0.93–1.04 with 10-year lag per ln increase in PFOA) or enlarged liver, fatty liver, or cirrhosis (HR 0.97, 95% CI 0.91–1.04 with no lag and HR 1.00, 95% CI 0.94–1.07 with 10-year lag per ln increase in PFOA).
Emmett et al. 2006b Cross-sectional study of 371 residents (aged 2.5–89 years) living in the Little Hocking Water Association district for ≥2 years; includes 18 residents with occupational exposure to PFOA	**Exposure:** Median serum PFOA level was 354 ng/mL	No significant correlations (p>0.05) between serum PFOA and AST, ALT, GGT, or total cholesterol were found. There were no significant (p>0.05) differences in the serum PFOA levels between residents with abnormal or normal ALT, GGT, or total cholesterol. Residents with abnormal AST levels had significantly (p=0.03) lower serum PFOA levels.
Fitz-Simon et al. 2013 Longitudinal study of 560 adults (54% females) participating in the C8 Health Project and not taking cholesterol-lowering medication; participants were examined twice, with an average of 4.4 years between examinations	**Exposure:** Geometric and arithmetic mean serum PFOA levels were 74.8 and 140.1 ng/mL (range: 1.0–2,495 ng/mL) at the first examination and 30.8 and 68.2 ng/mL (range: 0.25–2,140 ng/mL) at the second examinations **Regression model adjustments:** Age, sex, time between measurements, fasting status	A 50% decrease in serum PFOA levels would result in a predicted 3.58% (95% CI 1.47–5.66) decrease in LDL cholesterol levels and 1.65% (95% CI 0.32–2.97) decrease in total cholesterol levels. The predicted decreases in HDL cholesterol (1.33%, 95% CI -0.21–2.85) and triglycerides (-0.78, 95% CI -5.34–3.58) included unity in the CI.
Frisbee et al. 2010 Cross-sectional study of 12,476 children (1.0–11.9 ears of age) and adolescents (12.0–17.9 years of age) participants in the C8 Health Project	**Exposure:** The mean and median serum PFOA levels were 77.7 and 32.6 ng/mL in children and 61.8 and 26.3 ng/mL in adolescents **Linear regression model adjustments:** Age, BMI, duration of fast, exercise	In children and adolescents, differences of 5.8 mg/dL (p<0.001) and 4.2 mg/dL (p<0.001) in serum total cholesterol and 4.9 mg/dL (p=0.001) and 3.2 mg/dL (p=0.004) in LDL cholesterol were found between participants with serum PFOA levels in the 1st and 5th quintiles, respectively. No significant differences were found for HDL cholesterol (p=0.88 and p=0.20) or triglycerides (p=0.1 and p=0.1).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		The risks of abnormal cholesterol or LDL cholesterol levels were significantly associated with serum PFOA levels, the ORs (95% CI) were: Total cholesterol • 2nd quintile: 1.1 (1.0–1.3) • 3rd quintile: 1.2 (1.0–1.4) • 4th quintile: 1.2 (1.1–1.4) • 5th quintile: 1.2 (1.1–1.4) LDL cholesterol • 2nd quintile: 1.2 (1.0–1.5) • 3rd quintile: 1.2 (1.0–1.4) • 4th quintile: 1.2 (1.0–1.4) • 5th quintile: 1.4 (1.2–1.7).
Gallo et al. 2012 Cross-sectional study of 46,452 adult participants in the C8 Health Project	**Exposure:** Serum PFOA levels were used as the biomarker of exposure; mean and range of values not reported **Linear regression model adjustments:** Age, physical activity, BMI, average household income, educational level, race, alcohol consumption, cigarette smoking	Significant correlations ($p<0.001$) between serum PFOA and ALT and GGT levels were found; the correlation was not significant ($p>0.05$) for direct bilirubin levels. The odds of having an abnormally high ALT value (≥45 IU/L in men and 34 IU/L in women) were significantly higher in subjects with serum PFOA levels in the third or higher deciles (trend, $p<0.001$); OR (95% CI): • 3rd decile: 1.19 (1.03–1.37) • 4th decile: 1.26 (1.09–1.45) • 5th decile: 1.40 (1.22–1.62) • 6th decile: 1.39 (1.21–1.60) • 7th decile: 1.31 (1.14–1.52) • 8th decile: 1.42 (1.23–1.64) • 9th decile: 1.40 (1.21–1.62) • 10th decile: 1.54 (1.33–1.78). The associations were not significant for GGT (trend, $p=0.213$) or direct bilirubin (trend, $p=0.496$).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Steenland et al. 2009b Cross-sectional study of 46,294 adult participants in the C8 Health Project	**Exposure:** Mean and median serum PFOA levels were 80.3 and 26.6 ng/mL PFOA quartiles: • 1st quartile: 0–13.1 ng/mL • 2nd quartile: 13.2–26.5 ng/mL • 3rd quartile: 26.6–66.9 ng/mL • 4th quartile: ≥67.0 ng/mL **Regression model adjustments:** Age, sex, BMI, education, smoking, regular exercise, alcohol consumption	A monotonic increase in log cholesterol levels with increasing serum PFOA levels ($p<0.001$); the slope appears to decrease at a serum PFOA level of 40 ng/mL. There were significant ($p<0.05$) positive linear trends for LDL cholesterol and triglycerides, but not for HDL cholesterol. The risk of high cholesterol (total cholesterol ≥240 mg/dL) was significantly elevated for serum PFOA levels in the 2nd, 3rd, and 4th quartiles; OR (95% CI) • 2nd quartile: 1.21 (1.12–1.31) • 3rd quartile: 1.33 (1.23–1.43) • 4th quartile: 1.38 (1.28–1.50).
Wang et al. 2012 Cross-sectional study of 132 residents living near a fluorochemical plant in China for at least 5 years	**Exposure:** The mean and median serum PFOA levels were 378.30 and 284.34 ng/mL (range: 10.20–2,436.91 ng/mL) **Linear regression model adjustments:** Age, BMI	No significant correlations were found between serum PFOA and cholesterol ($p=0.85$), HDL cholesterol ($p=0.39$), LDL cholesterol ($p=0.97$), ratio of HDL to LDL cholesterol ($p=0.57$), triglycerides ($p=0.79$), ALT ($p=0.05$), or AST ($p=0.22$).
Winquist and Steenland 2014a Retrospective study of 28,541 participants in the C8 Health Project and a cohort of 3,713 workers at a DuPont Washington Works facility who worked at the plant between 1948 and 2002	**Exposure:** Serum PFOA levels based on estimated environmental levels on a fate and transport model to estimate PFOA levels in water and air per year since production began in 1951 and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life. Exposures of workers were estimated using a job history matrix. The mean serum PFOA level was of the combined cohort 86.6 ng/mL (70.9 ng/mL for community only cohort and 324.6 ng/mL for worker only cohort). Estimated cumulative PFOA levels were categorized into quintiles: • 2nd quintile: 142–<234 ng/mL • 3rd quintile: 234–<630 ng/mL	Significant association ($p=0.005$ for trend) between estimated cumulative serum PFOA and risk of hypercholesterolemia; HR (95% CI): • 2nd quintile: 1.24 (1.15–1.33) • 3rd quintile: 1.17 (1.09–1.26) • 4th quintile: 1.19 (1.11–1.27) • 5th quintile: 1.19 (1.11–1.28) The association between estimated cumulative serum PFOA and hypercholesterolemia was most pronounced in men aged 40–59 years.

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	• 4th quintile: 630–<3,579 ng/mL • 5th quintile: ≥3,579 ng/mL **Cox proportional hazards model adjustments:** Education, race, smoking, BMI, self-reported diabetes, alcohol consumption	
Eriksen et al. 2013 Cross-sectional study of 753 adults (663 men, 90 women) 50–65 years of age participating in the Danish Diet, Cancer, and Health study; the subjects did not report taking cholesterol-lowering medication	**Exposure:** Mean serum PFOA was 7.1 ng/mL **Regression model adjustments:** Sex, age, education, BMI, smoking status, animal fat intake, physical activity	A significant association (p=0.01) between serum PFOA levels and total cholesterol was found. The difference in levels per interquartile range of plasma PFOA was 4.4 (95% CI 1.1–7.8).
Fisher et al. 2013 Cross-sectional study of 2,368 adult (aged 18–74 years) participants in the Canadian Health Measures Survey (2007–2009); the subjects reported not taking cholesterol-lowering medication	**Exposure:** Serum PFOA geometric mean was 2.46 ng/mL; quartile ranges: • 1st quartile: 0.15–1.85 ng/mL • 2nd quartile: 1.86–2.58 ng/mL • 3rd quartile: 2.59–3.55 ng/mL • 4th quartile: ≥3.56 ng/mL **Linear regression model adjustments:** Age, sex, marital status, BMI, physical activity, smoking status, alcohol consumption	No significant associations between serum PFOA levels and total cholesterol (p=0.22), non-HDL (p=0.13), LDL (p=0.63), HDL (p=0.96), or the ratio of total cholesterol to HDL (p=0.22). No significant association (p=0.10) between serum PFOA and risk of high cholesterol levels was found; OR (95% CI) for the 4th quartile was 1.5 (0.86–2.62).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fu et al. 2014a Cross-sectional study of 133 male and female subjects from China aged 0.3–88 years The following serum lipid levels were considered abnormal: >5.18 and >4.40 mmol/L for total cholesterol in adults and children, respectively; >1.70 mmol/L for triglycerides; <1.04 mmol/L for HDL cholesterol; and >3.37 and >2.85 mmol/L for LDL cholesterol in adults and children, respectively.	**Exposure:** Median serum PFOA level 1.43 ng/mL **Linear regression model adjustments:** Age, sex, BMI	Significant associations between serum PFOA and total cholesterol (p=0.015) and LDL cholesterol (p=0.022); no association with triglyceride (p=0.298) or HDL cholesterol (p=0.260). No significant associations between serum PFOA and risk of abnormal serum lipid parameters; ORs (95% CI) for 4th quartile (2.95–39.46 ng/mL): • Total cholesterol: 0.55 (0.09–3.31) • Triglyceride: 1.97 (0.59–6.55) • HDL cholesterol: 0.67 (0.13–3.51) • LDL cholesterol: 0.71 (0.14–3.49).
Geiger et al. 2014b Cross-sectional study utilizing 1999–2008 NHANES data for 815 participants (≤18 years of age); criteria for dyslipidemia were elevated total cholesterol of >170 mg/dL, LDL of >110 mg/dL, HDL cholesterol of <40 mg/dL, and triglycerides of >150 mg/dL	**Exposure:** Mean serum PFOA 4.2 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, body weight (underweight, normal weight, overweight), household income, activity level, serum cotinine	Significant associations between serum PFOA and total cholesterol levels (p=0.0170 for trend) and LDL levels (p=0.0027 for trend). No significant associations between serum PFOA and HDL levels (p=0.1769 for trend) or triglyceride levels (p=0.9943 for trend). Significant association (p=0.0253 for trend) between serum PFOA and risk of elevated cholesterol; OR 1.44 (95% CI 1.11–1.88) for log-transformed PFOA. No significant associations between serum PFOA and risk of elevated LDL (p=0.0539 for trend) or triglyceride (p=0.5975 for trend) or decreased HDL (p=0.1493 for trend).
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum biomarkers of liver damage were considered elevated if they exceeded 75th percentile of 2007–2010 NHANES values	**Exposure:** Median serum concentrations of PFOA 3.7 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	Significant association between serum PFOA and ALT (p<0.001), GGT (p<0.01), AST (p<0.01), and total bilirubin (p<0.01). Significant association between serum PFOA and risk of elevated ALT (p=0.007 for trend), GGT (p=0.042 for trend), and total bilirubin (p<0.001). No significant associations between serum PFOA and AST (p=0.058 for trend).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFOA 1.88 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFOA and total cholesterol (β -2.256, 95% CI -11.490–6.978, p=0.630), LDL cholesterol (β 3.899, 95% CI -4.810–12.608, p=0.377), or triglycerides (β 0.020, 95% CI -0.134–0.175, p=0.796).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOA 1.81 ng/mL (WTCHR group) and 1.39 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFOA and serum cholesterol (β 0.09, 95% CI 0.04–0.14, p<0.001), LDL cholesterol (β 0.11, 95% CI 0.03–0.19, p=0.006) and triglycerides (β 0.14, 95% CI 0.02–0.27, p=0.03); no association with HDL cholesterol (β 0.04, 95% CI -0.04–0.12, p=0.34).
Lin et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 2,216 adults (>18 years of age)	**Exposure:** Geometric mean serum PFOA concentration: 5.05 ng/mL (males) and 4.06 ng/mL (females) **Linear regression model adjustments:** Age, sex, race/ethnicity, smoking, drinking status, education level, BMI, insulin resistance, metabolic syndrome, iron saturation	Significant associations between serum PFOA levels and serum ALT (p=0.005) and GGT (p=0.019), but not for serum total bilirubin (p=0.645). When PFOS, PFHxS, and PFNA were also entered into the regression model, the associations between serum PFOA and ALT (p=0.009) and GGT (p=0.001) remained significant.
Liu et al. 2018b Cross-sectional study utilizing 2013–2014 NHANES data for 1,871 adults	**Exposure:** Geometric mean serum PFOA 1.86 ng/mL **Statistical adjustments:** Age, sex, ethnicity, smoking status, alcohol intake, household income, waist circumference, medications (anti-hypertensive, anti-hyperglycemic, anti-lipidemic)	Associations between serum PFOA and total cholesterol (β 5.58, p<0.05) and HDL cholesterol (β 1.93, p<0.01). No associations between serum PFOA and LDL cholesterol (β 4.47, p>0.05) or triglyceride levels (β -0.08, p>0.05).
Maisonet et al. 2015b Prospective cohort study of girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; the girls were examined at age 7 (n=111) and 15 (n=88) years	**Exposure:** Mean maternal serum PFOA level was 4.2 ng/mL for the 7-year-old group and 4.5 ng/mL for the 15-year-old group • 1st tertiles: 1.1–3.1 ng/mL • 2nd tertile: 3.2–4.4 ng/mL • 3rd tertile: 4.5–16.4 ng/mL **Statistical adjustments:** Previous livebirths, maternal education, maternal age at delivery	Associations were found between serum PFOA and total cholesterol and LDL cholesterol levels for 7-year-old children with maternal PFOA levels in the first tertile, but not in the 2nd or 3rd tertiles: Total cholesterol • 1st tertile: β 13.75 (95% CI 0.05–27.45) • 2nd tertile: β -0.53 (95% CI -15.39–14.33) • 3rd tertile: β -1.53 (95% CI -4.61–1.54) LDL cholesterol

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		• 1st tertile: β 14.01 (95% CI 3.26–24.76) • 2nd tertile: β -5.56 (95% CI -17.22–6.10) • 3rd tertile: β 0.03 (95% CI -2.38–2.45) In the 15-year-olds, associations between maternal PFOA and total cholesterol LDL cholesterol was found for the 1st tertile, but not at higher tertiles: Total cholesterol • 1st tertile: β 17.19 (95% CI 0.45–33.93) • 2nd tertile: β -1.22 (95% CI -16.45–14.01) • 3rd tertile: β -2.09 (95% CI -5.59–1.40) LDL cholesterol • 1st tertile: β 14.26 (95% CI 0.25–28.26) • 2nd tertile: β -1.29 (95% CI -14.03–11.45) • 3rd tertile: β -1.41 (95% CI -4.33–1.51) No associations were found for HDL cholesterol or triglyceride levels in the 7-year-olds (3rd tertile: β -0.40, 95% CI -1.82–1.01 and β -0.020, 95% CI -0.068–0.029, respectively) or 15-year-olds (3rd tertile: β -0.52, 95% CI -2.10–1.06 and β -0.013, 95% CI -0.051–0.025, respectively).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFOA 2.32 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No associations at 4 years of age between maternal serum PFOA and total cholesterol (β -0.02, 95% CI -0.10–0.15), HDL-C (β -0.04, 95% CI -0.15–0.08), LDL-C (β 0.03, 95% CI -0.12–0.21) or triglycerides (β -0.01, 95% CI -0.17–0.16).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 860 adults (18–80 years of age); cholesterol analyses excluded subjects taking cholesterol-lowering medication	**Exposure:** Mean and median serum PFOA levels were 4.6 and 3.9 ng/mL (range: 0.1–37.3 ng/mL **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	A significant association between serum PFOA and non-HDL (includes LDL and VLDL, p=0.05), but not for total cholesterol (p=0.07), HDL (p=0.34), or LDL (p=0.84). The change in non-HDL cholesterol levels per ng/mL increase in PFOA was 1.38 mg/dL (95% CI 0.12–2.65)
Skuladottir et al. 2015 Cross-sectional study of 854 Danish women with singleton pregnancies	**Exposure:** Mean serum levels of PFOA (collected at gestation week 30) 4.1 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal smoking, parity, total caloric intake, maternal education, saturated fat intake	Significant association between serum PFOA levels and total cholesterol levels (p=0.01 for trend). Total cholesterol increased 0.39 mmol/L (95% CI 0.09–0.68) when 5th quintile levels of PFOA (>5.10 ng/mL) were compared with 1st quintile (≤2.65 ng/mL).
Starling et al. 2014a Cross-sectional study of 891 pregnant women participating in the Norwegian Mother and Child Study	**Exposure:** Median plasma level (50th percentile) (sample collected at gestation week 18) PFOA 2.25 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal education, smoking at mid-pregnancy, oily fish consumed, gestational age at blood collection, parity, breastfeeding duration in previous pregnancy	No association between plasma PFOA and total cholesterol, LDL cholesterol, or triglycerides; the β (95% CI) values per ln-unit increase in PFOA were 2.58 (95% CI -4.32–9.47) for cholesterol, 2.35 (-3.97–8.48) for LDL, and 0.00 (-0.07–0.06) for triglycerides. Plasma PFOA was associated with HDL cholesterol; β 3.42 (95% CI 0.56–6.28) for participants with PFOA levels in the 4th quartile.
Timmermann et al. 2014 Cross-sectional study of 499 Danish children (8–10 years of age) participants of the European Youth Heart Study	**Exposure:** Median plasma concentration of PFOA 9.3 ng/mL **Linear regression model adjustments:** Sex, age, ethnicity, paternal income, fast food consumption, fitness; model adjusted for height when using waist circumference as outcome measured	No significant associations (p=0.91) between PFOA and triglyceride levels among normal-weight children. Among overweight children, an increase of 10 ng/mL plasma PFOA was associated with a 76.2% (95% CI 22.8–153.0) increase in triglyceride levels (p=0.002).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Yamaguchi et al. 2013 Cross-sectional study of 307 men and 301 women (16–76 years of age) from various regions of Japan	**Exposure:** Mean blood concentrations of PFOA 2.1 ng/mL **Statistical adjustments:** Age, sex, BMI region, smoking status	Significant correlation between serum PFOA and serum levels of docosahexaenoic acid (p=0.003), eicosapentaenoic acid (p<0.0001), AST (p=0.001), ALT (p=0.02), and GGT (p=0.03).
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFOA 1.90 ng/mL (range of 0.6–5.0 ng/mL) **Statistical adjustments:** Age	Association between serum PFOA and triglycerides (β 2.3, 95% CI 0.77–8.38). No association with HDL cholesterol (β 0.15, 95% CI -0.17–0.46).
Zeng et al. 2015 Cross-sectional study of 225 Taiwanese children aged 12–15 years	**Exposure:** Mean serum PFOA levels 1.1 ng/mL in boys and 0.92 ng/mL in girls **Multivariate linear regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco exposure	Significant associations between serum PFOA and total cholesterol (p=0.001), LDL cholesterol (p=0.002), and triglycerides (p<0.001); no association with HDL cholesterol (p=0.06).
PFOS		
Alexander et al. 2003 Retrospective cohort mortality study of 2,083 workers (145 deaths) employed for at least 1 year by December 31, 1997	**Exposure:** Workers were assigned to an exposure category based on job history; geometric serum PFOS levels were assigned to each category based on monitoring data conducted in 1998 on 186 workers • Group 1: no direct workplace exposure • Group 2: low potential workplace exposure • Group 3: high potential workplace exposure **Reference population:** Alabama general population	No increases in deaths from liver cirrhosis were observed; the SMRs were less than unity for the whole and for the specific exposure groups (SMR 0.81, 95% CI 0.10–2.94 for Group 3).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Grice et al. 2007 A cohort study of 1,400 (81% males) current, retired, or former workers employed for at least 1 year at a PFOS-based fluorochemical manufacturing facility in Decatur, Alabama	**Exposure:** Workers were assigned to an exposure category based on job history; geometric serum PFOS levels were assigned to each category based on monitoring data conducted in 1998 on 186 workers • Group 1: no direct workplace exposure (serum PFOS 110–290 ng/mL) • Group 2: low potential workplace exposure (serum PFOS 390–890 ng/mL) • Group 3: high potential workplace exposure (serum PFOS 1,300–1,970 ng/mL) **Logistic regression model adjustments:** Group 1 used as a comparison group; ORs were adjusted for age and sex	Health conditions were self-reported. No significant associations between exposure to PFOS and cholelithiasis, cholecystitis, or liver disease (including cirrhosis and hepatitis). The ORs (95% CI) in the ever-exposed group (groups 2 and 3) and the high-exposure group (group 3) were: Cholelithiasis • Groups 2 and 3: 1.06 (0.71–1.59) • Group 3: 0.91 (0.57–1.46) Cholecystitis • Groups 2 and 3: 1.19 (0.71–1.98) • Group 3: 0.91 (0.57–1.46) Liver disease • Groups 2 and 3: 1.08 (0.54–2.17) • Group 3: 1.21 (0.56–2.60).
Olsen et al. 1999 Cross-sectional study of workers at two PFOS-based fluorochemical manufacturing facility in Decatur, Alabama or Antwerp, Belgium; workers were examined in 1995 (n=178) and 1997 (n=149); 61 workers participated in both years	**Exposure:** 20–22% of the workers in Decatur and 14–24% in Antwerp had serum PFOS levels of >3,000 ng/mL; the mean PFOS levels in 1995 and 1997 were 2,440 and 1,960 ng/mL in Decatur and 1,930 and 1,480 ng/mL in Antwerp	No significant differences in ALT (p=0.38 and 0.46 for trend in 1995 and 1997), AST (p=0.14 and 0.67 for trend in 1995 and 1997), or GGT (p=0.71 and 0.34 for trend in 1995 and 1997) levels were found between different exposure groups when analyzed by examination year. Significant decreases in total bilirubin levels with increasing serum PFOS levels were found when analyzed by examination year (p=0.005 or 0.04). When analyzed by location (collapsed across examination years), no significant correlations were found. For the 1997 examination, significant increases in cholesterol (p=0.006 for trend) and LDL (p=0.01) with increasing PFOS levels were found. No significant relationships were found in 1995 (cholesterol p=0.96; LDL p=0.87). Decreasing HDL levels with increasing serum PFOS levels were found in 1995 (p=0.04) but not in 1997 (p=0.34). No significant

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		correlations were found for triglyceride levels (p=0.35 and 0.67 for trend in 1995 and 1997). When analyzed by location (collapsed across examination years), no significant correlations were found.
Olsen et al. 2004a Cross-sectional study examining episodes of care among current or retired workers employed for at least 1 year at between 1993–1998 at a PFOS-based fluorochemical manufacturing facility in Decatur, Alabama.	**Exposure:** Workers at the chemical plant (n=652) were considered exposed to PFOS; these workers were divided into low and high potential subgroups. Workers at the film plant (n=659) were not considered exposed to PFOS and served as the comparison group. **Statistical Analysis:** Ratio of two indirect standardization methods was used to calculate RRE_pC, which was adjusted for age and sex	An increased RRE_pC was calculated for cholelithiasis or acute cholecystitis (8.6, 95% CI 1.1–>100). No significant increases in all liver disorders (1.2, 95% CI 0.2–8.6) or all biliary duct disorders (1.6, 95% CI 0.8–2.9) were found. Among workers employed for at least 10 years with high potential for exposure, the RRE_pCs for cholelithiasis or acute cholecystitis were 25 (95% CI 2.1–>100) and 2.6 (95% CI 1.2–5.5) for all biliary tract disorders.
Olsen et al. 2003a Cross-sectional study of workers at two fluorochemical manufacturing facility in Decatur, Alabama (n=263, 82% male) or Antwerp, Belgium (n=255, 81% male) with potential exposure to PFOA and PFOS; workers were examined in 2000; 174 workers participated in at least one other medical survey conducted in 1994/5 or 1997	**Exposure:** Mean serum PFOS levels were 1,320 ng/mL (range: 60–10,060 ng/mL) in Decatur and 800 ng/mL (range: 40–6,240 ng/mL) in Antwerp. Median PFOS levels in the 1st, 2nd, 3rd, and 4th quartiles were 290, 590, 1,170, and 2,460 ng/mL, respectively, for males and 80, 130, 370, and 1,340 ng/mL, respectively, in females. The mean serum PFOA levels were 1,780 ng/mL (range: 40–12,700 ng/mL) in Decatur and 840 ng/mL (range: 10–7,040 ng/mL) in Antwerp. **Regression model adjustments:** Age, BMI, current alcohol consumption, cigarette use, employment duration	Male workers with the highest PFOS levels (4th quartile) had significantly ($p<0.05$) higher mean triglyceride and ALT levels than workers with the lowest PFOS levels. There were no significant alterations for cholesterol, HDL, GGT, or AST. Female workers in the 4th quartile had significantly higher GGT levels than workers in the 1st quartile; no differences in cholesterol, HDL, triglyceride, ALT, or AST were found. No significant associations between the risk of having serum ALT or GGT levels above the reference range were found. The ORs (95% CI) for the 4th quartile workers were 2.1 (0.6–7.3) for ALT and 2.0 (0.7–5.8) for GGT. The OR for any liver marker being above the reference range was 1.6 (0.7–3.3). Total cholesterol and triglycerides were significantly associated with serum PFOS levels (p=0.04 and 0.01), but serum PFOS was only a minor contributor (R^2=0.06 and 0.27) to the

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		variance. Similar associations were found with serum PFOA. In longitudinal analyses, serum PFOS was not a significant predictor of cholesterol or triglyceride levels. PFOA was positively associated with cholesterol and triglyceride. The investigators noted that this was primarily due to Antwerp workers participating in all three medical surveys whose serum PFOA levels increased from 1,320 to 2,060 ng/mL and PFOS levels declined from 2,100 to 1,530 ng/mL. Cholesterol levels increased from 208 to 229 mg/dL and triglyceride levels increased from 85 to 123 mg/dL. It is noted that BMIs also increased from 23.4 to 24.3. No other significant alterations in liver function tests were found.
Fitz-Simon et al. 2013 Longitudinal study of 560 adults (54% females) participating in the C8 Health Project and not taking cholesterol-lowering medication; participants were examined twice, with an average of 4.4 years between examinations	**Exposure:** Geometric and arithmetic mean serum PFOS levels were 18.5 and 22.6 ng/mL (range: 0.25–90.5 ng/mL) at the first examination and 8.2 and 10.5 ng/mL (range: 0.1–61 ng/mL) at the second examinations **Regression model adjustments:** Age, sex, time between measurements, fasting status	A 50% decrease in serum PFOS levels would result in a predicted 4.99% (95% CI 2.46–7.44) decrease in LDL cholesterol levels and 3.20% (95% CI 1.63–4.76) decrease in total cholesterol levels, and 1.28% decrease in HDL cholesterol levels. The CIs for the predicted decreases in HDL cholesterol (1.28%, 95% CI -0.59–3.12) and triglyceride (2.49%, 95% CI -2.88–7.57) included unity.
Frisbee et al. 2010 Cross-sectional study of 12,476 children and adolescent participants (1.0–7.9 years of age) in the C8 Health Project	**Exposure:** The mean and median serum PFOS levels were 23.6 and 20.7 ng/mL in children and 21.9 and 19.3 ng/mL in adolescents **Linear regression model adjustments:** Age, BMI, duration of fast, exercise	In children and adolescents, differences of 5.5 mg/dL ($p<0.001$) and 9.5 mg/dL ($p<0.001$) in serum total cholesterol, 3.4 mg/dL ($=0.002$) and 7.5 mg/dL ($p<0.001$) in LDL cholesterol, and 1.6 mg/dL ($p=0.007$), and 1.5 mg/dL ($p=0.001$) in HDL cholesterol were found between participants with serum PFOS levels in the 1st and 5th quintiles, respectively. No significant differences were found for triglycerides ($p=0.99$ and $p=0.90$).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		The risks of abnormal cholesterol or LDL cholesterol levels were significantly associated with serum PFOS levels; the ORs (95% CI) were: Total cholesterol • 2nd quintile: 1.3 (1.1–1.4) • 3rd quintile: 1.3 (1.2–1.5) • 4th quintile: 1.3 (1.2–1.6) • 5th quintile: 1.6 (1.4–1.9) LDL cholesterol • 2nd quintile: 1.2 (1.0–1.5) • 3rd quintile: 1.2 (1.0–1.5) • 4th quintile: 1.3 (1.1–1.6) • 5th quintile: 1.6 (1.3–1.9) The associations with HDL cholesterol and triglycerides were not significant; ORs (95% CI) for the 5th quintile were 0.7 (0.6–0.9) and 1.2 (0.8–1.5).
Gallo et al. 2012 Cross-sectional study of 46,452 adult participants in the C8 Health Project	**Exposure:** Serum PFOS levels used as the biomarker of exposure; mean and range of values not reported **Linear regression model adjustments:** Age, physical activity, BMI, average household income, educational level, race, alcohol consumption, cigarette smoking	Significant correlations (p<0.001) between serum PFOS and ALT and direct bilirubin levels were found; the correlation was not significant (>0.05) for GGT. The odds of having an abnormally high ALT value (≥45 IU/L in men and 34 IU/L in women) were significantly higher in subjects with serum PFOS levels in the 5th or higher deciles (trend, p<0.001); ORs (95% CI): • 5th decile: 1.19 (1.04–1.37) • 6th decile: 1.19 (1.04–1.37) • 7th decile: 1.20 (1.04–1.38) • 8th decile: 1.24 (1.08–1.43) • 9th decile: 1.18 (1.02–1.36) • 10th decile: 1.25 (1.05–1.44) Significant trends were also found for GGT (p=0.047) and direct bilirubin (p=0.015); the

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		association was not significant for any of the deciles.
Steenland et al. 2009b Cross-sectional study of 46,294 adult participants in the C8 Health Project	**Exposure:** Mean and median serum PFOS levels were 22.4 and 19.6 ng/mL PFOS quartiles • 1st quartile: 0–13.2 ng/mL • 2nd quartile: 13.3–19.5 ng/mL • 3rd quartile: 19.6–28.0 ng/mL • 4th quartile: ≥28.4 ng/mL **Regression model adjustments:** Age, sex, BMI, education, smoking, regular exercise, alcohol consumption	A monotonic increase in log cholesterol levels with increasing serum PFOS levels ($p<0.001$); the slope appears to decrease at a serum PFOS level of 40 ng/mL. There were significant ($p<0.05$) positive linear trends for LDL cholesterol and triglycerides, but not for HDL cholesterol. The risk of high cholesterol (total cholesterol ≥240 mg/dL) was significantly elevated for serum PFOS levels in the 2nd, 3rd, and 4th quartiles; ORs (95% CI): • 2nd quartile: 1.14 (1.05–1.23) • 3rd quartile: 1.28 (1.19–1.39) • 4th quartile: 1.51 (1.40–1.64)
Château-Degat et al. 2010 Cross-sectional study of 723 Inuit adults living in Nunavik Canada with a high dietary exposure to n-3 polyunsaturated fatty acids found in traditional food items and not taking cholesterol-lowering medication	**Exposure:** Arithmetic and geometric mean serum PFOS levels were 25.7 and 18.6 ng/mL, respectively **Regression model adjustments:** Age, sex, smoking status, lipid lowering drugs, circulating n-3 PFUAs (total cholesterol, and HDL cholesterol only), BMI (triglyceride and LDL only), insulinemia (LDL only)	Significant positive associations were found between serum PFOS levels and HDL cholesterol in men ($p<0.001$) and women ($p=0.001$). There was a significant negative association between serum PFOS levels and triglycerides in women ($p=0.040$) and total cholesterol/HDL cholesterol ratio ($p<0.001$). No significant associations were found between serum PFOS and total cholesterol ($p=0.086$), triglycerides in men ($p=0.162$), LDL ($p=0.242$), or non-HDL cholesterol ($p=0.315$).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Eriksen et al. 2013 Cross-sectional study of 753 adults (663 men, 90 women) 50–65 years of age participating in the Danish Diet, Cancer, and Health study; the subjects did not report taking cholesterol-lowering medication	**Exposure:** Mean serum PFOS was 36.1 ng/mL **Regression model adjustments:** Sex, age, education, BMI, smoking status, animal fat intake, physical activity	A significant association (p=0.02) between serum PFOS levels and total cholesterol was found. The difference in levels per interquartile range of plasma PFOS was 4.6 (95% CI 0.8–8.5).
Fisher et al. 2013 Cross-sectional study of 2,368 adult (aged 18–74 years) participants in the Canadian Health Measures Survey (2007–2009); the subjects reported not taking cholesterol-lowering medication	**Exposure:** Serum PFOS geometric mean was 8.04 ng/mL; quartile ranges: • 1st quartile: 0.15–5.42 ng/mL • 2nd quartile: 5.43–8.54 ng/mL • 3rd quartile: 8.55–12.91 ng/mL • 4th quartile: ≥12.92 ng/mL **Linear regression model adjustments:** Age, sex, marital status, BMI, physical activity, smoking status, alcohol consumption	No significant associations between serum PFOS levels and total cholesterol (p=0.35), Non-HDL (p=0.14), LDL (p=0.42), HDL (p=0.33), or the ratio of total cholesterol to HDL (p=0.10). No significant association (p=0.13) between serum PFOS and risk of high cholesterol levels was found; OR (95% CI) for the 4th quartile was 1.36 (0.87–2.12).
Fu et al. 2014a Cross-sectional study of 133 male and female subjects from China aged 0.3–88 years; the following serum lipid levels were considered abnormal: >5.18 and >4.40 mmol/L for total cholesterol in adults and children, respectively; >1.70 mmol/L for triglycerides; <1.04 mmol/L for HDL cholesterol; and >3.37 and >2.85 mmol/L for LDL cholesterol in adults and children, respectively	**Exposure:** Median serum PFOS level 1.47 ng/mL **Linear regression model adjustments:** Age, sex, BMI	No significant associations between serum PFOS and total cholesterol (p=0.287), LDL cholesterol (p=0.357), triglyceride (p=0.711), or HDL cholesterol (p=0.260). No significant associations between serum PFOS and risk of abnormal serum lipid parameters; ORs (95% CI) for 4th quartile (2.15–10.20 ng/mL): • Total cholesterol: 2.27 (0.47–10.92) • Triglycerides: 1.26 (0.41–3.90) • HDL cholesterol: 0.29 (0.06–1.50) • LDL cholesterol: 2.27 (0.50–10.37)

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Geiger et al. 2014b Cross-sectional study utilizing 1999–2008 NHANES data for 815 participants (≤18 years of age); criteria for dyslipidemia were elevated total cholesterol of >170 mg/dL, LDL of >110 mg/dL, HDL cholesterol of <40 mg/dL, and triglycerides >150 mg/dL	**Exposure:** Mean serum PFOS 17.7 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, body weight (underweight, normal weight, overweight), household income, activity level, serum cotinine	Significant association between serum PFOS and LDL levels (p=0.0081 for trend). No significant associations between serum PFOA and total cholesterol levels (p=0.0512 for trend), HDL levels (p=0.9703), or triglyceride levels (p=0.1104 for trend). Significant associations between serum PFOS and risk of elevated cholesterol (OR 1.35, 95% CI 1.11–1.64, p=0.0183 for trend for log transformed PFOS) and LDL (OR 1.48, 95% CI 1.15–1.90, p=0.0178 for trend for log transformed PFOS). No significant associations between serum PFOA and risk of triglyceride (p=0.2418 for trend) or decreased HDL (p=0.9873 for trend).
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum biomarkers of liver damage were considered elevated if they exceeded 75th percentile of 2007–2010 NHANES values	**Exposure:** Median serum concentrations of PFOS 11.3 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	No significant association (p>0.01) between serum PFOS and ALT, GGT, AST, and total bilirubin. Significant association between serum PFOS and risk of elevated total bilirubin (p=0.028 for trend). No significant association between serum PFOS and risk of elevated ALT (p=0.370 for trend), AST (p=0.438 for trend), or GGT (p=0.654 for trend).
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFOS 5.68 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFOS and total cholesterol (β -0.450, 95% CI -10.667–9.768, p=0.931), LDL cholesterol (β 2.507, 95% CI -6.879–11.893, p=0.598), or triglycerides (β -0.020, 95% CI -0.186–0.146, p=0.809).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOS 3.72 ng/mL (WTCHR group) and 2.78 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFOS and serum cholesterol (β 0.08, 95% CI 0.05–0.12, p<0.001), LDL cholesterol (β 0.10, 95% CI 0.05–0.16, p<0.001) and HDL cholesterol (β 0.06, 95% CI 0.003–0.13, p=0.04); no association with triglycerides (β 0.04, 95% CI -0.05–0.13, p=0.36).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lin et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 2,216 adults (>18 years of age)	**Exposure:** Geometric mean serum PFOS concentration: 27.39 ng/mL (males) and 22.20 ng/mL (females) **Linear regression model adjustments:** Age, sex, race/ethnicity, smoking, drinking status, education level, BMI, insulin resistance, metabolic syndrome, iron saturation	No significant associations between serum PFOS levels and serum ALT (p=0.066), GGT (p=0.808), and total bilirubin (p=0.223). When PFOA, PFHxS, and PFNA were also entered into the regression model, significant associations between serum PFOS and GGT (p=0.025) and total bilirubin (p=0.001) were found; ALT was not significantly associated with PFOS (p=0.769).
Liu et al. 2018b Cross-sectional study utilizing 2013–2014 NHANES data for 1,871 adults	**Exposure:** Geometric mean serum PFOS 5.28 ng/mL **Statistical adjustments:** Age, sex, ethnicity, smoking status, alcohol intake, household income, waist circumference, medications (anti-hypertensive, anti-hyperglycemic, anti-lipidemic)	No associations between serum PFOA and total cholesterol (β 1.22, p>0.05), LDL cholesterol (β 0.88, p>0.05), HDL cholesterol (β 0.91, p>0.05), or triglyceride levels (β -0.08, p>0.05).
Maisonet et al. 2015b Prospective cohort study of girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; the girls were examined at age 7 (n=111) and 15 (n=88) years	**Exposure:** Mean maternal serum PFOA level was 4.2 ng/mL for the 7-year-old group and 4.5 ng/mL for the 15-year-old group • 1st tertiles: 7.6–17.2 ng/mL (7-year-olds) and 7.6–16.8 ng/mL (15-year-olds) • 2nd tertile: 17.3–23.4 ng/mL (7-year-olds) and 16.9–23.4 ng/mL (15-year-olds) • 3rd tertile: 23.5–94.5 ng/mL (7- and 15-year-olds) **Statistical adjustments:** Previous livebirths, maternal education, maternal age at delivery	No associations were found between serum PFOS and total cholesterol, LDL cholesterol, HDL cholesterol, or triglyceride levels for 7-year-olds (3rd tertile): • Total cholesterol: β -0.10 (95% CI -0.73–0.54) • LDL cholesterol: β 0.02 (95% CI -0.48–0.53) • HDL cholesterol: β -0.04 (95% CI -0.33–0.25) • Triglycerides: β -0.004 (95% CI -0.015–0.006) Inverse associations were found between maternal serum PFOS and total cholesterol and LDL cholesterol for the 3rd tertile; no associations were found for HDL cholesterol or triglycerides: • Total cholesterol: β -0.77 (95% CI -1.40 to -0.13)

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		• LDL cholesterol: β -0.54 (95% CI -1.08 to -0.003) • HDL cholesterol: β -0.18 (95% CI -0.47–0.12) • Triglycerides: β -0.004 (95% CI -0.011–0.004)
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFOS 5.80 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No associations at 4 years of age between maternal serum PFOS and total cholesterol (β -0.02, 95% CI -0.10–0.15), HDL-C (β -0.03, 95% CI -0.14–0.09), LDL-C (β 0.02, 95% CI -0.12–0.15) or triglycerides (β 0.05, 95% CI -0.06–0.17).
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 860 adults (18–80 years of age); cholesterol analyses excluded subjects taking cholesterol-lowering medication	**Exposure:** Serum mean and median PFOS levels were 25.3 and 21.0 ng/mL (range: 1.4–392.0 ng/mL) **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	Significant associations between serum PFOS and total cholesterol (p=0.01) and non-HDL (includes LDL and VLDL, p=0.02), but not for HDL (p=0.78) or LDL (p=0.27). The changes in total cholesterol and non-HDL cholesterol levels per ng/mL increase in PFOS were 0.27 mg/dL (95% CI 0.05–0.48) and 0.25 (95% CI 0–0.5), respectively.
Skuladottir et al. 2015 Cross-sectional study of 854 Danish women with singleton pregnancies	**Exposure:** Mean serum levels of PFOS (collected at gestation week 30) 22.3 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal smoking, parity, total caloric intake, maternal education, saturated fat intake	Significant association between serum PFOS levels and total cholesterol levels (p=0.01 for trend). Total cholesterol increased 0.39 mmol/L (95% CI 0.10–0.68) when 5th quintile levels of PFOS (>27.6 ng/mL) were compared with 1st quintile (≤16.0 ng/mL).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Starling et al. 2014a Cross-sectional study of 891 pregnant women participating in the Norwegian Mother and Child Study	**Exposure:** Median plasma level (50th percentile) (sample collected at gestation week 18) PFOS 13.03 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal education, smoking at mid-pregnancy, oily fish consumed, gestational age at blood collection, parity, breastfeeding duration in previous pregnancy	Plasma PFOS levels were significantly correlated with total cholesterol ($p<0.05$); the ln-unit increase in PFOS was 8.96 mg/dL (95% CI 1.70–16.22). Plasma PFOS was associated with HDL cholesterol; β 4.39 (95% CI 2.37–6.42) per ln-unit increase in PFOS. No association between plasma PFOS and LDL cholesterol or triglycerides; the β values (95% CI) per ln-unit increase in PFOS were -6.48 (-0.07–13.03) for LDL and -0.02 (-0.09–0.04) for triglycerides.
Timmermann et al. 2014 Cross-sectional study of 499 Danish children (8–10 years of age) participants of the European Youth Heart Study	**Exposure:** Median plasma concentration of PFOS 41.5 ng/mL **Linear regression model adjustments:** Sex, age, ethnicity, paternal income, fast food consumption, fitness; model adjusted for height when using waist circumference as outcome measured	No significant association ($p=0.78$) between PFOS and triglyceride levels among normal-weight children. Among overweight children, an increase of 10 ng/mL plasma PFOS was associated with an 8.6% (95% CI 1.2–16.5) increase in triglyceride levels ($p=0.02$).
Yamaguchi et al. 2013 Cross-sectional study of 307 men and 301 women (16–76 years of age) from various regions of Japan	**Exposure:** Mean blood concentrations of PFOS 5.8 ng/mL **Statistical adjustments:** Age, sex, BMI region, smoking status	Significant correlation between serum PFOS and serum levels of docosahexaenoic acid ($p<0.0001$), eicosapentaenoic acid ($p<0.0001$), AST ($p=0.01$), ALT ($p=0.003$), and GGT ($p=0.03$).
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFOS 3.00 ng/mL (range of 0.3–14.6 ng/mL) **Statistical adjustments:** Age	No association between serum PFOS and HDL cholesterol (β 0.02, 95% CI -0.17–0.2) or triglycerides (β 0.3, 95% CI -0.63–1.22).
Zeng et al. 2015 Cross-sectional study of 225 Taiwanese children aged 12–15 years	**Exposure:** Mean serum PFOS levels 32.4 and 34.2 ng/mL in boys and girls, respectively **Multivariate linear regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco exposure	Significant associations between serum PFOS and total cholesterol ($p<0.001$), LDL cholesterol ($p<0.001$), and triglycerides ($p=0.05$); no association with HDL cholesterol ($p=0.72$).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHxS		
Fisher et al. 2013 Cross-sectional study of 2,368 adult (aged 18–74 years) participants in the Canadian Health Measures Survey (2007–2009); the subjects reported not taking cholesterol-lowering medication	**Exposure:** Serum PFHxS geometric mean was 2.18 ng/mL; quartile ranges: • 1st quartile: 0.15–1.19 ng/mL • 2nd quartile: 1.20–2.10 ng/mL • 3rd quartile: 2.11–3.64 ng/mL • 4th quartile: ≥3.65 ng/mL **Linear regression model adjustments:** Age, sex, marital status, BMI, physical activity, smoking status, alcohol consumption	Significant association between serum PFHxS and total cholesterol (p=0.005), LDL (p=0.02), non-HDL (p=0.002), and total cholesterol/HDL ratio (p=0.006); no association was found for HDL (p=0.67) An increased odds of high cholesterol per increase in PFHxS was observed in participants with serum PFHxS levels in the 4th quartile (OR 1.27, 95% CI 1.11–1.45). A positive trend for increasing risk of high cholesterol with increasing PFHxS levels was found (p=0.001); however, the OR was not significant for a specific quartile. The OR (95% CI) for the 4th quartile was 1.57 (0.93–2.64)
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum biomarkers of liver damage were considered elevated if they exceeded 75th percentile value in 2007–2010 NHANES value	**Exposure:** Median serum concentrations of PFHxS 1.8 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	Significant association between serum PFHxS and ALT (p<0.01), AST (p<0.001), and total bilirubin (p<0.01). No significant association (p>0.01) between serum PFHxS and GGT. Significant association between serum PFHxS and risk of elevated total bilirubin (p=0.041 for trend). No significant association between serum PFHxS and risk of elevated ALT (p=0.484 for trend), AST (p=0.230 for trend), and GGT (p=0.415 for trend).
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFHxS 0.793 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFHxS and total cholesterol (β 0.989, 95% CI -9.526–11.503, p=0.853), LDL cholesterol (β -4.222, 95% CI -13.979–5.534, p=0.393), or triglycerides (β 0.081, 95% CI -0.092–0.253, p=0.355).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFHxS 0.67 ng/mL (WTCHR group) and 0.53 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFHxS and serum total cholesterol (β 0.04, 95% CI 0.04–0.06, p=0.01), and LDL cholesterol (β 0.05, 95% CI 0.01–0.09, p=0.02); no association with HDL cholesterol (β 0.03, 95% CI -0.02–0.07, p=0.26) or triglycerides (β 0.04, 95% CI -0.02–0.11, p=0.20).
Lin et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 2,216 adults (>18 years of age)	**Exposure:** Geometric mean serum PFHxS concentration: 2.29 ng/mL (males) and 1.72 ng/mL (females) **Linear regression model adjustments:** Age, sex, race/ethnicity, smoking, drinking status, education level, BMI, insulin resistance, metabolic syndrome, iron saturation	No significant associations between serum PFHxS levels and serum ALT (p=0.691), GGT (p=0.898), or total bilirubin (p=0.063). When PFOA, PFOS, and PFNA were also entered into the regression model, a significant association between serum PFHxS and total bilirubin (p=0.001) was found; ALT and GGT were not significantly associated with PFHxS (p=0.381 and p=0.376).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFHxS 0.61 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No associations at 4 years of age between maternal serum PFHxS and total cholesterol (β 0.02, 95% CI -0.09–0.12), HDL-C (β -0.01, 95% CI -0.11–0.10), or LDL-C (β -0.01, 95% CI -0.12–0.09). Association between maternal serum PFHxS and triglycerides at age 4 (β 0.11, 95% CI 0.01–0.21)
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 860 adults (20–80 years of age); cholesterol analyses excluded subjects taking cholesterol-lowering medication	**Exposure:** Serum mean and median PFHxS levels were 2.6 and 1.8 ng/mL (range: 0.2–27.1 ng/mL) **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	A significant negative association between serum PFHxS and non-HDL (includes LDL and VLDL, p=0.04), but not for total cholesterol (p=0.07), HDL (p=0.11), or LDL (p=0.10). The change in non-HDL cholesterol levels per ng/mL increase in PFHxS was -1.13 mg/dL (95% CI -1.90 to -0.35).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Starling et al. 2014a Cross-sectional study of 891 pregnant women participating in the Norwegian Mother and Child Study	**Exposure:** Median plasma level (50th percentile) (sample collected at gestation week 18) PFHxS 0.60 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal education, smoking at mid-pregnancy, oily fish consumed, gestational age at blood collection, parity, breastfeeding duration in previous pregnancy	No association between plasma PFHxS and total cholesterol, LDL cholesterol, or triglycerides; the β values (95% CI) per ln-unit increase in PFHxS were 3.00 (95% CI -1.75–7.76) for total cholesterol, 1.92 (-2.50–6.33) for LDL, and -0.01 (-0.05–0.03) for triglycerides. Plasma PFHxS was associated with HDL cholesterol; β 1.46 (95% CI 0.19–2.73) per ln-unit increase in PFHxS.
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFHxS 3.80 ng/mL (range of 0.1–9.8 ng/mL) **Statistical adjustments:** Age	Association between serum PFHxS and HDL cholesterol (β 0.22, 95% CI 0–0.43) or triglycerides (β 1.18, 95% CI 0.12–2.25).
Zeng et al. 2015 Cross-sectional study of 225 Taiwanese children aged 12–15 years	**Exposure:** Mean serum PFHxS levels 2.1 and 2.1 ng/mL in boys and girls, respectively **Multivariate linear regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco exposure	No significant associations between serum PFHxS and total cholesterol (p=0.23), LDL cholesterol (p=0.17), triglycerides (p=0.15), or HDL cholesterol (p=0.54).
PFNA		
Mundt et al. 2007 Longitudinal study of 592 workers (88% male) ever employed between 1989 and 2003 at a polymer production facility exposed to PFNA; workers underwent annual medical examinations, which involved measurement of clinical chemistry indices	**Exposure:** Workers were assigned to exposure categories based on serum PFNA levels in a subset of current workers **Adjustments:** Age, BMI	When comparing serum liver parameters between the male workers in each exposure category at the five different measurement periods, significant (p<0.05) differences in ALT were found between high-exposure and no-exposure groups only in 2001 and in total cholesterol levels between the high- and low-exposure groups in 1976 and 1989. Significant differences were not observed at other time points or for other endpoints (AST, GGT, bilirubin, triglycerides, HDL, LDL, VLDL); no differences were observed in female workers. In longitudinal analyses, there were no significant increases or decreases in total cholesterol, triglycerides, GGT, AST, ALT, or

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		bilirubin with unit increases in exposure intensity.
Fu et al. 2014a Cross-sectional study of 133 male and female subjects from China aged 0.3–88 years; the following serum lipid levels were considered abnormal: >5.18 and >4.40 mmol/L for total cholesterol in adults and children, respectively; >1.70 mmol/L for triglycerides; <1.04 mmol/L for HDL cholesterol; and >3.37 and >2.85 mmol/L for LDL cholesterol in adults and children, respectively	**Exposure:** Median serum PFNA level 0.37 ng/mL **Linear regression model adjustments:** Age, sex, BMI	Significant associations between serum PFNA and total cholesterol (p=0.002) and LDL cholesterol (p=0.004); no association with triglycerides (p=0.460) or HDL cholesterol (p=0.191). No significant associations between serum PFNA and risk of abnormal serum lipid parameters; ORs (95% CI) for 4th quartile (0.67–4.68 ng/mL): • Total cholesterol: 1.03 (0.24–4.46) • Triglycerides: 0.80 (0.26–2.49) • HDL cholesterol: 1.06 (0.20–5.57) • LDL cholesterol: 2.51 (0.59–10.74)
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum biomarkers of liver damage were considered elevated if they exceeded 75th percentile of 2007–2010 NHANES values	**Exposure:** Median serum concentrations of PFNA 1.4 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	Significant association between serum PFNA and ALT (p<0.001) and GGT (p<0.01). No significant association (p>0.01) between serum PFNA and AST and total bilirubin. No significant association between serum PFNA and risk of elevated ALT (p=0.042 for trend), AST (p=0.516 for trend), GGT (p=0.126 for trend), or elevated total bilirubin (p=0.614 for trend).
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFNA 0.938 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFNA and total cholesterol (β -1.624, 95% CI -10.218–6.970, p=0.709), LDL cholesterol (β 2.304, 95% CI -6.558–11.167, p=0.607), or triglycerides (β 0.065, 95% CI -0.092–0.221, p=0.820).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFNA 0.61 ng/mL (WTCHR group) and 0.49 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFNA and serum total cholesterol (β 0.05, 95% CI 0.01–0.09, p=0.01), and LDL cholesterol (β 0.07, 95% CI 0.01–0.14, p=0.01); no association with HDL cholesterol (β 0.05, 95% CI -0.02–0.12, p=0.13) or triglycerides (β -0.07, 95% CI -0.11–0.01, p=0.89).
Lin et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 2,216 adults (>18 years of age)	**Exposure:** Geometric mean serum PFNA concentration: 0.89 ng/mL (males) and 0.72 ng/mL (females) **Linear regression model adjustments:** Age, sex, race/ethnicity, smoking, drinking status, education level, BMI, insulin resistance, metabolic syndrome, iron saturation	No significant associations between serum PFNA levels and serum ALT (p=0.131), GGT (p=0.857), or total bilirubin (p=0.053). When PFOA, PFOS, and PFHxS were also entered into the regression model, a significant association between serum PFHxS and total bilirubin (p=0.004) was found; ALT and GGT were not significantly associated with PFHxS (p=0.721 and p=0.253).
Manzano-Salgado et al. 2017b Prospective study of 1,230 mother-child pairs participating in the INMA birth cohort study in Spain; children were assessed at age 4 and 7 years	**Exposure:** Geometric mean maternal serum PFNA 0.66 ng/mL (measured during first trimester) **Statistical adjustments:** Residence, country of birth, previous breastfeeding, age, prepregnancy BMI, age and sex of child	No associations at 4 years of age between maternal serum PFNA and total cholesterol (β -0.00, 95% CI -0.11–0.12), HDL-C (β -0.03, 95% CI -0.14–0.08), LDL-C (β 0.01, 95% CI -0.10–0.12) or triglycerides (β 0.03, 95% CI -0.07–0.14).
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 860 adults (18–80 years of age); cholesterol analyses excluded subjects taking cholesterol-lowering medication	**Exposure:** Serum mean and median PFNA levels were 1.3 and 1.0 ng/mL (range: 0.1–10.3 ng/mL) **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	Significant associations between serum PFNA and total cholesterol (p=0.04) and non-HDL (includes LDL and VLDL, p=0.04), but not for HDL (p=0.31) or LDL (p=0.08). The changes in total cholesterol and non-HDL cholesterol levels per ng/mL increase in PFNA were 2.01 mg/dL (95% CI -1.16–5.18) and 2.56 (95% CI -1.19–6.30), respectively.

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Starling et al. 2014a Cross-sectional study of 891 pregnant women participating in the Norwegian Mother and Child Study	**Exposure:** Median plasma level (50th percentile) (in sample collected at gestation week18) PFNA 0.39 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal education, smoking at mid-pregnancy, oily fish consumed, gestational age at blood collection, parity, breastfeeding duration in previous pregnancy	No association between plasma PFNA and total cholesterol, LDL cholesterol, or triglycerides; the β values (95% CI) per ln-unit increase in PFNA were 0.01 (95% CI -5.98–6.00) for total cholesterol, -2.15 (-7.31–3.02) for LDL, and -0.02 (-0.07–0.03) for triglycerides. Plasma PFNA was associated with HDL cholesterol; β 2.84 (95% CI 0.97–4.71) per ln-unit increase in PFNA.
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFNA 0.50 ng/mL (range of 0.1–1.1 ng/mL) **Statistical adjustments:** Age	Association between serum PFNA and HDL cholesterol (β 0.3, 95% CI 0.05–0.56) and triglycerides (β 1.54, 95% CI 0.27–2.8).
Zeng et al. 2015 Cross-sectional study of 225 Taiwanese children aged 12–15 years	**Exposure:** Mean serum PFNA levels 0.8 and 0.9 ng/mL in boys and girls, respectively **Multivariate linear regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco exposure	Significant associations between serum PFNA and total cholesterol (p=0.04), LDL cholesterol (p=0.05), and triglycerides (p=0.007); no association with HDL cholesterol (p=0.37).
PFDA		
Fu et al. 2014a Cross-sectional study of 133 male and female subjects from China aged 0.3–88 years; the following serum lipid levels were considered abnormal: >5.18 and >4.40 mmol/L for total cholesterol in adults and children, respectively; >1.70 mmol/L for triglycerides; <1.04 mmol/L for HDL cholesterol; and >3.37 and >2.85 mmol/L for LDL cholesterol in adults and children, respectively	**Exposure:** Median serum PFDA level 0.19 ng/mL **Linear regression model adjustments:** Age, sex, BMI	Significant associations between serum PFDA and total cholesterol (p=0.048) and HDL cholesterol (p=0.007); no associations with triglycerides (p=0.317) or LDL cholesterol (p=0.251). No significant associations between serum PFDA and risk of abnormal serum lipid parameters; ORs (95% CI) for 4th quartile (0.43–2.16 ng/mL): • Total cholesterol: 3.84 (0.87–16.95) • Triglycerides: 0.51 (0.17–1.58) • HDL cholesterol: 2.21 (0.49–10.07) • LDL cholesterol: 2.17 (0.52–9.04)

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFDA 0.0592 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFDA and total cholesterol (β -3.330, 95% CI -7.484–0.824, p=0.115), LDL cholesterol (β -1.858, 95% CI -5.694–1.979, p=0.339), or triglycerides (β -0.036, 95% CI -0.103–0.032, p=0.302).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFDA 0.14 ng/mL (WTCHR group) and 0.11 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFDA and serum total cholesterol (β 0.04, 95% CI 0.02–0.06, p<0.001), LDL cholesterol (β 0.04, 95% CI 0.02–0.06, p=0.03), and HDL cholesterol (β 0.05, 95% CI -0.02–0.09, p=0.003); no association with triglycerides (β 0.01, 95% CI -0.047–0.057, p=0.85).
Starling et al. 2014a Cross-sectional study of 891 pregnant women participating in the Norwegian Mother and Child Study	**Exposure:** Median plasma level (50th percentile) (sample collected at gestation week 18) PFDA 0.09 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal education, smoking at mid-pregnancy, oily fish consumed, gestational age at blood collection, parity, breastfeeding duration in previous pregnancy	No association between plasma PFDA and total cholesterol, LDL cholesterol, or triglycerides; the β values (95% CI) per ln-unit increase in PFDA were 1.84 (95% CI -2.12–5.79) for total cholesterol, 0.19 (-3.30–3.69) for LDL, and -0.03 (-0.07–0.01) for triglycerides. Plasma PFDA was associated with HDL cholesterol; β 2.54 (95% CI 1.22–3.87) per ln-unit increase in PFDA.
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFDA 0.40 ng/mL (range of 0.1–1.1 ng/mL) **Statistical adjustments:** Age	No association between serum PFDA and HDL cholesterol (β 0.24, 95% CI -0.04–0.52) or triglycerides (β 0.64, 95% CI -0.77–2.05).
Zeng et al. 2015 Cross-sectional study of 225 Taiwanese children aged 12–15 years	**Exposure:** Mean serum PFDA levels 1.0 and 1.0 ng/mL in boys and girls, respectively **Multivariate linear regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco exposure	No significant associations between serum PFDA and total cholesterol (p=0.74), LDL cholesterol (p=0.85), triglycerides (p=0.92), or HDL cholesterol (p=0.47).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFUnA		
Fu et al. 2014a Cross-sectional study of 133 male and female subjects from China aged 0.3–88 years; the following serum lipid levels were considered abnormal: >5.18 and >4.40 mmol/L for total cholesterol in adults and children, respectively; >1.70 mmol/L for triglycerides; <1.04 mmol/L for HDL cholesterol; and >3.37 and >2.85 mmol/L for LDL cholesterol in adults and children, respectively	**Exposure:** Median serum PFUnA level 0.26 ng/mL **Linear regression model adjustments:** Age, sex, BMI	No significant associations between serum PFUnA and total cholesterol (p=0.184), LDL cholesterol (p=0.270), triglycerides (p=0.755) or HDL cholesterol (p=0.279). No significant associations between serum PFUnA and risk of abnormal serum lipid parameters; ORs (95% CI) for 4th quartile (0.51–1.93 ng/mL): • Total cholesterol: 3.70 (0.76–18.03) • Triglycerides: 0.74 (0.25–2.21) • HDL cholesterol: 0.54 (0.11–2.57) • LDL cholesterol: 4.16 (0.96–18.00).
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFUnA 0.652 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	Associations between serum PFUnA and total cholesterol (β 7.906, 95% CI 2.681–13.131, p=0.003) and LDL cholesterol (β 7.101, 95% CI 2.448–11.754, p=0.003). No association between serum PFUnA and triglycerides (β 0.043, 95% CI -0.042–0.129, p=0.317).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFUnA 0.12 ng/mL (WTCHR group) and 0.04 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFUnA and serum HDL cholesterol (β 0.04, 95% CI 0.01–0.07, p=0.01); no association with total cholesterol (β 0.02, 95% CI 0–0.04, p=0.06), LDL cholesterol (β 0.01, 95% CI -0.02–0.04, p=0.49), or triglycerides (β -0.04, 95% CI -0.09–0.003, p=0.07).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Starling et al. 2014a Cross-sectional study of 891 pregnant women participating in the Norwegian Mother and Child Study	**Exposure:** Median plasma level (50th percentile) (sample collected at gestation week 18) PFUnA 0.22 ng/mL **Linear regression model adjustments:** Age, prepregnancy BMI, maternal education, smoking at mid-pregnancy, oily fish consumed, gestational age at blood collection, parity, breastfeeding duration in previous pregnancy	No association between plasma PFUnA and total cholesterol, LDL cholesterol, or triglycerides; the β values (95% CI) per ln-unit increase in PFUnA were 0.89 (95% CI -3.28–5.06) for total cholesterol, -2.36 (-5.97–1.25) for LDL, and -0.04 (-0.08–0.00) for triglycerides. Plasma PFUnA was associated with HDL cholesterol; β 4.05 (95% CI 2.75–5.35) per ln-unit increase in PFUnA.
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFUnA 0.30 ng/mL (range of 0.1–0.8 ng/mL) **Statistical adjustments:** Age	No association between serum PFUnA and HDL cholesterol (β 0.11, 95% CI -0.11–0.34) or triglycerides (β 0.61, 95% CI -0.48–1.7).
PFHpA		
Fu et al. 2014a Cross-sectional study of 133 male and female subjects from China aged 0.3–88 years	**Exposure:** Median serum PFHpA level 0.04 ng/mL **Linear regression model adjustments:** Age, sex, BMI	No significant associations (p>0.05) were reported between serum PFHpA levels and total cholesterol, triglyceride, HDL cholesterol, or LDL cholesterol levels.
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFHpA 0.20 ng/mL (range of 0.1–0.4 ng/mL) **Statistical adjustments:** Age	No association between serum PFHpA and HDL cholesterol (β -0.33, 95% CI -0.77–0.11) or triglycerides (β -0.92, 95% CI -3.12–1.28).
PFBS		
Zeng et al. 2015 Cross-sectional study of 225 Taiwanese children aged 12–15 years	**Exposure:** Mean serum PFBS levels 0.5 and 0.4 ng/mL in boys and girls, respectively **Multivariate linear regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco exposure	Significant association between serum PFBS and total cholesterol (p=0.04); no associations with LDL cholesterol (p=0.14), triglycerides (p=0.81), or HDL cholesterol (p=0.15).

Table 7. Hepatic Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFBA		
Fu et al. 2014a Cross-sectional study of 133 male and female subjects from China aged 0.3–88 years	**Exposure:** Median serum PFBA level 0.11 ng/mL **Linear regression model adjustments:** Age, sex, BMI	No significant associations (p>0.05) were reported between serum PFBA levels and total cholesterol, triglyceride, HDL cholesterol, or LDL cholesterol levels.
PFDoDA		
Zeng et al. 2015 Cross-sectional study of 225 Taiwanese children aged 12–15 years	**Exposure:** Mean serum PFDoDA levels 4.5 and 4.4 ng/mL in boys and girls, respectively **Multivariate linear regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco exposure	No significant associations between serum PFDoDA and total cholesterol (p=0.37), LDL cholesterol (p=0.44), triglycerides (p=0.40), or HDL cholesterol (p=0.68).

APFO = ammonium perfluorooctanoate; ALT = alanine aminotransferase; AST = aspartate aminotransferase; BMI = body mass index; GGT = gamma-glutamyl transferase; HDL = high density lipoprotein; HR = hazard ratio; INMA = INfancia y Medio Ambiente; LDL = low density lipoprotein; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PBPK = physiologically based pharmacokinetic; PFBA = perfluorobutanoic acid; PFBS = perfluorobutane sulfonic acid; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHpA = perfluoroheptanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; RREpC = risk ratio episode of care; SMR = standardized mortality ratio; SPR = standardized prevalence ratio; VLDL = very low-density lipoprotein

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Costa et al. 2009 Cohort study of 53 current (n=37) and former (n=16) male workers at a perfluoroalkyl manufacturing facility in Italy undergoing annual health examinations from 1978 to 2007; a control group of 107 male workers with no exposure to PFOA was also examined	**Exposure:** Mean and median serum PFOA levels measured in 2007 were 12,930 and 5,710 ng/mL (range: 200–47,040 ng/mL) in current workers and 6,810 and 4,430 ng/mL (range: 530–18,660 ng/mL) in former workers. Mean and median serum PFOA levels decreased over time; the mean levels were 18,800 ng/mL in 2000 and 11,600 ng/mL in 2007; the median levels were 11,920 and 3,890 ng/mL during those same times. **Regression model adjustments:** Age, years of exposure, year of PFOA sampling, BMI, smoking, alcohol consumption	No significant differences in serum urea nitrogen, creatinine, total proteins, α1 globulins, α2 globulins, β globulins, or γ globulins were found between 34 current PFOA workers and 34 matched controls. Significant differences (p=0.039) in serum uric acid levels between 34 current PFOA workers and 34 matched controls. When evaluating all workers (current, former, and non-exposed) who had concurrent measurements of serum PFOA and renal biomarkers (n=56), significant associations were found between serum PFOA and α2 globulins (p<0.01) and uric acid levels (p<0.05), but not for other renal parameters.
Lundin et al. 2009 Cohort mortality study of 3,992 (80% male) workers at an APFO manufacturing facility (Cottage Grove); 807 workers died during the follow-up period; cohort consisted of workers employed for at least 365 days prior to December 31, 1997	**Exposure:** Workers were divided into three exposure classifications: • Definite occupational exposure, workers were exposed on a regular basis with potential high exposure (group 1) • Probable occupational exposure, jobs in other chemical division where APFO exposure was possible, but likely lower or transient (group 2) • No or minimal occupational exposure (group 3) Serum PFOA levels measured in 2000 from 131 current workers ranged from 2,600 to 5,200 ng/mL in definite exposure jobs and from 300 to 1,500 ng/mL in the probable exposure jobs; no data were available for the no exposure jobs. **Reference population and adjustments:** Mortality rates were compared to rates from Minnesota general population; statistical	No significant increases in deaths from nephritis and nephrosis were observed compared to mortality rates from the state of Minnesota; the SMRs (95% CI) were: • Group 1: 5.2 (0.6–18.9) • Group 2: 0.7 (0.1–2.6) • Group 3: 0.9 (0.2–2.8).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	models were adjusted for sex, year of birth, age at entry into the cohort, smoking status, and wage type; Cox regression analyses were done with an internal referent population	
Olsen et al. 2003a Cross-sectional study of workers at two fluorochemical manufacturing facilities in Decatur, Alabama (n=263, 82% male) and Antwerp, Belgium (n=255, 81% male) with potential exposure to PFOA and PFOS; workers were examined in 2000; 174 workers participated in at least one other medical survey conducted in 1994/5 or 1997	**Exposure:** Mean serum PFOA levels were 1,780 ng/mL (range: 40–12,700 ng/mL) in Decatur and 840 ng/mL (range: 10–7,040 ng/mL) in Antwerp **Regression model adjustments:** Age, BMI, current alcohol consumption, cigarette use, employment duration	The investigators noted that there were no significant differences between serum PFOA quartiles for BUN or serum creatinine at either facility.
Raleigh et al. 2014 Retrospective cohort mortality study of 9,027 workers (84% male) at two 3M facilities in Minnesota; 4,668 workers at an APFO facility in Cottage Grove (3,993 of these workers were included in the Lundin et al. 2009 cohort) and 4,359 workers at a non-APFO facility in St. Paul; cohort consisted of workers employed for at least 1 year; the Cottage Grove cohort included workers in a non-chemical division without exposure to APFO	**Exposure:** Work history and industrial monitoring were used to estimate PFOA exposure. Cumulative exposure in the Cottage Grove workers was divided into quartiles: • 1st quartile: >2.9×10^{-5} µg/m^3 • 2nd quartile: ≤1.5×10^{-4} µg/m^3 • 3rd quartile: ≤7.9×10^{-4} µg/m^3 • 4th quartile: >7.9×10^{-4} µg/m^3 **Reference population:** Mortality rates were compared to rates from Minnesota general population; Cottage Grove cohort also compared to St. Paul cohort	As compared to the Minnesota population, no significant risk of death from chronic kidney disease (SMR 1.09, 95% CI 0.60–1.84) in the Cottage Grove cohort. As compared to the St. Paul cohort, no significant alterations in the risk of death from chronic kidney disease (HR 0.39, 95% CI 0.11–1.32) in Cottage Grove workers in the combined 3rd or 4th quartile or incidence of chronic kidney disease (HR 0.73, 95% CI 0.21–2.48) in Cottage Grove workers in the 4th quartile.

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Sakr et al. 2007b Cross-sectional study of 1,025 male (76%) and female (24%) workers at a fluoropolymers production plant (Washington Works)	**Exposure:** Median serum PFOA concentrations were 490 ng/mL (range: 17.4–9,550 ng/mL), 176 ng/mL (8.1–2,070 ng/mL), 195 ng/mL (8.6–2,590 ng/mL), and 114 ng/mL (4.6–963 ng/mL) among current workers (n=259), current workers with intermittent exposure (n=160), past occupational exposure to PFOA (n=264), or never assigned to APFO area (n=342), respectively. The mean and median concentrations in all workers were 428 ng/mL and 189 ng/mL, respectively, among current workers (n=259), current workers with intermittent exposure (n=160), past occupational exposure to PFOA (n=264), or never assigned to APFO area (n=342), respectively. **Linear regression model adjustments:** Age, sex, BMI, alcohol consumption, heart attack in a parent (lipid models only)	The investigators noted that serum uric acid levels were significantly associated with serum PFOA levels; no additional information was provided.
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was estimated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum levels PFOA in 2005–2006 were 325 and 113 ng/mL in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant associations between estimated cumulative serum PFOA and risk of chronic kidney disease (p=0.92 and 0.99 for trend with no lag or 10-year lag).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Steenland and Woskie 2012 Retrospective cohort mortality study of 1,084 deceased workers at a fluoropolymers production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between 1948 and 2002; deaths were obtained through 2008; this is an extension of the Leonard (2006) study	**Exposure:** Cumulative exposure was estimated using serum PFOA levels of workers measured between 1979 and 2004 (median of 580 ng/mL with a range of 160–2,880 ng/mL). Exposures over time were estimated for eight job categories. The mean estimated cumulative exposure was 7,800 ng/mL-years (median of 4,300 ng/mL-years) and an estimated average annual serum PFOA concentration of 350 ng/mL (median 230 ng/mL). **Reference population:** Population, of DuPont workers residing in West Virginia and seven neighboring states (excluding workers at Washington Works)	Significant increases in deaths from chronic renal disease were observed; the SMRS (95% CI) for the 2nd, 3rd, and 4th exposure quartiles were 3.79 (1.03–9.71), 1.83 (0.22–6.62), and 8.60 (3.46–17.22), and 3.11 (1.66–5.32) for all quartiles combined. Analyzing with a 10- or 20-year lag increased the risks in the 3rd and 4th quartile groups (3rd quartile: SMR 3.85, 95% CI 1.05–1.20 for 10-year lag and SMR 5.37, 95% CI 1.46–13.75 for 20-year lag and 4th quartile: SMR 9.12, 95% CI 3.67–18.80 for 10-year lag and SMR 9.04, 95% CI 3.32–19.67 for 20-year lag).
Anderson-Mahoney et al. 2008 Cross-sectional study of 566 adult residents (mean age of 49.9 years) living near a Teflon manufacturing facility in West Virginia for at least 1 year; most subjects were exposed to PFOA in drinking water provided by Lubeck Public Service District (37%) or Little Hocking water district (27%); some subjects also worked at the facility	**Exposure:** Individual biomonitoring data were not provided; reported PFOA levels in the Lubeck and Little Hocking water districts were 0.4–3.9 and 1.7–4.3 µg/L, respectively. **Reference population:** SPRs were estimated using NHANES data; statistical analyses were adjusted for age and sex	Incidence data were based on the results of participant completed health surveys. Significantly increased risk of kidney disease for the combined population (SPR 2.26; 95% CI 1.45–3.51).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Dhingra et al. 2016b Retrospective and prospective study of C8 Health Project participants (n=28,541) and a cohort of workers at a DuPont manufacturing facility (n=3,713) who worked at the plant between 1948 and 2002	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was estimated as the sum of yearly exposure estimates from birth to a given year. **Cox proportional hazards model adjustments:** Sex, self-reported hypertension, self-reported diabetes, self-reported high cholesterol, smoking, BMI, education	No significant association between serum PFOA levels and risk of chronic kidney disease in retrospective analysis with no lag (p=0.80 for trend) or 5-year lag (p=0.81 for trend), 10-year lag (p=0.88 for trend), or 20-year lag (p=0.30 for trend) or in the prospective analysis (p=0.77 for trend).
Emmett et al. 2006b Cross-sectional study of 371 residents (aged 2.5–89 years) who had resided in the Little Hocking Water Association district for ≥2 years; includes 18 residents with occupational exposure to PFOA	**Exposure:** Median serum PFOA level was 354 ng/mL	No significant correlations (p>0.05) between serum PFOA and BUN, serum creatinine, or total serum protein were found. There were no significant (p>0.05) differences in the serum PFOA levels between residents with abnormal or normal renal function parameters.
Steenland et al. 2010b Cross-sectional study of 54,591 adults (≥20 years of age) participating in the C8 Health Project	**Exposure:** Mean and median serum PFOA levels were 86.4 and 27.9 ng/mL • 1st quintile: 0–11.4 ng/mL • 2nd quintile: 11.5–20.6 ng/mL • 3rd quintile: 20.7–38.9 ng/mL • 4th quintile: 39.1–88.6 ng/mL • 5th quintile: ≥88.7 ng/mL **Statistical adjustments:** Age, sex, BMI, education, smoking, alcohol consumption, serum creatinine	A significant linear trend (p<0.0001) for increasing uric acid with increasing serum PFOA (unadjusted for covariates) was found. A significant association between serum PFOA and the risk of hyperuricemia (uric acid levels of >6.8 mg/dL for males and >6.0 mg/dL for females) was observed. The ORs (95% CI) were: • 2nd quintile 1.33 (1.24–1.43) • 3rd quintile: 1.35 (1.26–1.45) • 4th quintile: 1.47 (1.37–1.58) • 5th quintile: 1.47 (1.37–1.58).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Watkins et al. 2013 Cross-sectional study of 9,660 children (aged 1–<18 years) participating in the C8 Health Project	**Exposure:** Median serum PFOS level was 20.0 ng/mL **Linear regression model adjustments:** Age, sex, race, smoking, household income, BMI, regular exercise	A significant negative association (p=0.0001) between measured serum PFOS levels and estimated GFR was found.
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum uric acid levels were considered elevated if they exceeded 75th percentile of 2007–2010 NHANES values	**Exposure:** Median serum concentrations of PFOA 3.7 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	There was a significant association (p<0.001) between serum PFOA and uric acid levels. There was a significant association (p<0.001 for trend) between serum PFOA and risk of elevated uric acid levels.
Geiger et al. 2013 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,772 children and adolescents (<18 years of age)	**Exposure:** Mean serum PFOA level of 4.3 ng/mL • 1st quartile: <2.9 ng/mL • 2nd quartile: 2.9–4.0 ng/mL • 3rd quartile: 4.1–5.4 ng/mL • 4th quartile: >5.4 ng/mL **Linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, annual household income, activity, serum cotinine, serum cholesterol	A significant association (p=0.0001) between serum PFOA levels and uric acid levels was found. A significant association (p=0.0071) between serum PFOA and hyperuricemia uric acid levels >6 mg/dL) was found. The ORs (95%) were: • 2nd quartile: 0.94 (0.58–1.53) • 3rd quartile: 1.01 (0.62–1.63) • 4th quartile: 1.62 (1.10–2.37).
Kataria et al. 2015 Cross-sectional study utilizing 2003–2010 NHANES data for 1,960 adolescents (12–19 years of age)	**Exposure:** Serum PFOA levels • 1st quartile: <2.5 ng/mL • 2nd quartile: 2.5–3.5 ng/mL • 3rd quartile: 3.5–4.7 ng/mL • 4th quartile: ≥4.7 ng/mL **Multivariable logistic regression model adjustments:** Sex, poverty income ratio, caregiver education, serum cotinine, prehypertension, insulin resistance, BMI, hypercholesterolemia, race/ethnicity	Adolescents in the 4th quartile PFOA (≥4.7 ng/mL) had 6.61 mL/minute/1.73 m^2 lower estimated GFR than adolescents in the lowest quartile (<2.5 ng/mL) (95% CI -11.39 to -1.83; p<0.01). Adolescents in the 4th quartile PFOA (≥4.7 ng/mL) had 0.21 mg/dL lower serum uric acid levels than adolescents in the lowest quartile (<2.5 ng/mL) (95% CI 0.056–0.37; p<0.01). Investigators noted that estimated GFR and serum uric acid levels were within the normal range in all participants.

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFOA level 0.5 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine	Significant association between serum PFOA and uric acid levels (β 0.1463 mg/dL per ln-unit PFOA, 95% CI 0.0126–0.2801; p<0.05). Significant association between serum PFOA and the risk of elevated uric acid levels (≥6 mg/dL) in full cohort (OR 2.16, 95% CI 1.29–3.61, p<0.05) and in the boys only (OR 2.76, 95% CI 1.37–5.56, p<0.05).
Shankar et al. 2011a Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 4,587 adults (20–80 years of age	**Exposure:** Serum PFOA levels • 1st quartile: <2.8 ng/mL • 2nd quartile: 2.8–4.1 ng/mL • 3rd quartile: 4.2–5.9 ng/mL • 4th quartile: >5.9 ng/mL **Linear and logistic regression model adjustments:** Age, sex, race/ethnicity, educational level, BMI	Increasing levels of serum PFOA were negatively associated (p<0.001 for trend) with estimated GFR. A significant positive association between the risk of chronic kidney disease (defined as a GFR <60 mL/minute/1.73 m^2) and serum PFOA levels in the 4th quartile (OR 1.73, 95% CI 1.04–2.88).
Shankar et al. 2011b Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,883 adults (>20 years of age)	**Exposure:** Serum PFOA levels • 1st quartile: <2.4 ng/mL • 2nd quartile: 2.4–3.4 ng/mL • 3rd quartile: 3.5–5.1 ng/mL • 4th quartile: >5.1 ng/mL **Linear and logistic regression model adjustments:** Age, sex, race/ethnicity, educational level, smoking, alcohol consumption, BMI, hypertension, diabetes, serum total cholesterol	A significant association (p<0.0001) between serum PFOA levels and uric acid levels was found. Significant increases in the risk of hyperuricemia were observed for serum PFOA levels in the 3rd and 4th quartiles; ORs (95% CI) of 1.90 (1.35–2.69) and 1.97 (1.44–2.70), respectively.

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Olsen et al. 1998a Cross-sectional study of workers at two PFOS-based fluorochemical manufacturing facilities in Decatur, Alabama and Antwerp, Belgium; workers were examined in 1995 (n=178) and 1997 (n=149); 61 workers participated in both years; this is the same cohort of workers as Olsen et al. (1999)	**Exposure:** 20–22% of the workers in Decatur and 14–24% in Antwerp had serum PFOS levels of >3,000 ng/mL; the mean PFOS levels in 1995 and 1997 were 2,440 and 1,960 ng/mL in Decatur and 1,930 and 1,480 ng/mL in Antwerp **Multivariable regression model adjustments:** Age, BMI, alcohol consumption, smoking	An association between serum PFOS and serum creatinine was found in 1997 (p=0.06), but not in 1995 (p=0.13). When the facilities were analyzed separately, the association was found in 1997 at the Decatur facility (p=0.04) and in Antwerp in 1995 (p=0.1). No significant associations were found for BUN (p=0.91 and 0.60 in 1995 and 1997). When only workers (combined facilities) participating in both examination periods were examined, an association with serum creatinine was found in 1995 (p=0.06), but not in 1997 (p=0.11). No associations were found for BUN (p=0.75 and 0.22 for 1995 and 1997).
Olsen et al. 2003a Cross-sectional study of workers at two fluorochemical manufacturing facilities in Decatur, Alabama (n=263, 82% male) and Antwerp, Belgium (n=255, 81% male) with potential exposure to PFOA and PFOS; workers were examined in 2000; 174 workers participated in at least one other medical survey conducted in 1994/5 or 1997	**Exposure:** Mean serum PFOS levels were 1,320 ng/mL (range: 60–10,006 ng/mL) in Decatur and 800 ng/mL (range: 40–6,240 ng/mL) in Antwerp. Median PFOS levels in the 1st, 2nd, 3rd, and 4th quartiles were 290, 590, 1,170, and 2,460 ng/mL, respectively, for males and 80, 130, 370, and 1,340 ng/mL, respectively, in females. **Regression model adjustments:** Age, BMI, current alcohol consumption, cigarette use, employment duration	The investigators noted that there were no significant differences between serum PFOS quartiles for BUN or serum creatinine.

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Steenland et al. 2010b Cross-sectional study of 54,591 adults (≥20 years of age) participating in the C8 Health Project	**Exposure:** Mean and median serum PFOS levels were 23.4 and 20.29 ng/mL • 1st quintile: 0–12.1 ng/mL • 2nd quintile: 12.2–17.4 ng/mL • 3rd quintile: 17.5–23.2 ng/mL • 4th quintile: 23.2–31.8 ng/mL • 5th quintile: ≥31.9 ng/mL **Statistical adjustments:** Age, sex, BMI, education, smoking, alcohol consumption, serum creatinine	A significant linear trend (p<0.0001) for increasing uric acid with increasing serum PFOS (unadjusted for covariates) was found. A significant association between serum PFOS and the risk of hyperuricemia (uric acid levels of >6.8 mg/dL for males and >6.0 mg/dL for females) was observed. The ORs (95% CI) were: • 2nd quintile 1.02 (0.95–1.10) • 3rd quintile: 1.11 (1.04–1.20) • 4th quintile: 1.19 (1.11–1.27) • 5th quintile: 1.26 (1.17–1.35).
Watkins et al. 2013 Cross-sectional study of 9,660 children (aged 1–<18 years) participating in the C8 Health Project	**Exposure:** Median serum PFOS level was 20.0 ng/mL **Linear regression model adjustments:** Age, sex, race, smoking, household income, BMI, regular exercise	A significant negative association (p=0.0001) between measured serum PFOS levels and estimated GFR was found.
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum uric acid levels were considered elevated if they exceeded 75th percentile of 2007–2010 NHANES values	**Exposure:** Median serum concentrations of PFOS 11.3 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	Significant association (p<0.01) between serum PFOS and uric acid levels. No significant association (p=0.502 for trend) between serum PFOS and risk of elevated uric acid levels.
Geiger et al. 2013 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,772 children and adolescents (<18 years of age)	**Exposure:** Mean serum PFOS level of 18.4 ng/mL • 1st quartile: <10.7 ng/mL • 2nd quartile: 10.7–16.5 ng/mL • 3rd quartile: 16.6–25.5 ng/mL • 4th quartile: >25.5 ng/mL **Logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, annual household income, activity, serum cotinine, serum cholesterol	No significant association (p=0.0575) between serum PFOS levels and uric acid levels was found. A significant association (p=0.0221) between serum PFOS and hyperuricemia (uric acid levels >6 mg/dL) was found. The ORs (95%) were: • 2nd quartile: 1.17 (0.80–1.72) • 3rd quartile: 1.18 (0.74–1.87) • 4th quartile: 1.65 (1.10–2.49)
Kataria et al. 2015	**Exposure:** Serum PFOS levels: • 1st quartile: <7.9 ng/mL	Significantly lower estimated GFR levels were found in adolescents in the 2nd quartile

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cross-sectional study utilizing 2003–2010 NHANES data for 1,960 adolescents (12–19 years of age)	• 2nd quartile: 7.9–12.8 ng/mL • 3rd quartile: 12.8–19.4 ng/mL • 4th quartile: ≥19.4 ng/mL **Multivariable logistic regression model adjustments:** Sex, poverty income ratio, caregiver education, serum cotinine, prehypertension, insulin resistance, BMI, hypercholesterolemia, race/ethnicity	(β -5.24 mL/minute/1.73 m^2, 95% CI -9.75 to -0.73; p<0.05), 3rd quartile (β -7.21 mL/minute/1.73 m^2, 95% CI -12.21 to -2.21; p<0.01), or 4th quartile (β -9.47 mL/minute/1.73 m^2, 95% CI -14.68 to -4.25; p<0.0015), as compared to the 1st quartile. Adolescents in the 4th quartile PFOS (≥19.4 ng/mL) had 0.19 mg/dL lower serum uric acid levels than adolescents in the lowest quartile (<7.9 ng/mL) (95% CI 0.032–0.34; p<0.05). Investigators noted that estimated GFR and serum uric acid levels were within normal range in all participants.
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFOS level 28.9 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine Study examined associations between serum perfluoroalkyl compounds and serum uric acid levels	No significant association (p>0.05) between serum PFOS and uric acid levels. No significant association between serum PFOS and risk of elevated uric acid levels (≥6.0 mg/dL) in full cohort (OR 1.35, 95% CI 0.95–1.93; p>0.05).
Shankar et al. 2011a Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 4,587 adults (20–80 years of age	**Exposure:** Serum PFOS levels • 1st quartile: <11.7 ng/mL • 2nd quartile: 11.7–18.7 ng/mL • 3rd quartile: 18.8–29.5 ng/mL • 4th quartile: >29.5 ng/mL **Linear and logistic regression model adjustments:** Age, sex, race/ethnicity, educational level, BMI	Increasing levels of serum PFOS were inversely associated (p<0.001 for trend) with estimated GFR. A significant positive association between the risk of chronic kidney disease (defined as a GFR <60 mL/minute/1.73 m^2) and serum PFOS levels in the 4th quartile (OR 1.82, 95% CI 1.02–3.27).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Shankar et al. 2011b Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,883 adults (>20 years of age)	**Exposure:** Serum PFOS levels • 1st quartile: <11.2 ng/mL • 2nd quartile: 11.2–17.8 ng/mL • 3rd quartile: 17.9–27.9 ng/mL • 4th quartile: >27.9 ng/mL **Linear and logistic regression model adjustments:** Age, sex, race/ethnicity, educational level, smoking, alcohol consumption, BMI, hypertension, diabetes, serum total cholesterol	A significant association (p=0.0018) between serum PFOS levels and uric acid levels was found. Significant increases in the risk of hyperuricemia were observed for serum PFOS levels in the 2nd and 3rd quartiles; ORs (95% CI) of 1.46 (1.11–1.91) of 1.69 (1.19–2.40), respectively; the OR for the 4th quartile was1.48 (0.99–2.22).
PFHxS		
Watkins et al. 2013 Cross-sectional study of 9,660 children (aged 1–<18 years) participating in the C8 Health Project	**Exposure:** Median serum PFHxS level was 5.2 ng/mL **Linear regression model adjustments:** Age, sex, race, smoking, household income, BMI, regular exercise	A significant negative association (p=0.003) between measured serum PFHxS levels and estimated GFR was found.
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum uric acid levels were considered elevated if they exceeded 75th percentile of 2007–2010 NHANES values	**Exposure:** Median serum concentrations of PFHxS 1.8 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	No significant association between serum PFHxS and uric acid levels (p>0.01). No significant association (p=0.110 for trend) between serum PFHxS and risk of elevated uric acid levels.
Kataria et al. 2015 Cross-sectional study utilizing 2003–2010 NHANES data for 1,960 adolescents (12–19 years of age)	**Exposure:** Mean serum PFHxS levels not reported; 4th quartile PFHxS levels ≥4 ng/mL **Multivariable logistic regression model adjustments:** Sex, poverty income ratio, caregiver education, serum cotinine, prehypertension, insulin resistance, BMI, hypercholesterolemia, race/ethnicity	No significant associations between serum PFHxS and estimated GFR (p>0.05). No significant associations between serum PFHxS and serum uric acid levels (p>0.05).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFHxS level 1.3 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine Study examined associations between serum perfluoroalkyl compounds and serum uric acid levels	Significant association between serum PFHxS and uric acid levels (β 0.1372 mg/dL per ln-unit PFOA, 95% CI 0.0152–0.2593; p<0.05). No significant association between serum PFHxS and risk of elevated uric acid levels (≥6.0 mg/dL) in full cohort (OR 1.39, 95% CI 0.93–2.07, p>0.05).
PFNA		
Mundt et al. 2007 Study of 592 workers (88% male) ever employed between 1989 and 2003 at a polymer production facility exposed to PFNA; workers underwent annual medical examinations that involved measurement of clinical chemistry indices	**Exposure:** Workers were assigned to exposure categories (no exposure, low exposure, high exposure) based on serum PFNA levels in a subset of current workers **Adjustments:** Age, BMI	The investigators noted that the differences in serum BUN, creatinine, and serum uric acid levels between exposure groups were small and not clinically relevant (no additional information provided).
Watkins et al. 2013 Cross-sectional study of 9,660 children (aged 1–<18 years) participating in the C8 Health Project	**Exposure:** Median serum PFNA level was 1.5 ng/mL **Linear regression model adjustments:** Age, sex, race, smoking, household income, BMI, regular exercise	A significant negative association (p=0.002) between measured serum PFNA levels and estimated GFR was found.
Gleason et al. 2015 Cross-sectional study utilizing 2007–2008 and 2009–2010 NHANES data for 4,333 participants (≥12 years of age); serum uric acid levels were considered elevated if they exceeded 75th percentile of 2007–2010 NHANES values	**Exposure:** Median serum concentrations of PFNA 1.4 ng/mL **Multivariate linear and logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, poverty index, smoking, alcohol consumption	Significant association (p<0.001) between serum PFNA and uric acid levels. No significant association (p=0.042 for trend) between serum PFNA and risk of elevated uric acid levels.

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kataria et al. 2015 Cross-sectional study utilizing 2003–2010 NHANES data for 1,960 adolescents (12–19 years of age)	**Exposure:** Mean serum PFNA levels were not reported; 4th quartile PFNA levels were ≥1.5 ng/mL **Multivariable logistic regression model adjustments:** Sex, poverty income ratio, caregiver education, serum cotinine, prehypertension, insulin resistance, BMI, hypercholesterolemia, race/ethnicity	No significant associations between serum PFNA and estimated GFR (p>0.05). No significant associations between serum PFNA and serum uric acid levels (p>0.05).
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFNA level 0.8 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine Study examined associations between serum perfluoroalkyl compounds and serum uric acid levels	No significant association (p>0.05) between serum PFNA and uric acid levels. No significant association between serum PFNA and risk of elevated uric acid levels (≥6.0 mg/dL) in full cohort (OR 1.28, 95% CI 0.83–1.96, p>0.05).
PFDA		
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFDA level 0.9 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine Study examined associations between serum perfluoroalkyl compounds and serum uric acid levels	No significant association (p>0.05) between serum PFDA and uric acid levels. No significant association between serum PFDA and risk of elevated uric acid levels (≥6.0 mg/dL) in full cohort (OR 1.26, 95% CI 0.82–1.92, p>0.05).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFBS		
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFBS level 0.5 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine Study examined associations between serum perfluoroalkyl compounds and serum uric acid levels	No significant association ($p>0.05$) between serum PFBS and uric acid levels. No significant association between serum PFBS and risk of elevated uric acid levels (≥6.0 mg/dL) in full cohort (OR 1.23, 95% CI 0.86–1.75, $p>0.05$).
PFDoDA		
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFDoDA level 2.7 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine Study examined associations between serum perfluoroalkyl compounds and serum uric acid levels	No significant association ($p>0.05$) between serum PFDoDA and uric acid levels. No significant association between serum PFDoDA and risk of elevated uric acid levels (≥6.0 mg/dL) in full cohort (OR 0.93, 95% CI 0.65–1.34, $p>0.05$).

Table 8. Renal Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHxA		
Qin et al. 2016 Cross-sectional study of 225 Taiwanese children (12–15 years of age)	**Exposure:** Median serum PFHxA level 0.2 ng/mL **Logistic regression model adjustments:** Age, sex, BMI, exercise habits, parental education, environmental tobacco smoke exposure, serum creatinine Study examined associations between serum perfluoroalkyl compounds and serum uric acid levels	No significant association ($p>0.05$) between serum PFHxA and uric acid levels. No significant association between serum PFHxA and risk of elevated uric acid levels (≥6.0 mg/dL) in full cohort (OR 1.08, 95% CI 0.77–1.61, $p>0.05$).

APFO = ammonium perfluorooctanoate; BMI = body mass index; BUN = blood urea nitrogen; CI = confidence interval; GFR = glomerular filtration rate; HR = hazard ratio; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PFBS = perfluorobutane sulfonic acid; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; SMR = standardized mortality ratio; SPR = standard prevalence ratio

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
PFOA		
Costa et al. 2009 Cohort study of 53 current (n=37) and former (n=16) male workers at a perfluoroalkyl manufacturing facility in Italy undergoing annual health examinations from 1978–2007; a control group of 107 male workers with no exposure to PFOA was also examined	**Exposure:** Mean and median serum PFOA levels measured in 2007 were 12,930 and 5,710 ng/mL (range: 200–47,040 ng/mL) in current workers and 6,810 and 4,430 ng/mL (range: 530–18,660 ng/mL) in former workers. Mean and median serum PFOA levels decreased over time; the mean levels were 18,800 ng/mL in 2000 and 11,600 ng/mL in 2007; the median levels were 11,920 and 3,890 ng/mL during those same times. **Regression model adjustments:** Age, years of exposure, year of PFOA sampling, BMI, smoking, alcohol consumption	TSH, free T3, and free T4 levels were outside of the reference range in 2.6% of the workers.
Gilliland 1992 Cross-sectional study of 115 (79% male) current workers employed at a PFOA production facility in Cottage Grove, Minnesota between 1985 and1989; this is same cohort examined by Gilliland and Mandell (1996)	**Exposure:** Serum fluorine levels were used as surrogate for serum PFOA; workers were categorized into five exposure groups based on serum fluorine levels: <1, 1–3, >3–10, >10–15, and >15–26 ppm **Regression model adjustments:** Age, BMI, alcohol use, tobacco use	Association between serum fluorine levels and TSH levels (β 0.027, p=0.004).
Olsen et al. 1998b Cross-sectional study of male workers employed at a PFOA production facility in Cottage Grove, Minnesota; health surveys were conducted in 1993 (n=111) and 1995 (n=80); 68 workers participated in both surveys	**Exposure:** Ranges of serum PFOA levels were 0–80,000 ng/mL in 1993 (80,000 ng/mL was the upper limit of detection) and 0–115,000 ng/mL in 1995. Workers were categorized into four groups based on PFOA levels of 0–<1,000, 1,000–<10,000, 10,000–<30,000, and ≥30,000 ng/mL. **Multivariable regression modeling adjustments:** Age, BMI, alcohol use, cigarette use	Serum PFOA was not highly correlated with TSH. When workers were categorized by serum PFOA levels, no significant differences in TSH (p=0.09 for trend) in 1993 were found between groups. A significant trend (p=0.002) was found in the 1995 group. The increase in mean TSH levels was significantly (p<0.05) increased in the 10,000–<30,000 ng/mL group in 1995; it should be noted that there were only five workers in the >30,000 ng/mL group.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Olsen and Zobel 2007 Cross-sectional study of workers at three fluorochemical manufacturing facilities in Decatur, Alabama (n=215), Cottage Grove, Minnesota (n=131), and Antwerp, Belgium (n=206) with potential exposure to PFOA and PFOS; workers were examined in 2000; 92% of the workers reported that they did not take cholesterol-lowering medication	**Exposure:** Mean, median, and range of PFOA levels were 2,210, 1,100, and 10–92,030 ng/mL, respectively, and mean, median, and range of PFOS levels were 1,050, 720, and 20–6,240 ng/mL, respectively **Logistic and multiple regression adjustments:** Age, BMI, alcohol use	Significant correlations were found between serum PFOA and serum free T4 (p=0.01) and T3 (p=0.05). No significant correlations were found for TSH (p=0.08) or T4 (p=0.29). The investigators noted that these results were not clinically relevant since levels were within the normal reference ranges.
Sakr et al. 2007b Cross-sectional study of 1,025 male (76%) and female (24%) workers at a fluoropolymers production plant (Washington Works)	**Exposure:** Median serum PFOA concentrations were 490 ng/mL (range: 17.4–9,550 ng/mL), 176 (8.1–2,070 ng/mL), 195 ng/mL (8.6–2,590 ng/mL), and 114 ng/mL (4.6–963 ng/mL) among current workers (n=259), current workers with intermittent exposure (n=160), past occupational exposure to PFOA (n=264), or never assigned to APFO area (n=342), respectively. The mean and median concentrations in all workers were 428 and 189 ng/mL, respectively. **Linear regression model adjustments:** Age, sex, BMI, alcohol consumption, heart attack in a parent (lipid models only)	The investigators noted that TSH, T3, and T4 levels were within the reference range.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was estimated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum PFOA levels in 2005–2006 were 325 and 113 ng/mL in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant associations between estimated cumulative serum PFOA and risk of thyroid disease in males (p=0.98 and 0.55 for trend with no lag or 10-year lag), or thyroid disease in females (p=0.97 and 0.27 for trend with no lag or 10-year lag).
Anderson-Mahoney et al. 2008 Cross-sectional study of 566 adult residents (mean age of 49.9 years) living near a Teflon manufacturing facility in West Virginia for at least 1 year; most subjects were exposed to PFOA in drinking water provided by Lubeck Public Service District (37%) or Little Hocking water district (27%); some subjects also worked at the facility	**Exposure:** Individual biomonitoring data were not provided; reported PFOA levels in the Lubeck and Little Hocking water districts were 0.4–3.9 and 1.7–4.3 µg/L, respectively **Reference population:** SPRs were estimated using NHANES data; statistical analyses were adjusted for age and sex	Incidence data were based on the results of participant completed health surveys. Significantly increased risk of thyroid problems (combined population) (SPR 1.56; 95% CI 1.22–1.98).
Emmett et al. 2006b Cross-sectional study of 371 residents (aged 2.5–89 years) who had resided in the Little Hocking Water Association district for ≥2 years; includes 18 residents with occupational exposure to PFOA	**Exposure:** Median serum PFOA level was 354 ng/mL	No significant correlation (p>0.05) between serum PFOA and TSH was found. There was no significant (p>0.05) difference in the serum PFOA levels between residents with abnormal or normal TSH levels.
Knox et al. 2011a Cross-sectional study of 50,113 adult C8 Health Project participants	**Exposure:** Mean PFOA levels were 52.6, 91.0, 98.6, and 124.3 ng/mL in women 20–50 years, men 20–50 years, women >50 years, and men >50 years, respectively **Statistical adjustments:** Age, serum estradiol, alcohol	Significant association between serum PFOA and T4 levels in women 20–50 (p≤0.0001) and >50 (p<0.001) years of age and in men >50 years of age (p<0.001). Inverse association between serum PFOA and T3 uptake in women 20–50 years (p=0.0001) and >50 years (p=0.005) and in men

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
		>50 years (p=0.037). The investigators noted that T3 uptake in both groups of women were below 32%, which is the lower threshold of the range considered to be normal.
Lopez-Espinosa et al. 2012 Cross-sectional study of 10,725 children aged 1–17 years participating in the C8 Health Project study	**Exposure:** Median serum PFOA 29.3 ng/mL **Statistical adjustments:** Age, month, and time of sampling	Significant associations between serum PFOA and reported thyroid disease (OR 1.44, 95% CI 1.02–2.03) and hypothyroidism (1.54, 95% CI 1.00–2.37) per interquartile shift. No significant associations between serum PFOA and subclinical hypothyroidism (OR 0.98, 95% CI 0.86–1.15) or hyperthyroidism (OR 0.81, 95% CI 0.58–1.15) per interquartile shift. No significant associations between serum PFOA and measured TSH (β -1.1, 95% CI -5.3–3.4) or total T4 (β -0.1, 95% CI -1.7–1.4) were found for 4th quartile serum PFOA (67.7–2,071 ng/mL).
Winquist and Steenland 2014b Retrospective and prospective study of 28,541 participants in the C8 Health Project and a cohort of 3,713 workers at a DuPont Washington Works facility who worked at the plant between 1948 and 2002; functional thyroid disease was defined as a report of goiter, Graves' disease, hyperthyroidism, Hashimoto's disease, hypothyroidism, thyroiditis not otherwise specified, or a thyroid function problem of unknown type	**Exposure:** Serum PFOA levels based on estimated environmental levels on a fate and transport model to estimate PFOA levels in in water and air per year since production began in 1951 and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life. Exposures of workers were estimated using a job history matrix. The mean serum PFOA level of the combined cohort was 86.6 ng/mL. Estimated cumulative PFOA levels were categorized into quintiles: • 1st quintile: 0.1–<114.7 ng/mL-year • 2nd quintile: 114.7–<202.2 ng/mL-year • 3rd quintile: 202.2–<497.3 ng/mL-year • 4th quintile: 497.3–<2,676 ng/mL-year • 5th quintile: 2,676–97,396 ng/mL-year	In a retrospective analysis, estimated cumulative serum PFOA levels were significantly associated with the risk of functional thyroid disease among women; HR 1.24 (95% CI 1.02–1.51; p=0.031) for 2nd quintile, 1.27 (95% CI 1.04–1.55, p=0.019) for 3rd quintile, 1.36 (95% CI 1.12–1.66, p=0.002) for 4th quintile, and 1.37 (95% CI 1.11–1.68, p=0.003) for 5th quintile. No significant association for men (HR 1.01, 95% CI 0.94–1.07; p=0.853 per log linear increase in PFOA). No significant associations between estimated cumulative serum PFOA and hyperthyroidism (p=0.074 for women and p=0.858 for men) or hypothyroidism (p=0.076 for women and p=0.684 for men) in retrospective analysis.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
	Cox proportional hazards model adjustments: Education, race, smoking, BMI, self-reported diabetes, alcohol consumption	In retrospective analysis using yearly exposure estimates, significant associations between PFOA and functional thyroid disease (HR 1.04, 95% CI 1.01–1.08; p=0.008 per log linear increase in PFOA) and hyperthyroidism (HR 1.11, 95% CI 1.03–1.19; p=0.006 per log linear increase in PFOA) in women. No significant association between yearly PFOA estimates and functional thyroid disease in men (p=0.970), hyperthyroidism in men (p=0.766), or hypothyroidism in women (p=0.110) or men (p=0.993). In prospective analysis, significant association between estimated cumulative serum PFOA and hypothyroidism in men (HR 1.24, 95% CI 1.03–1.49; p=0.021) per log-unit PFOA. No significant associations between estimated cumulative serum PFOA and functional thyroid disease in women (p=0.549) or men (p=0.087), hyperthyroidism in women (p=0.268) or men (p=0.760), or hypothyroidism in women (p=0.247).
Berg et al. 2017 Prospective study of 370 pregnant women participating in the Northern Norway Mother-and-Child Contaminant Cohort Study	**Exposure:** Median maternal serum PFOA 1.53 ng/mL (measured during 2nd trimester) **Statistical adjustments:** Parity, age, physical activity BMI, sum of perfluoroalkyls, and/or sum of persistent organic pollutants	No associations (p>0.05) between maternal serum PFOA and TSH, total T4, free T4, total T3, free T3, or thyroxine binding capacity.
Bloom et al. 2010 Prospective cohort study of 31 participants (27 males and 4 females, mean age of 39.0 years) in the New York State Angler Cohort Study	**Exposure:** Geometric serum PFOA level 1.33 ng/mL (range: 0.57–2.58 ng/mL) **Linear regression model adjustments:** Age (TSH only)	No significant association between serum PFOA levels and TSH (p=0.871) or free T4 (p=0.896) were found.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Chan et al. 2011 Case-control study of women undergoing a prenatal screen for trisomy 18, Down's syndrome, and open spina bifida in Canada; 94 women with hypothyroxinemia and 175 matched controls	**Exposure:** Geometric mean serum PFOA levels were 1.28 and 1.37 ng/mL for cases and controls, respectively **Logistic regression adjustments:** Maternal age, maternal weight, gestational age at blood draw, race	No significant association between serum PFOA and hypothyroxinemia was observed; OR 0.94 (95% CI 0.74–1.18).
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in North Carolina and attempting to conceive for ≤3 months	**Exposure:** Geometric mean serum PFOA 2.79 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	Association between serum PFOA and T3 levels (β 6.05. p=0.03). No associations with TSH (p=0.37), total T4 (p=0.07), or free T4 (p=0.11) levels.
Dufour et al. 2018 Cross-sectional study of 214 pregnant women entering the hospital for delivery	**Exposure:** Cord blood mean PFOA 0.80 ng/mL; 0.44–0.68, 0.68–0.97, 0.98–3.40 ng/mL for 2nd, 3rd, and 4th quartiles **Statistical adjustments:** Maternal age, tobacco use	Association between cord blood PFOA and hypothyroid in mother, OR (95% CI): 2nd quartile: 4.42 (1.23–21.14) 3rd quartile: 3.22 (0.88–15.38) 4th quartile: 5.62 (1.64–26.11). No association between cord blood PFOA and TSH levels in infants (p=0.196).
Jain 2013 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 adults (≥12 years of age)	**Exposure:** Serum PFOA levels were not provided in publication **Multivariate linear regression model adjustments:** Age, sex, race, smoking status, iodine status, C-reactive protein, BMI, fasting time before blood was drawn, total calories consumed during the last 24 hours, perfluorinated compound variable	Significant association (p=0.013) between serum PFOA and total T3. No significant associations (p>0.05) between serum PFOA and TSH, free T3, free T4, total T4, or thyroglobulin.
Ji et al. 2012 Cross-sectional study of 633 children and adults (aged 12–>60 years) participating in a health study in Korea	**Exposure:** Median serum PFOA concentration was 2.74 ng/mL (range: 2.04–3.64) **Regression model adjustments:** Age, BMI, sex	No significant association between serum PFOA levels and T4 (p=0.2221) or TSH (p=0.4055) levels.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFOA 1.88 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No associations between serum PFOA and serum free T4 levels (β 0.044, 95% CI -0.005–0.093, p=0.075) or TSH levels (β -0.141, 95% CI -0.623–0.341, p=0.565).
Lewis et al. 2015 Cross-sectional study utilizing 2011–2012 NHANES data for 1,682 males and females 12–80 years of age	**Exposure:** Median serum PFOA levels tended to increase with age and ranged from 1.49 to 2.55 ng/mL **Multivariate linear regression model adjustments:** Age, BMI, poverty income ratio, race/ethnicity, serum cotinine	Significant association (p<0.05) between serum PFOA and TSH levels in 12–20-year-old females, free T4 levels in 20–<40-year-old females, and free T3 and total T3 levels in 60–80-year-old females. No significant associations (p>0.05) between serum PFOA and TSH, free T4, total T4, free T3, or total T3 were found for other ages or sexes. No association (p>0.05) between serum PFOA and serum testosterone.
Melzer et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,966 adults (≥20 years of age)	**Exposure:** Mean serum PFOA levels were 5.23 ng/mL (0.1–45.9 ng/mL) in men and 4.25 ng/mL (0.1–123.0 ng/mL) in women. Mean levels in each quartile: • 1st quartile: M 2.47 ng/mL; F 1.71 ng/mL • 2nd quartile: M 4.42 ng/mL; F 3.32 ng/mL • 3rd quartile: M 6.12 ng/mL; F 4.79 ng/mL • 4th quartile: M 10.39 ng/mL; F 9.47 ng/mL **Logistic regression model adjustments:** Age, ethnicity, study year, BMI, smoking status, alcohol consumption	There were significant associations between serum PFOA levels and female participants ever reporting physician-diagnosed thyroid disease; the ORs (95% CI) were: • 2nd quartile: 0.95 (0.62–1.47), p=0.875 • 3rd quartile: 1.11 (0.67–1.83), p=.679 • 4th quartile: 1.64 (1.09–2.46), p=0.019. The association was not significant in males; the OR for the 4th quartile was 1.58 (95% CI 0.74–3.39, p=0.233). Significant associations were also found between serum PFOA levels and female participants reporting current thyroid disease and taking thyroid medication; the ORs (95% CI) were: • 2nd quartile: 0.7 (0.41–1.22), p=0.205 • 3rd quartile: 0.89 (0.49–1.59), p=0.676 • 4th quartile: 1.86 (1.12–3.09), p=0.018. The association was not significant in males; the OR for the 4th quartile was 1.89 (95% CI 0.60–5.90, p=0.268).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Preston et al. 2018 Cross-sectional study of 732 mothers and 480 infants participating in Project Viva in Massachusetts	**Exposure:** Maternal median serum PFOA 5.6 ng/mL (range of 0.3–36.7 ng/mL measured during early pregnancy, median 9.6 weeks of gestation **Statistical adjustments:** Maternal age, race/ethnicity, smoking status, fish intake, parity, gestational week of blood draw	Inverse association between maternal PFOA and free T4 (β -1.87, 95% CI -3.40 to -0.31). No association between maternal PFOA and total T4 (β 0.09, 95% CI -0.08–0.27) or TSH (β 0.28, 95% CI -9.26–10.8). Inverse association between maternal serum PFOA and neonatal T4 (β -1.1, 95% CI -2.1 to -0.1) for the 4th quartile.
Raymer et al. 2012 Cross-sectional study of 256 men in Durham, North Carolina (mean age 41.6 years)	**Exposure:** Mean and median serum PFOA levels were 10.4 and 9.2 ng/mL **Statistical adjustments:** Age, period of abstinence, tobacco use	No significant associations (p>0.05) between serum PFOA levels and thyroid hormone (TSH, T3, T4) levels.
Shah-Kulkarni et al. 2016 Cross-sectional study of 279 pregnant women participating in the Ewha Birth and Growth Retrospective Cohort study	**Exposure:** Cord blood median PFOA 0.91 ng/mL (range of 0.05–2.4 ng/mL) **Statistical adjustments:** Maternal age, education, prepregnancy BMI, alcohol intake, child's parity, gestational age, sex	No association between cord blood PFOA and cord blood T4 (β 0.001, 95% CI -0.26–0.26, p=0.99), T3 (β -0.01, 95% CI -2.22–2.20, p=0.99), or TSH (β -0.79, 95% CI -2.13–0.55, p=0.24).
Shrestha et al. 2015 Cross-sectional study of 87 men and women 55–74 years of age living in New York; none of the participants had clinically diagnosed thyroid disease	**Exposure:** Geometric mean serum PFOA 9.17 ng/mL **Multivariable linear regression model adjustments:** Age, sex, years of education, serum ΣPCBs (lipid basis)	No significant associations between serum PFOA and TSH (p=0.176), free T4 (p=0.536), T4 (p=0.097), or T3 (p=0.208).
Tsai et al. 2017 Cross-sectional study of 118 mother-infant pairs participating in the Taiwan Birth Panel Study.	**Exposure:** Cord blood mean PFOA 3.14 ng/mL **Statistical adjustments:** Maternal age at delivery, BMI, education, newborn sex, gestational age, delivery type	No association between cord blood PFOA and cord blood T4 levels (β -0.031, 95% CI -0.414–0.342), T3 levels (β 0.025, 95% CI -0.054–0.103), or TSH (β 0.059, 95% CI -0.136–0.254).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Wang et al. 2013a Prospective cohort study of 903 pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Geometric mean serum PFOA levels in blood measured at approximately 18th week of gestation was 2.13 ng/mL **Statistical adjustments:** Age, gestation age at blood draw, parity, total seafood intake at mid-pregnancy, HDL blood concentrations	The investigators reported no significant associations between serum PFOA and TSH levels or the risk of elevated TSH (<7.5 in/mL).
Wang et al. 2014 Cross-sectional study of 285 healthy pregnant women and 116 neonates participating in the Taiwan Maternal and Infant cohort study	**Exposure:** Median plasma PFOA level (collected in the third trimester of pregnancy) 2.39 ng/mL **Multivariable linear regression model adjustments:** Age, maternal education, previous live births, family income, prepregnancy BMI, and maternal fish consumption during pregnancy.	No significant associations (p>0.05) between maternal serum PFOA and maternal levels of free T4, total T4, total T3, or TSH.
Webster et al. 2016 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 male and female adults (≥18 years of age)	**Exposure:** Geometric mean serum level PFOA 4.2 ng/mL **Multivariate linear regression model adjustments:** Age, log_{10}-transformed serum cotinine, race/ethnicity, sex, parity, pregnancy, menopause status	Significant association (p<0.05) between serum PFOA and free T3. No significant associations (p>0.05) between serum PFOA and free T4, ratio of free T3 to free T4, TSH, total T3, or total T4.
Wen et al. 2013 Cross-sectional study utilizing 2007–2010 NHANES data for 1,181 male and female adults	**Exposure:** Geometric mean serum PFOA 4.15 ng/mL **Statistical adjustments:** Age, race, drinking, smoking, and urinary iodine; regression analysis weighted for sampling strategy	Significant association between serum PFOA and total T3 in women (β 6.628, 95% CI 0.545–12.712, p=0.035), but not in men (β 0.775, 95% CI -3.048–4.598, p=0.673). No associations between total T4 (p=1.0 and p=0.705 in men and women), TSH (p=0.916 and 0.732 in men and women), or thyroglobulin (p=0.226 and 0.341 in men and women). When subjects were categorized by serum PFOA levels, there were significant differences in T3 levels between subjects with serum PFOA levels in the 3rd quartile (≤5.3 ng/mL) and 4th quartile (>5.3 ng/mL), as compared to the 1st quartile (≤2.4 ng/mL).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
		Significant association between serum PFOA and risk of subclinical hypothyroidism in women (OR 7.42, 95% CI 1.14–48.12, p<0.05), but not in men (OR1.29, 95% CI 0.40–4.10) and risk of subclinical hyperthyroidism in men (OR 0.38, 95% CI 0.16–0.95, p<0.05), but not in women (OR 0.99, 95% CI 0.13–7.59).
Yang et al. 2016a Cross-sectional study of 157 healthy pregnant women in China	**Exposure:** Mean and median maternal serum PFOA levels (collected 1–2 days before delivery) 1.95 and 1.64 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, delivery type, maternal income	No significant associations (p>0.05) were found between maternal serum PFOA and maternal levels of free T3, total T3, free T4, total T4, or TSH.
PFOS		
Olsen et al. 1998a Cross-sectional study of workers at two PFOS-based fluorochemical manufacturing facilities in Decatur, Alabama and Antwerp, Belgium; workers were examined in 1995 (n=178) and 1997 (n=149); 61 workers participated in both years; hormone levels were only measured in 88 workers in 1995; this is the same cohort of workers as Olsen et al. (1999)	**Exposure:** 20–22% of the workers in Decatur and 14–24% in Antwerp had serum PFOS levels of >3,000 ng/mL; the mean PFOS levels in 1995 and 1997 were 2,440 and 1,960 ng/mL in Decatur and 1,930 and 1,480 ng/mL in Antwerp **Multivariable regression model adjustments:** Age, BMI, alcohol consumption, smoking	No significant associations between serum PFOS and cortisol (p=0.45) or TSH (p=0.95) were found.
Olsen et al. 2003a Cohort study of workers at two fluorochemical manufacturing facilities in Decatur, Alabama (n=263, 82% male) and Antwerp, Belgium (n=255, 81% male) with potential exposure to PFOA and PFOS; workers were examined in 2000	**Exposure:** Mean serum PFOS levels were 1,320 ng/mL (range: 60–10,006 ng/mL) in Decatur and 800 ng/mL (range: 40–6,240 ng/mL) in Antwerp. Median PFOS levels in the 1st, 2nd, 3rd, and 4th quartiles were 290, 590, 1,170, and 2,460 ng/mL, respectively, for males and 80, 130, 370, and 1,340 ng/mL, respectively, in females. The mean serum PFOA levels were 1,780 ng/mL (range: 40–12,700 ng/mL) in Decatur and 840 ng/mL (range: 10–7,040 ng/mL) in Antwerp.	Male workers with the highest PFOS levels (4th quartile) had significantly (p<0.05) higher T3 levels than workers with the lowest PFOS levels (1st quartile). There were no significant alterations for T4 or TSH. No significant alterations were found for female workers. T3 levels were significantly associated with serum PFOS levels (p=0.04) and serum PFOA levels (p=0.01), but serum PFOS and PFOA were only minor contributors to the variance.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
	Regression model adjustments: Age, BMI, current alcohol consumption, cigarette use, employment duration	
Knox et al. 2011a Cross-sectional study of 50,113 adult C8 Health Project participants	**Exposure:** Mean PFOS levels were 17.3, 24.8, 25.7, and 29.1 ng/mL in women 20–50 years, men 20–50 year, women >50 years, and men >50 years **Statistical adjustments:** Age, serum estradiol, alcohol	Significant association between serum PFOA and T4 levels in women 20–50 ($p<0.0001$) and >50 ($p<0.0001$) years of age and in men 20–50 ($p=0.0001$) and >50 years of age ($p=0.0001$). Inverse association between serum PFOA and T3 uptake in women 20–50 years ($p<0.0001$) and >50 years ($p=0.0001$) and in men 20–50 years ($p=0.009$) and >50 years ($p<0.0001$). Investigators noted that there was no association with TSH.
Lopez-Espinosa et al. 2012 Cross-sectional study of 10,725 children aged 1–17 years participating in the C8 Health Project study	**Exposure:** Median serum PFOS 20.0 ng/mL **Statistical adjustments:** Age, month, and time of sampling	No significant associations between serum PFOS and reported thyroid disease (OR 0.8, 95% CI 0.62–1.08), hypothyroidism (0.91, 95% CI 0.63–1.31), subclinical hypothyroidism (OR 0.99, 95% CI 0.86–1.13), or subclinical hyperthyroidism (OR 0.80, 95% CI 0.62–1.02) per interquartile shift. Significant association between serum PFOS and total T4 (β 1.1, 95% CI 0.6–1.5) per interquartile shift; no association was found for TSH (β 1.0, 95% CI -0.3–2.3).
Berg et al. 2015 Longitudinal study of 391 pregnant women participating in the Northern Norway Mother and Child contaminant Cohort Study; thyroid hormone levels measured during the second trimester and 3 days and 6 weeks postpartum	**Exposure:** Median serum PFOS level (collected at gestation week 18) 8.03 ng/mL **Multivariable logistic regression model adjustments:** T4 binding capacity, parity	Significant association between maternal serum PFOS and TSH for women with PFOS levels in the 3rd quartile (8.1–11.0 ng/mL, $p=0.03$) or 4th quartile (11.1–35.9 ng/mL, $p=0.00$). Mean TSH levels were 24% higher in 4th quartile participants, compared to those in the 1st quartile (0.3–5.7 ng/mL). Because all values were within normal ranges, the investigators noted that the changes might

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
		have not been of clinical significance in the pregnant women.
Berg et al. 2017 Prospective study of 370 pregnant women participating in the Northern Norway Mother-and-Child Contaminant Cohort Study	**Exposure:** Median maternal serum PFOS 8.03 ng/mL (measured during 2nd trimester) **Statistical adjustments:** Parity, age, physical activity BMI, sum of perfluoroalkyls, and/or sum of persistent organic pollutants	Association ($p<0.05$) between serum PFOS and TSH concentration; however, association no longer significant after adjusting for exposure to other perfluoroalkyls and persistent organic pollutants. No associations ($p>0.05$) between serum PFOS and total T4, free T4, total T3, free T3, or thyroxine binding capacity.
Bloom et al. 2010 Prospective cohort study of 31 participants (27 males and 4 females, mean age of 39.0 years) in the New York State Angler Cohort Study	**Exposure:** Geometric serum PFOS level 19.57 ng/mL (range: 7.25–76.88 ng/mL) **Linear regression model adjustments:** Age (TSH only)	No significant association between serum PFOS levels and TSH ($p=0.896$) or free T4 ($p=0.623$) were found.
Chan et al. 2011 Case-control study of women undergoing a prenatal screen for trisomy 18, Down's syndrome, and open spina bifida in Canada; 94 women with hypothyroxinemia and 175 matched controls	**Exposure:** Geometric mean serum PFOS levels were 7.59 and 7.08 ng/mL for cases and controls, respectively **Logistic regression adjustments:** Maternal age, maternal weight, gestational age at blood draw, race	No significant association between serum PFOS and hypothyroxinemia was observed; OR 0.88 (95% CI 0.63–1.24).
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in North Carolina and attempting to conceive for ≤3 months	**Exposure:** Geometric mean serum PFOS 9.29 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	No associations between serum PFOS and TSH ($p=0.98$), T3 ($p=0.19$), total T4 ($p=0.28$), or free T4 ($p=0.42$) levels.
Dallaire et al. 2009 Cross-sectional study of 623 Inuit adults (18–73 years of age) living in Nunavik Canada with a high dietary exposure to n-3 polyunsaturated fatty acids found in traditional food items	**Exposure:** Geometric mean serum PFOS concentration was 18.28 ng/mL (range: 0.48–470.0 ng/mL) **Linear regression model adjustments:** Age, sex, BMI, plasma lipids, cigarette smoking, education, fish consumption, alcohol consumption	Significant negative associations between serum PFOS levels and TSH ($p\leq0.05$), T3 ($p\leq0.05$), and thyroxine-binding globulin ($p<0.01$), and a positive association with free T4 ($p\leq0.05$).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Dufour et al. 2018 Cross-sectional study of 214 pregnant women entering the hospital for delivery	**Exposure:** Cord blood mean PFOS 0.88 ng/mL; 0.52–0.71, 0.73–1.01, 1.01–9.21 ng/mL for 2nd, 3rd, and 4th quartiles **Statistical adjustments:** Maternal age, tobacco use	Association between cord blood PFOS and hypothyroid in mother, OR (95% CI) 2nd quartile: 1.76 (0.49–6.56) 3rd quartile: 3.22 (1.08–10.92) 4th quartile: 2.95 (0.98–10.07) No association between cord blood PFOS and TSH levels in infants (p=0.679).
Jain 2013 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 adults (≥12 years of age)	**Exposure:** Serum PFOS values were provided in publication **Multivariate linear regression model adjustments:** Age, sex, race, smoking status, iodine status, C-reactive protein, BMI, fasting time before blood was drawn, total calories consumed during the last 24 hours, perfluorinated compound variable	No significant association between serum PFOS and TSH, free T3, free T4, total T3, total T4, or thyroglobulin.
Ji et al. 2012 Cross-sectional study of 633 children and adults (aged 12–>60 years) participating in a health study in Korea	**Exposure:** Median serum PFOS concentration was 7.96 ng/mL (range: 5.58–12.10)	No significant association between serum PFOS levels and T4 (p=0.1134) or TSH (p=0.3537) levels.
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFOS 5.68 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No associations between serum PFOS and serum free T4 levels (β 0.000, 95% CI -0.055–0.054, p=0.987) or TSH levels (β -0.131, 95% CI -0.655–0.402, p=0.628).
Lewis et al. 2015 Cross-sectional study utilizing 2011–2012 NHANES data for 1,682 males and females 12–80 years of age	**Exposure:** Median PFOS levels tended to increase with age and ranged from 3.76 to 11.1 ng/mL **Multivariate linear regression model adjustments:** Age, BMI, poverty income ratio, race/ethnicity, serum cotinine	Significant association (p<0.05) between serum PFOS and free T4 levels in 20–<40-year-old females. No significant associations (p>0.05) between serum PFOS and TSH, free T4, total T4, free T3, or total T3 were found for other ages or sexes. No association (p>0.05) between serum PFOS and serum testosterone.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Melzer et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,966 adults (≥20 years of age)	**Exposure:** Mean serum PFOS levels were 29.57 ng/mL (0.3–435.0 ng/mL) in men and 23.24 ng/mL (0.14–406.0 ng/mL) in women. Mean levels in each quartile: • 1st quartile: M 12.29 ng/mL; F 8.13 ng/mL • 2nd quartile: M 21.82 ng/mL; F 15.75 ng/mL • 3rd quartile: M 30.81 ng/mL; F 24.21 ng/mL • 4th quartile: M 57.73 ng/mL; F 50.96 ng/mL **Logistic regression model adjustments:** Age, ethnicity, study year, BMI, smoking status, alcohol consumption	There were no significant associations between serum PFOS levels and participants ever reporting physician-diagnosed thyroid disease; the ORs for the 4th quartile were 1.58 (95% CI 0.72–3.47, p=0.251) in males and 1.15 (95% CI 0.7–1.91, p=0.568) in females. An association between serum PFOS and the risk of thyroid disease with current medication (OR 2.68, 95% CI 1.03–6.98, p=0.043) was found in men in the 4th quartile versus combined 1st and 2nd quartiles. No significant associations were found between serum PFOA levels and participants reporting current thyroid disease and taking thyroid medication; the ORs for the 4th quartile were 1.89 (95% CI 0.72–4.93, p=0.190) in males and 1.31 (95% CI 0.72–2.36, p=0.359) in females.
Preston et al. 2018 Cross-sectional study of 732 mothers and 480 infants participating in Project Viva in Massachusetts	**Exposure:** Maternal median serum PFOS 24.0 ng/mL (range of 2.8–115 ng/mL (measured during early pregnancy, median 9.6 weeks of gestation). **Statistical adjustments:** Maternal age, race/ethnicity, smoking status, fish intake, parity, gestational week of blood draw	No association between maternal PFOS and total T4 (β 0.01, 95% CI -0.14–0.16), free T4 (β -1.04, 95% CI -2.36–0.29), or TSH (β 0.90, 95% CI -7.27–9.80). When subjects were divided by maternal thyroid peroxides antibody (TPOAb) levels, an inverse association between maternal PFOS levels and TSH was found among TPOAb positive mothers (β -16.4, 95% CI -29.8 to -0.38). Inverse association between maternal serum PFOS and neonatal T4 (β -1.1, 95% CI -2.1 to -0.1) for the 4th quartile.
Raymer et al. 2012 Cross-sectional study of 256 men in Durham, North Carolina (mean age 41.6 years)	**Exposure:** Mean and median serum PFOS levels were 37.4 and 32.3 ng/mL **Statistical adjustments:** Age, period of abstinence, tobacco use	No significant associations (p>0.05) between serum PFOS levels and thyroid hormone (TSH, T3, T4) levels.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Shah-Kulkarni et al. 2016 Cross-sectional study of 279 pregnant women participating in the Ewha Birth and Growth Retrospective Cohort study	**Exposure:** Cord blood median PFOS 0.66 ng/mL (range of 0.07–5.9 ng/mL) **Statistical adjustments:** Maternal age, education, prepregnancy BMI, alcohol intake, child's parity, gestational age, sex	No association between cord blood PFOS and cord blood T4 (β 0.14, 95% CI -0.03–0.31, p=0.10), T3 (β 0.65, 95% CI -0.80–2.10, p=0.37), or TSH (β -0.15, 95% CI -1.03–0.73, p=0.73).
Shrestha et al. 2015 Cross-sectional study of 87 U.S. men and women 55–74 years of age without clinically diagnosed thyroid disease	**Exposure:** Geometric mean serum PFOS levels 31.6 ng/mL **Multivariable linear regression model adjustments:** Age, sex, years of education, serum ΣPCBs (lipid basis)	Significant associations between serum PFOS and free T4 (β 0.054, 95% CI 0.002–0.106; p=0.044) and T4 (β 0.766, 95% CI 0.327–1.205; p=0.001). No association with T3 (p=0.287) or TSH (p=0.094). Associations between perfluoroalkyls and thyroid hormones also were found to vary by age and levels of PCBs and PBDEs.
Tsai et al. 2017 Cross-sectional study of 118 mother-infant pairs participating in the Taiwan Birth Panel Study	**Exposure:** Cord blood mean PFOS 7.24 ng/mL **Statistical adjustments:** Maternal age at delivery, BMI, education, newborn sex, gestational age, delivery type	Inverse association between cord blood PFOS and cord blood T4 levels (β -0.458, 95% CI -0.916 to -0.001, p<0.05). Association between cord blood PFOS and cord blood TSH (β 0.346, 95% CI 0.101–0.591, p<0.05). No association between cord blood PFOS and cord blood T3 levels (β 0.027, 95% CI -0.072–0.125).
Wang et al. 2013a Prospective cohort study of 903 pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Geometric mean serum PFOS levels in blood collected at approximately 18th week of gestation was 12.77 ng/mL • 1st quartile: <10.30 ng/mL • 2nd quartile:>10.3–≤13.09 ng/mL • 3rd quartile: >13.09–≤16.58 ng/mL • 4th quartile: >16.58 ng/mL **Statistical adjustments:** Age, gestation age at blood draw, parity, total seafood intake at mid-pregnancy, HDL blood concentrations	Serum PFOS levels were significantly correlated (p=0.03) with TSH levels. Increasing trend in TSH levels across serum PFOS quartiles; only women in 3rd and 4th quartiles had significantly higher TSH levels than the referent group (1st quartile). The investigators reported no significant association between serum PFOS and the risk of elevated TSH (<7.5 µIU/mL).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Wang et al. 2014 Cross-sectional study of 285 healthy pregnant women and 116 neonates participating in the Taiwan Maternal and Infant cohort study	**Exposure:** Median plasma PFOS level (collected in the third trimester of pregnancy) 12.73 ng/mL **Multivariable linear regression model adjustments:** Age, maternal education, previous live births, family income, prepregnancy BMI, maternal fish consumption during pregnancy	No significant associations (p>0.05) between maternal serum PFOS and maternal levels of free T4, total T4, total T3, or TSH.
Webster et al. 2016 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 male and female adults (≥18 years of age)	**Exposure:** Geometric mean serum level PFOS 13.9 ng/mL **Multivariate linear regression model adjustments:** Age, log_{10}-transformed serum cotinine, race/ethnicity, sex, parity, pregnancy, menopause status	No significant associations (p>0.05) between serum PFOS and free T3, free T4, ratio of free T3 to free T4, TSH, total T3, and total T4.
Wen et al. 2013 Cross-sectional study utilizing 2007–2010 NHANES data for 1,181 male and female adults	**Exposure:** Geometric mean serum PFOS 14.2 ng/mL **Statistical adjustments:** Age, race, drinking, smoking, and urinary iodine; regression analysis weighted for sampling strategy	No associations between serum PFOS and total T4 (p=0.840 and 0.433 in men and women), T3 (p=0.404 and 0.384 in men and women), TSH (p=0.931 and 0.358 in men and women), or thyroglobulin (p=0.342 and 0.061 in men and women). Significant association between serum PFOS and risk of subclinical hypothyroidism in women (OR 3.03, 95% CI 1.14–8.07, p<0.05) and men (OR 1.98, 95% CI 1.19–3.28, p<0.05); no associations for the risk of subclinical hyperthyroidism in men (OR 0.92, 95% CI 0.19–4.46) or women (OR 1.90, 95% CI 0.53–6.80).
Yang et al. 2016a Cross-sectional study of 157 healthy pregnant women in China	**Exposure:** Mean and median maternal serum PFOS levels (collected 1–2 days before delivery) 5.08 and 4.41 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, delivery type, maternal income	Significant inverse association (p<0.01) between maternal serum PFOS and maternal levels of TSH. No significant associations (p>0.05) between maternal serum PFOS and maternal levels of free T3, total T3, free T4, or total T4.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
PFHxS		
Berg et al. 2017 Prospective study of 370 pregnant women participating in the Northern Norway Mother-and-Child Contaminant Cohort Study	**Exposure:** Median maternal serum PFHxS 0.44 ng/mL (measured during 2nd trimester) **Statistical adjustments:** Parity, age, physical activity BMI, sum of perfluoroalkyls, and/or sum of persistent organic pollutants	No associations (p>0.05) between serum PFHxS and TSH, total T4, free T4, total T3, free T3, or thyroxine binding capacity.
Bloom et al. 2010 Prospective cohort study of 31 participants (2 males and 4 females, mean age of 39.0 years) in the New York State Angler Cohort Study	**Exposure:** Geometric serum PFHxS level 0.75 ng/mL (range: 0.16–4.60 ng/mL) **Linear regression model adjustments:** Age (TSH only)	No significant association between serum PFHxS levels and TSH (p=0.956) or free T4 (p=0.567) were found.
Chan et al. 2011 Case-control study of women undergoing a prenatal screen for trisomy 18, Down's syndrome, and open spina bifida in Canada; 94 women with hypothyroxinemia and 175 matched controls	**Exposure:** Geometric mean serum PFHxS levels were 1.14 and 1.04 ng/mL for cases and controls, respectively **Logistic regression adjustments:** Maternal age, maternal weight, gestational age at blood draw, race	No significant association between serum PFHxS and hypothyroxinemia was observed; OR 1.12 (95% CI 0.89–1.41).
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in North Carolina and attempting to conceive for ≤3 months	**Exposure:** Geometric mean serum PFHxS 1.59 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	No associations between serum PFHxS and TSH (p=0.71), T3 (p=0.22), total T4 (p=0.50), or free T4 (p=0.84) levels.
Dufour et al. 2018 Cross-sectional study of 214 pregnant women entering the hospital for delivery	**Exposure:** Cord blood mean PFHxS 0.18 ng/mL **Statistical adjustments:** Maternal age, tobacco use	No association between cord blood PFHxS and hypothyroid in mother, OR 1.92 (95% CI 0.87–4.25), detected versus non-detected. No association between cord blood PFHxS and TSH levels in infants (p=0.894).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Jain 2013 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 adults (≥12 years of age)	**Exposure:** Serum PFHxS values were not provided in publication **Multivariate linear regression model adjustments:** Age, sex, race, smoking status, iodine status, C-reactive protein, BMI, fasting time before blood was drawn, total calories consumed during the last 24 hours, perfluorinated compound variable	No significant association between serum PFHxS and TSH, free T3, free T4, total T3, total T4, or thyroglobulin.
Ji et al. 2012 Cross-sectional study of 633 children and adults (aged 12–>60 years) participating in a health study in Korea	**Exposure:** Median serum PFHxS concentration was 1.51 ng/mL (range: 0.92–2.34) **Regression model adjustments:** Age, BMI, sex	No significant association between serum PFHxS levels and T4 (p=0.5147) or TSH (p=0.8144) levels.
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFHxS 0.793 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No associations between serum PFHxS and serum free T4 levels (β -0.029, 95% CI -0.085–0.027, p=0.308) or TSH levels (β -0.003, 95% CI -0.584–0.515, p=0.901)
Lewis et al. 2015 Cross-sectional study utilizing 2011–2012 NHANES data for 1,682 males and females 12–80 years of age	**Exposure:** Median PFHxS levels tended to increase with age and ranged from 0.69 to 1.81 ng/mL **Multivariate linear regression model adjustments:** Age, BMI, poverty income ratio, race/ethnicity, serum cotinine	No significant associations (p>0.05) between serum PFHxS and TSH, free T4, total T4, free T3, or total T3 were found in any age group in males or females. No association (p>0.05) between serum PFHxS and serum testosterone.
Preston et al. 2018 Cross-sectional study of 732 mothers and 480 infants participating in Project Viva in Massachusetts	**Exposure:** Maternal median serum PFHxS 2.4 ng/mL (range of <LOQ-43.2 ng/mL (measured during early pregnancy, median 9.6 weeks of gestation). **Statistical adjustments:** Maternal age, race/ethnicity, smoking status, fish intake, parity, gestational week of blood draw	No association between maternal PFHxS and total T4 (β -0.05, 95% CI -0.14–0.04), free T4 (β -0.60, 95% CI -1.39–0.19), or TSH (β 2.89, 95% CI -2.12–8.17). Inverse association between maternal serum PFHxS and neonatal T4 (β -1.1, 95% CI -2.1 to -0.1) for the 4th quartile.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Shah-Kulkarni et al. 2016 Cross-sectional study of 279 pregnant women participating in the Ewha Birth and Growth Retrospective Cohort study	**Exposure:** Cord blood median PFHxS 0.38 ng/mL (range of 0.11–1.31 ng/mL) **Statistical adjustments:** Maternal age, education, prepregnancy BMI, alcohol intake, child's parity, gestational age, sex	No association between cord blood PFHxS and cord blood T4 (β 0.03, 95% CI -0.26–0.32, p=0.83), T3 (β 1.81, 95% CI -0.66–4.28, p=0.15), or TSH (β -1.09, 95% CI -2.60–0.41, p=0.15). When the infants were divided by sex, an association between cord blood PFHxS and cord blood T3 was observed in girls (β 4.28, 95% CI 0.39–8.17, p=0.03), but not in boys (β 0.02, 95% CI -3.06–0.74, p=0.98).
Wang et al. 2013a Prospective cohort study of 903 pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Geometric mean serum PFHxS levels in blood collected at approximately 18th week of gestation was 0.62 ng/mL **Statistical adjustments:** Age, gestation age at blood draw, parity, total seafood intake at mid-pregnancy, HDL blood concentrations	The investigators reported no significant associations between serum PFHxS and TSH levels or the risk of elevated TSH (<7.5 µIU/mL).
Wang et al. 2014 Cross-sectional study of 285 healthy pregnant women and 116 neonates participating in the Taiwan Maternal and Infant cohort study	**Exposure:** Median plasma PFHxS level (collected in the third trimester of pregnancy) 0.81 ng/mL **Multivariable linear regression model adjustments:** Age, maternal education, previous live births, family income, prepregnancy BMI, maternal fish consumption during pregnancy	Significant association between maternal serum PFHxS and maternal TSH levels (β 0.105, 95% CI 0.002–0.207; p<0.05). No significant associations (p>0.05) between maternal serum PFHxS and maternal levels of free T4, total T4, or total T3.
Webster et al. 2016 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 male and female adults (≥18 years of age)	**Exposure:** Geometric mean serum level PFHxS 1.9 ng/mL **Multivariate linear regression model adjustments:** Age, log_{10}-transformed serum cotinine, race/ethnicity, sex, parity, pregnancy, menopause status	No significant associations (p>0.05) between serum PFHxS and free T3, free T4, ratio of free T3 to free T4, TSH, total T3, or total T4.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Wen et al. 2013 Cross-sectional study utilizing 2007–2010 NHANES data for 1,181 male and female adults	**Exposure:** Geometric mean serum PFHxS 2.0 ng/mL **Statistical adjustments:** Age, race, drinking, smoking, and urinary iodine; regression analysis weighted for sampling strategy	Significant associations between serum PFHxS and total T4 in women (β 0.260, 95% CI 0.108–0.413, p=0.002), but not in men (β -0.032, 95% CI -0.175–0.111, p=0.641) and total T3 in women (β 4.074, 95% CI 2.232–5.916, p<0.001), but not in men (β -0.081, 95% CI -1.698–1.536, p=0.917). No associations between TSH (p=0.608 and 0.720 in men and women) or thyroglobulin (p=0.455 and 0.725 in men and women). When subjects were categorized by serum PFHxS levels, there were significant differences in T3 and T4 levels for subjects with serum PFHxS levels in the 4th quartile (>3.1 ng/mL), as compared to the 1st quartile (≤1.0 ng/mL). Significant association between serum PFHxS and risk of subclinical hypothyroidism in women (OR 3.10, 95% CI 1.22–7.86, p<0.05), but not in men (OR 1.57, 95% CI 0.76–3.25); and an association for the risk of subclinical hyperthyroidism in women (OR 2.27, 95% CI 1.07–4.80), but not in men (OR 0.56, 95% CI 0.24–1.2).
Yang et al. 2016a Cross-sectional study of 157 healthy pregnant women in China	**Exposure:** Mean and median maternal serum PFHxS levels (collected 1–2 days before delivery) 0.63 and 0.50 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, delivery type, maternal income	No significant associations (p>0.05) between maternal serum PFHxS and maternal levels of free T3, total T3, free T4, total T4, or TSH.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
PFNA		
Mundt et al. 2007 Study of 592 workers (88% male) ever employed between 1989 and 2003 at a polymer production facility exposed to PFNA; workers underwent annual medical examinations that involved measurement of clinical chemistry indices	**Exposure:** Workers assigned to exposure categories (no exposure, low exposure, high exposure) based on serum PFNA levels in a subset of current workers **Adjustments:** Age, BMI	The investigators noted that the differences in serum TSH, T4, T3 uptake, and free T4 index levels between exposure groups were small and not clinically relevant (no additional information provided).
Lopez-Espinosa et al. 2012 Cross-sectional study of 10,725 children aged 1–17 years participating in the C8 Health Project study	**Exposure:** Median serum PFNA 1.50 ng/mL **Statistical adjustments:** Age, month, and time of sampling	No significant associations between serum PFNA and reported thyroid disease (OR 1.05, 95% CI 0.78–1.41), hypothyroidism (1.11, 95% CI 0.77–1.60), subclinical hypothyroidism (OR 0.99, 95% CI 0.88–1.12), or subclinical hyperthyroidism (OR 0.78, 95% CI 0.61–1.01) per interquartile shift. Significant association between serum PFNA and total T4 (β 1.1, 95% CI 0.7–1.5) per interquartile shift; no association was found for TSH (β 0.8, 95% CI -0.4–2.0).
Berg et al. 2017 Prospective study of 370 pregnant women participating in the Northern Norway Mother-and-Child Contaminant Cohort Study	**Exposure:** Median maternal serum PFNA 0.56 ng/mL (measured during 2nd trimester) **Statistical adjustments:** Parity, age, physical activity BMI, sum of perfluoroalkyls, and/or sum of persistent organic pollutants	No associations (p>0.05) between serum PFNA and TSH, total T4, free T4, total T3, free T3, or thyroxine binding capacity.
Bloom et al. 2010 Prospective cohort study of 31 participants (27 males and 4 females, mean age of 39.0 years) in the New York State Angler Cohort Study	**Exposure:** Geometric serum PFNA level 0.79 ng/mL (range: 0.35–2.08 ng/mL) **Linear regression model adjustments:** Age (TSH only)	No significant association between serum PFNA levels and TSH (p=0.789) or free T4 (p=0.424) were found.
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in North Carolina and attempting to conceive for ≤3 months	**Exposure:** Geometric mean serum PFNA 0.84 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	Associations between serum PFNA and T3 (β 5.65, p=0.02) and free T4 (β 0.08, p<0.01) levels. No associations with TSH (p=0.91) or total T4 (p=0.34).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Jain 2013 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 adults (≥12 years of age)	**Exposure:** Serum PFNA values were not provided in publication **Multivariate linear regression model adjustments:** Age, sex, race, smoking status, iodine status, C-reactive protein, BMI, fasting time before blood was drawn, total calories consumed during the last 24 hours, perfluorinated compound variable	No significant association between serum PFNA and TSH, free T3, free T4, total T3, total T4, or thyroglobulin.
Ji et al. 2012 Cross-sectional study of 633 children and adults (aged 12–>60 years) participating in a health study in Korea	**Exposure:** Median serum PFNA concentration was 2.09 ng/mL (range: 1.49–2.74) **Regression model adjustments:** Age, BMI, sex	No significant association between serum PFNA levels and T4 (p=0.7436) or TSH (p=0.1354) levels.
Dufour et al. 2018 Cross-sectional study of 214 pregnant women entering the hospital for delivery	**Exposure:** Cord blood mean PFNA 0.18 ng/mL; 0.10–0.15, 0.15–0.22, and 0.23–0.68 ng/mL for 2nd, 3rd, and 4th quartiles **Statistical adjustments:** Maternal age, tobacco use	No association between cord blood PFNA and hypothyroid in mother, OR (95% CI) 2nd quartile: 1.78 (0.60–5.71) 3rd quartile: 1.86 (0.64–5.95) 4th quartile: 1.17 (0.37–3.92) No association between cord blood PFNA and TSH levels in infants (p=0.064).
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFNA 0.938 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	Association between serum PFNA and serum free T4 levels (β 0.052, 95% CI 0.007–0.097, p=0.025). No association between serum PFNA and TSH levels (β -0.046, 95% CI -0.496–0.403, p=0.840).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Preston et al. 2018 Cross-sectional study of 732 mothers and 480 infants participating in Project Viva in Massachusetts	**Exposure:** Maternal median serum PFNA 0.6 ng/mL (range of <LOQ-6.0 ng/mL measured during early pregnancy, median 9.6 weeks of gestation) **Statistical adjustments:** Maternal age, race/ethnicity, smoking status, fish intake, parity, gestational week of blood draw	No association between maternal PFNA and total T4 (β -0.05, 95% CI -0.16–0.05), free T4 (β -0.57, 95% CI -1.52–0.40), or TSH (β -0.27, 95% CI -6.19–6.03). When subjects were divided by maternal TPOAb levels, an inverse association between maternal PFNA levels and TSH was found among TPOAb positive mothers (β -16.1, 95% CI -27.7 to -2.56). No association between maternal serum PFNA and neonatal T4 (β 0.05, 95% CI -0.29–0.39) per interquartile increase in maternal PFNA.
Shah-Kulkarni et al. 2016 Cross-sectional study of 279 pregnant women participating in the Ewha Birth and Growth Retrospective Cohort study	**Exposure:** Cord blood median PFNA 0.2 ng/mL (range of 0.03–1.24 ng/mL) **Statistical adjustments:** Maternal age, education, prepregnancy BMI, alcohol intake, child's parity, gestational age, sex	No association between cord blood PFNA and cord blood T4 (β 0.04, 95% CI -0.17–0.26, p=0.70), T3 (β 0.07, 95% CI -1.74–1.92, p=0.93), or TSH (β -0.83, 95% CI -1.95–0.28, p=0.14). When the infants were divided by sex, an inverse association between cord blood PFNA and cord blood TSH was observed in girls (β -1.69, 95% CI -3.31 to -0.08, p=0.04), but not in boys (β 0.41, 95% CI -1.15–1.98, p=0.60).
Tsai et al. 2017 Cross-sectional study of 118 mother-infant pairs participating in the Taiwan Birth Panel Study.	**Exposure:** Cord blood mean PFNA 7.55 ng/mL **Statistical adjustments:** Maternal age at delivery, BMI, education, newborn sex, gestational age, delivery type	No association between cord blood PFNA and cord blood T4 levels (β -0.067, 95% CI -0.252–0.009). T3 levels (β -0.03, 95% CI -0.069–0.103), or TSH (β 0.045, 95% CI -0.051–0.142).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Wang et al. 2013a Prospective cohort study of 903 pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Geometric mean serum PFNA levels in blood collected at approximately 18th week of gestation was 0.37 ng/mL **Statistical adjustments:** Age, gestation age at blood draw, parity, total seafood intake at mid-pregnancy, HDL blood concentrations	The investigators reported no significant associations between serum PFNA and TSH levels or the risk of elevated TSH (<7.5 µIU/mL).
Wang et al. 2014 Cross-sectional study of 285 healthy pregnant women and 116 neonates participating in the Taiwan Maternal and Infant cohort study	**Exposure:** Median plasma PFNA level (collected in the third trimester of pregnancy) 1.51 ng/mL **Multivariable linear regression model adjustments:** Age, maternal education, previous live births, family income, prepregnancy BMI, maternal fish consumption during pregnancy	Significant inverse associations between maternal serum PFNA and maternal free T4 (β -0.019, 95% CI -0.028 to -0.009; p<0.001) and total T4 (β -0.189, 95% CI -0.333 to -0.046; p<0.001). No significant associations (p>0.05) between maternal serum PFNA and maternal levels of total T3 or TSH.
Webster et al. 2016 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 male and female adults (≥18 years of age)	**Exposure:** Geometric mean serum level PFNA 1.5 ng/mL **Multivariate linear regression model adjustments:** Age, log_{10}-transformed serum cotinine, race/ethnicity, sex, parity, pregnancy, menopause status	No significant associations (p>0.05) between serum PFNA and free T3, free T4, ratio of free T3 to free T4, TSH, total T3, or total T4.
Wen et al. 2013 Cross-sectional study utilizing 2007–2010 NHANES data for 1,181 male and female adults	**Exposure:** Geometric mean serum PFNA 1.54 ng/mL **Statistical adjustments:** Age, race, drinking, smoking, and urinary iodine; regression analysis weighted for sampling strategy	No associations between serum PFNA and total T4 (p=0.097 and 0.632 in men and women), T3 (p=0.063 and 0.258 in men and women), TSH (p=0.973 and 0.407 in men and women), or thyroglobulin (p=0.537 and 0.395 in men and women). No significant associations between serum PFNA and risk of subclinical hypothyroidism in men (OR 1.30, 95% CI 0.65–2.60) or women (OR 2.54, 95% CI 0.40–16.05) subclinical hyperthyroidism in men (OR 2.41, 95% CI 0.48–12.04) or women (OR 1.91, 95% CI 0.83–4.38).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Yang et al. 2016a Cross-sectional study of 157 healthy pregnant women in China	**Exposure:** Mean and median maternal serum PFNA levels (collected 1–2 days before delivery) 0.52 and 0.46 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, delivery type, maternal income	Significant inverse association ($p<0.05$) between maternal serum PFNA and maternal levels of TSH. No significant associations ($p>0.05$) between maternal serum PFNA and maternal levels of free T3, total T3, free T4, or total T4.
PFDA		
Berg et al. 2015 Longitudinal study of 391 pregnant women participating in the Northern Norway Mother and Child contaminant Cohort Study; thyroid hormone levels measured during the second trimester and 3 days and 6 weeks postpartum	**Exposure:** Median serum PFDA level (collected at gestation week 18) 0.23 ng/mL **Multivariable logistic regression model adjustments:** Not totally clear, but appeared to include parity, age, thyroxin binding capacity, BMI	Significant inverse association between maternal serum PFDA and T3 for women with PFDA levels in the 4th quartile (0.31–2.34 ng/mL, $p=0.03$). Mean T3 levels were 4% lower in 4th quartile participants, compared to those in the 1st quartile (0.05–0.17 ng/mL). Because all values were within normal ranges, the investigators noted that the changes might not have been of clinical significance in the pregnant women.
Berg et al. 2017 Prospective study of 370 pregnant women participating in the Northern Norway Mother-and-Child Contaminant Cohort Study	**Exposure:** Median maternal serum PFDA 0.23 ng/mL (measured during 2nd trimester). Serum PFDA levels in the 2nd, 3rd, and 4th quartiles: 0.18–0.23, 0.24–0.31, 0.32–2.34 **Statistical adjustments:** Parity, age, physical activity BMI, sum of perfluoroalkyls, and/or sum of persistent organic pollutants	Inverse association between serum PFDA and total T3 (β, 95% CI): 2nd quartile: -0.01 (-0.030–0.007) 3rd quartile: -0.01 (-0.032–0.005) 4th quartile: -0.02 (-0.044 to -0.005) No associations ($p>0.05$) between serum PFDA and TSH, total T4, free T4, free T3, or thyroxine binding capacity.
Bloom et al. 2010 Prospective cohort study of 31 participants (27 males and 4 females, mean age of 39.0 years) in the New York State Angler Cohort Study	**Exposure:** Geometric serum PFDA level 0.21 ng/mL (range: 0.14–1.14 ng/mL); 64.5% of samples were greater than the LOD **Linear regression model adjustments:** Age (TSH only)	No significant association between serum PFDA levels and TSH ($p=0.365$) or free T4 ($p=0.107$) were found.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Jain 2013 Cross-sectional study utilizing 2007–2008 NHANES data for 1,525 adults (≥12 years of age)	**Exposure:** Serum PFDA values were not provided in publication **Multivariate linear regression model adjustments:** Age, sex, race, smoking status, iodine status, C-reactive protein, BMI, fasting time before blood was drawn, total calories consumed during the last 24 hours, perfluorinated compound variable	No significant association between serum PFDA and TSH, free T3, free T4, total T3, total T4, or thyroglobulin.
Ji et al. 2012 Cross-sectional study of 633 children and adults (aged 12–>60 years) participating in a health study in Korea	**Exposure:** Median serum PFDA concentration was 0.91 ng/mL (range: 0.58–1.45) **Regression model adjustments:** Age, BMI, sex	No significant association between serum PFDA levels and T4 (p=0.2176) or TSH (p=0.2721) levels.
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFDA 0.0592 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No associations between serum PFDA and serum free T4 levels (β 0.016, 95% CI -0.006–0.038, p=0.153) or TSH levels (β -0.089, 95% CI -0.308– 0.129, p=0.420).
Shah-Kulkarni et al. 2016 Cross-sectional study of 279 pregnant women participating in the Ewha Birth and Growth Retrospective Cohort study	**Exposure:** Cord blood median PFDA 0.1 ng/mL (range of 0.04–0.76 ng/mL) **Statistical adjustments:** Maternal age, education, prepregnancy BMI, alcohol intake, child's parity, gestational age, sex	No association between cord blood PFDA and cord blood T4 (β 0.13, 95% CI -0.18–0.45, p=0.40), T3 (β 2.40, 95% CI -0.27–5.09, p=0.07), or TSH (β -1.01, 95% CI -2.65–0.62, p=0.22).
Wang et al. 2013a Prospective cohort study of 903 pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Geometric mean serum PFDA levels in blood collected at approximately 18th week of gestation was 0.09 ng/mL; 69% of samples exceeded the LOD **Statistical adjustments:** Age, gestation age at blood draw, parity, total seafood intake at mid-pregnancy, HDL blood concentrations	The investigators reported no significant associations between serum PFDA and TSH levels or the risk of elevated TSH (<7.5 µIU/mL).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Wang et al. 2014 Cross-sectional study of 285 healthy pregnant women and 116 neonates participating in the Taiwan Maternal and Infant cohort study	**Exposure:** Median plasma PFDA level (collected in the third trimester of pregnancy) 0.46 ng/mL **Multivariable linear regression model adjustments:** Age, maternal education, previous live births, family income, prepregnancy BMI, maternal fish consumption during pregnancy	Significant association between maternal serum PFDA and maternal total T3 (β 0.002, 95% CI 0.000–0.003; p<0.01). No significant associations (p>0.05) between maternal serum PFDA and maternal levels of free T4, total T4, or TSH.
Yang et al. 2016a Cross-sectional study of 157 healthy pregnant women in China	**Exposure:** Mean and median maternal serum PFDA levels (collected 1–2 days before delivery) 0.45 and 0.37 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, delivery type, maternal income	Significant inverse association (p<0.01) between maternal serum PFDA and maternal levels of TSH. No significant associations (p>0.05) between maternal serum PFDA and maternal levels of free T3, total T3, free T4, or total T4.
PFUnA		
Berg et al. 2015 Longitudinal study of 391 pregnant women participating in the Northern Norway Mother and Child contaminant Cohort Study; thyroid hormone levels measured during the second trimester and 3 days and 6 weeks postpartum	**Exposure:** Median serum PFUnA level (collected at gestation week 18) 0.26 ng/mL **Multivariable logistic regression model adjustments:** Not totally clear, but appeared to include parity, age, thyroxin binding capacity, BMI	Significant inverse association between maternal serum PFUnA and free T3 for women with PFUnA levels in the 4th quartile (0.4–0.96 ng/mL, p=0.00). Mean free T3 levels were 3% lower in 4th quartile participants, compared to those in the 1s quartile (LOD–0.15 ng/mL). Because all values were within normal ranges, the investigators noted that the changes might have not been of clinical significance in the pregnant women.
Berg et al. 2017 Prospective study of 370 pregnant women participating in the Northern Norway Mother-and-Child Contaminant Cohort Study	**Exposure:** Median maternal serum PFUnA 0.26 ng/mL (measured during 2nd trimester). Serum PFUnA levels in the 2nd, 3rd, and 4th quartiles: 0.17–0.26, 0.27–0.38, 0.39–1.46 **Statistical adjustments:** Parity, age, physical activity BMI, sum of perfluoroalkyls, and/or sum of persistent organic pollutants	Inverse association (p<0.05) between serum PFUnA and free T3 (β, 95% CI): 2nd quartile: -0.01 (-0.024–0.004) 3rd quartile: -0.01 (-0.024–0.004) 4th quartile: -0.02 (-0.033 to -0.003). No associations (p>0.05) between serum PFUnA and TSH, total T4, free T4, total T3, or thyroxine binding capacity.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Bloom et al. 2010 Prospective cohort study of 31 participants (27 males and 4 females, mean age of 39.0 years) in the New York State Angler Cohort Study	**Exposure:** Geometric serum PFUnA level 0.20 ng/mL (range: 0.14–0.92 ng/mL); only 51.5% of the samples were above the LOD **Linear regression model adjustments:** Age (TSH only)	No significant association between serum PFUnA levels and TSH (p=0.527) or free T4 (p=0.204) were found.
Ji et al. 2012 Cross-sectional study of 633 children and adults (aged 12–>60 years) participating in a health study in Korea	**Exposure:** Median serum PFUnA concentration was 1.75 ng/mL (range: 1.11–4.58) **Regression model adjustments:** Age, BMI, sex	No significant association between serum PFUnA levels and T4 (p=0.0642) or TSH (p=0.5368) levels.
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFUnA 0.652 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No associations between serum PFUnA and serum free T4 levels (β -0.008, 95% CI -0.037–0.021, p=0.581) or TSH levels (β 0.094, 95% CI -0.188–0.376, p=0.510).
Shah-Kulkarni et al. 2016 Cross-sectional study of 279 pregnant women participating in the Ewha Birth and Growth Retrospective Cohort study	**Exposure:** Cord blood median PFUnA 0.26 ng/mL (range of 0.05–2.22 ng/mL) **Statistical adjustments:** Maternal age, education, prepregnancy BMI, alcohol intake, child's parity, gestational age, sex	No association between cord blood PFUnA and cord blood T4 (β -0.02, 95% CI -0.29–0.24, p=0.86), T3 (β 1.06, 95% CI -1.21–3.34, p=0.35), or TSH (β -0.62, 95% CI -2.01–0.76, p=0.37).
Tsai et al. 2017 Cross-sectional study of 118 mother-infant pairs participating in the Taiwan Birth Panel Study.	**Exposure:** Cord blood mean PFUnA 15.94 ng/mL **Statistical adjustments:** Maternal age at delivery, BMI, education, newborn sex, gestational age, delivery type	No association between cord blood PFUnA and cord blood T4 levels (β 0.045, 95% CI -0.223–0.313). T3 levels (β 0.048, 95% CI -0.008–0.104), or TSH (β 0.077, 95% CI -0.063–0.216).
Wang et al. 2013a Prospective cohort study of 903 pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Geometric mean serum PFUnA levels in blood collected at approximately 18th week of gestation was 0.20 ng/mL **Statistical adjustments:** Age, gestation age at blood draw, parity, total seafood intake at mid-pregnancy, HDL blood concentrations	The investigators reported no significant associations between serum PFUnA and TSH levels or the risk of elevated TSH (<7.5 µIU/mL).

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Wang et al. 2014 Cross-sectional study of 285 healthy pregnant women and 116 neonates participating in the Taiwan Maternal and Infant cohort study	**Exposure:** Median plasma PFUnA level (collected in the third trimester of pregnancy) 3.26 ng/mL **Multivariable linear regression model adjustments:** Age, maternal education, previous live births, family income, prepregnancy BMI, maternal fish consumption during pregnancy	Significant inverse associations between maternal serum PFUnA and maternal free T4 (β -0.004, 95% CI -0.007 to -0.002; p<0.001) and total T4 (β -0.062, 95% CI -0.097 to -0.026; p<0.001). No significant associations (p>0.05) between maternal serum PFUnA and maternal levels of total T3 or TSH.
Yang et al. 2016a Cross-sectional study of 157 healthy pregnant women in China.	**Exposure:** Mean and median maternal serum PFUnA levels (collected 1–2 days before delivery) 0.45 and 0.40 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, delivery type, maternal income	Significant inverse association (p<0.05) between maternal serum PFUnA and maternal levels of TSH. No significant associations (p>0.05) between maternal serum PFUnA and maternal levels of free T3, total T3, free T4, or total T4.
PFDoDA		
Ji et al. 2012 Cross-sectional study of 633 children and adults (aged 12–>60 years) participating in a health study in Korea	**Exposure:** Median serum PFDoDA concentration was 0.92 ng/mL (range: 0.21–1.13) **Regression model adjustments:** Age, BMI, sex	No significant association between serum PFDoDA levels and T4 (p=0.7153) or TSH (p=0.6925) levels.
Shah-Kulkarni et al. 2016 Cross-sectional study of 279 pregnant women participating in the Ewha Birth and Growth Retrospective Cohort study	**Exposure:** Cord blood median PFDoDA 0.08 ng/mL (range of 0.02–0.29 ng/mL) **Statistical adjustments:** Maternal age, education, prepregnancy BMI, alcohol intake, child's parity, gestational age, sex	No association between cord blood PFDoDA and cord blood T4 (β -0.07, 95% CI -0.46–0.31, p=0.69), T3 (β 1.69, 95% CI -1.57–4.96, p=0.30), or TSH (β -1.29, 95% CI -3.28–0.69, p=0.20).
Wang et al. 2014 Cross-sectional study of 285 healthy pregnant women and 116 neonates participating in the Taiwan Maternal and Infant cohort study	**Exposure:** Median plasma PFDoDA level (collected in the third trimester of pregnancy) 0.36 ng/mL **Multivariable linear regression model adjustments:** Age, maternal education, previous live births, family income, prepregnancy BMI, maternal fish consumption during pregnancy	Significant inverse associations between maternal serum PFDoDA and maternal free T4 (β -0.132, 95% CI -0.204 to -0.059; p<0.001) and total T4 (β -1.742, 95% CI -2.785 to -0.700; p<0.01). No significant associations (p>0.05) between maternal serum PFDoDA and maternal levels of total T3 or TSH.

Table 9. Endocrine Outcomes in Humans Exposed to Perfluoroalkyls[a]

Reference and study population	Exposure	Outcomes
Yang et al. 2016a Cross-sectional study of 157 healthy pregnant women in China	**Exposure:** Mean and median maternal serum PFDoDA levels (collected 1–2 days before delivery) 0.046 and 0.041 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, delivery type, maternal income	Significant inverse associations between maternal serum PFDoDA and maternal levels of free T3 ($p<0.01$), total T3 ($p<0.01$), free T4 ($p<0.05$), total T4 ($p<0.05$), and TSH ($p<0.01$).

[a]Reproductive hormone data are presented in Table 12 and insulin levels are presented in Table 14.

APFO = ammonium perfluorooctanoate; BMI = body mass index; CI = confidence interval; HDL = high density lipoprotein; HR = hazard ratio; LOD = limit of detection; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PBDEs = polybrominated diphenyl ethers; PBPK = physiologically based pharmacokinetic; PCBs = polychlorinated biphenyls; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; T3 = triiodothyronine; T4 = thyroxine; TSH = thyroid stimulating hormone

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was estimated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum PFOA levels in 2005–2006 were 325 and 113 ng/mL in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant association between estimated cumulative serum PFOA and risk medicated asthma (p=0.27 and 0.53 for trend with no lag or 10-year lag). Significant association (p=0.05 for trend) between estimated cumulative serum PFOA levels and risk of ulcerative colitis with or without a 10-year lag; the RR was significant for workers with estimated cumulative PFOA levels in the 4th quartile (RR 6.57, 95% CI 1.47–29.40). Medicated asthma (with no lag) and rheumatoid arthritis (without 10-year lag) showed categorical positive trends (p=0.05 and 0.04, respectively).
Anderson-Mahoney et al. 2008 Cross-sectional study of 566 adult residents (mean age of 49.9 years) living near a Teflon manufacturing facility in West Virginia for at least 1 year; most subjects were exposed to PFOA in drinking water provided by Lubeck Public Service District (37%) or Little Hocking water district (27%); some subjects also worked at the facility	**Exposure:** Individual biomonitoring data were not provided; reported PFOA levels in the Lubeck and Little Hocking water districts were 0.4–3.9 and 1.7–4.3 µg/L, respectively **Reference population:** SPRs were estimated using NHANES data; statistical analyses were adjusted for age and sex	Incidence data were based on the results of participant-completed health surveys (data from both water districts combined). Significantly increased risks of asthma SPR 1.82 (95% CI 1.47–2.25).
Looker et al. 2014 Cross-sectional study of 411 adults participating in a follow-up study to the C8 Health Project; all participants received an influenza vaccine and were examined prior to vaccination and 21 days post vaccination; 755 adults in the follow-up study participated in a survey evaluating self-reported colds and influenza episodes	**Exposure:** Geometric mean serum PFOA concentration was 33.74 ng/mL • 1st quartile: 0.25–13.7 ng/mL • 2nd quartile: 13.8–31.5 ng/mL • 3rd quartile: 31.6–90 ng/mL • 4th quartile: 90.4–2,140 ng/mL **Statistical adjustments:** Age, sex, mobility, history of previous influenza vaccination	A significant decrease in the geometric mean antibody titer rise (difference between pre and post vaccinations) to influenza type B vaccine was observed in participants with serum PFOA levels in the 4th quartile. However, other measures of response to the influenza type B vaccine were not affected. A significant decrease in seroprotection from A/H3N2 influenza virus for participants with serum PFOA levels in the 2nd (p=0.02),

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		3rd (p=0.01), or 4th (p=0.05) quartiles. The ORs (95% CI) were 0.34 (0.14–0.83), 0.28 (0.11–0.70), and 10.39 (0.15–0.99), respectively. Significant association between serum PFOA and Influenza A H1N1 seroprotection (p=0.02 for trend); no association for influenza type B (p=0.68 for trend). No significant associations (p>0.05) between serum PFOA levels and cold and flu infections or the frequency of colds.
Steenland et al. 2013 Retrospective and prospective studies of 28,541 adults participating in a follow-up study to the C8 Health Project and 3,713 workers at the PFOA facility	**Exposure:** Serum PFOA levels estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history; serum PFOA levels in workers estimated based on job history and combined with residential exposure **Statistical adjustments:** Sex, race/ethnicity, smoking, BMI, alcohol consumption	In retrospective analysis (1952 through 2008–2011), ulcerative colitis was significantly associated (p<0.0001) with estimated cumulative serum PFOA concentrations. The RRs (95% CI) for the 2nd, 3rd, and 4th quartiles were 1.76 (1.04–2.99), 2.63 (1.56–4.43), and 2.86 (1.65–4.96). In prospective analysis (2005–2006 through 2009–2011), the association was not statistically significant (p=0.21). No significant associations (p>0.05) were found for Crohn's disease, rheumatoid arthritis, type I diabetes, lupus, or multiple sclerosis in the retrospective and prospective analyses.
Ashley-Martin et al. 2015 Cohort study of 1,258 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Maternal serum PFOA levels measured during the first trimester **Bayesian model adjustments:** Maternal age, sex	No significant association between maternal serum PFOA levels and risk of elevated IL-33/TSLP levels in cord blood; OR (95% CI): • IL-33/TSLP: 1.1 (0.6–1.8) • IgE: 1.1 (0.6–1.9).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Buser and Scinicariello 2016 Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 (n=637) and 2007–2010 (n=701) data; food sensitization (at least 1 food specific serum IgE≥0.35 kU/L) and self-reported food allergies were evaluated in the 2005–2006 and 2007–2010 cohorts, respectively	**Exposure:** Geometric mean serum PFOA 3.59 ng/mL for NHANES 2005–2006 and 3.27 ng/mL NHANES 2007–2010 **Multivariable logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, serum cotinine	Significant association between serum PFOA and risk of food allergies; OR 9.09 (95% CI 3.52–24.90) for participants with serum PFOA levels in the 4th quartile (>4.47 ng/mL). No significant association between serum PFOA and risk of food sensitization (p=0.74 for trend).
Dalsager et al. 2016 Prospective cohort study of 359 children (aged 1–4 years) participating in the Odense Child Cohort in Denmark; parents responded to texts every other week regarding the child's symptoms of infection	**Exposure:** Median maternal serum PFOA level (measured at gestation age 10–16 weeks) 1.68 ng/mL **Regression model adjustments:** Maternal age, maternal educational level, parity, child's age	Significant association between maternal serum PFOA and number of days above the median with a fever (101.3°F); OR 1.97 (95% CI 1.07–3.62) for the 3rd tertile (2.04–10.12 ng/mL). However, when expressed as the number of days with fever, the association was not significant (OR 1.12, 95% CI 0.82–1.54). No significant associations (p>0.05) between maternal serum PFOA and days or days above or below median with other symptoms of infection (cough, nasal discharge, diarrhea, vomiting) were found.
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15 years) living in Taiwan; this is the same group of children evaluated by Zhu et al. (2016)	**Exposure:** Summary serum PFOA values not provided for the full cohort; mean serum PFOA levels were 1.5 and 1.0 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	Significant increases in odds of having asthma were observed for children with serum PFOA levels in the 3rd quartile (OR 2.67, 95% CI 1.49–4.79) and 4th quartile (OR 4.05, 95% CI 2.21–7.42), as compared to those in 1st quartile. No significant association between serum PFOA and asthma severity score was found (p=0.119 for trend). Among asthmatic children, significant associations were identified between serum PFOA and IgE (p=0.005), absolute eosinophil counts (p<0.001), and eosinophil cationic protein levels (p=0.01). In non-asthmatic children, no significant (p>0.05) associations were found between serum PFOA

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		and IgE, absolute eosinophil counts, or eosinophil cationic protein levels.
Fei et al. 2010 Prospective cohort study of 1,400 pregnant women participating in the Danish National Birth cohort study; offspring were monitored for hospitalization due to infections in early childhood (average age 8.2 years)	**Exposure:** Mean maternal serum PFOA level (measured at gestation week 12) 5.6 ng/mL **Statistical adjustments:** Parity, maternal age, prepregnancy BMI, breastfeeding, smoking during pregnancy, socio-occupational status, home density, child's age, sibling age difference, gestational age at blood drawing, birth year, birth season	No significant association between maternal PFOA and risk of hospitalization for infectious disease; IRR for trend 0.96 (95% CI 0.87–1.06). When categorized by sex, significant increases in risk for hospitalization were observed in girls (IRR 1.21, 95% CI 1.04–1.42 for trend); significant inverse association was seen in boys (IRR 0.83, 95% CI 0.73–0.95 for trend).
Goudarzi et al. 2016a Prospective study of 1,558 4-year-old children participating in the Hokkaido Study on Environment and Children's Health Study in Japan	**Exposure:** Mean maternal plasma PFOA 2.713 ng/mL (range of <0.2–24.88 ng/mL) (measured at 28–32 weeks of gestation) **Statistical adjustments:** Maternal age, education, parental allergic history, number of older siblings, breastfeeding, daycare attendance, external tobacco smoke, child's sex	No association between maternal plasma PFOA and prevalence of allergic disease (defined as cases with at least one of the following symptoms: eczema, wheezing, or rhinoconjuctivitis) (p=0.208 for trend); OR (95% CI): 2nd quartile: 1.07 (0.791–1.47) 3rd quartile: 0.954 (0.695–1.31) 4th quartile: 0.830 (0.591–1.16). No association between maternal plasma PFOA and prevalence of wheezing (p=0.699 for trend); OR (95% CI): 2nd quartile: 1.09 (0.743–1.60) 3rd quartile: 1.10 (0.749–1.62) 4th quartile: 1.09 (0.729–1.65).
Goudarzi et al. 2017b Prospective cohort study of 1,558 participants in the Hokkaido Study on Environmental and Children's Health; children were monitored for physician-diagnosed infectious disease up to 4 years of age	**Exposure:** Mean maternal serum PFOA level (measured at 28–32 weeks of gestation) 2.713 ng/mL **Statistical adjustments:** Maternal age, number of older siblings, maternal smoking during pregnancy, maternal education, infant sex, breastfeeding period	No significant associations between maternal serum PFOA and risk of total infectious diseases in early life OR 1.11 (95% CI 0.806–1.54) for 4th quartile, p=0.393 for trend. Similar results were observed when males and females were analyzed separately.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Grandjean et al. 2012; Mogensen et al. 2015a Prospective cohort study of children living in the Faroe Islands; children were examined prior to receiving vaccine boosters (5 years of age, n=532) for tetanus and diphtheria, 4 weeks after receiving the 5-year vaccine booster (n=456), and at age 7 (n=464)	**Exposure:** Median serum PFOA level was 4.1 ng/mL at age 5 and 4.4 ng/mL at age 7 years **Statistical adjustments:** Age, sex, time since vaccination, booster type	A significant negative difference at age 7 years between prebooster and postbooster serum tetanus antibody levels was found; the difference was -35.8% (95% CI -51.9 to -14.2) per 2-fold increase in PFOA levels. No significant differences were observed at age 5 years. Using PFOA levels at age 7, there was no association with tetanus antibody levels (-20.5%, 95% CI -38.2–2.1). A significant negative difference at age 7 years between prebooster and postbooster serum diphtheria antibody levels was found; the difference was -25.2% (95% CI -42.9 to -2.0) per 2-fold increase in PFOA levels. No significant differences were observed at age 5 years. Using PFOA levels at age 7, there was an inverse association with diphtheria antibody levels (-25.4%, 95% CI -40.9 to -5.8).
Grandjean et al. 2017 Prospective study of 516 children living in the Faroe Islands; serum antibodies to diphtheria and tetanus were measured at age 13 and compared to serum perfluoroalkyl levels at age 7 and 13	**Exposure:** Median serum PFOA levels 4.4 ng/mL at age 7 and 2.0 ng/mL at age 13 **Multivariate logistic regression model adjustments:** Age and sex (mandatory covariates), and age-5 booster type; prenatal PCB exposure included in separate analyses	No significant associations between serum PFOA levels at age 7 or 13 and diphtheria (p=0.742 and p=0.129) or tetanus (p=0.637 and p=0.856). When the cohort was restricted to children without possible unscheduled booster vaccines, significant associations were found between serum PFOA at age 13 and diphtheria antibodies (p=0.029), but not at age 7 (p=0.480).
Granum et al. 2013 Prospective birth cohort study, subcohort of the Norwegian Mother and Child Cohort study, examined 56 children examined annually to age 3 years; exclusion criteria included maternal use of steroids or anti-inflammatory drugs during pregnancy, as well as maternal autoimmune disease	**Exposure:** Maternal (measured at delivery; n=99) mean and median serum PFOA levels were 1.1 and 1.1 ng/mL (range: 0.2–2.7 ng/mL) **Multivariate regression model adjustments:** Maternal and paternal allergy, maternal education, child's sex, child's age	Maternal serum PFOA levels were inversely associated with rubella antibody levels (p=0.001); the association was not significant for measles, *Haemophilus influenza* type b, or tetanus (p>0.05) Maternal serum PFOA levels were significantly associated with the total number of episodes of the common cold or other upper respiratory tract infection (p<0.001) and gastroenteritis with

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		vomiting or diarrhea (p=0.048) from birth to 3 years of age. No significant associations (p>0.05) between maternal serum PFOA and eczema and itchiness, wheezing, otitis media, and doctor-diagnosed atopic eczema, asthma, or asthma bronchitis.
Humblet et al. 2014 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data; participants (n=1,877) were 12–19 years of age	**Exposure:** Median serum PFOA levels in children ever having asthma and never having asthma were 4.3 and 4.0 ng/mL, respectively **Regression model adjustments:** Sex, race/ethnicity, poverty income ratio, cigarette smoking, health insurance	Significant association between serum PFOA and self-reported having asthma in the last 12 months (OR 1.18, 95% CI 1.01–1.39, p=0.04 per doubling of PFOA concentration). However, when NHANES survey weights (to make results representative of the U.S. population) were incorporated into the model, the results were attenuated (OR 1.11, 95% CI 0.87–1.42). No significant associations between serum PFOA and risk of reporting wheezing (p=0.98) or self-reporting current asthma (p=0.26).
Impinen et al. 2018 Prospective study of 641 infants participating in the Environment and Childhood Asthma study in Norway; health outcomes were evaluated at 2 and 10 years of age	**Exposure:** Mean cord PFOA level 1.8 ng/mL (range 0.1–11 ng/mL) **Logistic regression model adjustments:** Sex; Bonferroni correction for multiple comparisons	No significant associations between number of common colds from 0 to 2 years of age (p=0.089). Significant association between cord PFOA and number of lower respiratory tract infections from 0 to 10 years of age, β 0.28 (95% CI 0.22–0.35; p<0.0001). No associations (after Bonferroni correction) between cord PFOA and asthma diagnosis, current asthma, asthma ever, wheezing, rhinitis, rhinoconjuctivitis, or allergic sensitization.
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4 and 10 days post-vaccination	**Exposure:** Median serum PFOA 1.69 ng/mL **Logistic regression model adjustments:** Sex, age	No significant associations (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFOA and change in diphtheria (p=0.250) or tetanus (p=0.970) antibody levels.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Okada et al. 2012 Prospective cohort study of 343 pregnant women in Japan; cord blood samples collected at delivery to measure total IgE levels; infant allergies and infectious disease information collected during first 18 months of age	**Exposure:** Median maternal serum PFOA (measured after second trimester) 1.3 ng/mL (range: ND–5.3 ng/mL) **Polynomial regression model adjustments:** Maternal age, maternal allergic history, distance from home to highway, infant sex, parity, birth season, blood sampling time	Significant inverse association ($p<0.05$) between maternal PFOA levels and cord blood IgE levels in female infants; no association in males ($p>0.05$). No association between maternal PFOA levels and infant food allergy (OR 1.67, 95% CI 0.52–5.37), eczema (OR 0.96, 95% CI 0.23–4.02), wheezing (OR 1.27, 95% CI 0.27–6.05), or otitis media (OR 1.51, 95% CI 0.45–5.12).
Okada et al. 2014 Prospective study of 2,603 infants whose mothers participated in the Hokkaido Study on Environment and Children's Health Study; mothers completed questionnaires regarding infant allergic disease, infectious diseases, and other diseases when infants were 12 and 24 months of age	**Exposure:** Maternal mean plasma PFOA (measured between 28 and 32 weeks of gestation) 2.67 ng/mL (range: <0.2–24.9 ng/mL) **Statistical adjustments:** Maternal age, education, parental allergic history, infant sex, breastfeeding, number of siblings, daycare attendance, environmental tobacco smoke exposure in infants at 24 months	Significant inverse association between maternal PFOA levels and risk of allergic diseases was observed in female infants; 4th PFOA quartile OR 0.64 (95% CI 0.42–0.97), but not in male infants OR 0.93 (95% CI 0.63–1.37). No significant association between maternal PFOA levels and risk of eczema was observed in the infants; 4th PFOA quartile OR 0.75 (95% CI 0.48–1.18) for males and OR 0.65 (95% CI 0.39–1.09) for females. However, there was an inverse association ($p=0.032$ for trend) for males and females combined. No significant associations (p-value not reported) between maternal PFOA and wheezing at 12 or 24 months of age.
Osuna et al. 2014 Prospective cohort study of 38 children (age 7 years) participating in the Children's Health and the Environment in the Faroes project	**Exposure:** Geometric mean cord blood PFOA and serum PFOA at age 7: 0.68 and 4.3 ng/mL **Statistical adjustments:** None	No significant associations ($p>0.05$) between cord PFOA or child serum PFOA and neural and non-neural specific antibody concentrations (NF-L, NF-M, NF-H, GFAP, MBP, ChAT, Actin, desmin, keratin).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Qin et al. 2017 Case control study of 132 nonsmoking children in Taiwan aged 10–15 years with asthma and 168 age- and sex-matched controls without asthma	**Exposure:** Median serum PFOA 1.02 ng/mL in cases and 0.50 ng/mL in controls **Statistical adjustments:** Age, sex, BMI, parental education level, exercise, environmental tobacco smoke exposure, month of survey	Association between serum PFOA and asthma occurrence (OR 2.76, 95% CI 1.82–4.17). Among asthmatic children, inverse associations between PFOA and FEV_1 (β -0.104, 95% CI -0.193 to -0.015) and FEF_{25-75} (β -0.223, 95% CI -0.400 to -0.045). No associations with FVC (β -0.067, 95% CI -0.167–0.032) or PEF (β -0.201, 95% CI -0.515–0.112). Among non-asthmatic children no associations between PFOA and FVC (β <-0.001, 95% CI -0.075–0.074), FEV_1 (β -0.006, 95% CI -0.081–0.069), PEF (β 0.049, 95% CI -0.180–0.279), or FEF_{25-75} (β 0.011, 95% CI -0.139–0.182).
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFOA levels (measured at any time during pregnancy) 0.97 and 1.79 ng/mL for Ukraine and Greenland cohorts, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	No significant associations between maternal serum PFOA and the risk in the combined cohort of ever having asthma (OR 0.80, 95% CI 0.62–1.04), ever having eczema (OR 0.97, 95% CI 0.81–1.17), ever having wheezing (OR 0.91, 95% CI 0.76–1.10), currently wheezing (OR 0.97, 95% CI 0.71–1.33), or currently having eczema (OR 1.01, 95% CI 0.79–1.29). Current symptoms were defined as those occurring in the past 12 months.
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 1999–2000 and 2003–2004 data (n=1,191)	**Exposure:** Geometric mean serum PFOA 4.13 ng/mL **Multivariable linear regression models adjustments:** Age, sex, race/ethnicity, serum cotinine, BMI	No significant association between serum PFOA and measles, mumps, and rubella antibody titers in all children (95% CI included unity). In seropositive children, a doubling of serum PFOA levels resulted in 6.6% decreases (95% CI -11.7 to -1.5) in mumps antibody titers and in 8.9% decreases (95% CI -14.6 to -2.9) in rubella antibody titers.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 data (n=640)	**Exposure:** Geometric mean serum PFOA 3.59 ng/mL **Multivariable logistic and linear regression models adjustments:** Age, sex, and race/ethnicity (added serum cotinine and BMI for vaccine study)	Significant association between serum PFOA and rhinitis (OR 1.35, 95% CI 1.10–1.66). No significant associations between serum PFOA levels and current asthma (OR 1.28, 95% CI 0.81–2.04), wheeze (OR 0.94, 95% CI 0.51–1.73), or allergy (OR 1.12, 95% CI 0.85–1.47). No significant association between serum PFOA and allergic sensitization to plants (OR 0.88, 95% CI 0.67–1.15), dust mites (OR 0.93, 95% CI 0.75–1.16), pets (OR 1.17, 95% CI 0.81–1.68), cockroach and/or shrimp (OR 0.79, 95% CI 0.55–1.13), rodents (OR 1.65, 95% CI 0.59–4.60), mold (OR 1.21, 95% CI 0.85–1.72), or food (OR 1.02, 95% CI 0.60–1.73).
Stein et al. 2016b Cross-sectional study of 78 healthy adults in New York city vaccinated during the 2010–2011 season with the intranasal FluMist influenza vaccine	**Exposure:** Geometric mean serum PFOA 2.28 ng/mL Serum cytokines (IFN-α2, IFN-γ, TNF-α, IP-10) and chemokines (MCP-1, MIP1a) were measured pre-vaccination and 3- and 30-days post vaccination; nasal cytokine (IP-10), chemokine (MCP-1), and nasal mucosal IgA were measured 3- and 30-days post vaccination **Multivariate linear regression model adjustments:** Age, sex, race/ethnicity	No significant association between serum PFOA and seroconversion as measured by hemagglutinin inhibition (p=0.07 for trend) or immunohistochemistry (p=0.27 for trend). No significant associations (p>0.05) between serum PFOA and changes in serum cytokine or chemokine levels or nasal cytokine, chemokine, or IgA levels.
Wang et al. 2011 Prospective cohort study of 244 children (2 years of age) whose mothers participated in the Taiwan Birth Panel cohort study; 43% developed atopic dermatitis as evaluated via a questionnaire and a dermatologist examination of a subset of the children	**Exposure:** Median cord blood PFOA 1.71 ng/mL (range: 0.75–17.40 ng/mL) **Logistic regression adjustments:** Sex, gestational age, parity, maternal age, pre-natal environmental tobacco smoke exposure; analyses of atopy disorder also adjusted for maternal history of atopy and duration of breastfeeding	No significant correlation (p=0.870) between cord blood PFOA and child blood IgE levels. Significant correlation between cord blood PFOA and cord blood IgE levels in males and females combined (p=0.047) and in males only (p=0.025). No significant association (p>0.05) between cord PFOA levels and atopic dermatitis.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Zhu et al. 2016 Case-control study of 231 asthmatic and 225 non-asthmatic children from Taiwan (9–16 years old); this is the same group of children evaluated by Dong et al. (2013)	**Exposure:** Mean serum levels PFOA 1.00 ng/mL in non-asthmatics and 1.51 ng/mL in asthmatics **Multivariate logistic regression model adjustments:** Age, sex, parental education, BMI, environmental tobacco smoke exposure, month of survey The study examined associations between exposure to perfluoroalkyl compounds and T-lymphocyte-related immunological markers of asthma; sex differences also examined	Significant association between serum PFOA and risk of asthma in children with serum PFOA levels in the 4th quartile; OR 4.24 (95% CI 1.91–9.42) in males and OR 3.68 (95% CI 1.43–9.48) in females. Significant associations between serum PFOA and serum T-helper 2 lymphocyte cytokines IL-4 (p=0.001 for trend) and IL-5 (p=0.004 for trend). No significant associations (p>0.05 for trend) with T-helper 1 lymphocyte cytokines IFN-γ or IL-2, or IgE levels. Asthmatic children had significantly higher serum levels of IgE, IL-4, and IL-5 and lower levels of IFN-γ and IL-2 than non-asthmatic children.
Zhou et al. 2017 Case control study of adolescents with asthma (n=231) or without asthma (n=225)	**Exposure:** Mean serum PFOA 1.16 ng/mL for cases and 0.52 ng/mL for controls **Statistical adjustments:** None	Serum PFOA levels were significantly higher (p<0.001) in the asthmatics.
PFOS		
Looker et al. 2014 411 adults participating in a follow-up study to the C8 Health Project; all participants received an influenza vaccine; 755 adults in the follow-up study participated in a survey evaluating self-reported colds and influenza episodes	**Exposure:** Geometric mean serum PFOS concentration was 8.32 ng/mL **Statistical adjustments:** Age, sex, mobility, history of previous influenza vaccination	No significant alterations in response to three strains of influenza (Influenza A H1N1, Influenza A H3N2, or Influenza Type B). No significant associations (p>0.05) between serum PFOS levels and cold and flu infections or the frequency of colds.
Ashley-Martin et al. 2015 Cohort study of 1,258 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Maternal serum PFOS levels measured during the first trimester **Bayesian model adjustments:** Maternal age, sex	No significant association between maternal serum PFOS levels and risk of elevated IL-33/TSLP levels or IgE levels in cord blood; OR (95% CI): • IL-33/TSLP: 1.1 (0.6–1.9) • IgE: 1.1 (0.6–1.9).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Buser and Scinicariello 2016 Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 (n=637) and 2007–2010 (n=701) data; food sensitization at least one food-specific serum IgE≥0.35 kU/L) and self-reported food allergies were evaluated in the 2005–2006 and 2007–2010 cohorts, respectively	**Exposure:** Geometric mean serum PFOS 14.98 ng/mL for NHANES 2005–2006 cohort and 8.74 ng/mL for NHANES 2007–2010 cohort **Multivariable logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, serum cotinine	Significant association between serum PFOS and risk of food allergies; however, the trend was not significant (p=0.27). OR 2.43 (95% CI 1.05–5.59) and OR 2.95 (95% CI 1.21–7.24) for participants with serum PFOS levels in the 3rd (9.17–13.75 ng/mL) and 4th (>13.74 ng/mL) quartiles. No significant association between serum PFOS and risk of food sensitization (p=0.49 for trend).
Dalsager et al. 2016 Prospective cohort study of 359 children (aged 1–4 years) participating in the Odense Child Cohort in Denmark. Parents responded to texts every other week regarding the child's symptoms of infection	**Exposure:** Median maternal serum PFOS level (measured at gestation age 10–16 weeks) 8.07 ng/mL **Regression model adjustments:** Maternal age, maternal educational level, parity, child's age	Significant association between maternal serum PFOS and number of days (above the median) with a fever (101.3°F); OR 2.35 (95% CI 1.34–4.11) for the 3rd tertile (10.19–25.10 ng/mL), as well as the number of days with fever; OR 1.65 (95% CI 1.24–2.18) for the 3rd tertile. No significant associations (p>0.05) between maternal serum PFOS and days or days above the median with other symptoms of infection (cough, nasal discharge, diarrhea, vomiting) were found.
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15) living in Taiwan; this is the same group of children evaluated by Zhu et al. (2016)	**Exposure:** Summary serum PFOS values not provided for the full cohort; mean serum PFOS levels were 45.5 and 33.4 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	Significant increases in odds of having asthma were observed for children with serum PFOS levels in the 4th quartile (OR 2.63, 95% CI 1.48–4.69), as compared to those in 1st quartile. Significant association between serum PFOS and asthma severity score was found (p=0.045 for trend). Among asthmatic children, significant associations between serum PFOS and absolute eosinophil counts (p=0.009), eosinophil cationic protein levels (p=0.001), and IgE (p=0.008). In non-asthmatic children, no significant (p>0.05) association were found between serum PFOS and IgE, absolute eosinophil counts, or eosinophil cationic protein levels.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fei et al. 2010 Prospective cohort study of 1,400 pregnant women participating in the Danish National Birth cohort study; offspring were monitored for hospitalization due to infections in early childhood (average age 8.2 years)	**Exposure:** Mean maternal PFOS level (measured at gestation week 12) 35.3 ng/mL **Statistical adjustments:** Parity, maternal age, prepregnancy BMI, breastfeeding, smoking during pregnancy, socio-occupational status, home density, child's age, sibling age difference, gestational age at blood drawing, birth year, birth season	No significant association between maternal PFOS and risk of hospitalization for infectious disease; IRR for trend 1.00 (95% CI 0.91–1.09). When categorized by sex, significant increases in risk for hospitalization were observed in girls (IRR 1.18, 95% CI 1.03–1.36 for trend), but not in boys (IRR 0.90, 95% CI 0.80–1.02 for trend).
Goudarzi et al. 2016a Prospective study of 1,558 4-year-old children participating in the Hokkaido Study on Environment and Children's Health Study in Japan	**Exposure:** Mean maternal plasma PFOS 5.456 ng/mL (range of 1.003–30.283 ng/mL) (measured at 28–32 weeks of gestation) **Statistical adjustments:** Maternal age, education, parental allergic history, number of older siblings, breastfeeding, daycare attendance, external tobacco smoke, child's sex	No association between maternal plasma PFOS and prevalence of allergic disease (defined as cases with at least one of the following symptoms: eczema, wheezing, or rhinoconjuctivitis) (p=0.391 for trend); OR (95% CI): 2nd quartile: 0.658 (0.481–0.898) 3rd quartile: 0.787 (0.577–1.07) 4th quartile: 0.815 (0.596–1.11). No association between maternal plasma PFOS and prevalence of wheezing (p=0.398 for trend); OR (95% CI): 2nd quartile: 0.753 (0.514–1.09) 3rd quartile: 0.980 (0.680–1.41) 4th quartile: 0.770 (0.526–1.12).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Goudarzi et al. 2017b Prospective cohort study of 1,558 participants in the Hokkaido Study on Environmental and Children's Health; children were monitored for physician-diagnosed infectious disease up to 4 years of age	**Exposure:** Mean maternal serum PFOS level (measured at 28–32 weeks of gestation) 5.456 ng/mL **Statistical adjustments:** Maternal age, number of older siblings, maternal smoking during pregnancy, maternal education, infant sex, breastfeeding period	Significant associations between maternal serum PFOS and risk of total infectious diseases in early life, p=0.008 for trend. OR (95% CI): 2nd quartile: 1.44 (1.06–1.96) 3rd quartile: 1.28 (0.949–1.73) 4th quartile: 1.61 (1.18–2.21). Similar results when males and females were analyzed separately, although significant associations were only found in the 4th quartile and the trend was only significant for females (p=0.036 for females and p=0.071 for males).
Grandjean et al. 2012; Mogensen et al. 2015a Prospective cohort study of children living in the Faroe Islands; children were examined prior to receiving vaccine boosters (5 years of age, n=532) for tetanus and diphtheria, 4 weeks after receiving the 5-year vaccine booster (n=456), and at age 7 (n=464)	**Exposure:** Median serum PFOS level was 17.3 ng/mL at age 5 and 15.5 ng/mL at age 7 **Statistical adjustments:** Age, sex, time since vaccination, booster type	A significant negative difference at age 5 years between prebooster and postbooster serum tetanus antibody levels was found; the difference was -28.5% (95% CI -45.5 to -6.1) per 2-fold increase in PFOS levels. No significant differences were observed at age 7 years. Using PFOS levels at age 7, there was no association with tetanus antibody levels (-9.1%, 95% CI -32.8–23.0). A significant negative difference at age 7 years between prebooster and postbooster serum diphtheria antibody levels was found; the difference was -27.6% (95% CI -45.8 to -3.3) per 2-fold increase in PFOS levels. No significant differences were observed at age 5 years. Using PFOS levels at age 7, there was an inverse association with diphtheria antibody levels (-30.3%, 95% CI -47.3 to -7.8).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Grandjean et al. 2017 Prospective study of 516 children living in the Faroe Islands; serum antibodies to diphtheria and tetanus were measured at age 13 and compared to serum perfluoroalkyl levels at age 7 and 13	**Exposure:** Median serum PFOS levels 15.3 ng/mL at age 7 and 6.7 ng/mL at age 13 **Multivariate logistic regression model adjustments:** Age and sex (mandatory covariates), and age-5 booster type; prenatal PCB exposure included in separate analyses	No significant associations between serum PFOS levels at age 7 or 13 and diphtheria (p=0.07 and p=0.454) or tetanus (p=0.240 and p=0.237). When the cohort was restricted to children without possible unscheduled booster vaccines, significant associations were found between serum PFOS at age 7 and tetanus antibodies (p=0.043); not significant at age 13 (p=0.144).
Granum et al. 2013 Prospective birth cohort study, subcohort of the Norwegian Mother and Child Cohort study, examined 56 children examined annually to age 3 years; exclusion criteria included maternal use of steroids or anti-inflammatory drugs during pregnancy, as well as maternal autoimmune disease	**Exposure:** Maternal (measured at delivery; n=99) mean and median serum PFOS levels were 5.6 and 5.5 ng/mL (range: 1.4–11.0 ng/mL) **Multivariate regression model adjustments:** Maternal and paternal allergy, maternal education, child's sex, child's age	Maternal serum PFOS levels were inversely associated with rubella antibody levels (p=0.007); the association was not significant for measles, *Haemophilus influenza* type b, or tetanus (p>0.05). Maternal serum PFOS levels were not significantly associated with the total number of episodes of the common cold or other upper respiratory tract infection (p=0.501) or gastroenteritis with vomiting or diarrhea (p=0.367). No significant associations (p>0.05) between maternal serum PFOS and eczema and itchiness, wheezing, otitis media, and doctor-diagnosed atopic eczema, or asthma.
Humblet et al. 2014 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data; participants (n=1,877) were 12–19 years of age	**Exposure:** Median serum PFOS in children ever having asthma and never having asthma: 17.0 and 16.8 ng/mL, respectively **Regression model adjustments:** Sex, race/ethnicity, poverty income ratio, cigarette smoking, health insurance	No significant associations between serum PFOS and self-reported having asthma in the last 12 months (p=0.13 per doubling of PFOS concentration), risk of reporting wheezing (p=0.08), or self-reporting current asthma (p=0.24).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Impinen et al. 2018 Prospective study of 641 infants participating in the Environment and Childhood Asthma study in Norway; health outcomes were evaluated at 2 and 10 years of age	**Exposure:** Mean cord PFOS level 5.6 ng/mL (range 0.5–21 ng/mL) **Logistic regression model adjustments:** Sex; Bonferroni correction for multiple comparisons	No significant associations between number of common colds from 0 to 2 years of age (p=0.173). Significant association between cord PFOS and number of lower respiratory tract infections from 0 to 10 years of age, β 0.50 (95% CI 0.42–0.57; p<0.0001). No associations (after Bonferroni correction) between cord PFOS and asthma diagnosis, current asthma, asthma ever, wheezing, rhinitis, rhinoconjuctivitis, or allergic sensitization.
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4- and 10-days post-vaccination	**Exposure:** Median serum PFOS 9.52 ng/mL **Logistic regression model adjustments:** Sex, age	Significant inverse association (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFOS and change in diphtheria (p=0.044) antibody levels; no association (p=0.420) with tetanus antibody levels.
Okada et al. 2012 Prospective cohort study of 343 pregnant women in Japan; cord blood samples collected at delivery to measure total IgE levels; infant allergies and infectious disease information collected during first 18 months of age	**Exposure:** Median maternal serum PFOS (measured after second trimester) 5.2 ng/mL (range: 1.3–16.2 ng/mL) **Polynomial regression model adjustments:** Maternal age, maternal allergic history, distance from home to highway, infant sex, parity, birth season, blood sampling time; allergies and infectious disease analysis also included adjustments for prepregnancy BMI, environmental tobacco exposure, daycare attendance	No significant inverse association (p>0.05) between maternal PFOS levels and cord blood IgE levels in male or female infants. No association between maternal PFOS levels and infant food allergy (OR 3.72, 95% CI 0.81–17.10), eczema (OR 0.87, 95% CI 0.15–5.08), wheezing (OR 2.68, 95% CI 0.39–18.30), or otitis media (OR 1.40, 95% CI 0.33–6.00).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Okada et al. 2014 Prospective study of 2,603 infants whose mothers participated in the Hokkaido Study on Environment and Children's Health Study; mothers completed questionnaires regarding infant allergic disease, infectious diseases, and other diseases when infants were 12 and 24 months of age	**Exposure:** Maternal mean plasma PFOS (measured between 28 and 32 weeks of gestation) 5.56 ng/mL (range: <1.00–30.3 ng/mL) **Statistical adjustments:** Maternal age, education, parental allergic history, infant sex, breastfeeding, number of siblings, daycare attendance, environmental tobacco smoke exposure in infants at 24 months	No significant associations between maternal PFOS levels and risk of allergic diseases or eczema were observed in the infants; 4th PFOS quartile OR 0.95 (95% CI 0.65–1.37) and OR 0.79 (95% CI 0.53–1.17) for allergic diseases in males and females and 0.98 (95% CI 0.63–1.53) and 0.84 (95% CI 0.51–1.38) for eczema in males and females.
Osuna et al. 2014 Prospective cohort study of 38 children (age 7 years) participating in the Children's Health and the Environment in the Faroes project	**Exposure:** Geometric mean cord blood PFOS and serum PFOS at age 7: 3.1 and 27 ng/mL **Statistical adjustments:** None	No significant associations (p>0.05) between child serum PFOS and neural- and non-neural specific antibody concentrations (NF-L, NF-M, NF-H, GFAP, MBP, ChAT, Actin, desmin, keratin). Significant associations (p≤0.05) between cord blood PFOS and actin-specific IgG. No significant associations with other neural- and non-neural specific antibody concentrations.
Qin et al. 2017 Case control study of 132 nonsmoking children in Taiwan aged 10–15 years with asthma and 168 age- and sex-matched controls without asthma	**Exposure:** Median serum PFOS 31.51 ng/mL in cases and 28.83 ng/mL in controls **Statistical adjustments:** Age, sex, BMI, parental education level, exercise, environmental tobacco smoke exposure, month of survey	Association between serum PFOS and asthma occurrence (OR 1.30, 95% CI 1.00–1.69). Among asthmatic children, inverse associations between PFOS and FVC (β -0.055, 95% CI -0.100 to -0.010) and FEV_1 (β -0.061, 95% CI -0.101 to -0.021). No associations with PEF (β -0.094, 95% CI -0.236–0.0497) or FEF_{25-75} (β -0.045, 95% CI -0.127–0.037). Among non-asthmatic children no associations between PFOS and FVC (β -0.005, 95% CI -0.046–0.036), FEV_1 (β -0.016, 95% CI -0.057–0.026), PEF (β 0.029, 95% CI -0.098–0.156), or FEF_{25-75} (β -0.046, 95% CI -0.129–0.161).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFOS levels (measured at any time during pregnancy) 4.88 and 20.6 ng/mL for Ukraine and Greenland cohorts, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	A significant inverse association between maternal PFOS and current wheezing was observed in the Ukraine cohort (OR 0.60, 0.38–0.92), but not in the Greenland cohort (OR 0.91, 95% CI 0.62–1.36) or the combined cohort (OR 0.76, 95% CI 0.56–1.01). No significant associations between maternal serum PFOS and the risk in the combined cohort of ever having asthma (OR 0.86, 95% CI 0.67–1.10), ever having eczema (OR 0.98, 95% CI 0.88–1.18), ever having wheezing (OR 0.83, 95% CI 0.69–1.00), or currently having eczema (OR 1.05, 95% CI 0.82–1.33).
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 1999–2000 and 2003–2004 data (n=1,191)	**Exposure:** Geometric mean serum PFOS 20.8 ng/mL **Multivariable linear regression models adjustments:** Age, sex, race/ethnicity, serum cotinine, BMI	A doubling of serum PFOS levels resulted in significant decreases in mumps antibody titers (7.4%, 95% CI -12.8 to -1.7). No significant association with measles or rubella. In seropositive children, a doubling of serum PFOS levels resulted in 5.9% decreases (95% CI -9.9 to -1.6) in mumps antibody titers and in 13.3% decreases (95% CI -19.9 to -6.2) in rubella antibody titers.
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 data (n=640)	**Exposure:** Geometric mean serum PFOS 15.0 ng/mL **Multivariable logistic regression models adjustments:** Age, sex, race/ethnicity	No significant associations between serum PFOS and current asthma (OR 1.20, 95% CI 0.88–1.63), wheeze (OR 0.76, 95% CI 0.45–1.19), allergy (OR 1.05, 95% CI 0.80–1.37), or rhinitis (OR 1.16, 95% CI 0.90–1.50). Significant inverse associations between serum PFOS and allergic sensitization to plants (OR 0.17, 95% CI 0.53–0.97) and cockroach and/or shrimp (OR 0.67, 95% CI 0.48–0.93). Significant association between serum PFOS and mold (OR 1.33, 95% CI 1.06–1.69). No significant association between serum PFOS and allergic sensitization to dust mites (OR 1.00, 95% CI 0.73–1.38), pets (OR 0.83, 95% CI 0.56–

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		1.22), rodents (OR 0.85, 95% CI 0.29–2.45), or food (OR 0.74, 95% CI 0.39–1.40).
Stein et al. 2016b Cross-sectional study of 78 healthy adults in New York city vaccinated during the 2010–2011 season with the intranasal FluMist influenza vaccine	**Exposure:** Geometric mean serum PFOS 5.22 ng/mL Serum cytokines (IFN-α2, IFN-γ, TNF-α, IP-10) and chemokines (MCP-1, MIP1a) were measured pre-vaccination and 3- and 30-days postvaccination; nasal cytokine (IP-10), chemokine (MCP-1), and nasal mucosal IgA were measured 3- and 30-days postvaccination **Multivariate linear regression model adjustments:** Age, sex, race/ethnicity	No significant association between serum PFOS and seroconversion as measured by hemagglutinin inhibition (p=0.81 for trend) or immunohistochemistry (p=0.12 for trend). No significant associations (p>0.05) between serum PFOS and changes in serum cytokine or chemokine levels or nasal cytokine, chemokine, or IgA levels.
Wang et al. 2011 Prospective cohort study of 244 children (2 years of age) whose mothers participated in the Taiwan Birth Panel cohort study; 43% developed atopic dermatitis as evaluated via a questionnaire and a dermatologist examination of a subset of the children	**Exposure:** Median cord blood PFOS 5.50 ng/mL (range: 0.11–48.36 ng/mL) **Logistic regression adjustments:** Sex, gestational age, parity, maternal age, pre-natal environmental tobacco smoke exposure; analyses of atopy disorder also adjusted for maternal history of atopy and duration of breastfeeding	No significant correlation (p=0.179) between cord blood PFOS and child blood IgE levels. Significant correlation between cord blood PFOS and cord blood IgE levels in males and females combined (p=0.017) and in males only (p=0.053). No significant association (p>0.05) between cord PFOS levels and atopic dermatitis.
Zhu et al. 2016 Case-control study of 231 asthmatic and 225 non-asthmatic children from Taiwan (9–16 years old); this is the same group of children evaluated by Dong et al. (2013)	**Exposure:** Mean serum levels PFOS 33.9 ng/mL in non-asthmatics and 45.86 ng/mL in asthmatics **Multivariate logistic regression model adjustments:** Age, sex, parental education, BMI, environmental tobacco smoke exposure, month of survey The study examined associations between exposure to perfluoroalkyl compounds and T-lymphocyte-related immunological markers of asthma; sex differences also examined	Significant association between serum PFOS and the presence of asthma in children with serum PFOS levels in the 4th quartile; OR 4.38 (95% CI 2.02–9.50) in males. No significant associations (p>0.05 for trend) between serum PFOS and T-helper 1 lymphocyte cytokines IFN-γ or IL-2, T-helper 2 lymphocyte cytokines IL-4 or IL-5, or IgE levels. Asthmatic children had significantly higher serum levels of IgE, IL-4, and IL-5 and lower levels of IFN-γ and IL-2 than non-asthmatic children.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Zhou et al. 2017 Case control study of adolescents with asthma (n=231) or without asthma (n=225)	**Exposure:** Mean serum PFOS 33.94 ng/mL for cases and 28.91 ng/mL for controls **Statistical adjustments:** None	Serum PFOS levels were significantly higher (p=002) in the asthmatics.
PFHxS		
Ashley-Martin et al. 2015 Cohort study of 1,258 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Maternal serum PFHxS levels measured during the first trimester **Bayesian model adjustments:** Maternal age, sex	No significant association between maternal serum PFHxS levels and risk of elevated IL-33/TSLP levels in cord blood; OR (95% CI): • IL-33/TSLP: 1.0 (0.7–1.4) • IgE: 1.0 (0.7–1.4).
Buser and Scinicariello 2016 Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 (n=637) and 2007–2010 (n=701) data; food sensitization at least 1 food specific serum IgE≥0.35 kU/L) and self-reported food allergies were evaluated in the 2005–2006 and 2007–2010 cohorts, respectively	**Exposure:** Geometric mean serum PFHxS 2.09 ng/mL for NHANES 2005–2006 and 2.19 ng/mL NHANES 2007–2010 **Multivariable logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, serum cotinine	Significant association between serum PFHxS and risk of food allergies; however, the trend was not significant (p=0.11). OR 3.06 (95% CI 1.35–6.93) for participants with serum PFHxS levels in the 4th quartile (>4.00 ng/mL). No significant association between serum PFOS and risk of food sensitization (p=0.72 for trend).
Dalsager et al. 2016 Prospective cohort study of 359 children (aged 1–4 years) participating in the Odense Child Cohort in Denmark. Parents responded to texts every other week regarding the child's symptoms of infection	**Exposure:** Median maternal serum PFHxS level (measured at gestation age 10–16 weeks) 0.32 ng/mL **Regression model adjustments:** Maternal age, maternal educational level, parity, child's age	No significant associations (p>0.05) between maternal serum PFHxS and days or days above/below the median with symptoms of infection (fever >101.3°F, cough, nasal discharge, diarrhea, vomiting) were found.
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15) living in Taiwan; this is the same group of children evaluated by Zhu et al. (2016)	**Exposure:** Summary serum PFHxS values were not provided for the full cohort; mean serum PFHxS levels were 3.9 and 2.1 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	Significant increases in odds of having asthma were observed for children with serum PFHxS levels in the 3rd quartile (OR 2.94, 95% CI 1.65–5.25) and 4th quartile (OR 3.83, 95% CI 2.11–6.932.63), as compared to those in the 1st quartile. No significant association between serum PFHxS and asthma severity score was found (p=0.722 for trend). Among asthmatic children, significant associations between serum PFHxS and

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		absolute eosinophil counts (p=0.029) and eosinophil cationic protein levels (p=0.024). No association (p=0.632) with IgE. In non-asthmatic children, no significant (p>0.05) associations with IgE, absolute eosinophil counts, or eosinophil cationic protein levels.
Goudarzi et al. 2016a Prospective study of 1,558 4-year-old children participating in the Hokkaido Study on Environment and Children's Health Study in Japan	**Exposure:** Mean maternal plasma PFHxS 0.322 ng/mL (range of <0.2–3.386 ng/mL) (measured at 28–32 weeks of gestation) **Statistical adjustments:** Maternal age, education, parental allergic history, number of older siblings, breastfeeding, daycare attendance, external tobacco smoke, child's sex	No association between maternal plasma PFHxS and prevalence of allergic disease (defined as cases with at least one of the following symptoms: eczema, wheezing, or rhinoconjuctivitis) (p=0.177 for trend); OR (95% CI) 2nd quartile: 0.917 (0.675–1.24) 3rd quartile: 0.771 (0.563–1.05) 4th quartile: 0.841 (0.615–1.151). Association between maternal plasma PFHxS and prevalence of wheezing (p=0.038 for trend); OR (95% CI) 2nd quartile: 0.8953 (0.624–1.28) 3rd quartile: 0.652 (0.443–0.954) 4th quartile: 0.728 (0.497–1.06).
Goudarzi et al. 2017b Prospective cohort study of 1,558 participants in the Hokkaido Study on Environmental and Children's Health; children were monitored for physician-diagnosed infectious disease up to 4 years of age	**Exposure:** Mean maternal serum PFHxS level (measured at 28–32 weeks of gestation) 0.322 ng/mL **Statistical adjustments:** Maternal age, number of older siblings, maternal smoking during pregnancy, maternal education, infant sex, breastfeeding period	No significant associations between maternal serum PFHxS and risk of total infectious diseases in early life OR 0.957 (95% CI 0.7.3–1.41) for 4th quartile, p=0.928 for trend. In females only, a significant trend between maternal serum PFHxS and risk of total infectious diseases in early life was found (p=0.045); OR (95% CI): 2nd quartile: 1.46 (0.938–2.29) 3rd quartile: 1.81 (1.14–2.88) 4th quartile: 1.55 (0.976–2.45). No associations between maternal PFHxS levels and risk of total infectious diseases in early life were found in male only analyses (p=0.223).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Grandjean et al. 2012; Mogensen et al. 2015a Prospective cohort study of children living in the Faroe Islands; the children were examined prior to receiving vaccine boosters (5 years of age, n=532) for tetanus and diphtheria, 4 weeks after receiving the 5-year vaccine booster (n=456), and at age 7 (n=464)	**Exposure:** Mean serum PFHxS level was 0.6 ng/mL at age 5 and 0.5 ng/mL at age 7 **Statistical adjustments:** Age, sex, time since vaccination, booster type	Significant negative differences at age 5 and 7 years between prebooster and postbooster serum tetanus antibody levels were found; the differences were -19.0% (95% CI -29.8 to -6.6) at 5 years and -19.7% (95% CI -31.6 to -5.7) at 7 years per 2-fold increase in PFHxS levels. Using PFHxS levels at age 7, there was an inverse association with tetanus antibody levels (-22.3%, 95% CI -36.3 to -5.2). No significant differences between prebooster and postbooster serum diphtheria antibody levels were found at age 5 or 7 years or when using PFHxS levels at age 7.
Grandjean et al. 2017 Prospective study of 516 children living in the Faroe Islands; serum antibodies to diphtheria and tetanus were measured at age 13 and compared to serum perfluoroalkyl levels at age 7 and 13	**Exposure:** Median serum PFHxS levels 0.5 ng/mL at age 7 and 0.4 ng/mL at age 13 **Multivariate logistic regression model adjustments:** Age and sex (mandatory covariates), and age-5 booster type; prenatal PCB exposure included in separate analyses	No significant associations between serum PFHxS levels at age 7 or 13 and serum diphtheria antibody levels (p=0.264 and p=0.583) or serum tetanus antibody levels (p=0.334 and p=0.568).
Granum et al. 2013 Prospective birth cohort study, subcohort of the Norwegian Mother and Child Cohort study, examined 56 children examined annually to age 3 years; exclusion criteria included maternal use of steroids or anti-inflammatory drugs during pregnancy, as well as maternal autoimmune disease	**Exposure:** Maternal (measured at delivery; n=99) mean and median serum PFHxS levels were 0.3 and 0.3 ng/mL (range: <0.05–2.8 ng/mL) **Multivariate regression model adjustments:** Maternal and paternal allergy, maternal education, child's sex, child's age	Maternal serum PFHxS levels were inversely associated with rubella antibody levels (p=0.008); the association was not significant for measles, *Haemophilus influenza* type b, or tetanus antibody levels (p>0.05). Maternal serum PFHxS levels were significantly associated with the total number of episodes of the common cold or other upper respiratory tract infection (p=0.078) and gastroenteritis with vomiting or diarrhea (p=0.007). No significant associations (p>0.05) between maternal serum PFHxS and eczema and itchiness, wheezing, otitis media, and doctor-diagnosed atopic eczema or asthma.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Impinen et al. 2018 Prospective study of 641 infants participating in the Environment and Childhood Asthma study in Norway; health outcomes were evaluated at 2 and 10 years of age.	**Exposure:** Mean cord PFHxS level 0.3 ng/mL (range <0.05–4.7 ng/mL) **Logistic regression model adjustments:** Sex; Bonferroni correction for multiple comparisons	No significant associations between number of common colds from 0 to 2 years of age (p=0.530). No significant association between cord PFHxS and number of lower respiratory tract infections from 0 to 10 years of age (p=0.119). No associations (after Bonferroni correction) between cord PFHxS and asthma diagnosis, current asthma, asthma ever, wheezing, rhinitis, rhinoconjuctivitis, or allergic sensitization.
Humblet et al. 2014 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data; participants (n=1,877) were 12–19 years of age	**Exposure:** Median serum PFHxS in children ever having asthma and never having asthma: 2.2 and 2.0 ng/mL, respectively **Regression model adjustments:** Sex, race/ethnicity, poverty income ratio, cigarette smoking, health insurance	No significant associations between serum PFHxS and self-reported having asthma in the last 12 months (p=0.66 per doubling of PFOS concentration), risk of reporting wheezing (p=0.92), or self-reporting current asthma (p=0.99).
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4- and 10-days post-vaccination	**Exposure:** Median serum PFHxS 0.37 ng/mL **Logistic regression model adjustments:** Sex, age	No significant associations (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFHxS and change in diphtheria (p=0.055) or tetanus (p=0.390) antibody levels.
Okada et al. 2014 Prospective study of 2,603 infants whose mothers participated in the Hokkaido Study on Environment and Children's Health Study; mothers completed questionnaires regarding infant allergic disease, infectious diseases, and other diseases when infants were 12 and 24 months of age	**Exposure:** Maternal mean plasma PFHxS (measured between 28 and 32 weeks of gestation) 0.324 ng/mL (range: <0.2–3.39 ng/mL) **Statistical adjustments:** Maternal age, education, parental allergic history, infant sex, breastfeeding, number of siblings, daycare attendance, environmental tobacco smoke exposure in infants at 24 months	No significant associations between maternal PFHxS levels and risk of allergic diseases or eczema were observed in the infants; 4th PFHxS quartile OR 0.81 (95% CI 0.56–1.16) and OR 1.13 (95% CI 0.75–1.69) for allergic diseases in males and females and 0.78 (95% CI 0.51–1.19) and 0.82 (95% CI 0.49–1.36) for eczema in males and females.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Qin et al. 2017 Case control study of 132 nonsmoking children in Taiwan aged 10–15 years with asthma and 168 age- and sex-matched controls without asthma	**Exposure:** Median serum PFHxS 2.38 ng/mL in cases and 1.07 ng/mL in controls **Statistical adjustments:** Age, sex, BMI, parental education level, exercise, environmental tobacco smoke exposure, month of survey	Association between serum PFHxS and asthma occurrence (OR 2.14, 95% CI 1.48–3.11). Among asthmatic children, inverse associations between PFHxS and FVC (β -0.075, 95% CI -0.148 to -0.002), FEV_1 (β -0.101, 95% CI -0.166 to -0.036) and FEF_{25-75} (β -0.195, 95% CI -0.325 to -0.065). No association with PEF (β -0.093, 95% CI -0.326–0.139). Among non-asthmatic children no associations between PFHxS and FVC (β -0.059, 95% CI -0.132–0.015), FEV_1 (β -0.044, 95% CI -0.448–0.031), PEF (β 0.011, 95% CI -0.218–0.240), or FEF_{25-75} (β 0.008, 95% CI -0.141–0.158).
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFHxS levels (measured at any time during pregnancy) 1.53 and 2.14 ng/mL for Ukraine and Greenland cohort, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	No significant associations between maternal serum PFHxS and the risk in the combined cohort of ever having asthma (OR 0.91, 95% CI 0.69–1.18), ever having eczema (OR 1.03, 95% CI 0.86–1.24), ever having wheezing (OR 0.96, 95% CI 0.79–1.17), currently wheezing (OR 0.93, 95% CI 0.68–1.27), or currently having eczema (OR 0.93, 95% CI 0.73–1.20).
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 1999–2000 and 2003–2004 data (n=1,191)	**Exposure:** Geometric mean serum PFHxS 2.47 ng/mL **Multivariable linear regression models adjustments:** Age, sex, race/ethnicity, serum cotinine, BMI	No significant associations of serum PFHxS levels and measles, mumps, or rubella antibody titers (95% CI included unity). In seropositive children, a doubling of serum PFHxS levels resulted in 6.0% decreases (95% CI -9.6 to -2.2) in rubella antibody titers.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 data (n=640)	**Exposure:** Geometric mean serum PFHxS 2.09 ng/mL **Multivariable logistic regression models adjustments:** Age, sex, race/ethnicity	No significant associations between serum PFHxS and current asthma (OR 0.98, 95% CI 0.51–1.87), wheeze (OR 0.99, 95% CI 0.68–1.44), allergy (OR 0.83, 95% CI 0.59–1.17), or rhinitis (OR 0.81, 95% CI 0.57–1.16). No significant association between serum PFHxS and allergic sensitization to plants (OR 0.93, 95% CI 0.62–1.39), dust mites (OR 1.01, 95% CI 0.84–1.22), pets (OR 0.96, 95% CI 0.71–1.30), cockroach/shrimp (OR 0.72, 95% CI 0.56–0.93), rodents (OR 0.81, 95% CI 0.54–1.21), mold (OR 0.98, 95% CI 0.65–1.47), or food (OR 1.03, 95% CI 0.74–1.42).
Stein et al. 2016b Cross-sectional study of 78 healthy adults in New York city vaccinated during the 2010–2011 season with the intranasal FluMist influenza vaccine	**Exposure:** Geometric mean serum PFHxS 1.1 ng/mL Serum cytokines (IFN-α2, IFN-γ, TNF-α, IP-10) and chemokines (MCP-1, MIP1a) were measured pre-vaccination and 3- and 30-days post vaccination; nasal cytokine (IP-10), chemokine (MCP-1), and nasal mucosal IgA were measured 3- and 30-days post vaccination **Multivariate linear regression model adjustments:** Age, sex, race/ethnicity	No significant association between serum PFHxS and seroconversion as measured by hemagglutinin inhibition (p=0.22 for trend) or immunohistochemistry (p=0.34 for trend). Significant associations between serum PFHxS and changes in the serum cytokines IFN-γ (p=0.05) and TNF-α (p=0.04). No significant associations (p>0.05) for other serum cytokines or chemokine levels or nasal cytokine, chemokine, or IgA levels.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Zhu et al. 2016 Case-control study of 231 asthmatic and 225 non-asthmatic children from Taiwan (9–16 years old); this is the same group of children evaluated by Dong et al. (2013)	**Exposure:** Mean serum levels PFHxS 2.10 ng/mL in non-asthmatics and 3.86 ng/mL in asthmatics **Multivariate logistic regression model adjustments:** Age, sex, parental education, BMI, environmental tobacco smoke exposure, month of survey The study examined associations between exposure to perfluoroalkyl compounds and T-lymphocyte-related immunological markers of asthma; sex differences also examined	Significant association between serum PFHxS and presence of asthma in children with serum PFHxS levels in the 4th quartile; OR 2.97 (95% CI 1.33–6.64) in males and OR 5.02 (95% CI 2.05–12.30) in females. No significant associations between serum PFHxS and serum T-helper 1 lymphocyte cytokines IFN-γ or IL-2; T-helper 2 lymphocyte cytokines IL-4 or IL-5; or IgE levels. Asthmatic children had significantly higher serum levels of IgE, IL-4, and IL-5 and lower levels of IFN-γ and IL-2 than non-asthmatic children.
Zhou et al. 2017 Case control study of adolescents with asthma (n=231) or without asthma (n=225)	**Exposure:** Mean serum PFHxS 2.47 ng/mL for cases and 1.32 ng/mL for controls **Statistical adjustments:** None	Serum PFHxS levels were significantly higher ($p<0.001$) in the asthmatics.
PFNA		
Buser and Scinicariello 2016 Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 (n=637) and 2007–2010 (n=701) data; food sensitization at least 1 food specific serum IgE≥0.35 kU/L) and self-reported food allergies were evaluated in the 2005–2006 and 2007–2010 cohorts, respectively	**Exposure:** Geometric mean serum PFNA 0.93 ng/mL for NHANES 2005–2006 and 1.13 ng/mL NHANES 2007–2010. **Multivariable logistic regression model adjustments:** Age, sex, race/ethnicity, BMI, serum cotinine	No significant association between serum PFNA and risk of food allergies ($p=0.28$ for trend). No significant association between serum PFNA and risk of food sensitization ($p=0.15$ for trend). However, an inverse association was observed for PFNA levels in the 4th quartile (>1.36 ng/mL), OR 0.51 (95% CI 0.28–0.92).
Dalsager et al. 2016 Prospective cohort study of 359 children (aged 1–4 years) participating in the Odense Child Cohort in Denmark; parents responded to texts every other week regarding the child's symptoms of infection	**Exposure:** Median maternal serum PFNA level (measured at gestation age 10–16 weeks) 0.70 ng/mL **Regression model adjustments:** Maternal age, maternal educational level, parity, child's age	Significant inverse association between maternal PFNA levels and number of days above the median reporting nasal discharge; OR 0.53 (95% CI 0.31–0.92) for 2nd tertile (0.56–0.81 ng/mL) and 0.55 (95% CI 0.31–0.97) for 3rd tertile (0.82–3.64 ng/mL); this was not observed when the number of days of nasal discharge was analyzed (OR 1.12, 95% CI 0.84–1.49). A significant association between maternal PFNA and number of days with diarrhea was

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		observed in the 2nd tertile (OR 0.46, 95% CI 0.26–0.81), but not the 3rd tertile (OR 0.74, 95% CI 0.42–1.30). No significant associations (p>0.05) between maternal serum PFNA and days or days above/below the median with other symptoms of infection (fever >101.3°F, cough, diarrhea, vomiting) were found.
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15) living in Taiwan; this is the same group of children evaluated by Zhu et al. (2016)	**Exposure:** Summary serum PFNA values were not provided for the full cohort; mean serum PFNA levels were 1.1 and 0.9 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	Significant increases in odds of having asthma were observed for children with serum PFNA levels in the 4th quartile (OR 2.56, 95% CI 1.41–4.65), as compared to those in 1st quartile. No significant association between serum PFNA and asthma severity score was found (p=0.217 for trend). Among asthmatic children, significant associations between serum PFNA and IgE (p=0.001), absolute eosinophil counts (p<0.001), and eosinophil cationic protein levels (p=0.003). In non-asthmatic children, no significant (p>0.05) associations with IgE, absolute eosinophil counts, or eosinophil cationic protein levels.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Goudarzi et al. 2016a Prospective study of 1,558 4-year-old children participating in the Hokkaido Study on Environment and Children's Health Study in Japan	**Exposure:** Mean maternal plasma PFNA 1.402 ng/mL (range of <0.3–13.189 ng/mL) (measured at 28–32 weeks of gestation) **Statistical adjustments:** Maternal age, education, parental allergic history, number of older siblings, breastfeeding, daycare attendance, external tobacco smoke, child's sex	No association between maternal plasma PFNA and prevalence of allergic disease (defined as cases with at least one of the following symptoms: eczema, wheezing, or rhinoconjuctivitis) (p=0.137 for trend); OR (95% CI): 2nd quartile: 1.36 (0.891–2.08) 3rd quartile: 0.694 (0.442–1.08) 4th quartile: 0.873 (0.562–1.35). No association between maternal plasma PFNA and prevalence of wheezing (p=0.875 for trend); OR (95% CI): 2nd quartile: 1.16 (0.803–1.67) 3rd quartile: 0.910 (0.617–1.33) 4th quartile: 1.11 (0.760–1.63).
Goudarzi et al. 2017b Prospective cohort study of 1,558 participants in the Hokkaido Study on Environmental and Children's Health; children were monitored for physician-diagnosed infectious disease up to 4 years of age.	**Exposure:** Mean maternal serum PFNA level (measured at 28–32 weeks of gestation) 1.402 ng/mL **Statistical adjustments:** Maternal age, number of older siblings, maternal smoking during pregnancy, maternal education, infant sex, breastfeeding period	No significant associations between maternal serum PFNA and risk of total infectious diseases in early life OR 0.918 (95% CI 0.672–1.25) for 4th quartile, p=0.748 for trend. Similar results were observed when males and females were analyzed separately.
Grandjean et al. 2012; Mogensen et al. 2015a Prospective cohort study of children living in the Faroe Islands; the children were examined prior to receiving vaccine boosters (5 years of age, n=532) for tetanus and diphtheria, 4 weeks after receiving the 5-year vaccine booster (n=456), and at age 7 (n=464)	**Exposure:** Geometric serum PFNA level at age 5 was 1.00 ng/mL **Statistical adjustments:** Age, sex, time since vaccination, booster type	No significant differences between prebooster and postbooster serum tetanus antibody levels were found at age 5 or 7 years. A significant negative difference at age 5 years between prebooster and postbooster serum diphtheria antibody levels was found; difference was -16.1% (95% CI -28.8 to -1.0) per 2-fold increase in PFNA levels. No significant differences were observed at age 7 years.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Grandjean et al. 2017 Prospective study of 516 children living in the Faroe Islands; serum antibodies to diphtheria and tetanus were measured at age 13 and compared to serum perfluoroalkyl levels at age 7 and 13	**Exposure:** Median serum PFNA levels 1.1 ng/mL at age 7 and 0.7 ng/mL at age 13 **Multivariate logistic regression model adjustments:** Age and sex (mandatory covariates), and age-5 booster type; prenatal PCB exposure included in separate analyses	No significant associations between serum PFNA levels at age 7 or 13 and diphtheria antibody levels (p=0.243 and p=0.693) or tetanus antibody levels (p=0.075 and p=0.394).
Granum et al. 2013 Prospective birth cohort study, subcohort of the Norwegian Mother and Child Cohort study, examined 56 children examined annually to age 3 years; exclusion criteria included maternal use of steroids or anti-inflammatory drugs during pregnancy, as well as maternal autoimmune disease	**Exposure:** Maternal (measured at delivery; n=99) mean and median serum PFNA levels were 0.3 and 0.3 ng/mL (range: <0.05–0.9 ng/mL) **Multivariate regression model adjustments:** Maternal and paternal allergy, maternal education, child's sex, child's age	Maternal serum PFNA levels were inversely associated with rubella antibody levels (p=0.007); the association was not significant for measles, *Haemophilus influenza* type b, or tetanus antibody levels (p>0.05). Maternal serum PFNA levels were significantly associated with the total number of episodes of the common cold or other upper respiratory tract infection (p=0.035), but not with the number of episodes of gastroenteritis with vomiting or diarrhea (p=0.883). No significant associations (p>0.05) between maternal serum PFNA and eczema and itchiness, wheezing, otitis media, and doctor-diagnosed atopic eczema, or asthma.
Humblet et al. 2014 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data; participants (n=1,877) were 12–19 years of age	**Exposure:** Median serum PFNA in children ever having asthma and never having asthma: 0.9 and 0.8 ng/mL, respectively **Regression model adjustments:** Sex, race/ethnicity, poverty income ratio, cigarette smoking, health insurance	No significant associations between serum PFNA and self-reported having asthma in the last 12 months (p=0.92 per doubling of PFNA concentration), risk of reporting wheezing (p=0.94), or self-reporting current asthma (p=0.97).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Impinen et al. 2018 Prospective study of 641 infants participating in the Environment and Childhood Asthma study in Norway; health outcomes were evaluated at 2 and 10 years of age	**Exposure:** Mean cord PFNA level 0.2 ng/mL (range <0.05–5.0 ng/mL) **Logistic regression model adjustments:** Sex; Bonferroni correction for multiple comparisons	No significant associations between number of common colds from 0 to 2 years of age (p=0.983). Significant association between cord PFNA and number of lower respiratory tract infections from 0 to 10 years of age, β 0.0.09 (95% CI 0.03–0.14; p=0.001). No associations (after Bonferroni correction) between cord PFNA and asthma diagnosis, current asthma, asthma ever, wheezing, rhinitis, rhinoconjuctivitis, or allergic sensitization.
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4- and 10-days post-vaccination	**Exposure:** Median serum PFNA 0.66 ng/mL **Logistic regression model adjustments:** Sex, age	Significant inverse association (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFNA and change in diphtheria (p=0.004) antibody levels; no association (p=0.250) with tetanus antibody levels.
Okada et al. 2014 Prospective study of 2,603 infants whose mothers participated in the Hokkaido Study on Environment and Children's Health Study; mothers completed questionnaires regarding infant allergic disease, infectious diseases, and other diseases when infants were 12 and 24 months of age	**Exposure:** Maternal mean plasma PFNA (measured between 28 and 32 weeks of gestation) 1.36 ng/mL (range: <0.3–13.2 ng/mL) **Statistical adjustments:** Maternal age, education, parental allergic history, infant sex, breastfeeding, number of siblings, daycare attendance, environmental tobacco smoke exposure in infants at 24 months	Significant inverse association between maternal PFNA levels and risk of allergic diseases was observed in female infants; 4th PFNA quartile OR 0.55 (95% CI 0.36–0.82), but not in male infants OR 0.95 (95% CI 0.66–1.38). No significant association between maternal PFNA levels and risk of eczema was observed in the infants; 4th PFOA quartile OR 0.96 (95% CI 0.61–1.52) for males and OR 0.63 (95% CI 0.38–1.02) for females.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Qin et al. 2017 Case control study of 132 nonsmoking children in Taiwan aged 10–15 years with asthma and 168 age- and sex-matched controls without asthma	**Exposure:** Median serum PFNA 1.00 ng/mL in cases and 0.80 ng/mL in controls **Statistical adjustments:** Age, sex, BMI, parental education level, exercise, environmental tobacco smoke exposure, month of survey	Association between serum PFNA and asthma occurrence (OR 1.61, 95% CI 1.12–2.31). Among asthmatic children, inverse associations between PFNA and FVC (β -0.165, 95% CI -0.321 to -0.009) and FEV_1 (β -0.199, 95% CI -0.338 to -0.060). No associations with PEF (β -0.211, 95% CI -0.708–0.285) or FEF_{25-75} (β -0.277, 95% CI -0.560–0.006). Among non-asthmatic children, association between PFNA and PEF (β 0.630, 95% CI 0.115–1.144). No associations with FVC (β 0.011, 95% CI -0.159–0.189), FEV_1 (β -0.068, 95% CI -0.102–0.238), or FEF_{25-75} (β 0.278, 95% CI -0.061 to -0.616).
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFNA levels (measured at any time during pregnancy) 0.62 and 0.73 ng/mL for Ukraine and Greenland cohorts, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	No significant associations between maternal serum PFNA and the risk in the combined cohort of ever having asthma (OR 0.90, 95% CI 0.70–1.14), ever having eczema (OR 0.94, 95% CI 0.78–1.14), ever having wheezing (OR 0.91, 95% CI 0.75–1.09), currently wheezing (OR 0.90, 95% CI 0.66–1.23), or currently having eczema (OR 1.03, 95% CI 0.82–1.30).
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 1999–2000 and 2003–2004 data (n=1,191)	**Exposure:** Geometric mean serum PFNA 0.765 ng/mL **Multivariable linear regression models adjustments:** Age, sex, race/ethnicity serum cotinine, BMI	No significant associations of serum PFNA levels and measles, mumps, or rubella antibody titers (95% CI included unity).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Stein et al. 2016a Cross-sectional study of adolescents (12–19 years of age) utilizing NHANES 2005–2006 data (n=640)	**Exposure:** Geometric mean serum PFNA 0.929 ng/mL **Multivariable logistic regression models adjustments:** Age, sex, race/ethnicity	No significant associations between serum PFNA and current asthma (OR 1.26, 95% CI 0.79–2.01), wheeze (OR 0.99, 95% CI 0.58–1.68), allergy (OR 1.12, 95% CI 0.85–1.47), or rhinitis (OR 1.24, 95% CI 0.97–1.60). No significant association between serum PFNA and allergic sensitization to plants (OR 0.96, 95% CI 0.74–1.23), dust mites (OR 1.05, 95% CI 0.78–1.41), pets (OR 1.26, 95% CI 0.85–1.87), cockroach/shrimp (OR 0.86, 95% CI 0.60–1.24), rodents (OR 2.25, 95% CI 0.83–6.10), mold (OR 1.31, 95% CI 0.83–2.06), or food (OR 0.91, 95% CI 0.55–1.50).
Stein et al. 2016b Cross-sectional study of 78 healthy adults in New York city vaccinated during the 2010–2011 season with the intranasal FluMist influenza vaccine	**Exposure:** Geometric mean serum PFNA 0.77 ng/mL Serum cytokines (IFN-α2, IFN-γ, TNF-α, IP-10) and chemokines (MCP-1, MIP1a) were measured pre-vaccination and 3- and 30-days post vaccination; nasal cytokine (IP-10), chemokine (MCP-1), and nasal mucosal IgA were measured 3- and 30-days post vaccination **Multivariate linear regression model adjustments:** Age, sex, race/ethnicity	No significant association between serum PFNA and seroconversion as measured by hemagglutinin inhibition (p=0.33 for trend) or immunohistochemistry (p=0.40 for trend). No significant associations (p>0.05) between serum PFNA and changes in serum cytokine or chemokine levels or nasal cytokine, chemokine, or IgA levels.
Wang et al. 2011 Prospective cohort study of 244 children (2 years of age) whose mothers participated in the Taiwan Birth Panel cohort study; 43% developed atopic dermatitis as evaluated via a questionnaire and a dermatologist examination of a subset of the children	**Exposure:** Median cord blood PFNA 2.30 ng/mL (range: 0.38–63.87 ng/mL) **Logistic regression adjustments:** Sex, gestational age, parity, maternal age, pre-natal environmental tobacco smoke exposure; analyses of atopy disorder also adjusted for maternal history of atopy and duration of breastfeeding	No significant correlation between cord blood PFNA and child blood IgE levels (p=0.837) or cord blood IgE levels (p=0.908). No significant association (p>0.05) between cord PFNA levels and atopic dermatitis.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Zhu et al. 2016 Case-control study of 231 asthmatic and 225 non-asthmatic children from Taiwan (9–16 years old); this is the same group of children evaluated by Dong et al. (2013)	**Exposure:** Mean serum levels PFNA 0.87 ng/mL in non-asthmatics and 1.07 ng/mL in asthmatics **Multivariate logistic regression model adjustments:** Age, sex, parental education, BMI, environmental tobacco smoke exposure, month of survey The study examined associations between exposure to perfluoroalkyl compounds and T-lymphocyte-related immunological markers of asthma; sex differences also examined	Significant association between serum PFNA and presence of asthma in male children with serum PFNA levels in the 4th quartile; OR 3.33 (95% CI 1.46–7.58); no association was found in females. Significant associations between serum PFNA and serum IgE (p=0.008 for trend), T-helper 2 lymphocyte cytokines IL-4 (p=0.031 for trend) or IL-5 (p=0.011 for trend). No significant associations (p>0.05 for trend) with T-helper 1 lymphocyte cytokines IFN-γ or IL-2 levels. Asthmatic children had significantly higher serum levels of IgE, IL-4, and IL-5 and lower levels of IFN-γ and IL-2 than non-asthmatic children.
Zhou et al. 2017 Case control study of adolescents with asthma (n=231) or without asthma (n=225)	**Exposure:** Mean serum PFNA 1.00 ng/mL for cases and 0.83 ng/mL for controls **Statistical adjustments:** None	Serum PFNA levels were significantly higher (p<0.001) in the asthmatics.
PFDA		
Dalsager et al. 2016 Prospective cohort study of 359 children (aged 1–4 years) participating in the Odense Child Cohort in Denmark; parents responded to texts every other week regarding the child's symptoms of infection	**Exposure:** Median maternal serum PFDA level (measured at gestation age 10–16 weeks) 0.27 ng/mL **Regression model adjustments:** Maternal age, maternal educational level, parity, child's age	No significant associations (p>0.05) between maternal serum PFDA and days or days above/below the median with symptoms of infection (fever >101.3°F, cough, nasal discharge, diarrhea, vomiting) were found.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15) living in Taiwan; this is the same group of children evaluated by Zhu et al. (2016)	**Exposure:** Summary serum PFDA values not provided for the full cohort; mean serum PFDA levels were 1.2 and 1.0 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	Significant increases in odds of having asthma were observed for children with serum PFDA levels in the 4th quartile (OR 3.22, 95% CI 1.75–5.94), as compared to those in 1st quartile. Significant association between serum PFDA and asthma severity score was found (p=0.005 for trend). Among asthmatic children, significant associations between serum PFDA and IgE (p0.001), absolute eosinophil counts (p=0.004), and eosinophil cationic protein levels (p=0.001). In non-asthmatic children, significant association (p=0.004) between serum PFDA and eosinophil cationic protein levels. No significant (p>0.05) associations with IgE or absolute eosinophil counts.
Goudarzi et al. 2016a Prospective study of 1,558 4-year-old children participating in the Hokkaido Study on Environment and Children's Health Study in Japan	**Exposure:** Mean maternal plasma PFDA 0.575 ng/mL (range of <0.1–2.434 ng/mL) (measured at 28–32 weeks of gestation) **Statistical adjustments:** Maternal age, education, parental allergic history, number of older siblings, breastfeeding, daycare attendance, external tobacco smoke, child's sex	No association between maternal plasma PFDA and prevalence of allergic disease (defined as cases with at least one of the following symptoms: eczema, wheezing, or rhinoconjuctivitis) (p=0.391 for trend); OR (95% CI): 2nd quartile: 0.886 (0.652–1.20) 3rd quartile: 0.880 (0.646–1.19) 4th quartile: 0.906 (0.663–1.23). No association between maternal plasma PFDA and prevalence of wheezing (p=0.917 for trend); OR (95% CI): 2nd quartile: 0.785 (0.537–1.14) 3rd quartile: 1.08 (0.756–1.56) 4th quartile: 0.879 (0.602–1.28).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Goudarzi et al. 2017b Prospective cohort study of 1,558 participants in the Hokkaido Study on Environmental and Children's Health; children were monitored for physician-diagnosed infectious disease up to 4 years of age	**Exposure:** Mean maternal serum PFDA level (measured at 28–32 weeks of gestation) 0.575 ng/mL **Statistical adjustments:** Maternal age, number of older siblings, maternal smoking during pregnancy, maternal education, infant sex, breastfeeding period	No significant associations between maternal serum PFDA and risk of total infectious diseases in early life OR 0.799 (95% CI 0.588–1.08) for 4th quartile, p=0.114 for trend. Similar results were observed when males and females were analyzed separately.
Grandjean et al. 2012; Mogensen et al. 2015a Prospective cohort study of children living in the Faroe Islands; the children were examined prior to receiving vaccine boosters (5 years of age, n=532) for tetanus and diphtheria, 4 weeks after receiving the 5-year vaccine booster (n=456), and at age 7 (n=464)	**Exposure:** Geometric serum PFDA level at age 5 was 0.28 ng/mL **Statistical adjustments:** Age, sex, time since vaccination, booster type	Significant negative differences at age 5 and 7 years between prebooster and postbooster serum tetanus antibody levels were found; difference was -19.9% (95% CI -33.1 to -3.9) at 5 years and -22.3 (95% CI -35.8 to -5.8) at 7 years per 2-fold increase in PFDA levels. No significant differences between prebooster and postbooster serum diphtheria antibody levels were found at age 5 or 7 years.
Grandjean et al. 2017 Prospective study of 516 children living in the Faroe Islands; serum antibodies to diphtheria and tetanus were measured at age 13 and compared to serum perfluoroalkyl levels at age 7 and 13	**Exposure:** Median **s**erum PFDA levels 0.4 ng/mL at age 7 and 0.3 ng/mL at age 13 **Multivariate logistic regression model adjustments:** Age and sex (mandatory covariates), and age-5 booster type; prenatal PCB exposure included in separate analyses	Significant association between serum PFDA and antibodies for tetanus at age 7 (p=0.022), but not at age 13 (p=0.258). Significant association between serum PFDA levels at age 7 and diphtheria antibody levels (p=0.008), but not at age 13 (p=0.726).
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4- and 10-days post-vaccination	**Exposure:** Median serum PFDA 0.30 ng/mL **Logistic regression model adjustments:** Sex, age	Significant inverse association (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFDA and change in diphtheria (p=0.009) antibody levels; no association (p=0.130) with tetanus antibody levels.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Okada et al. 2014 Prospective study of 2,603 infants whose mothers participated in the Hokkaido Study on Environment and Children's Health Study; mothers completed questionnaires regarding infant allergic disease, infectious diseases, and other diseases when infants were 12 and 24 months of age	**Exposure:** Maternal mean plasma PFDA (measured between 28 and 32 weeks of gestation) 0.563 ng/mL (range: <0.1–2.43 ng/mL) **Statistical adjustments:** Maternal age, education, parental allergic history, infant sex, breastfeeding, number of siblings, daycare attendance, environmental tobacco smoke exposure in infants at 24 months	No significant associations between maternal PFDA levels and risk of allergic diseases or eczema were observed in the infants; 4th PFDA quartile OR 1.13 (95% CI 0.78–1.64) and OR 0.70 (95% CI 0.47–1.04) for allergic diseases in males and females and 0.93 (95% CI 0.60–1.44) and 0.78 (95% CI 0.49–1.25) for eczema in males and females, respectively.
Qin et al. 2017 Case-control study of 132 nonsmoking children in Taiwan aged 10–15 years with asthma and 168 age- and sex-matched controls without asthma	**Exposure:** Median serum PFDA 1.13 ng/mL in cases and 0.93 ng/mL in controls **Statistical adjustments:** Age, sex, BMI, parental education level, exercise, environmental tobacco smoke exposure, month of survey	No association between serum PFDA and asthma occurrence (OR 1.24, 95% CI 0.97–1.58). Among asthmatic children, no associations between PFDA and FVC (β -0.039, 95% CI -0.148–0.070), FEV_1 (β -0.053, 95% CI -0.152–0.042), PEF (β -0.087, 95% CI -0.429–0.256), or FEF_{25-75} (β -0.070, 95% CI -0.267–0.128). Among non-asthmatic children no associations between PFDA and FVC (β -0.005, 95% CI -0.114–0.103), FEV_1 (β -0.008, 95% CI -0.101–0.117), PEF (β 0.188, 95% CI -0.145–0.520), or FEF_{25-75} (β 0.058, 95% CI -0.160–0.276).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFDA levels (measured at any time during pregnancy) 0.16 and 0.42 ng/mL for Ukraine and Greenland cohorts, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	No significant associations between maternal serum PFDA and the risk in the combined cohort of ever having asthma (OR 0.92, 95% CI 0.73–1.16), ever having eczema (OR 0.88, 95% CI 0.73–1.06), ever having wheezing (OR 0.85, 95% CI 0.70–1.01), currently wheezing (OR 0.76, 95% CI 0.56–1.04), or currently having eczema (OR 0.95, 95% CI 0.75–1.20).
Zhu et al. 2016 Case-control study of 231 asthmatic and 225 non-asthmatic children from Taiwan (9–16 years old); this is the same group of children evaluated by Dong et al. (2013)	**Exposure:** Mean serum levels PFDA 1.02 ng/mL in non-asthmatics and 1.24 ng/mL in asthmatics **Multivariate logistic regression model adjustments:** Age, sex, parental education, BMI, environmental tobacco smoke exposure, month of survey The study examined associations between exposure to perfluoroalkyl compounds and T-lymphocyte-related immunological markers of asthma; sex differences also examined	Significant association between serum PFDA and presence of asthma in children with serum PFDA levels in the 4th quartile; OR 3.45 (95% CI 1.51–7.88) in males and OR 3.68 (95% CI 1.43–9.48) in females. Significant association between serum PFDA and serum IgE levels (p=0.002 for trend). No significant associations (p>0.05 for trend) with T-helper 1 lymphocyte cytokines IFN-γ or IL-2, T-helper 2 or lymphocyte cytokines IL-4 or IL-5 levels. Asthmatic children had significantly higher serum levels of IgE, IL-4, and IL-5 and lower levels of IFN-γ and IL-2 than non-asthmatic children.
Zhou et al. 2017 Case-control study of adolescents with asthma (n=231) or without asthma (n=225)	**Exposure:** Mean serum PFDA 1.14 ng/mL for cases and 0.95 ng/mL for controls **Statistical adjustments:** None	Serum PFDA levels were significantly higher (p<0.001) in the asthmatics.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFUnA		
Goudarzi et al. 2016a Prospective study of 1,558 4-year-old children participating in the Hokkaido Study on Environment and Children's Health Study in Japan	**Exposure:** Mean maternal plasma PFUnA 1.534 ng/mL (range of <0.1–5.89 ng/mL) (measured at 28–32 weeks of gestation) **Statistical adjustments:** Maternal age, education, parental allergic history, number of older siblings, breastfeeding, daycare attendance, external tobacco smoke, child's sex	No association between maternal plasma PFUnA and prevalence of allergic disease (defined as cases with at least one of the following symptoms: eczema, wheezing, or rhinoconjuctivitis) (p=0.085 for trend); OR (95% CI): 2nd quartile: 0.859 (0.631–1.16) 3rd quartile: 0.905 (0.667–1.22) 4th quartile: 0.736 (0.538–1.00). No association between maternal plasma PFUnA and prevalence of wheezing (p=0.706 for trend); OR (95% CI): 2nd quartile: 0.994 (0.682–1.44) 3rd quartile: 1.10 (0.762–1.60) 4th quartile: 1.04 (0.714–1.51).
Goudarzi et al. 2017b Prospective cohort study of 1,558 participants in the Hokkaido Study on Environmental and Children's Health; children were monitored for physician-diagnosed infectious disease up to 4 years of age	**Exposure:** Mean maternal serum PFUnA level (measured at 28–32 weeks of gestation) 1.534 ng/mL **Statistical adjustments:** Maternal age, number of older siblings, maternal smoking during pregnancy, maternal education, infant sex, breastfeeding period	No significant associations between maternal serum PFUnA and risk of total infectious diseases in early life OR 1.03 (95% CI 0.764–1.40) for 4th quartile, p=0.786 for trend. Similar results were observed when males and females were analyzed separately.
Impinen et al. 2018 Prospective study of 641 infants participating in the Environment and Childhood Asthma study in Norway; health outcomes were evaluated at 2 and 10 years of age	**Exposure:** Mean cord PFUnA level 0.1 ng/mL (range <0.05–0.4 ng/mL) **Logistic regression model adjustments:** Sex; Bonferroni correction for multiple comparisons	Significant associations between cord PFUnA and number of common colds from 0 to 2 years of age, β 0.11 (95% CI 0.08–0.14; p<0.0001). Significant association between cord PFUnA and number of lower respiratory tract infections from 0 to 10 years of age, β 0.18 (95% CI 0.13–0.23; p<0.0001). No associations (after Bonferroni correction) between cord PFUnA and asthma diagnosis, current asthma, asthma ever, wheezing, rhinitis, rhinoconjuctivitis, or allergic sensitization.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4- and 10-days post-vaccination	**Exposure:** Median serum PFUnA 0.21 ng/mL **Logistic regression model adjustments:** Sex, age	Significant inverse associations (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFUnA and change in diphtheria (p=0.036) or tetanus (p=0.039) antibody levels.
Okada et al. 2014 Prospective study of 2,603 infants whose mothers participated in the Hokkaido Study on Environment and Children's Health Study; mothers completed questionnaires regarding infant allergic disease, infectious diseases, and other diseases when infants were 12 and 24 months of age	**Exposure:** Maternal mean plasma PFUnA (measured between 28 and 32 weeks of gestation) 1.50 ng/mL (range: <0.1–5.89 ng/mL) **Statistical adjustments:** Maternal age, education, parental allergic history, infant sex, breastfeeding, number of siblings, daycare attendance, environmental tobacco smoke exposure in infants at 24 months	Significant inverse association between maternal PFUnA levels and risk of allergic diseases was observed in female infants; 4th PFUnA quartile OR 0.58 (95% CI 0.39–0.86), but not in male infants OR 1.13 (95% CI 0.79–1.63). Significant inverse association between maternal PFUnA levels and risk of eczema was observed in female infants, 4th PFUnA quartile OR 0.50 (95% CI 0.30–0.81), but not in male infants OR 1.16 (95% CI 0.75–1.81).
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFUnA levels (measured at any time during pregnancy) 0.16 and 0.68 ng/mL for Ukraine and Greenland cohorts, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	No significant associations between maternal serum PFUnA and the risk in the combined cohort of ever having asthma (OR 0.96, 95% CI 0.77–1.21), ever having eczema (OR 0.95, 95% CI 0.79–1.15), ever having wheezing (OR 0.84, 95% CI 0.70–1.00), currently wheezing (OR 0.87, 95% CI 0.65–1.17), or currently having eczema (OR 1.07, 95% CI 0.85–1.34).
PFHpA		
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4- and 10-days post-vaccination	**Exposure:** Median serum PFHpA 0.12 ng/mL **Logistic regression model adjustments:** Sex, age	No significant associations (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFHpA and change in diphtheria (p=0.750) or tetanus (p=0.280) antibody levels.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFHpA levels (measured at any time during pregnancy) 0.03 and 0.05 ng/mL for Ukraine and Greenland cohorts, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	A significant inverse association between maternal PFHpA and current wheezing was observed in the Ukraine cohort (OR 0.62, 95% CI 0.40–0.97), but not in the Greenland cohort (OR 1.24, 95% CI 0.79–1.93) or the combined cohort (OR 0.88, 95% CI 0.64–1.20). No significant associations between maternal serum PFOS and the risk in the combined cohort of ever having asthma (OR 0.93, 95% CI 0.71–1.22), ever having eczema (OR 0.93, 95% CI 0.78–1.11), ever having wheezing (OR 1.03, 95% CI 0.84–1.25), or currently having eczema (OR 0.90, 95% CI 0.70–1.15).
PFBS		
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15) living in Taiwan; this is the same group of children evaluated by Zhu et al. (2016)	**Exposure:** Summary serum PFBS values were not provided for the full cohort; mean serum PFBS levels were 0.5 and 0.5 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	Significant increases in odds of having asthma were observed for children with serum PFBS levels in the 4th quartile (OR 1.90, 95% CI 1.08–3.37), as compared to those in 1st quartile. No significant association between serum PFBS and asthma severity score was found (p=0.092 for trend). Among asthmatic children, significant associations between serum PFBS and absolute eosinophil counts (p=0.009). No association (p>0.05) with IgE or eosinophil cationic protein levels. In non-asthmatic children, no significant (p>0.05) association were found between serum PFBS and IgE, absolute eosinophil counts, or eosinophil cationic protein levels.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Qin et al. 2017 Case-control study of 132 nonsmoking children in Taiwan aged 10–15 years with asthma and 168 age- and sex-matched controls without asthma	**Exposure:** Median serum PFBS 0.48 ng/mL in cases and 0.48 ng/mL in controls **Statistical adjustments:** Age, sex, BMI, parental education level, exercise, environmental tobacco smoke exposure, month of survey	No association between serum PFBS and asthma occurrence (OR 1.06, 95% CI 0.93–1.20). Among asthmatic children, no associations between PFBS and FVC (β 0.180, 95% CI -0.041–0.401), FEV_1 (β 0.096, 95% CI -0.106–0.297), PEF (β -0.205, 95% CI -0.904–0.494), or FEF_{25-75} (β 0.022, 95% CI -0.382–0.425). Among non-asthmatic children no associations between PFBS and FVC (β -0.010, 95% CI -0.122–0.102), FEV_1 (β -0.020, 95% CI -0.132–0.093), PEF (β -0.125, 95% CI -0.469–0.219), or FEF_{25-75} (β -0.081, 95% CI -0.305–0.143).
Zhu et al. 2016 Case-control study of 231 asthmatic and 225 non-asthmatic children from Taiwan (9–16 years old); this is the same group of children evaluated by Dong et al. (2013)	**Exposure:** Mean serum levels PFBS 0.48 ng/mL in non-asthmatics and 0.53 ng/mL in asthmatics **Multivariate logistic regression model adjustments:** Age, sex, parental education, BMI, environmental tobacco smoke exposure, month of survey The study examined associations between exposure to perfluoroalkyl compounds and T-lymphocyte-related immunological markers of asthma; sex differences also examined	Significant association between serum PFBS and risk of asthma in male children with serum PFBS levels in the 4^{th} quartile (OR 2.59, 95% CI 1.14–5.87); no association in females. Significant association between serum PFBS and serum T-helper 2 lymphocyte cytokine IL-5 (p=0.023 for trend). No significant associations (p>0.05 for trend) with T-helper 1 lymphocyte cytokines IFN-γ or IL-2, T-helper 2 lymphocyte cytokine IL-4, or IgE levels. Asthmatic children had significantly higher serum levels of IgE, IL-4, and IL-5 and lower levels of IFN-γ and IL-2 than non-asthmatic children.

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFDoDA		
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15) living in Taiwan	**Exposure:** Summary serum PFDoDA values not provided for the full cohort; mean serum PFDoDA levels were 5.8 and 4.5 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	Significant increases in odds of having asthma were observed for children with serum PFDoDA levels in the 4th quartile (OR 1.81, 95% CI 1.02–3.23), as compared to those in 1st quartile. Significant association between serum PFDoDA and asthma severity score was found (p=0.024 for trend). Among asthmatic children, significant associations between serum PFDoDA and IgE (p=0.016), absolute eosinophil counts (p=0.011), and eosinophil cationic protein levels (p=0.003). In non-asthmatic children, significant association (p=0.001) between serum PFDoDA and eosinophil cationic protein levels. No significant (p>0.05) associations with IgE or absolute eosinophil counts.
Goudarzi et al. 2016a Prospective study of 1,558 4-year-old children participating in the Hokkaido Study on Environment and Children's Health Study in Japan	**Exposure:** Mean maternal plasma PFDoDA 0.191 ng/mL (range of <0.1–0.729 ng/mL) (measured at 28–32 weeks of gestation) **Statistical adjustments:** Maternal age, education, parental allergic history, number of older siblings, breastfeeding, daycare attendance, external tobacco smoke, child's sex	Inverse association between maternal plasma PFDoDA and prevalence of allergic disease (defined as cases with at least one of the following symptoms: eczema, wheezing, or rhinoconjuctivitis) (p=0.008 for trend); OR (95% CI): 2nd quartile: 0.735 (0.540–0.999) 3rd quartile: 0.810 (0.597–1.09) 4th quartile: 0.621 (0.454–0.847). No association between maternal plasma PFDoDA and prevalence of wheezing (p=0.794 for trend); OR (95% CI): 2nd quartile: 0.962 (0.659–1.40) 3rd quartile: 1.12 (0.778–1.63) 4th quartile: 0.999 (0.684–1.45).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Goudarzi et al. 2017b Prospective cohort study of 1,558 participants in the Hokkaido Study on Environmental and Children's Health; children were monitored for physician-diagnosed infectious disease up to 4 years of age	**Exposure:** mean maternal serum PFDoDA level (measured at 28–32 weeks of gestation) 0.191 ng/mL **Statistical adjustments:** Maternal age, number of older siblings, maternal smoking during pregnancy, maternal education, infant sex, breastfeeding period	No significant associations between maternal serum PFDoDA and risk of total infectious diseases in early life OR 1.07 (95% CI 0.790–1.46) for 4th quartile, p=0.502 for trend. Similar results were observed when males and females were analyzed separately.
Kielsen et al. 2016 Prospective study of 12 adults in Denmark administered a booster vaccine for tetanus and diphtheria; antibody concentrations were measured 4- and 10-days post-vaccination	**Exposure:** Median serum PFDoDA 0.039 ng/mL **Logistic regression model adjustments:** Sex, age	Significant inverse associations (unadjusted results, adjusting for sex and age showed similar results but were not reported) between serum PFDoDA and change in diphtheria (p=0.038) or tetanus (p=0.038) antibody levels.
Okada et al. 2014 Prospective study of 2,603 infants whose mothers participated in the Hokkaido Study on Environment and Children's Health Study; mothers completed questionnaires regarding infant allergic disease, infectious diseases, and other diseases when infants were 12 and 24 months of age	**Exposure:** Maternal mean plasma PFDoDA (measured between 28 and 32 weeks of gestation) 0.188 ng/mL (range: <0.1–0.729 ng/mL) **Statistical adjustments:** Maternal age, education, parental allergic history, infant sex, breastfeeding, number of siblings, daycare attendance, environmental tobacco smoke exposure in infants at 24 months	Significant inverse association between maternal PFDoDA levels and risk of allergic diseases was observed in female infants (4th PFDoDA quartile OR 0.58, 95% CI 0.39–0.85), but not in male infants (OR 0.93, 95% CI 0.65–1.34). No significant association between maternal PFDoDA levels and risk of eczema was observed in the infants; 4th PFOA quartile OR (1.00, 95% CI 0.64–1.55) for males and OR (0.73, 95% CI 0.45–1.18) for females.
Smit et al. 2015 Retrospective study of 1,024 children whose mothers participated in the INUENDO cohort in Greenland (n=532) and Ukraine (n=492); parents completed questionnaires when the children were 5–9 years of age	**Exposure:** Maternal mean serum PFDoDA levels (measured at any time during pregnancy) 0.04 and 0.13 ng/mL for Ukraine and Greenland cohorts, respectively **Statistical adjustments:** Unclear whether ORs were adjusted in the single variate analyses	No significant associations between maternal serum PFDoDA and the risk in the combined cohort of ever having asthma (OR 1.03, 95% CI 0.81–1.30), ever having eczema (OR 0.90, 95% CI 0.75–1.08), ever having wheezing (OR 0.97, 95% CI 0.80–1.16), currently wheezing (OR 0.87, 95% CI 0.64–1.18), or currently having eczema (OR 0.88, 95% CI 0.70–1.14).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHxA		
Dong et al. 2013 Case-control study of 231 asthmatic and 225 non-asthmatic children (aged 10–15) living in Taiwan	**Exposure:** Summary serum PFHxA values not provided for the full cohort; mean serum PFHxA levels were 0.3 and 0.2 ng/mL in the asthmatic and non-asthmatic children, respectively **Logistic regression model adjustments:** Sex, age, BMI, parental education, environmental tobacco smoke exposure, month of survey	No association between odds of having asthma and serum PFHxA levels observed (OR 1.60, 95% CI 0.90–2.86, 4th quartile). No association between serum PFHxA and asthma severity score was found (p=0.854 for trend). No associations (p>0.05) between serum PFHxA and IgE, absolute eosinophil counts, and eosinophil cationic protein levels were observed in asthmatic and non-asthmatic children.
Qin et al. 2017 Case-control study of 132 nonsmoking children in Taiwan aged 10–15 years with asthma and 168 age- and sex-matched controls without asthma	**Exposure:** Median serum PFHxA 0.20 ng/mL in cases and 0.18 ng/mL in controls **Statistical adjustments:** Age, sex, BMI, parental education level, exercise, environmental tobacco smoke exposure, month of survey	No association between serum PFHxA and asthma occurrence (OR 0.99, 95% CI 0.80–1.21). Among asthmatic children, no associations between PFHxA and FVC (β -0.047, 95% CI -0.128–0.035), FEV_1 (β -0.030, 95% CI -0.104–0.044), PEF (β 0.049, 95% CI -0.208–0.306), or FEF_{25-75} (β -0.124, 95% CI -0.181–0.115). Among non-asthmatic children no associations between PFHxA and FVC (β 0.035, 95% CI -0.040–0.111), FEV_1 (β 0.042, 95% CI -0.033–0.118), PEF (β 0.138, 95% CI -0.094–0.370), or FEF_{25-75} (β 0.077, 95% CI -0.074–0.288).

Table 10. Immunological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
FOSA		
Impinen et al. 2018 Prospective study of 641 infants participating in the Environment and Childhood Asthma study in Norway; health outcomes were evaluated at 2 and 10 years of age	**Exposure:** Mean cord FOSA level 0.4 ng/mL (range <0.05–2.3 ng/mL) **Logistic regression model adjustments:** Sex; Bonferroni correction for multiple comparisons	No significant associations between number of common colds from 0 to 2 years of age (p=0.477). Significant association between cord FOSA and number of lower respiratory tract infections from 0–10 years of age, β 0.10 (95% CI 0.06–0.14; p<0.0001). No associations (after Bonferroni correction) between cord FOSA and asthma diagnosis, current asthma, asthma ever, wheezing, rhinitis, rhinoconjuctivitis, or allergic sensitization.

BMI = body mass index; CI = confidence interval; FEF = forced expiratory flow; FEV_1 = forced expiratory volume in 1 second; FOSA = perfluorooctane sulfonamide; FVC = forced vital capacity; IFN-α-2 = interferon-α2; IFN-γ = interferon-γ; IgA = immunoglobulin A; IgE = immunoglobulin E; IL-4 = interleukin-4; IL-5 = interleukin 5; IP-10 = interferon-γ-inducible protein 10; IRR = incidence rate ratio; MCP-1 = monocyte chemoattractant protein-1; MIP-1a = macrophage inflammatory protein 1a; ND = not detected; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PCB = polychlorinated biphenyl; PEF = peak expiratory flow; PFBS = perfluorobutane sulfonic acid; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHpA = perfluoroheptanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; TNF-α = tumor necrosis factor-α; RR = rate ratio; TSLP = thymic stromal lymphopoietin

Table 11. Neurological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Gallo et al. 2013 Cross-sectional study of 21,024 older adults (>50 years; mean age 60.5 years) participating in the C8 Health Project	**Exposure:** Serum PFOA level • 1st quintile: 0.25–14.0 ng/mL • 2nd quintile: 14.1–27.0 ng/mL • 3rd quintile: 27.1–53.8 ng/mL • 4th quintile: 53.9–118.1 ng/mL • 5th quintile: 118.3–22,412 ng/mL **Statistical adjustments:** Age, race, sex, educational level, average household income, physical activity, alcohol consumption, cigarette smoking	A significant inverse association (trend p<0.001) between serum PFOA levels and self-reported memory loss was found; ORs (95% CI) were: • 2nd quintile: 0.88 (0.79–0.97) • 3rd quintile: 0.83 (0.75–0.92) • 4th quintile: 0.79 (0.71–0.88) • 5th quintile: 0.79 (0.71–0.88). When participants were categorized on diabetic status, there were significant differences in the OR for memory loss when diabetics were compared to nondiabetics (p=0.014) with higher OR in the diabetics.
Power et al. 2013 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,766 adults aged 60–<85 years	**Exposure:** Geometric mean serum PFOA level was 4.08 ng/mL **Statistical adjustments:** Age, race/ethnicity, sex, NHANES cycle, education, poverty-income ratio, food security, health insurance, social support, recreational physical activity, smoking, alcohol consumption	No significant association between doubling serum PFOA levels and self-reported limitation due to difficulty remembering or periods of confusion was found (OR 0.92, 95% CI 0.78–1.09). Categorizing subjects based on diabetic status, did not result in significant associations with serum PFOA (p>0.05).
Shrestha et al. 2017 Cross-sectional study of 126 older adults (aged 55–74 years) in New York	**Exposure:** Median serum PFOA 8.1 ng/mL (range of 0.6–42.7 ng/mL) **Statistical adjustments:** Age, sex, education, serum PCB	Association (p=0.03) between serum PFOA and performance on tests for memory and learning corresponding to a 6% higher mean score. Inverse association (p=0.04, p=0.03) between serum PFOA and performance on tests of executive function resulting in 16–18% less perseverative errors and responses. No association between serum PFOA and tests of visual and spatial function, reaction time, affective state, or motor function.
PFOS		
Gallo et al. 2013	**Exposure:** Serum PFOS level • 1st quintile: 0.25–14.4 ng/mL	A significant inverse association (trend p<0.001) between serum PFOS levels and self-

Table 11. Neurological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cross-sectional study of 21,024 older adults (>50 years; mean age 60.5 years) participating in the C8 Health Project	• 2nd quintile:14.5–20.4 ng/mL • 3rd quintile: 20.5–27.1 ng/mL • 4th quintile: 27.2–37.2 ng/mL • 5th quintile: 37.3–759.2 ng/mL **Statistical adjustments:** Age, race, sex, educational level, average household income, physical activity, alcohol consumption, cigarette smoking	reported memory loss was found; ORs (95% CI) were: • 2nd quintile: 0.96 (0.87–1.07) • 3rd quintile: 0.86 (0.78–0.96) • 4th quintile: 0.87 (0.78–0.96) • 5th quintile: 0.85 (0.76–0.94).
Power et al. 2013 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,766 adults aged 60–<85 years	**Exposure:** Geometric mean serum PFOS level was 22.63 ng/mL **Statistical adjustments:** Age, race/ethnicity, sex, NHANES cycle, education, poverty-income ratio, food security, health insurance, social support, recreational physical activity, smoking, alcohol consumption	No significant association between doubling serum PFOS levels and self-reported limitation due to difficulty remembering or periods of confusion was found (OR 0.90, 95% CI 0.78–1.03). When participants were categorized based on diabetic status, a significant inverse association was found between doubling serum PFOS levels and self-reported limitation due to difficulty remembering or periods of confusion in diabetics not using medication (OR 0.39, 95% CI 0.19–0.78). This association was not observed in diabetics taking medication or in nondiabetics (p>0.05).
Shrestha et al. 2017 Cross-sectional study of 126 older adults (aged 55–74 years) in New York	**Exposure:** Median serum PFOS 33.7 ng/mL (range of 5.3–217 ng/mL) **Statistical adjustments:** Age, sex, education, serum PCB	Association between serum PFOS and tests of visual reproduction delayed recall (p=0.04) resulting in 11% higher scores and tests of visual and spatial function (p=0.05) resulting in 8% higher mean score. No association between serum PFOS and tests of executive function, reaction time, affective state, or motor function.

Table 11. Neurological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHxS		
Gallo et al. 2013 Cross-sectional study of 21,024 older adults (>50 years; mean age 60.5 years) participating in the C8 Health Project	**Exposure:** Serum PFHxS level • 1st quintile: 0.25–1.7 ng/mL • 2nd quintile: 1.8–2.6 ng/mL • 3rd quintile: 2.7–3.6 ng/mL • 4th quintile: 3.7–5.6 ng/mL • 5th quintile: 5.7–232.6 ng/mL **Statistical adjustments:** Age, race, sex, educational level, average household income, physical activity, alcohol consumption, cigarette smoking	A significant inverse association (trend p=0.009) between serum PFHxS levels and self-reported memory loss was found; ORs (95% CI) were: • 2nd quintile: 1.01 (0.91–1.12) • 3rd quintile: 1.02 (0.91–1.13) • 4th quintile: 0.93 (0.84–1.04) • 5th quintile: 0.89 (0.79–0.99).
Power et al. 2013 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,766 adults aged 60–<85 years	**Exposure:** Geometric mean serum PFHxS level was 2.05 ng/mL **Statistical adjustments:** Age, race/ethnicity, sex, NHANES cycle, education, poverty-income ratio, food security, health insurance, social support, recreational physical activity, smoking, alcohol consumption	No significant association between doubling serum PFHxS levels and self-reported limitation due to difficulty remembering or periods of confusion was found (OR 0.93, 95% CI 0.82–1.06). When participants were categorized based on diabetic status, a significant inverse association was found between doubling serum PFOS levels and self-reported limitation due to difficulty remembering or periods of confusion in diabetics not using medication (OR 0.49, 95% CI 0.29–0.84). This association was not observed in diabetics taking medication or in nondiabetics (p>0.05).

Table 11. Neurological Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFNA		
Gallo et al. 2013 Cross-sectional study of 21,024 older adults (>50 years; mean age 60.5 years) participating in the C8 Health Project	**Exposure:** Serum PFNA level • 1st quintile: 0.25–0.90 ng/mL • 2nd quintile: 1.0–1.2 ng/mL • 3rd quintile: 1.3–1.4 ng/mL • 4th quintile: 1.5–1.9 ng/mL • 5th quintile: 2.0–28.6 ng/mL **Statistical adjustments:** Age, race, sex, educational level, average household income, physical activity, alcohol consumption, cigarette smoking	A significant inverse association (trend p=0.053) between serum PFNA levels and self-reported memory loss was found; ORs (95% CI) were: • 2nd quintile: 0.86 (0.78–0.96) • 3rd quintile: 0.87 (0.77–0.98) • 4th quintile: 0.86 (0.77–0.95) • 5th quintile: 0.89 (0.80–0.99).
Power et al. 2013 Cross-sectional study utilizing 1999–2000 and 2003–2008 NHANES data for 1,766 adults aged 60–<85 years	**Exposure:** Geometric mean serum PFNA level was 1.01 ng/mL **Statistical adjustments:** Age, race/ethnicity, sex, NHANES cycle, education, poverty-income ratio, food security, health insurance, social support, recreational physical activity, smoking, alcohol consumption	No significant association between doubling serum PFNA levels and self-reported limitation due to difficulty remembering or periods of confusion was found (OR 0.91, 95% CI 0.79–1.04). When participants were categorized based on diabetic status, a significant inverse association was found between doubling serum PFOS levels and self-reported limitation due to difficulty remembering or periods of confusion in diabetics not using medication (OR 0.43, 95% CI 0.21–0.87). This association was not observed in diabetics taking medication or in nondiabetics (p>0.05).

CI = confidence interval; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PCB = polychlorinated biphenyl; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Costa et al. 2009	**Exposure:** Mean and median serum PFOA levels measured in 2007 were 12,930 and 5,710 ng/mL (range: 200–	Serum testosterone and estradiol levels were outside of the reference range in 5.1 and 2.6%, respectively, of the workers.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cohort study of 53 current (n=37) and former (n=16) male workers at a perfluoroalkyl manufacturing facility in Italy undergoing annual health examinations from 1978–2007; a control group of 107 male workers with no exposure to PFOA was also examined	47,040 ng/mL) in current workers and 6,810 and 4,430 ng/mL (range: 530–18,660 ng/mL) in former workers. Mean and median serum PFOA levels decreased over time; the mean levels were 18,800 ng/mL in 2000 and 11,600 ng/mL in 2007; the median levels were 11,920 and 3,890 ng/mL during those same times. **Regression model adjustments:** Age, years of exposure, year of PFOA sampling, BMI, smoking, alcohol consumption	
Gilliland 1992 Cross-sectional study of 115 (79% male) current workers employed at a PFOA production facility in Cottage Grove, Minnesota between 1985 and1989; this is same cohort examined by Gilliland and Mandell (1996)	**Exposure:** Serum fluorine levels were used as surrogate for serum PFOA; workers were categorized into five exposure groups based on serum fluorine levels: <1, 1–3, >3–10, >10–15, and >15–26 ppm **Regression model adjustments:** Age, BMI, alcohol use, tobacco use	Inverse associations between serum fluorine levels and bound testosterone (β -148, p=0.05), and free testosterone (β -3.56, p=0.03). Associations between serum fluorine levels and estradiol levels (β 0.03, p=0.03) and prolactin levels (β 1.43, p=0.0002). No association between serum fluorine levels and LH levels (β 0.001, p=0.93) or FSH levels (β0.004, p=0.91)
Olsen et al. 1998b Cross-sectional study of male workers employed at a PFOA production facility in Cottage Grove, Minnesota; health surveys were conducted in 1993 (n=111) and 1995 (n=80); 68 workers participated in both surveys	**Exposure:** Ranges of serum PFOA levels were 0–80,000 ng/mL in 1993 (80,000 ng/mL was the upper limit of detection) and 0–115,000 ng/mL in 1995; workers were categorized into four groups based on PFOA levels of 0–<1,000, 1,000–<10,000, 10,000–<30,000, and ≥30,000 ng/mL **Multivariable regression modeling adjustments:** Age, BMI, alcohol use, cigarette use	Significant associations between serum PFOA and reproductive hormone levels was limited to a significant association with prolactin in 1993 (p=0.01 for trend), which was due to a significantly higher level in the 10,000–<30,000 ng/mL group only; no significant association was found in 1995 (p=0.58 for trend). No significant associations between serum PFOA in 1993 or 1995 and levels of estradiol (p=0.66 and p=0.56 for trend), 17-HP (p=0.21 and p=0.18 for trend), or bound (p=0.07 and 0.85 for trend) or free (p=0.15 or p=0.82 for trend) testosterone.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Sakr et al. 2007b Cross-sectional study of 1,025 male (76%) and female (24%) workers at a fluoropolymers production plant (Washington Works)	**Exposure:** Median serum PFOA concentrations were 490 ng/mL (range: 17.4–9,550 ng/mL), 176 (8.1–2,070 ng/mL), 195 ng/mL (8.6–2,590 ng/mL), and 114 ng/mL (4.6–963 ng/mL) among current workers (n=259), current workers with intermittent exposure (n=160), past occupational exposure to PFOA (n=264), or never assigned to APFO area (n=342), respectively. The mean and median concentrations in all workers were 428 and 189 ng/mL, respectively. **Linear regression model adjustments:** Age, sex, BMI, alcohol consumption, heart attack in a parent (lipid models only)	Association between serum PFOA levels and estradiol (regression coefficient 22.3, p=0.017) and testosterone (regression coefficient 0.6, p=0.034) levels in males.
Dhingra et al. 2016a Retrospective study of 8,759 women (age >40 years) participating in the C8 Science Panel study; follow-up began in 1951 or age 40 (whichever was later)	**Exposure:** Cumulative exposure was estimated based on modeled serum PFOA levels (estimated using environmental fate and transport data, historical air and water PFOA concentrations, and PBPK modeling) **Statistical adjustments:** Smoking status, education, parity	No significant association between estimated cumulative PFOA exposure and age of natural menopause was found; the HRs (5th quintile, >2,130 ng/mL x year) were 1.11 (95% CI 0.97–1.26, p=0.14) in a subcohort excluding women with hysterectomies and 1.06 (95% CI 0.93–1.21, p=0.40) in hysterectomy censored analysis. No significant associations between 5-year (p=0.45), 10-year (p=0.58), 15-year (p=0.57), or 20-year (p=0.20) lagged estimated cumulative PFOA exposure and risk of early menopause were found in the subcohort that excluded hysterectomies. Similarly, no associations were found in the hysterectomy censored analysis (5-year lag p=0.58, 10-year lag p=0.66, 15-year lag p=0.60, 20-year lag p=0.17).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Dhingra et al. 2016a Prospective study of 3,334 women (age >40 years, all were premenopausal at study enrollment) participating in the C8 Science Panel study; follow-up began in 2005–2006 or age 40 (whichever was later)	**Exposure:** Cumulative PFOA exposure was estimated using historical air and water PFOA concentrations, environmental fate and transport data, and PBPK modeling; measured PFOA levels were based on blood samples collected in 2005–2006 **Statistical adjustments:** Smoking status, education, parity	No significant association between estimated cumulative PFOA exposure and age of natural menopause was found; the HRs (5th quintile, >4,670 ng/mL x year) were 1.10 (95% CI 0.84–1.43, p=0.51) in a subcohort excluding women with hysterectomies (trend p=0.63) and 1.10 (95% CI 0.85–1.44, p=0.47) in hysterectomy censored analysis (trend p=0.61). No significant association between measured PFOA levels and age of natural menopause was found; the HRs (5th quintile, >80.8 ng/mL) were 1.12 (95% CI 0.86–1.45, p=0.40) in a subcohort excluding women with hysterectomies (trend p=0.20) and 1.14 (95% CI 0.88–1.47, p=0.33) in hysterectomy censored analysis (trend p=0.19).
Knox et al. 2011b Cross-sectional study of 25,957 women (>18 years of age) participating in C8 Health Project; childbearing group (n=13,458; 18–≤42 years of age), perimenopausal group (n=5,782; >42–≤51 years of age), menopausal group (n=6,717, >51–≤65 years of age)	**Exposure:** Median serum PFOA levels in childbearing, perimenopausal, and menopausal groups: 16.7, 23.4, and 32.5 ng/mL • 1st quintile: 0.25–11.2 ng/mL • 2nd quintile: 11.3–19.8 ng/mL • 3rd quintile: 19.9–36.7 ng/mL • 4th quintile: 36.8–84.9 ng/mL • 5th quintile: 85.0–22,412.0 ng/mL **Logistic regression model adjustments:** Smoking, age, BMI, alcohol consumption, regular exercise	Increased odds of experiencing menopause were observed; the ORs (95% CI) were: Menopausal group • 2nd quintile: 1.5 (1.1–2.1) • 3rd quintile: 1.6 (1.2–2.2) • 4th quintile: 1.4 (1.1–1.9) • 5th quintile: 1.7 (1.3–2.3) Perimenopausal group • 2nd quintile: 1.4 (1.1–1.8) • 3rd quintile: 1.2 (0.9–1.6) • 4th quintile: 1.4 (1.1–1.9) • 5th quintile: 1.4 (1.1–1.8) No significant associations (p>0.05) between serum PFOA and estradiol concentration were observed in the perimenopausal and menopausal groups.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Bach et al. 2015a Cross-sectional study of 1,372 nulliparous women in the Aarhus Birth Cohort in Denmark; infertility defined as TTP of >12 months or infertility treatment before current pregnancy	**Exposure:** Median serum PFOA levels (measured between gestation week 9 and 20): 2.0 ng/mL **Statistical adjustments:** Maternal age at delivery, prepregnancy BMI, maternal education	No differences in fecundability were observed; the fecundability ratio was 1.00 (95% CI 0.99–1.01) per 0.1 ng/mL PFOA. No significant association between serum PFOA and the risk of infertility was observed; OR 1.00 (95% CI 0.98–1.01) per 0.1 ng/mL PFOA.
Bach et al. 2015c, 2015d Cross-sectional study of 440 women participating in the Danish National Birth Cohort women served as controls in the Liew et al. (2014) case-control study	**Exposure:** Median serum PFOA (measured in first or second trimester): 4.0 ng/mL • 1st quartile: 0.6–3.0 ng/mL • 2nd quartile: 3.1–4.0 ng/mL • 3rd quartile: 4.1–5.52 ng/mL • 4th quartile: 5.6–7.7 ng/mL **Statistical adjustments:** Age, prepregnancy BMI, socio-occupational status, parity	No significant associations between serum PFOA and fecundability ratios was found; OR for the 4th quartile was 0.86 (95% CI 0.63–1.19). No significant association between serum PFOA and risk of infertility (TTP >12 months or infertility treatment); OR for the 4th quartile was 1.67 (95% CI 0.70–4.00). When participants were stratified by parity, no significant associations were found between serum PFOA and fecundability ratio for parous women (4th quartile OR 0.74, 95% CI 0.48–1.13) or nulliparous women (4th quartile OR 0.99, 95% CI 0.64–1.54). No significant association between serum PFOA and risk of infertility (TTP >12 months or infertility treatment) in parous women (4th quartile OR 1.74, 95% CI 0.46–6.55) or nulliparous women (4th quartile OR 1.56, 95% CI 0.55–4.42).
Bach et al. 2015c, 2015d Cross-sectional study of 1,161 women participating in the Danish National Birth Cohort; women were also examined in the Fei et al. (2009) study	**Exposure:** Median serum PFOA (measured during pregnancy): 5.4 ng/mL • 1st quartile: 0.5–4.0 ng/mL • 2nd quartile: 4.1–5.4 ng/mL • 3rd quartile: 5.4–7.1 ng/mL • 4th quartile: 7.2–41.5 ng/mL **Statistical adjustments:** Age, prepregnancy BMI, socio-occupational status, parity	Significant inverse associations between serum PFOA and fecundability ratios were found; OR (95% CI): • 2nd quartile: 0.78 (0.65–0.94) • 3rd quartile: 0.83 (0.69–1.00) • 4th quartile: 0.74 (0.60–0.90) Significant associations between serum PFOA and risk of infertility (TTP >12 months or infertility treatment); OR (95% CI): • 2nd quartile: 1.91 (1.16–3.13)

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		• 3rd quartile: 1.43 (0.85–2.40) • 4th quartile: 2.07 (1.24–3.48) When participants were stratified by parity, significant associations were found between serum PFOA and fecundability ratio for parous women; OR (95% CI): • 2nd quartile: 0.76 (0.59–0.96) • 3rd quartile: 0.71 (0.56–0.90) • 4th quartile: 0.78 (0.61–0.99) Significant associations were also found among nulliparous women; OR (95% CI): • 2nd quartile: 0.93 (0.71–1.23) • 3rd quartile: 0.80 (0.71–1.07) • 4th quartile: 0.74 (0.56–0.98) Significant associations were found between serum PFOA and risk of infertility in parous women; OR (95% CI): • 2nd quartile: 2.30 (1.09–4.87) • 3rd quartile: 2.44 (1.17–5.07) • 4th quartile: 2.16 (1.02–4.56) No significant associations were also found among nulliparous women; OR (95% CI): • 2nd quartile: 0.75 (0.38–1.46) • 3rd quartile: 1.39 (0.75–2.61) • 4th quartile: 1.48 (0.80–2.75).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Barrett et al. 2015 Prospective study of 178 women participating in the Energy Balance and Breast Cancer Aspects study in Norway; subjects collected waking saliva samples every day for the duration of a single menstrual cycle	**Exposure:** Mean and median serum PFOA (measured at baseline): 3.61 and 3.36 ng/mL in nulliparous women and 2.31 and 2.03 ng/mL in parous women **Statistical adjustments:** Age, BMI, history of use of oral contraceptives, alcohol consumption, smoking, marital status, physical activity, parity	No significant associations (95% CI included unity) between serum PFOA levels and follicular estradiol or luteal progesterone levels in all women and when nulliparous and parous women were analyzed separately.
Buck Louis et al. 2012 Cross-sectional study of 473 women in Salt Lake City, Utah or San Francisco, California scheduled for laparoscopic or laparotomy surgery or served or served by the same clinic (190 and 283 were diagnosed with or without endometriosis, respectively) and a matched referent group of 127 women (14 and 113 with or without endometriosis, respectively); endometriosis was diagnosed by surgical visualization or pelvic MRI	**Exposure:** Geometric mean serum PFOA levels were 2.65 and 2.15 ng/mL in women in the clinic group with endometriosis or without endometriosis, and 2.49 and 2.3 ng/mL in women in the referent group with or without endometriosis **Statistical adjustments:** Age, BMI, parity	A significant association between serum PFOA and odds of endometriosis was observed in the clinic group when adjusted for age and BMI; OR 1.89 (95% CI 1.17–3.06), but was not significant when also adjusted for parity (OR 1.62, 95% CI 0.99–2.66). No significant association was found for the referent group (OR 1.28, 95% CI 0.35–4.62 when adjusted for age and BMI). Among the clinic group, serum PFOA was associated with an increased risk of moderate or severe endometriosis (stages 3 and 4), the age and BMI adjusted OR 2.58 (95% CI 1.18–5.64) and the age, BMI, and parity adjusted OR 1.86 (95% CI 0.81–4.24).
Buck Louis et al. 2013 Prospective study of 501 couples in Michigan and Texas participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Geometric mean serum PFOA levels in women and men who became pregnant were 3.112 and 5.016 ng/mL, respectively, and in women and men who withdrew or were not pregnant during followup were 3.101 and 4.749 ng/mL, respectively **Statistical adjustments:** Serum concentrations for other perfluoroalkyls, age, BMI, cotinine, site	No association between female or male serum PFOA concentration and fecundability odds ratio (OR 0.95, 95% CI 0.82–1.11 and OR 1.01, 95% CI 0.88–1.17, respectively).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Buck Louis et al. 2015 Cross-sectional study of 462 male partners in Michigan (n=96) and Texas (n=366) participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Median serum PFOA levels 4.6 ng/mL for Michigan site and 5.3 ng/mL for Texas site **Statistical adjustments:** Age, BMI, serum cotinine, abstinence, sample age, research site	Significant associations ($p<0.05$) with some sperm quality parameters: increased curvilinear velocity, increased percentage of sperm head acrosome area, and reduction of percentage of sperm with coiled tail. No significant association ($p>0.05$) with other sperm quality parameters including sperm viability, sperm count, and most parameters for sperm motility or sperm morphology.
Campbell et al. 2016 Cross-sectional study of 753 women aged 20–50 years participating in the 2003–2006 NHANES	**Exposure:** Geometric mean serum PFOA 3.48 ng/mL in women with endometriosis and 2.84 ng/mL in women without endometriosis; 1.80–2.69, 2.70–3.99, and 4.00–20.60 ng/mL, 2nd, 3rd, 4th quartile PFOA **Statistical adjustments:** Age, race, BMI, poverty income ratio, cotinine	Association between serum PFOA and self-reported endometriosis ($p=0.007$, for trend); OR (95% CI) 2nd quartile: 1.07 (0.20–5.78) 3rd quartile: 5.45 (1.19–25.04) 4th quartile: 1.33 (0.82–2.17).
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in North Carolina and attempting to conceive for ≤3 months	**Exposure:** Geometric mean serum PFOA 2.79 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	No association between serum PFOA and fertility; fecundability ratio of 1.15 (95% CI 0.66–2.01).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fei et al. 2009 Cohort study of 1,240 women enrolled in Danish National Birth Cohort; participants self-reported TTP	**Exposure:** Median plasma PFOA: at gestation week 12 was 5.6 ng/mL • 1st quartile: LLOQ–3.91 ng/mL • 2nd quartile: 3.91–5.20 ng/mL • 3rd quartile: 5.21–6.96 ng/mL • 4th quartile: ≥6.97 ng/mL **Logistic regression model adjustments:** Maternal age at delivery, parity, prepregnancy BMI, maternal socio-occupational status, paternal education, paternal age, alcohol consumption prior to pregnancy	Increased serum PFOA levels in women with longer TTP, as compared to women getting pregnant within 6 months (p<0.001). Increased infertility (TTP >12 months), OR (95% CI): • 2nd quartile: 2.06 (1.22–3.51) • 3rd quartile: 1.60 (0.93–2.78) • 4th quartile: 2.54 (1.47–4.29). Decreased fecundity (odds of successful conception) in three highest PFOA quartiles, OR (95% CI): • 2nd quartile: 0.72 (0.57–0.90) • 3rd quartile: 0.73 (0.58–0.92) • 4th quartile: 0.60 (0.47–0.76).
Fei et al. 2010 Cohort study of 1,347 women enrolled in Danish National Birth Cohort; participants self-reported breastfeeding duration 6 and 18 months after birth	**Exposure:** Plasma PFOA (at gestation weeks 4–14) • 1st quartile: LLOQ–3.90 ng/mL • 2nd quartile: 3.91–5.20 ng/mL • 3rd quartile: 5.21–6.96 ng/mL • 4th quartile: ≥6.97 ng/mL **Logistic regression model adjustments:** Maternal age at delivery, parity, prepregnancy BMI, maternal socio-occupational status, alcohol consumption prior to pregnancy, gestational age at blood draw	Increases in the risk of weaning before 3 or 6 months were observed at the three highest PFOA quartiles (OR, 95% CI): ≤3 months: • 2nd quartile: 1.98 (1.17–3.24) • 3rd quartile: 2.02 (1.21–3.38) • 4th quartile: 2.68 (1.02–1.15). ≤6 months: • 2nd quartile: 1.88 (1.31–2.72) • 3rd quartile: 2.22 (1.54–3.22) • 4th quartile: 2.60 (1.78–3.81). When the women were segregated by parity, the increase in risk of breastfeeding for <3 or 6 months was only found in the multiparous women.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fei et al. 2012 Re-analysis of data from Fei et al. (2009) stratified by parity		Increased infertility in parous women with three highest PFOA quartiles (p=0.01), OR (95% CI): • 2nd quartile: 3.39 (1.75–6.53) • 3rd quartile: 2.92 (1.44–5.93) • 4th quartile: 2.99 (1.28–6.98). No significant association between serum PFOA and infertility in nulliparous women (p=0.082). Significant inverse associations between serum PFOA and fecundity. Parous women (p=0.004), OR (95% CI): • 2nd quartile: 0.61 (0.46–0.80) • 3rd quartile: 0.62 (0.46–0.83) • 4th quartile: 0.63 (0.44–0.91). • Nulliparous women (p=0.002), OR (95% CI): • 2nd quartile: 0.98 (0.59–1.64) • 3rd quartile: 0.93 (0.56–1.54) • 4th quartile: 0.63 (0.39–1.04).
Joensen et al. 2009 Cross-sectional study of 105 young men (median age approximately 19 years) in Denmark; 53 men had high testosterone levels and 52 men had low testosterone levels	**Exposure:** Median serum PFOA: 4.9 ng/mL; median serum PFOS: 24.5 ng/mL	Significant decreases in percentage (p=0.030) and number (p=0.037) of morphologically normal spermatozoa in the high combined PFOA and PFOS group (adjusted for duration of abstinence). When PFOA and PFOS were analyzed separately, no significant associations were found with sperm parameters. No significant alterations (p>0.05) in reproductive hormone levels (testosterone, estradiol, SHBG, LH, FSH) or other sperm parameters (volume, concentration, total count, percent motile sperm).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Joensen et al. 2013 Cross-sectional study of 247 young men (median age 19.2 years) in Denmark	**Exposure:** Mean serum PFOA level was 3.46 ng/mL **Statistical adjustments:** BMI (hormone levels), smoking (hormone levels), abstinence time (sperm parameters)	No significant association ($p>0.05$) between serum PFOA levels and reproductive hormones (testosterone, free testosterone, free androgen index, LH, estradiol, SHBG, FSH, testosterone/LH ratio, free testosterone/LH ratio, and free androgen/LH ratio). No significant association ($p>0.05$) between serum PFOA levels and sperm parameters (volume, concentration, total count, progressively motile, morphologically normal).
Jørgensen et al. 2014a, 2014b Retrospective study of 938 women participating in the INUENDO cohort in Greenland (n=448), Ukraine (n=287), and Poland (n=203)	**Exposure:** Median serum PFOA: 1.65 ng/mL (full cohort), 1.83 ng/mL (Greenland), 2.67 ng/mL (Poland), 0.92 ng/mL (Ukraine) **Statistical adjustments:** Parity, gestational week of sampling, smoking status, maternal age, BMI	No significant association between serum PFOA levels and TTP; the fecundability ratios were 1.04 (95% CI 0.87–1.25) for the full cohort, 0.97 (95% CI 0.73–1.27) for Greenland, 1.21 (95% CI 0.79–1.84) for Poland, and 1.20 (0.87–1.67) for Ukraine. Sensitivity analysis restricted to primiparous women, found significant associations between serum PFOA levels and fecundability ratios (1.31, 95% CI 1.03–1.68 for full cohort and 1.46, 95% CI 1.02–2.08 for Ukraine cohort); these results suggest a shorter TTP is association with higher serum PFOA levels. No significant association between serum PFOA levels and risk of infertility (TTP >13 months); OR 1.11 (95% CI 0.74–1.66) for the full cohort, 1.20 (95% CI 0.61–2.37) for Greenland, 1.11 (95% CI 0.44–2.80) for Poland, and 0.79 (0.40–1.54) for Ukraine.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kvist et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=161, median age 30.9 years), Poland (n=122, 30.3 years), and Ukraine (n=131, 26 years)	**Exposure:** Respective mean serum PFOA in Greenland, Poland, and Ukraine groups: 4.84, 5.19, and 1.91 ng/mL **Statistical adjustments:** Age, abstinence time, alcohol intake, and serum levels of 2,2',4,4',5,5'-hexachlorobiphenyl	No significant association (p>0.05) was found between serum PFOA levels and sperm Y:X chromosome ratios in combined group.
Lum et al. 2017 Prospective study of 501 couples participating in the Longitudinal Investigation of Fertility and the Environment Study in Michigan and Texas	**Exposure:** Median serum PFOA of 3.1, 3.5, and 3.1 ng/mL in women with menstrual cycles of ≤24 days, 25–31 days, or ≥32 days; and 2.50–4.10 and ≥4.20 ng/mL for 2nd and 3rd tertiles **Statistical adjustments:** Female age, BMI, and active smoking at enrollment	No association between serum PFOA and menstrual cycle length, OR (95% CI): 2nd tertile: 0.98 (0.95–1.01) 3rd tertile: 0.98 (0.96–1.00) No association between women's serum PFOA and probability of pregnancy OR (95% CI): 2nd tertile: 1.0 (0.7–1.5) 3rd tertile: 0.7 (0.5–1.1)
Lyngsø et al. 2014 Cross-sectional study of 1,623 pregnant women participating in the INUENDO cohort in Greenland (n=528), Ukraine (n=643), and Poland (n=452); self-reported information on menstrual cycle length	**Exposure:** Respective median serum PFOA in Greenland, Poland, Ukraine, and pooled groups: 1.8, 2.7, 1.0, and 1.5 ng/mL **Statistical adjustments:** Age at menarche, age at pregnancy, parity, prepregnancy BMI, smoking	A significant association between serum PFOA and the risk of a long menstrual cycle (OR 1.7, 95% CI 1.1–2.6). No associations with the risk of irregular menstrual cycle (≥7 days of variation) (OR 1.4, 95% CI 0.9–2.2) or short menstrual cycle (OR 0.7, 95% CI 0.3–1.5).
Raymer et al. 2012 Cross-sectional study of 256 men in Durham, North Carolina (mean age 41.6 years)	**Exposure:** Mean and median serum PFOA levels were 10.4 and 9.2 ng/mL **Statistical adjustments:** Age, period of abstinence, tobacco use	Serum PFOA levels were significantly correlated with LH (p=0.011) levels and free testosterone levels (p=0.015), but not with other reproductive hormone levels (p>0.05) (estradiol, prolactin, FSH, total testosterone). No significant associations (p>0.05) between semen parameters (volume, pH, concentration, motility) and serum PFOA levels were found.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Romano et al. 2016 Longitudinal cohort study of Prospective study of 336 women participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; women completed telephone surveys on breastfeeding practices every 3 months until breastfeeding was discontinued or the child's 3rd birthday	**Exposure:** Median maternal serum PFOA levels (measured at 16 weeks of gestation) 5.5 ng/mL • 1st quartile: <3.8 ng/mL • 2nd quartile: 3.8–5.4 ng/mL • 3rd quartile: 5.5–7.6 ng/mL • 4th quartile: >7.6 ng/mL **Multivariable Poisson regression adjustments:** Maternal age at delivery, household income, total weeks of prior breastfeeding, gestational age at blood draw, marital status, race, maternal serum cotinine during pregnancy, alcohol use during pregnancy	Significant association (trend p=0.003) between maternal serum PFOA and stopping any breastfeeding by 3 months; RR (95% CI): • 2nd quartile: 1.32 (0.92–1.88) • 3rd quartile: 1.63 (1.16–2.28) • 4th quartile: 1.77 (1.23–2.54). Significant association (trend p=0.038) between maternal serum PFOA and stopping any breastfeeding by 6 months; RR (95% CI): • 2nd quartile: 1.25 (0.96–1.62) • 3rd quartile: 1.38 (1.06–1.79) • 4th quartile: 1.41 (1.06–1.87).
Specht et al. 2012 Cross-sectional study of 604 male partners of pregnant women in Greenland (n=199, median age 30.6 years), Poland (n=197, 29.6 years), and Ukraine (n=208, 25.1 years)	**Exposure:** Respective median serum PFOA in Greenland, Poland, and Ukraine groups: 4.5, 4.8, and 1.3 ng/mL **Statistical adjustments:** Age, BMI, caffeinated drinks, cotinine, fever, spillage, abstinence time, genital infections, testicular disorders	No significant associations (p=0.39 for trend) between serum PFOA levels and SHBG levels. The investigators noted no consistent associations with testosterone, estradiol, FSH, or LH.
Taylor et al. 2014 Cross-sectional study of 2,151 women aged 20–65 years participating in NHANES 1999–2000 and 2003–2010	**Exposure:** Serum PFOA • 1st tertile: 0.07–2.5 ng/mL • 2nd tertile: >2.5–4.4 ng/mL • 3rd tertile: >4.4 mg/mL **Statistical adjustments:** Age, race/ethnicity, education, smoking status, parity	Significant association between serum PFOA and rate of menopause (HR 1.36, 95% CI 1.05–1.75 for comparisons between 1st and 3rd tertiles) and for hysterectomy (HR 1.83, 95% CI 1.31–2.56 for comparisons between 1st and 2nd tertiles); HR 2.81 (95% CI 2.12–3.71) for comparisons between 1st and 3rd tertiles.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Timmermann et al. 2017 Cross-sectional study of 1,130 woman participating in study of two birth cohorts (1997–2000, n=640 or 2007–2009, n=490) in the Faroe Islands	**Exposure:** Median maternal serum PFOA (measured between 34 and 36 weeks of gestation) 2.40 ng/mL **Statistical adjustments:** Maternal parity, age, prepregnancy BMI, pregnancy alcohol intake, pregnancy smoking, education, employment, cohort	Significant inverse association between maternal PFOA and duration of breastfeeding (β -1.3, 95% CI -1.9 to -0.7) and length of exclusive breastfeeding (β -0.5, 95% CI -0.7 to -0.3) in months with a doubling of serum PFOA levels. No significant differences in duration or exclusiveness between primiparous and multiparous women (p=0.45 and 0.55, respectively).
Toft et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=196, median age 31.3 years), Poland (n=189, 29.6 years), and Ukraine (n=203, 26.2 years)	**Exposure:** Median serum PFOA: 3.8 ng/mL **Statistical adjustments:** Age, abstinence time, spillage, smoking, urogenital infections, BMI, county	Significant association (p<0.05) between serum PFOA and the percent motile sperm in the whole cohort; the percentage of motile sperm was 19% higher in the 3rd tertile (>4.7 ng/mL), as compared to the 1st tertile. The strongest association was observed in the Greenland cohort (36%). No significant association (p>0.05) for the whole cohort for sperm concentration, volume, total count, or morphology.
Tsai et al. 2015 Cross-sectional study of 540 12–30-year-olds in Taiwan	**Exposure:** Geometric mean serum PFOA 2.74 ng/mL **Linear regression adjustments:** Age, sex, BMI, high fat diet	Significant inverse association between serum PFOA levels and SHBG (p<0.05 for trend) among females 12–17 years old. No significant associations (p>0.05 for trend) between serum PFOA and FSH or testosterone.
Vagi et al. 2014 Case-control study 52 women with polycystic ovary syndrome and 50 controls in California	**Exposure:** Geometric mean serum PFOA 4.1 ng/mL (cases) and 2.3 ng/mL (controls) **Logistic regression adjustments:** Age, BMI, race	Significant association between serum PFOA and risk of polycystic ovary syndrome; OR 6.93 (95% CI 1.79–29.92, p=0.003) for comparisons of the 3rd tertile to 1st tertile.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vélez et al. 2015 Cohort study of 1,743 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Median maternal serum PFOA (measured in first trimester) 1.7 ng/mL **Regression adjustments:** Gestational age at blood draw, maternal age, country of birth, education, household income, maternal and paternal smoking, prepregnancy BMI	Significant inverse association between serum PFOA and fecundability OR (longer TTP) 0.89 (95% CI 0.83–0.94, p<0.001). Significant association between serum PFOA and risk of infertility (TTP >12 months or infertility treatment) OR 1.31 (95% CI 1.11–1.53, p=0.001).
Vestergaard et al. 2012 Prospective study of 222 Danish nulliparous couples discontinuing birth control and followed for six menstrual cycles or until clinically recognized pregnancy; mean age of women was 26.6 years	**Exposure:** Median serum PFOA levels were 5.58 ng/mL in women with no pregnancy and 5.61 ng/mL in women becoming pregnant **Logistic regression model adjustments:** Female age, BMI, smoking habits, length of menstrual cycle, female diseases affecting fecundability, oligospermia	Serum PFOA concentrations did not differ between women becoming pregnant and those who did not (p=0.66). No association between serum PFOA above the median and the odds of not becoming pregnant within first six cycles; OR 1.21 (95% CI 0.67–2.18) No significant associations between serum PFOA and the fecundability ratio (monthly probability of conceiving); OR 1.18 (95% CI 0.78–1.78).
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFOA of 14.67 ng/mL in cases and 12.09 ng/mL in controls; 2nd and 3rd tertile PFOA >8.74–19.6 and >19.6–72.1 ng/mL **Statistical adjustments:** Age, BMI, household income, education	No association between serum PFOA and endometriosis-related infertility, OR (95% CI): 2nd tertile: 0.89 (0.50–1.59) 3rd tertile: 1.05 (0.58–1.91).
Whitworth et al. 2012b Case-control study of pregnant women enrolled in the Norwegian Mother and Child Cohort Study in 2003–2004; 416 subfecund women, 494 controls	**Exposure:** Median serum PFOA levels (blood samples measured at gestation week 17) were 2 and 2 ng/mL in the subfecund and control groups • 1st quartile: <1.66 ng/mL • 2nd quartile: 1.66–2.24 ng/mL • 3rd quartile: 2.25–3.02 ng/mL • 4th quartile: ≥3.02 ng/mL	Significant association (p<0.001 for trend) between serum PFOA levels and subfecundity (>12 months TTP); OR (95% CI: • 2nd quartile: 1.6 (1.1–2.3) • 3rd quartile: 2.2 (1.5–3.2) • 4th quartile: 2.0 (1.4–3.0) When stratified by parity, no significant association in primiparous women; OR 0.5 (95% CI 0.2–1.2) for 4th quartile. Significant association in parous women:

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	Logistic regression model adjustments: Maternal age, prepregnancy BMI, alcohol intake	• 2nd quartile: 1.5 (0.9–2.5) • 3rd quartile: 2.4 (1.4–4.1) • 4th quartile: 2.1 (1.0–4.4).
Whitworth et al. 2016 Retrospective study of 451 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum PFOA 2.8 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum PFOA and fecundability; OR 1.0 (0.90–1.2).
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFOA in boys and girls 0.5 and 0.5 ng/mL **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	No association between serum PFOA and testosterone levels in boys (β -0.0549, 95% CI -0.1186–0.0088) or girls (β -0.1627, 95% CI -0.1627–0.0233). An association between serum PFOA and estradiol levels in boys (β 0.0921, 95% CI 0.0186–0.1656), but not in girls (β 0.1015, 95% CI -0.0023–0.0033).
PFOS		
Olsen et al. 1998a Cross-sectional study of workers at two PFOS-based fluorochemical manufacturing facilities in Decatur, Alabama and Antwerp, Belgium. Workers were examined in 1995 (n=178) and 1997 (n=149); 61 workers participated in both years; hormone levels were only measured in 88 workers in 1995; this is the same cohort of workers as Olsen et al. (1999)	**Exposure:** 20–22% of the workers in Decatur and 14–24% in Antwerp had serum PFOS levels of >3,000 ng/mL; the mean PFOS levels in 1995 and 1997 were 2,440 and 1,960 ng/mL in Decatur and 1,930 and 1,480 ng/mL in Antwerp **Multivariable regression model adjustments:** Age, BMI, alcohol consumption, smoking	No significant association between serum PFOS and DHEAS (p=0.60), FSH (p=0.91), 17-hydroxyprogesterone (p=0.99), LH (p=0.69), prolactin (p=0.25), SHBG (p=0.77), or free or bound testosterone (p=0.90 and p=0.35) were found. A significant association was found for estradiol levels (p=0.01); however, this was due to one worker; when the worker was removed from the analysis, the association was no longer statistically significant (p=0.14).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Knox et al. 2011b Cross-sectional study of 25,957 women (>18 years of age) participating in C8 Health Project; childbearing group (n=13,458; 18–≤42 years of age), perimenopausal group (n=5,782; >42–≤51 years of age), menopausal group (n=6,717, >51–≤65 years of age)	**Exposure:** Median serum PFOS in childbearing, perimenopausal, and menopausal groups:16.7, 23.4, and 32.5 ng/mL • 1st quintile: 0.25–11.8 ng/mL • 2nd quintile: 11.9–17.0 ng/mL • 3rd quintile: 17.1–22.4 ng/mL • 4th quintile: 22.5–30.7 ng/mL • 5th quintile: 30.8–564.3 ng/mL **Logistic regression model adjustments:** Smoking, age, BMI, alcohol consumption, regular exercise	Increased odds of experiencing menopause were observed; the ORs (95% CI) were: Menopausal group • 2nd quintile: 1.5 (1.1–2.1) • 3rd quintile: 1.8 (1.3–2.5) • 4th quintile: 2.0 (1.5–2.6) • 5th quintile: 2.1 (1.6–2.8) Perimenopausal group • 2nd quintile: 1.2 (0.9–1.5) • 3rd quintile: 1.1 (1.1–1.8) • 4th quintile: 1.4 (1.1–1.8) • 5th quintile: 1.4 (1.1–1.8) Serum PFOS was inversely associated with estradiol concentration in perimenopausal (p<0.0001) and menopausal (p=0.007) groups.
Bach et al. 2015a Cross-sectional study of 1,372 nulliparous women in the Aarhus Birth Cohort in Denmark; infertility defined as TTP of >12 months or infertility treatment before current pregnancy	**Exposure:** Median serum PFOS levels (measured between gestation week 9 and 20): 8.3 ng/mL **Statistical adjustments:** Maternal age at delivery, prepregnancy BMI, maternal education	No differences in fecundability were observed; the fecundability ratio was 1.00 (95% CI 1.00–1.00) per 0.1 ng/mL PFOS. No significant association between serum PFOS and the risk of infertility was observed; OR 1.00 (95% CI 0.99–1.00) per 0.1 ng/mL PFOS.
Bach et al. 2015c, 2015d Cross-sectional study of 440 women participating in the Danish National Birth Cohort; women served as controls in the Liew et al. (2014) case-control study	**Exposure:** Group 1: Median serum PFOS (measured in first or second trimester): 27.9 ng/mL • 1st quartile: 5.6–21.0 ng/mL • 2nd quartile: 21.1–27.8 ng/mL • 3rd quartile: 27.9–36.2 ng/mL • 4th quartile: 36.3–103.8 ng/mL **Statistical adjustments:** Age, prepregnancy BMI, socio-occupational status, parity	No significant associations between serum PFOS and fecundability ratios was found; OR for the 4th quartile was 0.96 (95% CI 0.75–1.24). No significant association between serum PFOS and risk of infertility (TTP >12 months or infertility treatment); OR for the 4th quartile was 1.03 (95% CI 0.54–2.00). When participants were stratified by parity, no significant associations were found between serum PFOS and fecundability ratio for parous women (4th quartile OR 1.04, 95% CI 0.70–1.55)

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		or nulliparous women (4th quartile OR 0.97, 95% CI 0.62–1.51). No significant association between serum PFOS and risk of infertility (TTP >12 months or infertility treatment) in parous women (4th quartile OR 0.70, 95% CI 0.16–3.11) or nulliparous women (4th quartile OR 1.23, 95% CI 0.452–3.39).
Bach et al. 2015c, 2015d Cross-sectional study of 1,161 women participating in the Danish National Birth Cohort; women were also examined in the Fei et al. (2009) study	**Exposure:** Median serum PFOS (measured during pregnancy): 34.2 ng/mL • 1st quartile: 6.4–26.90 ng/mL • 2nd quartile: 27.0–34.2 ng/mL • 3rd quartile: 34.3–43.8 ng/mL • 4th quartile: 43.9–106.7 ng/mL **Statistical adjustments:** Age, prepregnancy BMI, socio-occupational status, parity	Significant inverse associations between serum PFOS and fecundability ratios were found; OR (95% CI): • 2nd quartile: 0.79 (0.66–0.95) • 3rd quartile: 0.78 (0.65–0.95) • 4th quartile: 0.78 (0.65–0.94). Significant associations between serum PFOS and risk of infertility (TTP >12 months or infertility treatment); OR (95% CI): • 2nd quartile: 1.65 (1.01–2.68) • 3rd quartile: 1.85 (1.13–3.02) • 4th quartile: 1.89 (1.16–3.08). When participants were stratified by parity, no consistent significant associations were found between serum PFOS and fecundability ratio for parous women; OR (95% CI): • 2nd quartile: 0.88 (0.69–1.12) • 3rd quartile: 0.72 (0.56–0.94) • 4th quartile: 0.90 (0.70–1.14). Significant associations were found among nulliparous women; OR (95% CI): • 2nd quartile: 0.89 (0.68–1.17) • 3rd quartile: 0.68 (0.52–0.91) • 4th quartile: 0.69 (0.53–0.91).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		No consistent significant associations were found between serum PFOS and risk of infertility for parous women; OR (95% CI): • 2nd quartile: 1.44 (0.79–2.99) • 3rd quartile: 2.44 (1.23–4.85) • 4th quartile: 1.60 (0.78–3.28). Significant associations were found among nulliparous women; OR (95% CI): • 2nd quartile: 1.47 (0.74–2.91) • 3rd quartile: 2.71 (1.38–5.30) • 4th quartile: 2.11 (1.08–4.15).
Barrett et al. 2015 Prospective study of 178 women participating in the Energy Balance and Breast Cancer Aspects study in Norway; subjects collected waking saliva samples every day for the duration of a single menstrual cycle	**Exposure:** Mean and median serum PFOS (measured at baseline): 16.44 and 14.78 ng/mL in nulliparous women and 14.18 and 12.65 ng/mL in parous women **Statistical adjustments:** Age, BMI, history of use of oral contraceptives, alcohol consumption, smoking, marital status, physical activity, parity	A significant inverse association between serum PFOS levels and follicular estradiol levels (β -0.013, 95% CI -0.023 to -0.001) was observed. When women were categorized based on parity, a significant inverse association was only observed in nulliparous women (β -0.025, 95% CI -0.043 to -0.007). No significant association between serum PFOS and luteal progesterone levels (95% CI included unity) was found.
Buck Louis et al. 2012 Cross-sectional study of 473 women in Salt Lake City, Utah and San Francisco, California scheduled for laparoscopic or laparotomy surgery or served by the same clinic (190 and 283 were diagnosed with or without endometriosis, respectively) and a matched referent group of 127 women (14 and 113 women with or without endometriosis, respectively); endometriosis was diagnosed by surgical visualization or pelvic MRI	**Exposure:** Geometric mean serum PFOS levels were 7.20 and 6.11 ng/mL in women in the clinic group with endometriosis or without endometriosis, and 7.41 and 6.74 ng/mL in women in the referent group with or without endometriosis, respectively. **Statistical adjustments:** Age, BMI, parity	No significant associations (when adjusted for age and BMI) were found between serum PFOS and odds of endometriosis in the clinic group (OR 1.39 95% CI 0.98–1.98) or referent group (OR 1.29, 95% CI 0.48–3.45); also adjusting for parity did not change the outcome (OR 1.25, 95% CI 0.87–3.45 for the clinic group and OR 1.37, 95% CI 0.48–3.90 for the referent group). Among the clinic group, serum PFOS was associated with an increased risk of moderate or severe endometriosis (stages 3 and 4), the age and BMI adjusted OR 1.86 (95% CI 1.05–3.30) and the age, BMI, and parity adjusted OR 1.50 (95% CI 0.82–2.74).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Buck Louis et al. 2013 Prospective study of 501 couples in Michigan and Texas participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Geometric mean serum PFOS levels in women and men who became pregnant were 11.764 and 20.867 ng/mL, respectively, and woman and men who withdrew or were not pregnant during followup were 11.088 and 19.765 ng/mL, respectively **Statistical adjustments:** Serum concentrations for other perfluoroalkyls, age, BMI, cotinine, site	No association between female or male serum PFOS concentration and fecundability odds ratio (OR 0.99, 95% CI 0.85–1.17 and OR 0.96, 95% CI 0.80–1.15, respectively).
Buck Louis et al. 2015 Cross-sectional study of 462 male partners in Michigan (n=96) and Texas (n=366) participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Median serum PFOS levels 19.15 ng/mL for Michigan site and 21.6 ng/mL for Texas site **Statistical adjustments:** Age, BMI, serum cotinine, abstinence, sample age, research site	Significant association ($p<0.05$) between serum PFOS levels and increased distance sperm traveled. No significant association ($p>0.05$) with other sperm quality parameters including sperm viability, sperm count, sperm motility, or sperm morphology.
Campbell et al. 2016 Cross-sectional study of 753 women aged 20–50 years participating in the 2003–2006 NHANES	**Exposure:** Geometric mean serum PFOS 16.28 ng/mL in women with endometriosis and 13.36 ng/mL in women without endometriosis; 8.00–12.29, 12.30–18.19, and 18.20–392.00 ng/mL 2nd, 3rd, and 4th quartile PFOS **Statistical adjustments:** Age, race, BMI, poverty income ratio, cotinine	Association between serum PFOS and self-reported endometriosis ($p=0.003$, for trend); OR (95% CI) 2nd quartile: 1.89 (0.35–10.17) 3rd quartile: 3.56 (0.86–14.74) 4th quartile: 3.48 (1.00–12.00).
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in North Carolina and attempting to conceive for ≤3 months	**Exposure:** Geometric mean serum PFOS 9.29 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	No association between serum PFOS and fertility; fecundability ratio of 0.89 (CI 0.49–1.60).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fei et al. 2009 Cohort study of 1,240 women enrolled in Danish National Birth Cohort; participants self-reported TTP	**Exposure:** Median plasma PFOS: at gestation week 12 was 35.5 ng/mL • 1st quartile: 6.4–26.0 ng/mL • 2nd quartile: 26.1 to -33.3 ng/mL • 3rd quartile: 33.4–43.2 ng/mL • 4th quartile: ≥43.3 ng/mL **Logistic regression model adjustments:** Maternal age at delivery, parity, prepregnancy BMI, maternal socio-occupational status, paternal education, paternal age, alcohol consumption prior to pregnancy	Increased serum PFOS levels in women with longer TTP, as compared to women getting pregnant within 6 months (p<0.001). Increased infertility (TTP >12 months), OR (95% CI): • 2nd quartile: 1.70 (95% CI 1.01–2.86) • 3rd quartile: 2.34 (1.40–3.89) • 4th quartile: 1.77 (1.06–2.95) Decreased fecundity (odds of successful conception) in three highest PFOS quartiles, OR (95% CI): • 2nd quartile: 0.70 (0.56–0.87) • 3rd quartile: 0.67 (0.53–0.84) • 4th quartile: 0.74 (0.58–0.93).
Fei et al. 2010 Cohort study of 1,347 women enrolled in Danish National Birth Cohort; participants self-reported breastfeeding duration 6 and 18 months after birth	**Exposure:** Plasma PFOS (gestation weeks 4–14) • 1st quartile: 6.4–26.0 ng/mL • 2nd quartile: 26.1 to -33.3 ng/mL • 3rd quartile: 33.4–43.2 ng/mL • 4th quartile: ≥43.3 ng/mL **Logistic regression model adjustments:** Maternal age at delivery, parity, prepregnancy BMI, maternal socio-occupational status, alcohol consumption prior to pregnancy, gestational age at blood draw	Increases in the risk of weaning before 3 months or before 6 months were observed (OR, 95% CI): ≤3 months • 2nd quartile: 1.26 (0.78–2.0.3) • 3rd quartile: 1.26 (0.78–2.04) • 4th quartile: 1.89 (1.19–3.01) ≤6 months • 2nd quartile: 1.56 (1.10–2.22) • 3rd quartile: 1.54 (1.08–2.19) • 4th quartile: 2.07 (1.46–2.93) When the women were segregated by parity, the increase in risk of breastfeeding for <3 or 6 months was only found in the multiparous women with serum PFOS levels in the 2nd, 3rd, and 4th quartiles.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fei et al. 2012 Re-analysis of data from Fei et al. (2009) stratified by parity		No significant trend for increasing fertility with increasing serum PFOS levels (p=0.26) in parous women, although the ORs for the 2nd and 3rd quartiles were significant, OR (95% CI): • 2nd quartile: 2.07 (1.04–4.11) • 3rd quartile: 2.52 (1.24–5.13) • 4th quartile: 1.59 (0.75–3.37) Significant inverse associations between serum PFOS and infertility. Nulliparous women (p=0.036), OR (95% CI): • 2nd quartile: 1.37 (0.61–3.08) • 3rd quartile: 2.50 (1.16–5.37) • 4th quartile: 2.14 (1.00–4.60) No association between serum PFOS and fecundity was found in parous women (p=0.32). In nulliparous women, there was a significant inverse association between serum PFOS and fecundity (p=0.006), OR (95% CI): • 2nd quartile: 0.79 (0.54–1.16) • 3rd quartile: 0.63 (0.43–0.91) • 4th quartile: 0.60 (0.41–0.97).
Joensen et al. 2013 Cross-sectional study of 247 young men (median age 19.2 years) in Denmark	**Exposure:** Mean serum PFOS level was 8.46 ng/mL **Statistical adjustments:** BMI (hormone levels), smoking (hormone levels), abstinence time (sperm parameters)	Inverse association (p<0.05) between serum PFOS levels and testosterone, free testosterone, free androgen index, testosterone/LH ratio, free testosterone/LH ratio, and free androgen/LH ratio. No significant association (p>0.05) between serum PFOS and estradiol, SHBG, LH, or FSH levels. No significant association (p>0.05) between serum PFOS levels and sperm parameters (volume, concentration, total count, progressively motile, morphologically normal).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Jørgensen et al. 2014a, 2014b Retrospective study of 938 women participating in the INUENDO cohort in Greenland (n=448), Ukraine (n=287), and Poland (n=203)	**Exposure:** Median serum PFOS: 10.60 ng/mL (full cohort), 20.32 ng/mL (Greenland), 7.97 ng/mL (Poland), 4.93 ng/mL (Ukraine) **Statistical adjustments:** Parity, gestational week of sampling, smoking status, maternal age, BMI	No significant association between serum PFOS levels and TTP; the fecundability ratios were 0.90 (95% CI 0.76–1.07) for the full cohort, 0.83 (95% CI 0.64–1.07) for Greenland, 0.94 (95% CI 0.58–1.50) for Poland, and 1.06 (0.78–1.45) for Ukraine. No significant association between serum PFOS levels and risk of infertility (TTP >13 months); OR 1.39 (95% CI 0.93–2.07) for the full cohort, 1.74 (95% CI 0.97–3.13) for Greenland, 2.06 (95% CI 0.69–6.12) for Poland, and 0.77 (0.41–1.43) for Ukraine.
Kvist et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=161, median age 30.9 years), Poland (n=122, 30.3 years), and Ukraine (n=131, 26 years)	**Exposure:** Respective mean serum PFOS in Greenland, Poland, and Ukraine groups: 51.65, 12.12, and 8.20 ng/mL **Statistical adjustments:** Age, abstinence time, alcohol intake, serum levels of 2,2',4,4',5,5'-hexachlorobiphenyl	Positive association ($p<0.05$) between serum PFOS and sperm Y:X chromosome ratios in combined group. A significant negative trend (p=0.044) was found between categorized serum PFOS levels and sperm Y:X chromosome ratios in Greenland population.
Lum et al. 2017 Prospective study of 501 women participating in the Longitudinal Investigation of Fertility and the Environment Study in Michigan and Texas	**Exposure:** Median serum PFOS of 12.3, 12.6, and 11.5 ng/mL in women with menstrual cycles of ≤24, 25–31, or ≥32 days; 9.50–15.10 and ≥15.20 ng/mL for 2nd and 3rd tertiles **Statistical adjustments:** Female age, BMI, and active smoking at enrollment	No association between serum PFOS and menstrual cycle length, OR (95% CI) 2nd tertile: 1.01 (0.98–1.03 3rd tertile: 1.01 (0.98–1.03) No association between women's serum PFOS and probability of pregnancy OR (95% CI) 2nd tertile: 1.0 (0.7–1.5) 3rd tertile: 0.9 (0.6–1.3).
Lyngsø et al. 2014 Cross-sectional study of 1,623 pregnant women participating in the INUENDO cohort in Greenland (n=528), Ukraine (n=643), and Poland (n=452); self-reported information on menstrual cycle length	**Exposure:** Respective median serum PFOS in Greenland, Poland, Ukraine, and pooled groups: 20.2, 8.0, 5.0, and 8.0 ng/mL **Statistical adjustments:** Age at menarche, age at pregnancy, parity, prepregnancy BMI, smoking	No associations with the risk of irregular menstrual cycle (≥7 days of variation) (OR 1.0, 95% CI 0.6–1.6), short menstrual cycle (OR 0.7, 95% CI 0.3–1.5), or long menstrual cycle (OR 0.7, 95% CI 0.4–1.2).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Raymer et al. 2012 Cross-sectional study of 256 men in Durham, North Carolina (mean age 41.6 years)	**Exposure:** Mean and median serum PFOS levels were 37.4 and 32.3 ng/mL **Statistical adjustments:** Age, period of abstinence, tobacco use	No significant associations (p>0.05) between semen parameters (volume, pH, concentration, motility) or reproductive hormone levels (estradiol, prolactin, FSH, free testosterone, total testosterone, LH) and serum or sperm PFOS levels were found.
Romano et al. 2016 Longitudinal cohort study of Prospective study of 336 women participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; women completed telephone surveys on breastfeeding practices every 3 months until breastfeeding was discontinued or the child's 3rd birthday	**Exposure:** Median maternal serum PFOS levels (measured at 16 weeks of gestation) 13.9 ng/mL **Multivariable Poisson regression adjustments:** Maternal age at delivery, household income, total weeks of prior breastfeeding, gestational age at blood draw, marital status, race, maternal serum cotinine during pregnancy, alcohol use during pregnancy	No significant associations between maternal serum PFOS and stopping any breastfeeding by 3 months (trend p=0.065) or by 6 months (trend p=0.111).
Specht et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=199, median age 30.6 years), Poland (n=197, 29.6 years), and Ukraine (n=208, 25.1 years)	**Exposure:** Respective median serum PFOS in Greenland, Poland, and Ukraine groups: 44.7, 18.5, and 7.6 ng/mL **Statistical adjustments:** Age, BMI, caffeinated drinks, cotinine, fever, spillage, abstinence time, genital infections, testicular disorders	The investigators noted no consistent associations with testosterone, estradiol, FSH, LH, or SHBG.
Taylor et al. 2014 Cross-sectional study of 2,151 women aged 20–65 years participating in NHANES 1999–2000 and 2003–2010	**Exposure:** Serum PFOS • 1st tertile: 0.14–9 ng/mL • 2nd tertile: >9–18.4 ng/mL • 3rd tertile: >18.4 mg/mL **Statistical adjustments:** Age, race/ethnicity, education, smoking status, parity	No significant association between serum PFOS and rate of menopause (HR 1.16, 95% CI 0.91–1.48 for comparisons between 1st and 3rd tertiles). Significant association between serum PFOS and rate of hysterectomy (HR 1.44, 95% CI 1.12–1.85 for comparisons between 1st and 2nd tertiles; HR 2.56, 95% CI 1.90–3.43 for comparisons between 1st and 3rd tertiles).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Timmermann et al. 2017 Cross-sectional study of 1,130 woman participating in study of two birth cohorts (1997–2000, n=640 or 2007–2009, n=490) in the Faroe Islands	**Exposure:** Maternal serum PFOS (measured between 34 and 36 weeks of gestation) 19.47 ng/mL **Statistical adjustments:** Maternal parity, age, prepregnancy BMI, pregnancy alcohol intake, pregnancy smoking, education, employment, cohort	Significant inverse association between maternal PFOS and duration of breastfeeding (β -1.4, 95% CI -2.1 to -0.6) and length of exclusive breastfeeding (β -0.3, 95% CI -0.6 to -0.1) in months with a doubling of serum PFOS levels. No significant differences in duration or exclusiveness between primiparous and multiparous women (p=0.75 and 0.52, respectively).
Toft et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=196, median age 31.3 years), Poland (n=189, 29.6 years), and Ukraine (n=203, 26.2 years)	**Exposure:** Median serum PFOS: 18.4 ng/mL **Statistical adjustments:** Age, abstinence time, spillage, smoking, urogenital infections, BMI, county	Significant inverse association ($p<0.05$) between serum PFOS levels and the percentage of normal sperm cells in participants with serum PFOS levels in the 2nd and 3rd tertiles (>11.9 ng/mL); the percentage of normal sperm cells was 22 and 35% lower in the 2nd and 3rd tertiles than in the 1st tertile. Significant decrease in sperm concentration and total count were observed in the Polish cohort but was significant only in the second tertile. No significant association ($p>0.05$) for the whole cohort for sperm concentration, volume, total count, or percent motile sperm.
Tsai et al. 2015 Cross-sectional study of 540 12–30-year-olds in Taiwan	**Exposure:** Geometric mean serum PFOS 7.78 ng/mL **Linear regression adjustments:** Age, sex, BMI, high fat diet	Significant inverse association ($p<0.05$ for trend) between serum PFOS levels and FSH among males 12–17 years old and testosterone among females 12–17 years old. No significant associations ($p>0.05$ for trend) between serum PFOS and SHBG.
Vagi et al. 2014 Case-control study 52 women with polycystic ovary syndrome and 50 controls in California	**Exposure:** Geometric mean serum PFOS 8.2 ng/mL (cases) and 4.9 ng/mL (controls) **Logistic regression adjustments:** Age, BMI, race	Significant association between serum PFOS and risk of polycystic ovary syndrome; OR 5.79 (95% CI 1.58–24.12, p=0.005) for comparisons of the 3rd tertile to 1st tertile.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vélez et al. 2015 Cohort study of 1,743 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Median maternal serum PFOS (measured in first trimester) 4.7 ng/mL **Regression adjustments:** Gestational age at blood draw, maternal age, country of birth, education, household income, maternal and paternal smoking, prepregnancy BMI	No significant association between serum PFOS and fecundity odds ratio (longer TTP) 0.96 (95% CI 0.91–1.02, p=0.17). No significant association between serum PFOS and risk of infertility (TTP >12 months or infertility treatment) OR 1.14 (95% CI 0.98–1.34, p=0.09).
Vestergaard et al. 2012 Cross-sectional study of 222 Danish nulliparous couples discontinuing birth control and followed for six menstrual cycles or until clinically recognized pregnancy; mean age of women was 26.6 years	**Exposure:** Median serum PFOS levels were 35.75 ng/mL in women with no pregnancy and 36.29 ng/mL in women becoming pregnant **Logistic regression model adjustments:** Female age, BMI, smoking habits, length of menstrual cycle, female diseases affecting fecundability, oligospermia	Serum PFOS concentrations did not differ between women becoming pregnant and those who did not (p=0.29). No association between serum PFOS above the median and the odds of not becoming pregnant within first six cycles; OR 0.98 (95% CI 0.54–1.77). No significant associations between serum PFOS and the fecundability ratio (monthly probability of conceiving); OR 1.39 (95% CI 0.92–2.09).
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFOS of 6.40 ng/mL in cases and 6.60 ng/mL in controls; 2nd and 3rd tertile PFOS >4.70–9.36 and >9.36–138 ng/mL **Statistical adjustments:** Age, BMI, household income, education	No association between serum PFOS and endometriosis-related infertility, OR (95% CI): 2nd tertile: 1.11 (0.61–1.91) 3rd tertile: 0.66 (0.36–1.21).
Whitworth et al. 2012b Case-control study of pregnant women enrolled in the Norwegian Mother and Child Cohort Study in 2003–2004; 416 subfecund women (TTP >12 months), 494 controls	**Exposure:** Median serum PFOS levels (blood samples measured at gestation week 17) were 14 and 13 ng/mL in the subfecund and control groups • 1st quartile: <10.34 ng/mL • 2nd quartile: 10.34–13.09 ng/mL • 3rd quartile: 13.10–16.60 ng/mL • 4th quartile: ≥16.61 ng/mL	Significant association (p<0.001 for trend) between serum PFOS levels and subfecundity (>12 months TTP); OR (95% CI: • 2nd quartile: 1.3 (0.9–1.9) • 3rd quartile: 1.4 (1.0–2.0) • 4th quartile: 1.6 (1.1–2.3) When stratified by parity, no significant association in primiparous women; OR 0.7 (95% CI 0.4–1.3) for 4th quartile. Significant association in parous women:

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	Logistic regression model adjustments: Maternal age, prepregnancy BMI, alcohol intake	• 2nd quartile: 1.5 (0.9–2.5) • 3rd quartile: 1.5 (0.9–2.6) • 4th quartile: 2.1 (1.2–3.8)
Whitworth et al. 2016 Retrospective study of 451 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum PFOS 14.6 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum PFOS and fecundability; OR 1.00 (0.88–1.1).
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFOS in boys and girls 29.9 and 28.8 ng/mL, respectively **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	Inverse association between serum PFOS and testosterone levels in boys (β -0.0029, 95% CI -0.0055 to -0.0003), but not in girls (β 0.0005, 95% CI -0.0018–0.0028). No association between serum PFOS and estradiol levels in boys (β 0.0024, 95% CI -0.0007–0.0055) or girls (β 0.0005, 95% CI -0.0023–0.0033).
PFHxS		
Bach et al. 2015a Cross-sectional study of 1,372 nulliparous women in the Aarhus Birth Cohort in Denmark; infertility defined as TTP of >12 months or infertility treatment before current pregnancy	**Exposure:** Median serum PFHxS levels (measured between gestation week 9 and 20): 0.5 ng/mL **Statistical adjustments:** Maternal age at delivery, prepregnancy BMI, maternal education	No differences in fecundability were observed; the fecundability ratio was 1.00 (95% CI 0.99–1.01) per 0.1 ng/mL PFHxS. No significant association between serum PFHxS and the risk of infertility was observed; OR 0.98 (95% CI 0.93–1.03) per 0.1 ng/mL PFHxS.
Barrett et al. 2015 Prospective study of 178 women participating in the Energy Balance and Breast Cancer Aspects study in Norway; subjects collected waking saliva samples every day for the duration of a single menstrual cycle	**Exposure:** Mean and median serum PFHxS (measured at baseline): 1.22 and 1.05 ng/mL in nulliparous women and 1.65 and 0.71 ng/mL in parous women **Statistical adjustments:** Age, BMI, history of use of oral contraceptives, alcohol consumption, smoking, marital status, physical activity, parity	No significant associations (95% CI included unity) between serum PFHxS levels and follicular estradiol or luteal progesterone levels in all women and when nulliparous and parous women were analyzed separately.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Buck Louis et al. 2012 Cross-sectional study of 473 women in Salt Lake City, Utah and San Francisco, California scheduled for laparoscopic or laparotomy surgery or served by the same clinic (190 and 283 were diagnosed with or without endometriosis, respectively) and a matched referent group of 127 women (14 and 113 women with or without endometriosis, respectively); endometriosis was diagnosed by surgical visualization or pelvic MRI	**Exposure:** Geometric mean serum PFHxS levels were 0.48 and 0.43 ng/mL women in the clinic group with endometriosis or without endometriosis and 0.59 and 0.51 ng/mL in women in the referent group with or without endometriosis. **Statistical adjustments:** Age, BMI, parity	No significant associations (when adjusted for age and BMI) were found between serum PFHxS and odds of endometriosis in the clinic group (OR 1.14 95% CI 0.58–2.24) or referent group (OR 1.52, 95% CI 0.40–5.80); also adjusting for parity did not change the outcome (OR 0.85, 95% CI 0.42–1.73 for the clinic group and OR 1.65, 95% CI 0.41–6.61 for the referent group). Among the clinic group, there was no significant association between serum PFHxS with the risk of moderate or severe endometriosis (stages 3 and 4), the age and BMI adjusted OR 2.12 (95% CI 0.85–5.27) and the age, BMI, and parity adjusted OR 1.24 (95% CI 0.47–3.31).
Campbell et al. 2016 Cross-sectional study of 753 women aged 20–50 years participating in the 2003–2006 NHANES	**Exposure:** Geometric mean serum PFHxS 1.31 ng/mL in women with endometriosis and 1.23 ng/mL in women without endometriosis; 060–1.19, 1.20–2.19, 2.20–19.40 ng/mL 2nd, 3rd, 4th quartile PFHxS **Statistical adjustments:** Age, race, BMI, poverty income ratio, cotinine	No association between serum PFHxS and self-reported endometriosis (p=0.61, for trend); OR (95% CI) 2nd quartile: 1.74 (0.41–7.35) 3rd quartile: 1.70 (0.57–5.07) 4th quartile: 1.47 (0.40–1.41).
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in North Carolina and attempting to conceive for ≤3 months	**Exposure:** Geometric mean serum PFHxS 1.59 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	No association between serum PFHxS and fertility; fecundability ratio of 0.84 (95% CI 0.46–1.54).
Joensen et al. 2013 Cross-sectional study of 247 young men (median age 19.2 years) in Denmark	**Exposure:** Mean serum PFHxS level was 0.81 ng/mL; median serum PFHxS: 0.67 ng/mL **Statistical adjustments:** BMI (hormone levels), smoking (hormone levels), abstinence time (sperm parameters)	No significant association (p>0.05) between serum PFHxS levels and reproductive hormones (testosterone, free testosterone, free androgen index, LH, estradiol, SHBG, FSH, testosterone/LH ratio, free testosterone/LH ratio, and free androgen/LH ratio).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		No significant association (p>0.05) between serum PFHxS levels and sperm parameters (volume, concentration, total count, progressively motile, morphologically normal).
Jørgensen et al. 2014a, 2014b Retrospective study of 938 women participating in the INUENDO cohort in Greenland (n=448), Ukraine (n=287), and Poland (n=203)	**Exposure:** Median serum PFHxS: 1.94 ng/mL (full cohort), 2.04 ng/mL (Greenland), 2.35 ng/mL (Poland), 1.55 ng/mL (Ukraine) **Statistical adjustments:** Parity, gestational week of sampling, smoking status, maternal age, BMI	No significant association between serum PFHxS levels and TTP; the fecundability ratios were 0.97 (95% CI 0.85–1.11) for the full cohort, 0.97 (95% CI 0.78–1.20) for Greenland, 0.90 (95% CI 0.65–1.24) for Poland, and 1.05 (0.84–1.31) for Ukraine. No significant association between serum PFHxS levels and risk of infertility (TTP >13 months); OR 0.99 (95% CI 0.73–1.33) for the full cohort, 0.99 (95% CI 0.59–1.65) for Greenland, 1.05 (95% CI 0.50–2.20) for Poland, and 0.76 (0.47–1.24) for Ukraine.
Romano et al. 2016 Longitudinal cohort study of Prospective study of 336 women participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; women completed telephone surveys on breastfeeding practices every 3 months until breastfeeding was discontinued or the child's 3rd birthday	**Exposure:** Median maternal serum PFHxS levels (measured at 16 weeks of gestation) 1.5 ng/mL) **Multivariable Poisson regression adjustments:** Maternal age at delivery, household income, total weeks of prior breastfeeding, gestational age at blood draw, marital status, race, maternal serum cotinine during pregnancy, alcohol use during pregnancy	No significant associations between maternal serum PFHxS and stopping any breastfeeding by 3 months (trend p=0.124) or by 6 months (trend p=0.087).
Specht et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=199, median age 30.6 years), Poland (n=197, 29.6 years), and Ukraine (n=208, 25.1 years)	**Exposure:** Respective median serum PFHxS in Greenland, Poland, and Ukraine groups: 2.2, 1.2, and 0.3 ng/mL **Statistical adjustments:** Age, BMI, caffeinated drinks, cotinine, fever, spillage, abstinence time, genital infections, testicular disorders	The investigators noted no consistent associations with testosterone, estradiol, FSH, LH, or SHBG.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Taylor et al. 2014 Cross-sectional study of 2,151 women aged 20–65 years participating in NHANES 1999–2000 and 2003–2010	**Exposure:** Serum PFHxS • 1st tertile: 0.07–0.90 ng/mL • 2nd tertile: >0.90–1.8 ng/mL • 3rd tertile: >1.8 mg/mL **Statistical adjustments:** Age, race/ethnicity, education, smoking status, parity	Significant association between serum PFHxS and rate of menopause in the 2nd (HR 1.42, 95% CI 1.08–1.87) and 3rd tertiles (HR 1.70, 95% CI 1.36–2.12) and for hysterectomy in the 2nd (HR 2.22, 95% CI 1.66–2.98) and 3rd tertiles (HR 3.50, 95% CI 2.72–4.50).
Timmermann et al. 2017 Cross-sectional study of 1,130 woman participating in study of two birth cohorts (1997–2000, n=640 or 2007–2009, n=490) in the Faroe Islands	**Exposure:** Maternal serum PFHxS (measured between 34 and 36 weeks of gestation) 1.45 ng/mL **Statistical adjustments:** Maternal parity, age, prepregnancy BMI, pregnancy alcohol intake, pregnancy smoking, education, employment, cohort	No significant association between maternal PFHxS and duration of breastfeeding (β -0.2, 95% CI -0.5–0.2) and length of exclusive breastfeeding (β -0.1 95% CI -0.2–0.2) in months with a doubling of serum PFHxS levels. No significant differences in breastfeeding duration or exclusiveness between primiparous and multiparous women (p=0.66 and 0.28, respectively).
Toft et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=196, median age 31.3 years), Poland (n=189, 29.6 years), and Ukraine (n=203, 26.2 years)	Exposure: Median serum PFHxS: 1.1 ng/mL **Statistical adjustments:** Age, abstinence time, spillage, smoking, urogenital infections, BMI, county	Significant inverse association (p<0.05) between serum PFHxS levels and the percentage of normal sperm cells in participants with serum PFOS levels in the 3rd tertile (>1.5 ng/mL); the percentage of normal sperm cells was 35% lower in the 3rd tertile than in the 1st tertile. No significant association (p>0.05) for the whole cohort between serum PFHxS and sperm concentration, volume, total count, or percent motile sperm.
Vagi et al. 2014 Case-control study 52 women with polycystic ovary syndrome and 50 controls in California	**Exposure:** Geometric mean serum PFHxS 1.1 ng/mL (cases) and 0.7 ng/mL (controls) **Logistic regression adjustments:** Age, BMI, race	No significant association between serum PFHxS and risk of polycystic ovary syndrome; OR 1.20 (95% CI 0.35–4.07) for comparisons of the 3rd tertile to 1st tertile.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vélez et al. 2015 Cohort study of 1,743 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Median maternal serum PFHxS (measured in first trimester) 1 ng/mL **Regression adjustments:** Gestational age at blood draw, maternal age, country of birth, education, household income, maternal and paternal smoking, prepregnancy BMI	Significant inverse association between serum PFHxS and fecundity OR (longer TTP) 0.91 (95% CI 0.86–0.97, 0.002). Significant association between serum PFHxS and risk of infertility (TTP >12 months or infertility treatment) OR 1.27 (95% CI 1.09–1.48, p=0.003).
Vestergaard et al. 2012 Cross-sectional study of 222 Danish nulliparous couples discontinuing birth control and followed for six menstrual cycles or until clinically recognized pregnancy; mean age of women was 26.6 years	**Exposure:** Median serum PFHxS levels were 1.12 ng/mL in women with no pregnancy and 1.22 ng/mL in women becoming pregnant **Logistic regression model adjustments:** Female age, BMI, smoking habits, length of menstrual cycle, female diseases affecting fecundability, oligospermia	Serum PFHxS concentrations did not differ between women becoming pregnant and those who did not (p=0.06). No association between serum PFHxS above the median and the odds of not becoming pregnant within first six cycles; OR 0.67 (95% CI 0.37–1.20). A significant association was found between serum PFHxS and the fecundability ratio (monthly probability of conceiving); OR 1.33 (95% CI 1.01–1.75).
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFHxS of 0.30 ng/mL in cases and 0.32 ng/mL in controls; 2nd and 3rd tertile PFHxS >0.25–0.39 and >0.39–1.69 ng/mL **Statistical adjustments:** Age, BMI, household income, education	Inverse association between serum PFHxS and endometriosis-related infertility, OR (95% CI): 2nd tertile: 0.66 (0.37–1.19) 3rd tertile: 0.47 (0.26–0.87).
Whitworth et al. 2016 Retrospective study of 450 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum PFHxS 7.0 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum PFHxS and fecundability; OR 0.97 (0.90–1.1).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFHxS in boys and girls 1.4 and 1.2 ng/mL, respectively **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	No association between serum PFHxS and testosterone levels in boys (β 0.0173, 95% CI -0.0211–0.0588) or girls (β -0.0182, 95% CI -0.0451–0.0087). An association between serum PFHxS and estradiol levels in boys (β 0.0462, 95% CI 0.0020–0.0925), but not in girls (β 0.0017, 95% CI -0.0154–0.0496).
PFNA		
Bach et al. 2015a Cross-sectional study of 1,372 nulliparous women in the Aarhus Birth Cohort in Denmark; infertility defined as TTP of >12 months or infertility treatment before current pregnancy	**Exposure:** Median serum PFNA levels (measured between gestation week 9 and 20): 0.8 ng/mL **Statistical adjustments:** Maternal age at delivery, prepregnancy BMI, maternal education	No differences in fecundability were observed; the fecundability ratio was 1.00 (95% CI 0.98–1.02) per 0.1 ng/mL PFNA. No significant association between serum PFNA and the risk of infertility was observed; OR 0.99 (95% CI 0.95–1.03) per 0.1 ng/mL PFNA.
Barrett et al. 2015 Prospective study of 178 women participating in the Energy Balance and Breast Cancer Aspects study in Norway; subjects collected waking saliva samples every day for the duration of a single menstrual cycle	**Exposure:** Mean and median serum PFNA (measured at baseline): 0.67 and 0.61 ng/mL in nulliparous women and 0.60 and 0.55 ng/mL in parous women **Statistical adjustments:** Age, BMI, history of use of oral contraceptives, alcohol consumption, smoking, marital status, physical activity, parity	No significant associations (95% CI included unity) between serum PFNA levels and follicular estradiol or luteal progesterone levels in all women and when nulliparous and parous women were analyzed separately.
Buck Louis et al. 2012 Cross-sectional study of 473 women in Salt Lake City, Utah and San Francisco, California scheduled for laparoscopic or laparotomy surgery or served by the same clinic (190 and 283 were diagnosed with or without endometriosis, respectively) and a matched referent group of 127 women (14 and 113 women with or without endometriosis, respectively); endometriosis was diagnosed by surgical visualization or pelvic MRI	**Exposure:** Geometric mean serum PFNA levels 0.69 and 0.58 ng/mL in women in the clinic group with endometriosis or without endometriosis, respectively, and 0.71 and 0.64 ng/mL in women in the referent group with or without endometriosis, respectively **Statistical adjustments:** Age, BMI, parity	A significant association between serum PFNA and odds of endometriosis was observed in the clinic group when adjusted for age and BMI; OR 2.20 (95% CI 1.02–4.75), but was not significant when also adjusted for parity (OR 1.99, 95% CI 0.91–4.33). No significant association was found for the referent group (OR 1.52, 95% 0.15–15.1 when adjusted for age and BMI and OR 1.63, 95% CI 0.16–16.9 when also adjusted for parity).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		Among the clinic group, there was no significant association between serum PFNA with the risk of moderate or severe endometriosis (stages 3 and 4), the age and BMI adjusted OR 1.21 (95% CI 0.35–4.19) and the age, BMI, and parity adjusted OR 0.99 (95% CI 0.27–3.65).
Buck Louis et al. 2013 Prospective study of 501 couples in Michigan and Texas participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Geometric mean serum PFNA levels in women and men who became pregnant were 1.176 and 1.558 ng/mL, respectively, and in men and women who withdrew or were not pregnant during followup were 1.112 and 1.422 ng/mL, respectively **Statistical adjustments:** Serum concentrations for other perfluoroalkyls, age, BMI, cotinine, site	No association between female or male serum PFNA concentration and fecundability odds ratio (OR 1.00, 95% CI 0.84–1.19 and OR 1.09, 95% CI 0.90–1.32, respectively).
Buck Louis et al. 2015 Cross-sectional study of 462 male partners in Michigan (n=96) and Texas (n=366) participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Median serum PFNA levels 1.0 ng/mL for Michigan site and 1.65 ng/mL for Texas site **Statistical adjustments:** Age, BMI, serum cotinine, abstinence, sample age, research site	Significant associations ($p<0.05$) with some sperm quality parameters: reduction of percentage of sperm with coiled tail and increase in percentage of morphologically normal sperm. No significant association ($p>0.05$) with other sperm quality parameters including sperm viability, sperm count, sperm motility, or sperm morphology.
Campbell et al. 2016 Cross-sectional study of 753 women aged 20–50 years participating in the 2003–2006 NHANES	**Exposure:** Geometric mean serum PFNA 1.00 ng/mL in women with endometriosis and 0.84 ng/mL in women without endometriosis; 0.60–0.79, 0.80–1.19, and 1.20–15.40 2nd, 3rd, and 4th quartile PFNA **Statistical adjustments:** Age, race, BMI, poverty income ratio, cotinine	Association between serum PFNA and self-reported endometriosis (p=0.01, for trend); OR (95% CI) 2nd quartile: 3.76 (0.69–20.66 3rd quartile: 5.27 (1.20–23.06) 4th quartile: 3.24 (0.81–12.91).
Crawford et al. 2017 Prospective study of 99 30–44-year-old women participating in the Time to Conceive cohort study in	**Exposure:** Geometric mean serum PFNA 0.84 ng/mL **Statistical adjustments:** Age and full menstrual cycle length	No association between serum PFNA and fertility; fecundability ratio of 1.40 (95% CI 0.79–2.49).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
North Carolina and attempting to conceive for ≤3 months		
Joensen et al. 2013 Cross-sectional study of 247 young men (median age 19.2 years) in Denmark	**Exposure:** Mean serum PFNA level was 1.23 ng/mL **Statistical adjustments:** BMI (hormone levels), smoking (hormone levels), abstinence time (sperm parameters)	Significant association ($p<0.05$) between serum PFNA and estradiol level. No significant association ($p>0.05$) between serum PFNA levels and other reproductive hormones (testosterone, free testosterone, free androgen index, LH, SHBG, FSH, testosterone/LH ratio, free testosterone/LH ratio, and free androgen/LH ratio). No significant association ($p>0.05$) between serum PFNA levels and sperm parameters (volume, concentration, total count, progressively motile, morphologically normal).
Jørgensen et al. 2014a, 2014b Retrospective study of 938 women participating in the INUENDO cohort in Greenland (n=448), Ukraine (n=287), and Poland (n=203)	**Exposure:** Median serum PFNA: 0.64 ng/mL (full cohort), 0.70 ng/mL (Greenland), 0.60 ng/mL (Poland), 0.60 ng/mL (Ukraine) **Statistical adjustments:** Parity, gestational week of sampling, smoking status, maternal age, BMI	Significant inverse association between serum PFNA levels and TTP; the fecundability ratios were 0.80 (95% CI 0.69–0.94) for the full cohort, 0.72 (95% CI 0.58–0.89) for Greenland, 1.35 (95% CI 0.93–1.95) for Poland, and 0.74 (0.53–1.04) for Ukraine. Sensitivity analysis restricted to primiparous women, did not find significant associations between serum PFNA levels and fecundability ratios (0.99, 95% CI 0.80–1.22 for full cohort and 0.87, 95% CI 0.60–1.28 for Greenland cohort). Significant association between serum PFOA levels and risk of infertility (TTP >13 months); OR 1.53 (95% CI 1.08–2.15) for the full cohort, 1.97 (95% CI 1.22–3.19) for Greenland, 0.74 (95% CI 0.32–1.72) for Poland, and 1.26 (0.66–2.40) for Ukraine.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lum et al. 2017 Prospective study of 501 women participating in the Longitudinal Investigation of Fertility and the Environment Study in Michigan and Texas	**Exposure:** Median serum PFNA of 1.3, 1.2, and 1.1 ng/mL in women with menstrual cycles of ≤24, 25–31, or ≥32 days; 0.10–1.40 and ≥1.50 ng/mL for 2nd and 3rd tertiles **Statistical adjustments:** Female age, BMI, and active smoking at enrollment	No association between serum PFNA and menstrual cycle length, OR (95% CI): 2nd tertile: 1.02 (0.99–1.04) 3rd tertile: 1.01 (0.99–1.04) No association between women's serum PFNA and probability of pregnancy OR (95% CI): 2nd tertile: 0.7 (0.5–1.0) 3rd tertile: 0.8 (0.6–1.2).
Romano et al. 2016 Longitudinal cohort study of Prospective study of 336 women participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; women completed telephone surveys on breastfeeding practices every 3 months until breastfeeding was discontinued or the child's 3rd birthday	**Exposure:** Median maternal serum PFNA levels (measured at 16 weeks of gestation) 0.9 ng/mL **Multivariable Poisson regression adjustments:** Maternal age at delivery, household income, total weeks of prior breastfeeding, gestational age at blood draw, marital status, race, maternal serum cotinine during pregnancy, alcohol use during pregnancy	No significant associations between maternal serum PFNA and stopping any breastfeeding by 3 months (trend p=0.591) or by 6 months (trend p=0.349).
Specht et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=199, median age 30.6 years), Poland (n=197, 29.6 years), and Ukraine (n=208, 25.1 years)	**Exposure:** Respective median serum PFNA in Greenland, Poland, and Ukraine groups: 1.4, 1.2, and 1.0 ng/mL **Statistical adjustments:** Age, BMI, caffeinated drinks, cotinine, fever, spillage, abstinence time, genital infections, testicular disorders	The investigators noted no consistent associations with testosterone, estradiol, FSH, LH, or SHBG.
Taylor et al. 2014 Cross-sectional study of 2,151 women aged 20–65 years participating in NHANES 1999–2000 and 2003–2010	**Exposure:** Serum PFNA • 1st tertile: 0.07–0.80 ng/mL • 2nd tertile: >0.80–1.5 ng/mL • 3rd tertile: >1.5 mg/mL **Statistical adjustments:** Age, race/ethnicity, education, smoking status, parity	Significant association between serum PFNA and rate of menopause (HR 1.47, 95% CI 1.14–1.90 for comparisons between 1st and 3rd tertiles) and for hysterectomy (HR 1.39, 95% CI 1.08–1.80 for comparisons between 1st and 2nd tertiles; HR 1.78, 95% CI 1.33–2.37 for comparisons between 1st and 3rd tertiles).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Timmermann et al. 2017 Cross-sectional study of 1,130 woman participating in study of two birth cohorts (1997–2000, n=640 or 2007–2009, n=490) in the Faroe Islands	**Exposure:** Maternal serum PFNA (measured between 34 and 36 weeks of gestation) 0.62 ng/mL **Statistical adjustments:** Maternal parity, age, prepregnancy BMI, pregnancy alcohol intake, pregnancy smoking, education, employment, cohort	Significant inverse association between maternal PFNA and duration of breastfeeding (β -1.3, 95% CI -2.0 to -0.7) and length of exclusive breastfeeding (β -0.2, 95% CI -0.5 to -0.0) in months with a doubling of serum PFNA levels. No significant differences in breastfeeding duration or exclusiveness between primiparous and multiparous women (p=0.60 and 0.64, respectively).
Toft et al. 2012 Cross-sectional study of 588 male partners of pregnant women in Greenland (n=196, median age 31.3 years), Poland (n=189, 29.6 years), and Ukraine (n=203, 26.2 years)	**Exposure:** Median serum PFNA: 1.2 ng/mL **Statistical adjustments:** Age, abstinence time, spillage, smoking, urogenital infections, BMI, county	No significant association (p>0.05) for the whole cohort between serum PFNA and sperm concentration, volume, total count, percent motile sperm, or percent normal sperm.
Tsai et al. 2015 Cross-sectional study of 540 12–30-year-olds in Taiwan	**Exposure:** Geometric mean serum PFNA 1.10 ng/mL **Linear regression adjustments:** Age, sex, BMI, high fat diet	No significant associations (p>0.05 for trend) between serum PFNA and SHBG, FSH, or testosterone.
Vagi et al. 2014 Case-control study 52 women with polycystic ovary syndrome and 50 controls in California	**Exposure:** Geometric mean serum PFNA 1.2 ng/mL (cases) and 0.9 ng/mL (controls) **Logistic regression adjustments:** Age, BMI, race	No significant association between serum PFNA and risk of polycystic ovary syndrome; OR 2.25 (95% CI 0.67–8.00) for comparisons of the 3rd tertile to 1st tertile.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vestergaard et al. 2012 Cross-sectional study of 222 Danish nulliparous couples discontinuing birth control and followed for six menstrual cycles or until clinically recognized pregnancy; mean age of women was 26.6 years	**Exposure:** Median serum PFNA levels were 0.45 ng/mL in women with no pregnancy and 0.51 ng/mL in women becoming pregnant **Logistic regression model adjustments:** Female age, BMI, smoking habits, length of menstrual cycle, female diseases affecting fecundability, oligospermia	Serum PFNA concentrations did not differ between women becoming pregnant and those who did not (p=0.48). No association between serum PFNA above the median and the odds of not becoming pregnant within first six cycles; OR 0.67 (95% CI 0.37–1.25). No significant associations between serum PFNA and the fecundability ratio (monthly probability of conceiving); OR 1.17 (95% CI 0.88–1.54).
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFNA of 1.05 ng/mL in cases and 1.20 ng/mL in controls; PFNA >0.83–1.50 and >1.50–7.10 ng/mL **Statistical adjustments:** Age, BMI, household income, education	Inverse association between serum PFNA and endometriosis-related infertility, OR (95% CI): 2nd tertile: 0.71 (0.39–1.28) 3rd tertile: 0.52 (0.28–0.95).
Whitworth et al. 2016 Retrospective study of 451 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum PFNA 0.43 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum PFNA and fecundability; OR 1.1 (0.92–1.3).
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFNA in boys and girls 0.8 and 0.9 ng/mL, respectively **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	Inverse association between serum PFNA and testosterone levels in boys (β -0.4233, 95% CI -0.6998 to -0.1467), but not in girls (β -0.1018, 95% CI -0.2684–0.0648). No association between serum PFNA and estradiol levels in boys (β 0.3204, 95% CI -0.0115–0.6522) or girls (β 0.1252, 95% CI -0.0758–0.3263).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFDA		
Bach et al. 2015a Cross-sectional study of 1,372 nulliparous women in the Aarhus Birth Cohort in Denmark; infertility defined as TTP of >12 months or infertility treatment before current pregnancy	**Exposure:** Median serum PFDA levels (measured between gestation week 9 and 20): 0.3 ng/mL **Statistical adjustments:** Maternal age at delivery, prepregnancy BMI, maternal education	No differences in fecundability were observed; the fecundability ratio was 1.00 (95% CI 0.97–1.03) per 0.1 ng/mL PFDA. No significant association between serum PFDA and the risk of infertility was observed; OR 0.99 (95% CI 0.92–1.07) per 0.1 ng/mL PFDA.
Barrett et al. 2015 Prospective study of 178 women participating in the Energy Balance and Breast Cancer Aspects study in Norway; subjects collected waking saliva samples every day for the duration of a single menstrual cycle	**Exposure:** Mean and median serum PFDA (measured at baseline): 0.25 and 0.23 ng/mL in nulliparous women and 0.24 and 0.22 ng/mL in parous women **Statistical adjustments:** Age, BMI, history of use of oral contraceptives, alcohol consumption, smoking, marital status, physical activity, parity	No significant associations (95% CI included unity) between serum PFDA levels and follicular estradiol or luteal progesterone levels in all women and when nulliparous and parous women were analyzed separately.
Buck Louis et al. 2012 Cross-sectional study of 473 women in Salt Lake City, Utah and San Francisco, California scheduled for laparoscopic or laparotomy surgery or served by the same clinic (190 and 283 were diagnosed with or without endometriosis, respectively) and a matched referent group of 127 women (14 and 113 women with or without endometriosis, respectively); endometriosis was diagnosed by surgical visualization or pelvic MRI	**Exposure:** Geometric mean serum PFDA levels were 0.20 and 0.18 ng/mL in women in the clinic group with endometriosis or without endometriosis, respectively, and 0.17 and 0.19 ng/mL in women in the referent group with or without endometriosis, respectively **Statistical adjustments:** Age, BMI, parity	No significant associations (when adjusted for age and BMI) were found between serum PFDA and odds of endometriosis in the clinic group (OR 2.95 95% CI 0.72–12.1) or referent group (OR 0.06, 95% CI 0.00–12.3); also adjusting for parity did not change the outcome (OR 2.60, 95% CI 0.62–10.9 for the clinic group and OR 0.06, 95% CI 0.00–13.3 for the referent group). Among the clinic group, there was no significant association between serum PFDA with the risk of moderate or severe endometriosis (stages 3 and 4), the age and BMI adjusted OR 0.72 (95% CI 0.06–8.09) and the age, BMI, and parity adjusted OR 0.58 (95% CI 0.04–7.42).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Buck Louis et al. 2013 Prospective study of 501 couples in Michigan and Texas participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Geometric mean serum PFDA levels in women and men who became pregnant were 0.385 and 0.448 ng/mL, respectively, and men and women who withdrew or were not pregnant during followup were 0.349 and 0.416 ng/mL, respectively **Statistical adjustments:** Serum concentrations for other perfluoroalkyls, age, BMI, cotinine, site	No association between female or male serum PFDA concentration and fecundability odds ratio (OR 1.11, 95% CI 0.95–1.29 and OR 1.08, 95% CI 0.93–1.26, respectively).
Buck Louis et al. 2015 Cross-sectional study of 462 male partners in Michigan (n=96) and Texas (n=366) participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Median serum PFDA levels 0.3 ng/mL for Michigan site and 0.5 ng/mL for Texas site **Statistical adjustments:** Age, BMI, serum cotinine, abstinence, sample age, research site	Significant associations ($p<0.05$) with some sperm quality parameters: decreased sperm head length and reduction of percentage of sperm with coiled tail. No significant association ($p>0.05$) with other sperm quality parameters including sperm viability, sperm count, sperm motility, or most parameters of sperm morphology.
Joensen et al. 2013 Cross-sectional study of 247 young men (median age 19.2 years) in Denmark	**Exposure:** Mean serum PFDA level was 0.38 ng/mL **Statistical adjustments:** BMI (hormone levels), smoking (hormone levels), abstinence time (sperm parameters)	No significant association ($p>0.05$) between serum PFDA levels and reproductive hormones (testosterone, free testosterone, free androgen index, LH, estradiol, SHBG, FSH, testosterone/LH ratio, free testosterone/LH ratio, and free androgen/LH ratio). No significant association ($p>0.05$) between serum PFDA levels and sperm parameters (volume, concentration, total count, progressively motile, morphologically normal).
Lum et al. 2017 Prospective study of 501 women participating in the Longitudinal Investigation of Fertility and the Environment Study in Michigan and Texas	**Exposure:** Median serum PFDA of 0.4, 0.4, and 0.4 ng/mL in women with menstrual cycles of ≤24, 25–31, or ≥32 days; 0.03–0.04 and ≥0.05 ng/mL for 2nd and 3rd tertiles **Statistical adjustments:** Female age, BMI, and active smoking at enrollment	No association between serum PFDA and menstrual cycle length, OR (95% CI): 2nd tertile: 1.03 (1.00–1.05) 3rd tertile: 1.01 (0.99–1.04). No association between women's serum PFDA and probability of pregnancy OR (95% CI): 2nd tertile: 0.7 (0.5–1.1)

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		3rd tertile: 0.9 (0.6–1.3).
Timmermann et al. 2017 Cross-sectional study of 1,130 woman participating in study of two birth cohorts (1997–2000, n=640 or 2007–2009, n=490) in the Faroe Islands	**Exposure:** Maternal serum PFDA (measured between 34 and 36 weeks of gestation) 0.28 ng/mL **Statistical adjustments:** Maternal parity, age, prepregnancy BMI, pregnancy alcohol intake, pregnancy smoking, education, employment, cohort	Significant inverse association between maternal PFDA and duration of breastfeeding (β -0.8, 95% CI -1.4 to -0.3) in months with a doubling of serum PFDA levels. No association between maternal PDA and length of exclusive breastfeeding (β -0.2, 95% CI -0.4–0.0). No significant differences in breastfeeding duration or exclusiveness between primiparous and multiparous women (p=0.06 and 0.06, respectively).
Vestergaard et al. 2012 Cross-sectional study of 222 Danish nulliparous couples discontinuing birth control and followed for six menstrual cycles or until clinically recognized pregnancy; mean age of women was 26.6 years	**Exposure:** Median serum PFDA levels were 0.10 ng/mL in women with no pregnancy and 0.11 ng/mL in women becoming pregnant **Logistic regression model adjustments:** Female age, BMI, smoking habits, length of menstrual cycle, female diseases affecting fecundability, oligospermia	Serum PFDA concentrations did not differ between women becoming pregnant and those who did not (p=0.45). No association between serum PFDA above the median and the odds of not becoming pregnant within first six cycles; OR 0.61 (95% CI 0.33–1.12). No significant associations between serum PFOA and the fecundability ratio (monthly probability of conceiving); OR 1.15 (95% CI 0.89–1.49).
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFDA of 1.29 ng/mL in cases and 1.34 ng/mL in controls; PFDA >0.95–1.79 and >1.79–11.2 ng/mL **Statistical adjustments:** Age, BMI, household income, education	No association between serum PFDA and endometriosis-related infertility, OR (95% CI): 2nd tertile: 0.93 (0.51–1.70) 3rd tertile: 0.74 (0.40–1.35).
Whitworth et al. 2016 Retrospective study of 429 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum PFDA 0.11 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum PFOA and fecundability; OR 1.00 (0.85–1.2).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFDA in boys and girls 0.9 and 1.0 ng/mL, respectively **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	Inverse association between serum PFDA and testosterone levels in boys (β -0.2565, 95% CI -0.4135 to -0.0994), but not in girls (β -0.0626, 95% CI -0.1730–0.0477). No association between serum PFDA and estradiol levels in boys (β 0.0734, 95% CI -0.1189–0.2657) or girls (β 0.0131, 95% CI -0.1208–0.1469).
PFUnA		
Bach et al. 2015a Cross-sectional study of 1,372 nulliparous women in the Aarhus Birth Cohort in Denmark; infertility defined as TTP of >12 months or infertility treatment before current pregnancy	**Exposure:** Median serum PFUnA levels (measured between gestation week 9 and 20): 0.3 ng/mL **Statistical adjustments:** Maternal age at delivery, prepregnancy BMI, maternal education	No differences in fecundability were observed; the fecundability ratio was 1.01 (95% CI 0.98–1.03) per 0.1 ng/mL PFUnA. No significant association between serum PFUnA and the risk of infertility was observed; OR 0.98 (95% CI 0.92–1.04) per 0.1 ng/mL PFUnA.
Barrett et al. 2015 Prospective study of 178 women participating in the Energy Balance and Breast Cancer Aspects study in Norway.; subjects collected waking saliva samples every day for the duration of a single menstrual cycle	**Exposure:** Mean and median serum PFUnA (measured at baseline): 0.40 and 0.36 ng/mL in nulliparous women and 0.42 and 0.39 ng/mL in parous women **Statistical adjustments:** Age, BMI, history of use of oral contraceptives, alcohol consumption, smoking, marital status, physical activity, parity	No significant associations (95% CI included unity) between serum PFUnA levels and follicular estradiol or luteal progesterone levels in all women and when nulliparous and parous women were analyzed separately.
Tsai et al. 2015 Cross-sectional study of 540 12–30-year-olds in Taiwan	**Exposure:** Geometric mean serum PFUnA 5.84 ng/mL **Linear regression adjustments:** Age, sex, BMI, high fat diet	Significant inverse association between serum PFUnA levels and FSH ($p<0.05$ for trend) among girls 12–17 years of age. No significant associations ($p>0.05$ for trend) between serum PFUnA and SHBG or testosterone.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFUnA of 0.98 ng/mL in cases and 1.04 ng/mL in controls; PFUnA >0.73–1.42 and >1.42–5.34 ng/mL **Statistical adjustments:** Age, BMI, household income, education	No association between serum PFUnA and endometriosis-related infertility, OR (95% CI): 2nd tertile: 0.63 (0.34–1.14) 3rd tertile: 0.61 (0.33–1.13).
Whitworth et al. 2016 Retrospective study of 447 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum PFUnA 0.23 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum PFUnA and fecundability; OR 0.93 (0.78–1.1).
PFBS		
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFBS of 0.091 ng/mL in cases and 0.089 ng/mL in controls; PFBS >0.086–0.094 and >0.094–1.25 ng/mL **Statistical adjustments:** Age, BMI, household income, education	Association between serum PFBS and endometriosis-related infertility, OR (95% CI): 2nd tertile: 3.74 (2.04—6.84) 3rd tertile: 3.04 (1.65–5.57).
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFBS in boys and girls 0.5 and 0.5 ng/mL, respectively **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	No association between serum PFBS and testosterone levels in boys (β -0.0387, 95% CI -0.3261–0.2487) or girls (β 0.1326, 95% CI -0.3576–0.6229). No association between serum PFBS and estradiol levels in boys (β 0.0149, 95% CI -0.3216–0.3513) or girls (β 0.3129, 95% CI -0.2771–0.9028).
PFDoDA		
Wang et al. 2017 Case-control study of 157 women with endometriosis-related infertility and 178 controls	**Exposure:** Median serum PFDoDA of 0.22 ng/mL in cases and 0.23 ng/mL in controls; PFDoDA >0.19–0.27 and >0.27–1.02 ng/mL **Statistical adjustments:** Age, BMI, household income, education	No association between serum PFDoDA and endometriosis-related infertility, OR (95% CI): 2nd tertile: 0.88 (0.50–1.56) 3rd tertile: 0.61 (0.34–1.11).

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Whitworth et al. 2016 Retrospective study of 410 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum PFDoDA 0.04 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum PFDoDA and fecundability; OR 0.91 (0.77–1.1).
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFDoDA in boys and girls 2.4 and 3.1 ng/mL, respectively **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	Inverse association between serum PFDoDA and testosterone levels in girls (β -0.0119, 95% CI -0.0227 to -0.0010), but not in boys (β 0.0056, 95% CI -0.0056–0.0168). No association between serum PFDoDA and estradiol levels in boys (β -0.0007, 95% CI -0.0139–0.0124) or girls (β 0.0106, 95% CI -0.0026–0.0218).
PFHxA		
Zhou et al. 2016 Cross-sectional study of 225 adolescents (13–15 years of age) in Taiwan	**Exposure:** Median serum PFHxA in boys and girls 0.2 and 0.2 ng/mL, respectively **Statistical adjustments:** Age, BMI, environmental tobacco smoke exposure, parental education, regular exercise, month of survey	Inverse association between serum PFHxA and testosterone levels in boys (β -0.3095, 95% CI -0.5942 to -0.0248), but not in girls (β -0.1896, 95% CI -0.4387–0.0595). No association between serum PFHxA and estradiol levels in boys (β 0.0600, 95% CI -0.2803–0.4003) or girls (β -0.1492, 95% CI -0.4515–0.1531).
FOSA		
Barrett et al. 2015 Prospective study of 178 women participating in the Energy Balance and Breast Cancer Aspects study in Norway; subjects collected waking saliva samples every day for the duration of a single menstrual cycle	**Exposure:** Mean and median serum FOSA (measured at baseline): 0.25 and 0.20 ng/mL in nulliparous women and 0.23 and 0.17 ng/mL in parous women **Statistical adjustments:** Age, BMI, history of use of oral contraceptives, alcohol consumption, smoking, marital status, physical activity, parity	No significant associations (95% CI included unity) between serum FOSA levels and follicular estradiol or luteal progesterone levels in all women and when nulliparous and parous women were analyzed separately.

Table 12. Reproductive Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Buck Louis et al. 2013 Prospective study of 501 couples in Michigan and Texas participating in the LIFE study cohort who discontinued contraception for the purpose of becoming pregnant	**Exposure:** Geometric mean serum FOSA levels in women and men who became pregnant were 0.110 and 0.112 ng/mL, respectively, and women and men who withdrew or were not pregnant during followup were 0.126 and 0.129 ng/mL, respectively **Statistical adjustments:** Serum concentrations for other perfluoroalkyls, age, BMI, cotinine, site	Significant inverse association between female serum FOSA levels and fecundability odds ratio (OR 0.81, 95% CI 0.70–0.94). Including parity in the analysis did not alter the results. Results should be interpreted cautiously since 90% of population had FOSA levels below the detection limit. No association between male serum FOSA levels and fecundability odds ratio (OR 0.89, 95% CI 0.78–1.02).
Vestergaard et al. 2012 Cross-sectional study of 222 Danish nulliparous couples discontinuing birth control and followed for six menstrual cycles or until clinically recognized pregnancy; mean age of women was 26.6 years	**Exposure:** Median serum FOSA levels were 0.10 ng/mL in women with no pregnancy and 0.11 ng/mL in women becoming pregnant **Logistic regression model adjustments:** Female age, BMI, smoking habits, length of menstrual cycle, female diseases affecting fecundability, oligospermia	Serum FOSA concentrations did not differ between women becoming pregnant and those who did not (p=0.48). No association between serum FOSA above the median and the odds of not becoming pregnant within first six cycles; OR 0.81 (95% CI 0.45–1.46). No significant associations between serum FOSA and the fecundability ratio (monthly probability of conceiving); OR 1.01 (95% CI 0.86–1.18).
Whitworth et al. 2016 Retrospective study of 226 primiparous pregnant women participating in the Norwegian Mother and Child Cohort Study	**Exposure:** Median serum FOSA 0.03 ng/mL (measured at gestation week 18) **Statistical adjustments:** Maternal age at conception, prepregnancy BMI	No association between serum FOSA and fecundability; OR 0.91 (0.71–1.2).

APFO = ammonium perfluorooctanoate; BMI = body mass index; CI = confidence interval; DHEAS= dehydroepiandrosterone sulfate; DNA = deoxyribonucleic acid; FOSA = perfluorooctane sulfonamide; FSH = follicle stimulating hormone; HR = hazard ratio; LH = luteinizing hormone; LLOQ = lower limit of quantification; MRI = magnetic resonance imaging; NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PBPK = physiologically based pharmacokinetic; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; TTP = time-to-pregnancy

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Darrow et al. 2013 Cross-sectional study of 1,330 women participating in the C8 Health Project and giving birth between 2005 and 2010; maternal blood samples collected in 2005–2006; birth outcome data self-reported and taken from Ohio and West Virginia health departments	**Exposure:** Mean and geometric mean serum PFOA were 31.0 and 16.2 ng/mL (range: 0.6–459.5 ng/mL) • 1st quintile: 0–<6.9 ng/mL • 2nd quintile: 6.9–<11.1 ng/mL • 3rd quintile: 11.1–<18.9 ng/mL • 4th quintile: 18.9–<37.2 ng/mL • 5th quintile: ≥37.2 ng/mL **Logistic regression model adjustments:** Maternal age, educational level, smoking, parity, BMI, self-reported diabetes, time between conception and serum measurement	No significant trend (p=0.701) for decreased birth weight and PFOA levels across serum PFOA quintiles. No association between PFOA levels and preterm birth or LBW. The ORs (95% CI) for the 5th quintile were: • Preterm birth: 1.01 (0.55–1.86) • LBW: 0.92 (0.44–1.95).
Darrow et al. 2014 Cross-sectional study of 1,129 women participating in the C8 Health Project and reporting pregnancies in follow-up interviews between 2008 and 2011; maternal blood samples collected in 2005–2006; birth outcome data self-reported	**Exposure:** Mean and geometric mean serum PFOA levels were 33.7 and 18.0 ng/mL (range: 0.6–516.2 ng/mL) **Statistical adjustments:** Smoking status, maternal age at time of conception, education, BMI at enrollment, race, self-reported diabetes, time between conception and serum measurement	No significant association between serum PFOA levels and risk of miscarriage was observed, the OR for the 5th quintile (>39.4 ng/mL) was 1.00 (95% CI 0.63–1.58). No associations were found among nulliparous women (OR 0.81, 95% CI 0.38–1.71 for 5th quintile) or parous women (OR 1.06, 95% CI 0.57–1.97).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lopez-Espinosa et al. 2011 Cross-sectional study of 3,076 boys and 2,931 girls aged 8–18 years participating in the C8 Health Project and C8 Science Panel studies	**Exposure:** Median serum PFOA levels in boys and girls were 26 and 20 ng/mL, respectively **Logistic regression model adjustments:** Age, time of day for blood sampling (boys only)	No significant association between PFOA levels and the age of puberty in boys (as assessed by total testosterone levels); OR 0.95 (95% CI 0.84–1.07). Significant association between PFOA and age of puberty in girls (as assessed by self-reported menarche or estradiol levels); OR (95% CI) using menarche criteria: • 2nd quartile: 0.54 (0.35–0.84) • 3rd quartile: 0.50 (0.32–0.77) • 4th quartile: 0.57 (0.37–0.89). The delays in the 2nd, 3rd, and 4th quartiles were 142, 163, and 130 days, respectively.
Lopez-Espinosa et al. 2016 Cross-sectional study of 1,169 boys and 1,123 girls aged 6–9 years participating in the C8 Health Project study; sexual maturation	**Exposure:** Median serum PFOA 34.8 ng/mL in boys and 30.1 ng/mL in girls **Statistical adjustments:** Age, month, time of sampling	Significant inverse association between serum PFOA and total testosterone in boys (percent difference between 75th and 25th PFOA levels, -4.9, 95% CI -8.7 to -0.8) and insulin-like growth factor-1 (-3.6, 95% CI -6.6 to -0.5) in girls. No significant associations between serum PFOA and estradiol (4.3, 95% CI -0.4–9.1) or insulin-like growth factor-1 (-0.4, 95% CI -3.4–2.7) in boys or estradiol (4.2, 95% CI -0.7–9.4) or total testosterone (-2.5, 95% CI -6.7–1.8) in girls.
Nolan et al. 2009 Cross-sectional study of 1,555 singleton neonates, 11% born to mothers living in area with PFOA contaminated drinking water from the LHWA, 13% living in area partially serviced by LHWA, and 76% living in area without service from LHWA; birth outcome data taken from the Ohio Department of Health	**Exposure:** No biomonitoring performed **Logistic regression model adjustments:** Neonatal sex, race, gestational age, gestational age squared, gestational age cubed, maternal age, socioeconomic status index	Lower incidence of LBW in partial (3.8%) and exclusive (3.6%) LHWA groups as compared to the national incidence (8.1%) ($p<0.01$). Lower adjusted odds of LBW (OR 0.37, 95% CI 0.16–0.86) in partial LHWA group, as compared to the no LHWA group. No significant associations ($p>0.05$) between residence area and birth weights, LBW mean gestational age, or preterm births.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Nolan et al. 2010 Cross-sectional study of 1,548 singleton neonates, 11% living in area with PFOA contaminated drinking water from the LHWA; 13% partial LHWA, and 76% no LHWA (see Nolan et al. 2009)	**Exposure:** No biomonitoring performed **Logistic regression model adjustments:** Race, parity, preterm birth, maternal age, maternal education, diabetic status, tobacco and alcohol use during pregnancy	No significant association between residence area and the likelihood of congenital anomalies; OR 1.1 (95% CI 0.34–3.3) in comparison between exclusive LHWA and no LHWA.
Savitz et al. 2012a Cross-sectional study of 11,737 singleton infants born to mothers living in an area of the Mid-Ohio Valley with known PFOA contamination from 1990 to 2006 and with birth records linked to the C8 Health Project; birth outcome data taken from Ohio and West Virginia health departments	**Exposure:** Maternal PFOA blood levels based on environmental levels of PFOA (based on maternal lifetime residential history) and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life; used a Bayesian time-dependent calibration that used measured serum concentrations (2005–2006) to update estimates Median maternal serum PFOA: 6.0, 10.7, and 15.9 ng/mL in the 1990–1994, 1995–1999, and 2000–2005 time periods • 1st quartile: 3.9–<6.8 ng/mL • 2nd quartile: 6.8–<16.6 ng/mL • 3rd quartile: 16.6–<63.1 ng/mL • 4th quartile: 63.1–934.3 ng/mL **Regression model adjustments:** Maternal age, parity, education, smoking status	No associations between PFOA levels and odds of miscarriage, stillbirth, preterm birth, LBW, or birth defects were found; the ORs (95% CI) for the 4th quartile were: • Miscarriage: 0.9 (0.7–1.0) • Stillbirth: 1.0 (0.5–1.8) • LBW: 0.8 (0.4–1.4) • Birth defect: 1.0 (0.8–1.3).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Savitz et al. 2012b Case-control study of singleton pregnancy of women living in Mid-Ohio Valley with known PFOA contamination from 1990 to 2004; birth outcome data taken from Ohio and West Virginia health departments; cases of stillbirth (n=106), preterm birth (n=3,613), term LBW (n=918), term SGA (n=353), and birth weight (n=8,253) were compared to controls with term births	**Exposure:** Maternal PFOA levels based on estimated environmental levels of PFOA (based on maternal address on birth certificate and assumption that mother lived at address for 6 years) and PBPK model using standard assumptions about water intake, body weight, PFOA half-life Median estimated maternal serum PFOA: 7.7 ng/mL (range: 1.0–717.6 ng/mL) **Logistic and multiple linear regression model adjustments:** Maternal age, education, tobacco use, exposure year, state of residence	No significant associations between estimated serum PFOA levels and stillbirth, preterm birth, LBW, SGA, and birth weight were found. ORs (95% CI) per 100 ng/mL increase in PFOA: • Stillbirth: 0.8 (0.5–1.5): • Preterm birth (<37 weeks): 1.02 (0.94–1.10) • Preterm birth (<32 weeks): 0.90 (0.74–1.10) • Term LBW:1.0 (0.86–1.15) • Term SGA: 0.86 (0.67–1.11). There were no monotonic gradient decrements in continuous birth weight; change per 100 ng/mL PFOA was 14.80 g lower (95% CI -43.28–13.68 g).
Savitz et al. 2012b Case-control study of 4,547 singleton infants born to mothers living in an area of the Mid-Ohio Valley with known PFOA contamination from 1990 to 2004 and with birth records linked to the C8 Health Project; birth outcome data taken from Ohio and West Virginia health departments; cases of preterm birth (n=405), term LBW (n=99), term SGA (n=362), and birth weight (n=4,547) were compared to controls with term births	**Exposure:** Serum PFOA levels from the mother estimated for the early pregnancy period. Serum levels were estimated based on plant operations and chemical releases, address, and age- and sex-specific PBPK modeling with standards for water intake, body weights and PFOA half-life. Bayesian time-dependent calibration that used measured serum concentrations (2005–2006) to update estimates. Median maternal serum PFOA: 13.4 ng/mL (range: 3.9–921.3 ng/mL) **Logistic and multiple linear regression model adjustments:** Maternal age, education, tobacco use, exposure year, state of residence, gestational age (birth weight only)	Association between serum PFOA and SGA, no association between estimated serum PFOA levels and preterm birth, LBW, change in birth weight. ORs (95% CI) per 100 ng/mL increase in PFOA: • Preterm birth (<37 weeks): 1.09 (1.00–1.18) • Preterm birth (<32 weeks): 1.10 (0.86–1.40) • Term LBW:1.07 (0.96–1.18) • Term SGA: 1.08 (1.01–1.16) • Change in birth weight: -12.76 (-26.08–0.57). The investigators noted that analysis of continuous birth weight showed some support of an association with uncalibrated and Bayesian calibrated serum PFOA levels. A decrement of 33.3 g (95% CI -73.1–6.5 g) in the 5th quintile for uncalibrated serum levels and 32.3 g (95% CI -71.5–6.8 g).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Stein et al. 2009 Cross-sectional study of 1,845 pregnancies (1,589 live births) in Mid-Ohio Valley residents that occurred within the 5 years preceding blood sample collections for the C8 Health Project; self-reported birth outcome	**Exposure:** Mean and median serum PFOA: 48.8 and 21.2 ng/mL (range: 0.25–894.4 ng/mL) • 1st quartile: 0.25–<21.3 ng/mL • 2nd quartile:21.3–<50.0 ng/mL • 3rd quartile:50.0–<120.6 ng/mL • 4th quartile: 120.6–894.4 ng/mL **Logistic linear regression model adjustments:** Maternal age, parity, education, smoking status	No association between PFOA levels and odds of miscarriage, pre-term birth, LBW, or birth defects. ORs (95% CI) for the 4th quartile: • Miscarriage: 0.9 (0.5–1.6) • Preterm: 0.9 (0.6–1.5) • LBW: 0.8 (0.3–1.9) • Birth defects: 1.7 (0.8–3.6).
Stein et al. 2013 Cross-sectional study of 320 6–12-year-old children (mean age of 9.9 years) participating in the C8 Health Project; neuropsychological tests were conducted by trained examiners	**Exposure:** Estimated maternal serum PFOA level based on documented PFOA releases, environmental fate and transport modeling, residential history, and toxicokinetic properties; estimated mean and median *in utero* PFOA: 115.9 and 43.7 ng/mL Mean and median measured child PFOA: 91.9 and 35.0 ng/mL **Linear regression adjustments:** Child's age at assessment, sex, cognitive and emotional Home Observation for Measurement of the Environment scores, test examiner maternal Full-Scale IQ	An association between *in utero* PFOA levels and increases in IQ for children with PFOA levels in the 4th quartile (β 4.61 95% CI 0.68–8.54). No association between reading and math skills and *in utero* or measured PFOA were found. Increases in *in utero* PFOA were associated with improved scores on tests of ADHD (clinical CI β -8.49, 95% CI -16.14 to -0.84) for 4th quartile.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Stein et al. 2014a, 2014b Cross-sectional study of 321 children 6–12 years of age (mean 9.9 years) participating in the C8 Health Project; mothers and teachers completed 3 surveys to assess the child's executive function, ADHD-like behaviors, and behavioral problems and emotional disturbances	**Exposure:** Median serum PFOA level in blood samples collected 3–4 years prior to behavioral assessments was 35.1 ng/mL • 1st quartile: 0.7–<15.8 ng/mL • 2nd quartile: 15.8–<35.1 ng/mL • 3rd quartile: 35.1–<94.1 ng/mL • 4th quartile: 94.1–838.6 ng/mL **Linear regression adjustments:** Age, sex, maternal IQ, a measure of quality and extent of stimulation at home, maternal age, maternal employment for mother's survey results, age and sex for teacher's survey results	Associations (β, 95% CI; comparisons between 1st and 4th quartiles), based on the mother's survey: Executive function scores • Boys: -6.39 (-11.43 to -1.35); for comparisons between 1st and 3rd quartiles • Girls: -6.39 (-0.03–8.87) • Combined: -0.85 (-4.46–2.77) ADHD-like behaviors • Boys: -3.82 (-8.96–1.31) • Girls: 6.99 (2.47–11.51) • Combined: 2.30 (-1.18–5.77) Behavioral problems and emotional disturbances • Boys: -1.55 (-5.91–2.82) • Girls: 4.63 (0.72–8.53) • Combined: 1.90 (-1.09–4.88). Associations (β, 95% CI; comparisons between 1st and 4th quartiles), based on the teacher's survey: Executive function scores • Boys: -6.42 (-13.29–0.45) • Girls: -1.92 (-10.39–6.55) • Combined: -3.81 (-9.81–2.18) ADHD-like behaviors • Boys: -9.25 (-18.78–0.27) • Girls: -3.65 (-10.85–3.51) • Combined: -6.03 (-11.40 to -0.66) Behavioral problems and emotional disturbances • Boys: -2.47 (-8.24–3.30) • Girls: -0.91 (-6.19–4.37) • Combined: -1.55 (-5.78–2.69).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Stein et al. 2014c Cross-sectional study of 10,262 infants whose mothers are participating in the C8 Health Project; mothers reported whether the infants had any major birth defects	**Exposure:** Estimated maternal serum PFOA level based on documented PFOA releases, environmental fate and transport modeling, residential history, and toxicokinetic properties; estimated mean and median *in utero* PFOA: 61.3 and 10.4 ng/mL **Regression adjustments:** Year of conception	A significant association between maternal serum PFOA and the risk of brain defects was found (OR for interquartile range increase 2.6, 95% CI 1.3–5.1); however, this was only based on 13 cases. No significant associations between maternal serum PFOA and the risk of other defects (interquartile increase OR, 95% CI): gastrointestinal (0.7, 0.3–1.4), kidney 0.7, 0.3–1.8), craniofacial (0.6, 0.3–1.3), eye (1.1, 0.6–2.1), limb (1.2, 0.7–2.0), genitourinary (1.0, 0.6–1.7), or heart (1.2, 0.8–1.7).
Stein and Savitz 2011 Cross-sectional study of 10,546 non-Hispanic white children aged 5–18 years participating in the C8 Health Project; ADHD diagnosis and learning problems were reported by parents	**Exposure:** Mean serum PFOA level of 66.3 ng/mL (range: 0.6–2,070.6 ng/mL) • 1st quartile: 0.6–<13.0 ng/mL • 2nd quartile:13.0–<28.2 ng/mL • 3rd quartile: 28.2–<65.3 ng/mL • 4th quartile: 65.3–2,070.6 ng/mL **Logistic regression model adjustments:** Age, sex	An inverse association between serum PFOA and risk of ADHD and ADHD with medication was found in 5–18-year-olds; OR (95% CI) ADHD: • 2nd quartile: 1.10 (0.94–1.30) • 3rd quartile: 0.98 (0.83–1.15) • 4th quartile: 0.76 (0.64–0.90). ADHD with medication: • 2nd quartile: 1.20 (0.94–1.53) • 3rd quartile: 1.04 (0.81–1.32) • 4th quartile: 0.72 (0.55–0.94). These associations were not significant the 12–15-year-olds; OR (95% CI) for 4th quartile: 0.79 (0.60–1.04) and 0.87 (0.58–1.32). No significant associations between serum PFOA and risk of learning problems; the ORs (95% CI) for 12–15-year-old participants and 5–18-year-old participants with serum PFOA levels in the 4th quartile (65.3–2,070.6 ng/mL), were 0.96 (0.73–1.26) and 0.90 (0.76–1.06), respectively.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Alkhalawi et al. 2016 Retrospective study of 156 mother-child pairs participating in the Duisburg Birth Cohort study in Germany; weight and length recorded at birth and at 1, 4, 6, and 12 months of age.	**Exposure:** Geometric mean maternal serum PFOA 2.43 ng/mL; 1st quartile: <0.4–1.97 ng/mL, 2nd quartile: 1.99–2.73 ng/mL, 3rd quartile: 2.75–3.48 ng/mL, 4th quartile: 3.52–9.20 ng/mL **Statistical adjustments:** Pregnancy duration, maternal BMI before pregnancy, maternal height, maternal blood lead levels, infant sex, mode of delivery, mother place of birth, smoking during pregnancy	Inverse association between maternal PFOA and ponderal index at birth (β -0.412, 95% CI -0.788 to -0.037). No association (p>0.05) between maternal PFOA and birth weight or length.
Apelberg et al. 2007b Cross-sectional study of 341 singleton births in Baltimore Maryland; maternal and neonatal data collected from hospital records	**Exposure:** Median cord blood serum PFOA level 1.6 ng/mL (range: 0.3–7.1 ng/mL) **Linear regression model adjustments:** Gestational age, maternal age, BMI, race, parity, smoking, baby sex, height, net weight gain, diabetes, hypertension, delivery mode (head circumference only)	No significant association (p>0.05) between cord blood serum PFOA levels and gestational age, birth weight, or length. Significant inverse associations between cord blood serum PFOA levels and head circumference and ponderal index.
Ashley-Martin et al. 2016 Cohort study of 1,723 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada; GWG was based on weekly weight gain during the 2nd and 3rd trimesters	**Exposure:** Median serum PFOA (measured during first trimester) and cord blood PFOA: 1.70 and 0.39 ng/mL **Logistic regression adjustments:** Maternal age, prepregnancy BMI	No significant association (p>0.1) between serum PFOA and GWG when subjects were stratified by BMI. GWG was significantly associated with increased odds of high cord blood PFOA (>0.39 ng/mL); OR 1.04 (95% CI 1.02–1.06) per 1 kg increase in GWG.
Ashley-Martin et al. 2017 Cross-sectional study of 1,705 mother-infant pairs participating in the Maternal Infant Research on Environmental Chemicals in Canada	**Exposure:** Median maternal plasma PFOA 1.7 ng/mL (measured during first trimester) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, household income, smoking	No association between maternal PFOA and birth weight (β -0.10, 95% CI -0.34–0.13), leptin (β 0.01, 95% CI -0.15–0.13), or adiponectin (β 0.04, 95% CI -0.05–0.12). Similar findings when cord blood PFOA used as biomarker of exposure.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Bach et al. 2016 Cohort study of 1,507 nulliparous women and their children in the Aarhus Birth Cohort in Denmark	**Exposure:** Median serum PFOA levels (measured between gestation week 9 and 20): 2.0 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, maternal education	No consistent alterations in birth weight, birth length, or head circumference were found in comparisons across serum PFOA quartiles.
Bae et al. 2015 Prospective study of 233 couples from Michigan and Texas participating in the Longitudinal Investigation of Fertility and the Environment Study	**Exposure:** Geometric mean serum PFOA levels 5.01 and 4.05 ng/mL in male and female nulliparous parents and 5.00 and 2.54 ng/mL in male and female parous parents (measured at the time of pregnancy testing) **Logistic regression adjustments:** Age, research site, household income, maternal parity	No significant association between maternal or paternal PFOA levels and the odds of a male birth (maternal: OR 0.93, 95% CI 0.68–1.26; paternal: OR 0.94, 95% CI 0.72–1.23).
Braun et al. 2014 Prospective study of 175 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; social responsiveness scale measures (measurement of autistic behavior) was evaluated when children were 4 and 5 years of age	**Exposure:** Median maternal serum PFOA levels (measured at 16 weeks of gestation): 5.5 ng/mL **Bayesian regression adjustments:** Maternal age at delivery, race, marital status, education, parity, insurance status, employment, household income, prenatal vitamin use, maternal depressive symptoms, maternal IQ, child sex, caregiving environment, maternal serum cotinine	An inverse association between maternal serum PFOA levels and social responsiveness scale scores; however, the 95% CI of the regression betas included unity (β -2.0, 95% CI -4.4–0.4).
Buck Louis et al. 2016 Prospective study of 332 couples followed from preconception to 7 weeks post-conception	**Exposure:** Median serum PFOA in women 3.3 ng/mL **Statistical adjustments:** Age, BMI, prior pregnancy loss, alcohol consumption, cigarette smoking during pregnancy	No association between maternal serum PFOA and pregnancy loss (HR 0.93, 95% CI 0.75–1.16.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Callan et al. 2016 Cross-sectional study of 98 pregnant women in Australia	**Exposure:** Median serum PFOA 0.86 ng/mL (range of 0.21–3.1 ng/mL) (measured 2 weeks prior to due date) **Statistical adjustments:** Gestational age, maternal height, prepregnancy BMI, weight gain during pregnancy, infant sex	No association between maternal PFOA and birth weight (β -48 g, 95% CI -203–108), birth length (β 0.06, 95% CI -0.70–0.81), head circumference (β -0.40, 95% CI -0.96–0.16), or ponderal index (β -0.06, 95% CI -0.16–0.05).
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFOA 1.59 ng/mL; 1st tertile <0.99 ng/mL, 2nd tertile 0.99–1.59 ng/mL, 3rd tertile >1.59 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	Inverse association between cord PFOA and birth length (β, 95% CI): 2nd tertile: -0.21 (-0.56–0.14) 3rd tertile: -0.45 (-0.79 to -0.10). No association between cord PFOA and birth weight (p=0.58) or ponderal index (p=0.21).
Chen et al. 2012a Cross-sectional study of 429 infants participating in Taiwan Birth Panel Study	**Exposure:** Geometric mean cord blood PFOA level 1.84 ng/mL **Linear and logistic regression model adjustments:** Maternal age, prepregnancy BMI, education level, type of delivery, parity, infant sex, gestational age (for birth weight, birth length, heard circumference, ponderal index, LBW)	No significant associations (p>0.05) between cord blood PFOA and gestational age, birth weight, birth length, head circumference, or ponderal index. No significant association between cord blood PFOA and odds preterm birth (OR 0.64, 95% CI 0.40–1.02), LBW (OR 0.53, 95% CI 0.18–1.55), or SGA (OR 1.24, 95% CI 0.75–2.05).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Chen et al. 2013 Cross-sectional study of 239 2-year-old children participating in Taiwan Birth Panel Study; scores on the Comprehensive Developmental Inventory for Infants and Toddlers test were used to assess neurodevelopment	**Exposure:** Mean cord blood PFOA level 2.5 ng/mL **Linear and logistic regression model adjustments:** Maternal education, family income, infant sex and gestational age, breastfeeding, HOME score at 24 months of age, cord blood cotinine level, postnatal environmental smoke exposure	No associations between cord blood PFOA and scores on the full test or on tests of cognitive, language, gross motor, fine motor, social, or self-help tests (CIs on the change in outcome for a shift from 25th to 75th percentile included unity). Among children with the lowest 10% of scores, a 10 ng/mL increase in cord blood PFOA was not associated with an increased risk of poor performance on whole test (OR 0.6, 95% CI 0.08–4.8), cognitive (OR1.3, 95% CI 0.3–6.2), language (OR 0.5, 95% CI 0.06–4.0), gross motor (OR 0.8, 95% CI 0.1–4.7), fine motor (OR 2.8, 95% CI 0.6–13.5), social (OR 0.3, 95% CI 0.02–2.7), or self-help (OR 3.2, 95% CI 0.7–14.3) tests.
Christensen et al. 2011 Case-control study of 448 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; case-control study of girls with early menarche (<11.5 years of age, n=218) and controls (menarche ≥11.5 years, n=230)	**Exposure:** Median maternal (blood samples measured at gestation week 15) serum PFOA 3.7 ng/mL **Logistic regression model adjustments:** Birth order, maternal age at delivery	No significant association between maternal PFOA and odds of earlier age at menarche (OR 1.01, 95% CI 0.61–1.68).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Donauer et al. 2015 Prospective study of 349 infants who whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; neurobehavior was evaluated at 5 weeks of age using the Neonatal Intensive Care Unit Network Neurobehavioral Scale	**Exposure:** Geometric mean maternal serum PFOA (most measured at gestation week 16; 10% measured at gestation week 26, and 5% at delivery): 5.49 ng/mL **Statistical adjustments:** Infant sex and age at examination, maternal age, race, household income, marital status, maternal depression, maternal BMI at 13–19 weeks of gestation, alcohol and marijuana use during pregnancy, maternal serum cotinine, infant weight change per month from birth to 5 weeks, maternal blood lead level during pregnancy, variable of high risk infants (gestation age <37 weeks, birth weight <2,500 g and/or stay in NICU after birth)	No significant (p>0.05) associations between maternal serum PFOA levels and neurobehavioral outcomes were found. Significant association (p=0.0322) between maternal serum PFOA and the likelihood of infants being categorized as hypotonic, as compared to social/easy going OR 3.79 (95% CI 1.1–12.8). However, there was no alteration (p=0.3533 without statistical adjustments) in the likelihood of infants being categorized as high arousal/difficult.
Fei et al. 2007, 2008a Cross-sectional study of 1,400 pregnant women participating in Danish National Birth Cohort study; birth outcome data obtained from National Discharge Register at the National Board of Health	**Exposure:** Median maternal serum PFOA levels (measured during first trimester) 5.6 ng/mL (range: <LLOQ [1.0]–41.5 ng/mL) • 1st quartile: <LLOQ–3.91 ng/mL • 2nd quartile: 3.91–5.20 ng/mL • 3rd quartile: 5.21–6.96 ng/mL • 4th quartile: ≥6.97 ng/mL **Statistical adjustments:** Maternal age, parity, socio-occupational status, prepregnancy BMI, smoking during pregnancy, infant sex, gestational week at blood drawing	Maternal PFOA levels inversely associated with birth weight (β -10.63, 95% CI -20.79 to -0.47), birth length (β -0.069, 95% CI -0.113 to -0.024), and abdominal circumference (β -0.059, 95% CI -0.106 to -0.012). No association between maternal PFOA and head circumference (β -0.030, 95% CI -0.064–0.004). No significant associations between PFOA and gestation length (p>0.01), preterm birth (OR 1.71, 95% CI 0.55–5.28 for 4th quartile), LBW (OR 2.44, 95% CI 0.27–22.25 for 4th quartile), or SGA (OR 0.97, 95% CI 0.55–1.70 for 4th quartile); maternal serum PFOA levels for the 4th quartile were >6.97 ng/mL.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fei et al. 2008b Cross-sectional study of 1,400 pregnant women participating in Danish National Birth Cohort study; birth outcome data obtained from National Discharge Register at the National Board of Health, Infants were examined at birth (Apgar score) and at 5–7 and 18–20 months of age (neurodevelopmental milestones)	**Exposure:** Median maternal serum PFOA levels (measured during first trimester) 5.6 ng/mL (range: <LLOQ [1.0]–41.5 ng/mL) • 1st quartile: <LLOQ–3.91 ng/mL • 2nd quartile: 3.91–5.20 ng/mL • 3rd quartile: 5.21–6.96 ng/mL • 4th quartile: ≥6.97 ng/mL **Statistical adjustments:** Maternal age, parity, socio-occupational status, prepregnancy BMI, smoking during pregnancy, infant sex, gestational week at blood drawing	No significant association between maternal PFOA and risk of Apgar scores <10 (assessed 5 minutes after birth); OR 1.14 (95% CI 0.57–2.25). No significant trends (p>0.05) for associations between maternal PFOA levels and gross motor, fine motor, attention, cognition, or language developmental milestones assessed at 18 months of age or in motor or mental development at 6 months of age.
Fei and Olsen 2011 Subgroup of the Fei et al. (2007, 2008a, 2008b) cohort consisting of 526–787 children; mothers completed questionnaires regarding behavioral and social development when the children were 7 years of age	**Exposure:** Median maternal serum PFOA levels (measured during first trimester) 5.4 ng/mL (range: 0.5–21.9 ng/mL) **Statistical adjustments:** Parity, maternal age, prepregnancy BMI, smoking and alcohol consumption during pregnancy, socioeconomic status, sex of child, breastfeeding, birth year, home density, gestational age at blood drawing, parental behavioral problem scores during their childhood (not used for developmental coordination disorder analyses)	No significant trends between maternal PFOA levels and the risk of abnormal scores on tests of behavioral health (p>0.15 for trend) or motor coordination (p=0.89 for trend) in children. Some significant inverse associations between maternal PFOA levels and the risk of abnormal scores were found at maternal serum PFOA levels in the 2nd (3.96–5.32 ng/mL) and 3rd (5.35–7.11 ng/mL) quartiles, but were not found in the 4th quartile.
Forns et al. 2015 Prospective study of 843 infants of mothers participating in the Norwegian Human Milk Study; neurobehavioral assessment, as measured using the Ages and Stages Questionnaire-II, was conducted at 6 and 24 months of age.	**Exposure:** Median PFOA breast milk level (measured 2 weeks after giving birth) 40 ng/L **Logistic regression adjustments:** Child's age at milk sample collection, fish consumption during pregnancy, maternal age, maternal education, parity, prepregnancy BMI, maternal smoking during pregnancy, interpregnancy interval, duration of total breastfeeding of previous children, child's sex	No alteration in the risk of an abnormal score on neurobehavioral assessment questionnaire at 6 months (OR 1.05, 95% CI 0.77–1.44) or 24 months (OR 1.0, 95% CI 0.78–1.28) of age.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Goudarzi et al. 2016b Prospective study of infants of mothers participating in the Hakkaido Study on Environment and Children's Health in Japan; neurodevelopment was assess using the MDI and PDI tests at age 6 months (n=173) and 18 months (n=133)	**Exposure:** Median maternal serum PFOA levels (measured after second trimester): 1.2 ng/mL for 6-month evaluation group and 1.2 ng/mL for 18-month evaluation group **Statistical adjustments:** Gestational age, maternal age, parity, education, alcohol use, smoking, caffeine during pregnancy, blood sampling period, breastfeeding	No significant association ($p>0.05$) between maternal serum PFOA levels and performance on the MDI and PDI tests at 6 months. When stratified by sex, a significant inverse association ($p<0.05$) between PFOA and MDI scores was observed in female infants at 6 months; further stratification by maternal PFOA quintile levels, resulted in a significant inverse association for the 5th quintile. No significant associations between serum PFOA and MDI and PDI test scores were found at 18 months.
Govarts et al. 2016b Cross-sectional study of 202 infants of mothers participating in the Flemish Human Environmental Health Survey in Belgium	**Exposure:** Geometric mean cord blood serum PFOA: 1.52 ng/mL **Linear Regression adjustments:** Gestational age, child's sex, smoking during pregnancy, parity, prepregnancy BMI	No significant association ($p=0.473$) between cord blood PFOA and birth weight was found.
Govarts et al. 2018 Compilation of data from 4 birth cohort studies in Europe	**Exposure:** Median cord serum PFOA 0.550 ng/mL; exposure estimate based on measured cord PFOA from one cohort, estimated cord PFOA based on measured breast milk levels from two cohorts; and measured and estimated cord PFOA from one cohort **Statistical adjustments:** Maternal education, age at delivery, height, and prepregnancy BMI, parity, child's sex	No association between cord PFOA and risk of small for gestational age (OR 1.637, 95% CI 0.971–2.761). Among women who smoked during pregnancy, association between cord PFOA and risk of small for gestational age (OR 2.177, 95% CI 1.022–4.643). No association found in nonsmoking women (OR 0.511, 95% CI 0.869–2.632).
Gump et al. 2011 Cross-sectional study of 83 children aged 9–11 years (mean 10.13 years; 36.1% female) living in New York	**Exposure:** Mean and median serum PFOA: 3.23 and 3.28 ng/mL **Statistical adjustments:** Blood lead, sex, body fat, patent's education, family history of high blood pressure, asthma	No significant ($p>0.05$) association between serum PFOA and performance on a task requiring behavioral inhibition.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Hamm et al. 2010 Cross-sectional study of 252 pregnant women in Alberta Canada undergoing prenatal screening for Down's syndrome, trisomy 18, and open spina bifida; birth outcome data obtained from medical records	**Exposure:** Mean serum PFOA levels (measured in early second trimester) 2.1 ng/mL (range:<LOD [0.25]–18 ng/mL) **Statistical adjustments:** Maternal age, maternal weight, maternal height, smoking status during pregnancy, infant sex, maternal race, parity	No associations between maternal serum PFOA levels and birth weight (change in birth weight for 3rd tertile of 14.80 (95% CI -107.29–136.89). No significant associations between maternal serum PFOA and the risk for SGA or preterm delivery; the RRs (95% CI) for serum PFOA levels in the 3rd tertile (>2.1–18 ng/mL) were 0.99 (0.25–3.92) and 1.31 (0.38–4.45).
Hoffman et al. 2010 Cross-sectional study of 571 children aged 12–15 years participating in NHANES 1999–2000 or 2003–2004	**Exposure:** Median serum PFOA: 4.4 ng/mL (range: 0.4–21.7 ng/mL) **Logistic regression model adjustments:** NHANES sample cycle, age, race/ethnicity, sex, environmental tobacco smoke, and maternal smoking during pregnancy	Significant association between serum PFOA levels and parent-reported ADHD; the OR for each 1 ng/mL increase in serum PFOA was 1.12 (95% CI 1.01–1.23).
Høyer et al. 2015a Prospective study of 1,106 children of mothers participating in the INUENDO cohort in Greenland, Ukraine, and Poland; parents completed questionnaires when the children were between 5 and 9 years of age to evaluate behavior and motor development	**Exposure:** Median maternal serum PFOA (measured at any time during pregnancy): 1.4 ng/mL **Statistical adjustments:** Maternal cotinine level during pregnancy, alcohol consumption at conception, maternal age at pregnancy, child sex, gestational age at blood sampling	No significant associations between maternal serum PFOA and motor skills were found (β -0.2, 95% CI -1.2–0.9). Significant association between maternal serum PFOA levels and risk of abnormal behavior was observed; OR 2.7 (95% CI 1.2–6.3) for children with maternal serum PFOA levels in the 3rd tertile (1.9–9.8 ng/mL). Significant association between maternal serum PFOA levels and risk of hyperactivity was observed; OR 3.1 (95% CI 1.3–7.2) for children with maternal serum PFOA levels in the 3rd tertile. When segregated by country, a significant association was found in the Greenland cohort (OR 6.3, 95% CI 1.3–30.1) for the 3rd tertile (2.2–5.1), but not in the Ukraine cohort (OR 0.9, 95% CI 0.3–2.4; 3rd tertile PFOA levels of 1.1–9.8 ng/mL). Analysis not conducted in the Poland cohort.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Itoh et al. 2016 Prospective study of 189 infants whose mothers were participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Maternal median serum PFOA levels (measured after the second trimester): 1.4 ng/mL **Linear regression adjustments:** Maternal age, parity, prepregnancy BMI, annual income smoking and caffeine consumption during pregnancy, gestational week of blood sampling, gestational age at birth	Significant association between maternal serum PFOA levels and cord blood inhibin B levels in male infants (p=0.040). No significant associations (p>0.05) with estradiol, testosterone, testosterone:estradiol ratio, progesterone, LH, FSH, SHBG, testosterone:SHBG ratio, or insulin-like factor-3 in male and female infants or inhibin B in female infants.
Jeddy et al. 2017 Prospective study of 432 mother-daughter pairs participating in the Avon Longitudinal Study of Parents and Children in the Great Britain; children were assessed at 15 and 38 months of age	**Exposure:** Maternal median serum PFOA 3.7 ng/mL (measured at 15 weeks of gestation) **Statistical adjustments:** Parity, maternal age, maternal education, maternal smoking status, gestational age at blood sample collection	No association between maternal PFOA and verbal comprehension, vocabulary comprehension and production, nonverbal communication, or social developmental scores in 15-month-old children (p>0.05). When children were categorized by maternal age at delivery, an inverse association between maternal PFOA and vocabulary comprehension and production scores was found in 15-month infants with mothers <25 years of age (β -11.39, 95% CI -22.76 to -0.02). Inverse association between maternal PFOA and intelligibility scores (β -0.04, 95% CI -0.08 to -0.01) in children 38 months of age. When children were categorized by maternal age at delivery, an inverse association between maternal PFOA and intelligibility scores was found in 38-month children with mothers >30 years of age (β -0.06, 95% CI -0.11 to -0.01). No association with maternal PFOA for language or communicative scores in 38-month-old children (p>0.05).
Jensen et al. 2015	**Exposure:** Median maternal serum PFOA levels (measured prior to gestation week 12): 1.58 ng/mL	No significant association between maternal serum PFOA levels and the risk of miscarriage

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Case-control study of 56 women in Denmark having a miscarriage before gestation week 12 and 336 matched controls	**Logistic regression adjustments:** Age, BMI, parity, and gestational age at serum sampling	before gestation week 12; OR 0.64 (95% CI 0.36–1.18).
Kim et al. 2011 Cross-sectional study of 44 pregnant women in South Korea; birth outcome data obtained from questionnaires	**Exposure:** Median maternal serum PFOA (mostly measured during the third trimester) 1.46 ng/mL (range: 1.15–1.91 ng/mL). Cord blood serum PFOA level 1.15 ng/mL (range: 0.95–1.86 ng/mL) **Statistical adjustments:** Maternal age, gestational age, maternal BMI (T4, TSH, and body weight only)	Significant ($p<0.05$) correlation between maternal serum PFOA levels and fetal cord TSH levels. No significant correlations ($p>0.05$) with T3 or T4 levels. No significant correlations ($p>0.05$) between cord blood PFOA and fetal cord T3, T4, or TSH levels. No significant correlations ($p>0.05$) between maternal serum PFOA or cord blood PFOA levels and birth weight.
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFOA: 5.398 ng/mL (cases) and 2.12 ng/mL (controls)	Serum PFOA levels were significantly ($p<0.01$) higher than in cases than controls. Significant inverse correlation ($p<0.05$) between serum PFOA levels and thyroid stimulating immunoglobulin levels in infants with congenital hypothyroidism. No significant correlation ($p>0.05$) between serum PFOA and TSH, free T4, T3, and microsomal antibodies.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kishi et al. 2015 Prospective study of 306 infants whose mothers were participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Mean and median maternal serum PFOA levels (measured after the second trimester): 1.52 and 1.40 ng/mL **Linear regression adjustments:** Maternal age, parity, annual income smoking and alcohol consumption during pregnancy, gestational week of blood sampling	Significant association between maternal serum PFOA and palmitic acid (p=0.027) levels. No significant associations between maternal serum PFOA and triglycerides (p=0.273), palmitoleic acid (p=0.333), stearic acid (p=0.352), oleic acid (p=0.067), linoleic acid (p=0.385), α-linolenic acid (p=0.675), arachidonic acid (p=0.619), eicosapentaenoic acid (p=0.854), docosahexaenoic acid (p=0.377), essential fatty acids (p=0.384), omega 6 (p=0.440), or omega 3 (p=0.479).
Kobayashi et al. 2017 Cross-sectional study of 177 mother-infant pairs participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Mean maternal serum PFOA (measured at gestation weeks 24–42) 1.6 ng/mL (range of ND–5.3 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, maternal education, maternal smoking during pregnancy, gestational age, infant sex, maternal blood sampling period	No association between maternal PFOA and birth weight (β -49.4, 95% CI -130.4–31.6), birth length (β 0.01, 95% CI -0.37–0.40), or ponderal index (β -0.44, 95% CI -0.99–0.12).
Kristensen et al. 2013 Prospective study of 343 women whose mothers participated in a Danish pregnancy cohort study	**Exposure:** Median maternal serum PFOA (measured at gestation week 30): 3.6 ng/mL **Statistical adjustments:** Maternal smoking during pregnancy, household income, daughter's BMI, daughter's smoking (menstrual cycle length, reproductive hormones, follicle number), menstrual cycle phase (FSH, LH, estradiol)	A significant association between maternal serum PFOA levels and age of menarche of the daughters (p=0.01). The age of menarche was 5.3 months longer in daughters whose mothers were in the 3rd tertile (4.4–19.8 ng/mL) compared to those in the 1st tertile (0.1–3.0 ng/mL). No significant associations (p>0.05) between maternal serum PFOA levels and menstrual cycle length, total testosterone, SHBG, free androgen index, dehydroepiandrosterone sulphate, anti-Müllerian hormone, or number of follicles/ovary in daughters using or not using hormonal contraceptives

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lauritzen et al. 2017 Case-cohort study of 265 mother-infant pairs participating in a prospective study in Norway	**Exposure:** Median maternal serum PFOA 1.62 ng/mL (range of 0.31–7.97) (measured in gestation weeks 17–20) **Statistical adjustments:** Maternal age, height, prepregnancy BMI, education, parity, smoking status at conception, interpregnancy interval, child's sex	No association between maternal PFOA and birth weight (p=0.590), birth length (p=0.656), head circumference (p=0.354), or gestational age (p=0.431). No association with risk of SGA (OR 0.66, 95% CI 0.33–1.33).
Lauritzen et al. 2017 Case-cohort study of 159 mother-infant pairs participating in a prospective study in Sweden	**Exposure:** Median maternal serum PFOA 2.33 ng/mL (0.60–6.70 ng/mL) (measured in gestation weeks 17–20) **Statistical adjustments:** Maternal age, height, prepregnancy BMI, education, parity, smoking status at conception, interpregnancy interval, child's sex	Inverse association between maternal PFOA and birth weight (β -359, 95% CI -596 to -122; p=0.003), birth length (β -1.3, 95% CI -2.3 to -0.3, p=0.010). When infants were categorized by sex, associations with birth weight (p=0.001) and birth length (p=0.012) were only observed in boys. No association between maternal PFOA and head circumference (p=0.115), or gestational age (p=0.318). Association with risk of SGA and maternal PFOA (OR 5.25, 95% CI 1.68–16.4). When infants were divided by sex, association was observed in boys (OR 6.55, 95% CI 1.14–37.45), but not in girls (OR 4.73, 95% CI 0.79–28.3).
Lee et al. 2013 Cross-sectional study of 59 pregnant women in South Korea; birth outcome data obtained from medical records	**Exposure:** Mean maternal serum PFOA (measured at delivery) 2.73 ng/mL (range: 1.20–5.72 ng/mL). Mean cord blood serum PFOA level 2.09 ng/mL (range: 0.75–5.44 ng/mL) **Logistic regression model adjustments:** Maternal age, gestational age	Maternal PFOA levels significantly higher in infants whose birth weight (p=0.04), birth length (p=0.04), and ponderal index (ratio of birth weight to length) (p=0.04) were below the median level; no significant association with head circumference (p=0.12). These are unadjusted values. After adjustments for confounders, no significant associations between maternal PFOA levels and birth weight (OR 0.54, 95% CI 0.17–3.03), birth length (OR 0.44, 95% CI

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		0.12–1.58), ponderal index (OR 0.56, 95% CI 0.16–2.01), or head circumference (OR 0.82, 95% CI 0.24–13.65). No significant associations between cord blood PFOA levels and birth weight (p=0.78), birth length (p=0.99), head circumference (p=0.35), or ponderal index (p=0.67).
Lee et al. 2016 Cross-sectional study of 85 newborns in South Korea; birth outcome data from medical records	**Exposure:** Mean cord blood serum PFOA: 1.11 ng/mL **Multiple regression adjustments:** Gestational age, maternal age, infant sex, variable to control for sampling bias	No significant association (p>0.05) between cord blood PFOA levels and birth weight.
Lenters et al. 2016a, 2016b Prospective study of 1,250 infants whose mothers participated in the INUENDO cohort in Greenland (n=513), Ukraine (n=557), and Poland (n=180)	**Exposure:** Median maternal serum PFOA levels: 1.84 ng/mL for Greenland cohort, 2.51 ng/mL for Poland cohort, and 0.96 ng/mL for Ukraine cohort **Regression model adjustments:** Study population, maternal age, parity, gestational age, infant sex, maternal height, alcohol consumption, cotinine, vitamin D	Significant association (p=0.009) between maternal PFOA levels and term birth weight. In linear regression analysis that adjusted for exposure to other environmental exposures (diethyl hexyl phthalate and diisononyl phthalate metabolites and *p,p'*-DDE, the association between maternal serum PFOA and term birth weight remained significant (p=0.035); β -63.77 (95% CI -122.83 to -4.71) per 2 SD increase in ln transformed PFOA.
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFOA 1.2 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	Inverse association between cord PFOA and birth weight (β -112.7, 95% CI -171.9 to -53.5). No association between cord PFOA and gestational age (β 0.16, 95% CI -0.02–0.33).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lien et al. 2016 Prospective study of 282 7-year-old children whose mothers participated in the Taiwan Birth Panel Study or Taiwan Early-Life Cohort; psychometric symptoms related to attention deficit/hyperactivity disorder were assessed using three parent completed questionnaires	**Exposure:** Weighted average cord blood serum PFOA: 1.55 ng/mL **Linear regression adjustments:** Child sex, breastfeeding, maternal age, maternal education, parity, maternal environmental tobacco smoke during pregnancy, alcohol consumption during pregnancy, annual income, gestational age, birth weight, cord blood lead, study cohort	No significant associations between cord blood PFOA and scores on tests measuring inattention (p=0.7758), hyperactivity/impulsivity (p=0.2997), oppositional defiant disorder (p=0.9459), internalizing problems (p=0.1911), externalizing problems (p=0.6421), emotional symptoms (p=0.691), conduct problems (p=0.2664), hyperactivity/inattention (p=0.774), peer problems (p=0.9047), or pro-social behavior (p=0.7983).
Liew et al. 2014 Case-control study using data from the Danish National Birth Cohort study; 156 children were diagnosed with congenital cerebral palsy (cases) and 550 randomly selected children served as controls	**Exposure:** Median maternal serum PFOA (86% measured during first trimester and 14% during the second trimester). Cases: • boys 4.56 ng/mL • girls 3.90 ng/mL Controls: • boys 4.00 ng/mL • girls 4.04 ng/mL **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness	Significant association between maternal PFOA levels and risk of congenital cerebral palsy in boys (RR 2.1, 95% CI 1.2–3.6), but not in girls (RR 0.8, 95% CI 0.4–1.5).
Liew et al. 2015 Nested case control study using data from the Danish National Birth Cohort study; 215 cases of ADHD, 213 cases of autism, and 545 randomly selected children served as controls	**Exposure:** Median maternal serum PFOA (87% measured during first trimester and 13% during the second trimester): 4.06 ng/mL for ADHD cases, 3.88 ng/mL for autism cases, 4.00 ng/mL for controls **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness, gestational week of blood drawn, child's sex, birth year	No significant association between maternal PFOA levels and the risk of ADHD (RR 0.98, 95% CI 0.82–1.16) or autism (RR 0.98, 95% CI 0.73–1.31).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Maisonet et al. 2012 Prospective cohort study of 447 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data obtained from medical records; weight and height at age 2 and 20 months were measured	**Exposure:** Median maternal serum PFOA (measured at gestation week 15) 3.7 ng/mL (range: 1.0–16.4 ng/mL) **Linear regression (with inverse probability) adjustments:** Maternal smoking during pregnancy (birth weight and length only), maternal prepregnancy BMI, previous live births, gestational age, maternal education (birth length only)	Significant inverse trend between maternal serum PFOA levels and birth weight (p=0.0120); no significant trends for birth length (p=0.0978) or ponderal index (p=0.5920). No significant association between maternal serum PFOA and weight at 20 months (unadjusted p=0.9642, adjusted by birth weight p=0.4892, adjusted for height at 20 months p=0.9269, or adjusted by height at 20 months and birth weight p=0.4147).
Maisonet et al. 2015a Prospective cohort study of 72 girls (aged 15 years) participating in Avon Longitudinal Study of Parents and Children in Great Britain	**Exposure:** Median maternal serum PFOA (measured at gestation week 16) 3.6 ng/mL (range: 1.1–14.6 ng/mL) **Statistical adjustments:** SHBG concentration (testosterone), maternal education, maternal age at delivery, maternal prepregnancy BMI, maternal smoking during pregnancy, time of day daughter's blood sample obtained, daughter's age at menarche, daughter's BMI at age 15 years	Serum testosterone levels were 0.24 nmol/L (95% CI 0.05–0.43) higher in girls whose maternal serum PFOA levels were in the 3rd tertile (>4.1 ng/mL). No association between serum PFOA and SHBG (5.02, 95% CI -13.07–11.00).
Manzano-Salgado et al. 2017a Prospective study of 1,202 mother-infant pairs participating in the Environment and Childhood Study in Spain	**Exposure:** Mean maternal serum PFOA 2.35 ng/mL (measured during first trimester) **Statistical adjustments:** Maternal age, parity, prepregnancy BMI, fish intake during pregnancy	No association between maternal PFOA and birth weight (β -9.33, 95% CI -38.81–20.16) length (β -0.01, 95% CI -0.15–0.14), head circumference (β 0.07, 95% CI -0.17–0.03), or gestational age (β -0.05, 95% CI -0.12–0.08). No associations between maternal PFOA and risk of small for gestational age (OR 0.92, 95% CI 0.72–1.19), preterm (OR 0.90, 95% CI 0.60–1.35), low birth weight (OR 0.90, 95% CI 0.63–1.29), or low birth weight at term (OR 0.85, 95% CI 0.53–1.34).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Monroy et al. 2008 Prospective study of 101 pregnant women participating in the Family Study in Ontario Canada; birth outcome data obtained from medical records	**Exposure:** Median maternal serum PFOA (measured at delivery) 1.81 ng/mL (range: 1.33–2.64 ng/mL); median cord blood PFOA 1.58 ng/mL (range: 1.09–2.37 ng/mL) **Linear regression model adjustments:** Parity, gestational length, maternal BMI, sex, smoking status	No significant correlations (p>0.05) between maternal serum PFOA or cord blood PFOA and birth weight.
Minatoya et al. 2017 Cross-sectional study of 168 mother-infant pairs participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Median maternal serum PFOA 1.4 ng/mL (measured at gestation weeks 23–35) **Statistical adjustments:** Maternal BMI, parity, smoking during pregnancy, blood sampling period, gestational age, infant sex	Inverse association between maternal PFOA and birth weight (β -197, 95% CI -391 to -3, p=0.047); no association with ponderal index (β -1.32, 95% CI -2.66–0.02, p=0.054). No associations between maternal PFOA and cord blood total adiponectin levels (p=0.377), high molecular weight adiponectin levels (p=0.575), or leptin levels (p=0.830).
Ode et al. 2014 Case-control study of 206 children with ADHD in Sweden and 206 matched controls; children were 5–17 years old at the time of diagnosis	**Exposure:** Median cord blood serum level of PFOA 1.80 ng/mL for cases and 1.83 ng/mL for controls **Logistic regression adjustments:** Maternal smoking, parity, gestational age at birth	No significant association between cord blood PFOA and risk of ADHD; OR 0.98 (95% CI 0.91–1.02 for 1 ng/mL increase in cord blood PFOA).
Oulhote et al. 2016 Prospective study of 567 7-year-old children; behavioral development was assessed using a Strengths and Difficulties Questionnaire	**Exposure:** Geometric mean PFOA levels: maternal 3.19 ng/mL (range of 0.82–8.43 ng/mL) (measured at 16 weeks of gestation), 5-year-old child 4.09 ng/mL (range of 1.33–15.44 ng/mL), 7-year-old child 4.51 ng/mL (range of 1.72–19.16 ng/mL) **Statistical adjustments:** Child's age, sex, maternal age, prepregnancy BMI, parity, socio-economic status, alcohol and tobacco use during pregnancy, breastfeeding duration, birth weight	No associations between maternal PFOA levels and behavioral development scores. Association between child's PFOA levels at age 5 years and total questionnaire score (indicative of higher difficulties) and higher internalizing problems, peer relationship score, and autism screening score. No associations between child's PFOA levels at age 7 years and behavioral development scores.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Quaak et al. 2016 Prospective study of 76 infants whose mothers participated in the Linking Maternal Nutrition to Child Health study in the Netherlands; child behavior was assessed at 18 months of age via a parent completed questionnaire	**Exposure:** Mean and median cord blood plasma PFOA 0.9056 and 0.8700 ng/mL **Linear regression adjustments:** Parental educational level, maternal smoking and alcohol use, family history of ADHD	No significant associations between cord plasma PFOA levels and scores on an ADHD scale (p=0.70 and p=0.72 for the 2nd and 3rd tertiles, respectively) or the externalizing problem scale (p=0.12 and p=0.31 for 2nd and 3rd tertiles). Stratifying by sex did not alter the scores on the ADHD scale (p=0.22 and p=0.31 for boys and girls in the 3rd tertile, respectively). A significant inverse association was found on the externalizing problem scale in boys (p=0.05 and p=0.09 for the 2nd and 3rd tertiles); the association was not significant in girls (p=0.10 and p=0.74 for the 2nd and 3rd tertiles).
Robledo et al. 2015a, 2015b Cross-sectional study of 234 couples in Michigan and Texas participating in the LIFE study cohort; women reported birth size characteristics after delivery	**Exposure:** Geometric mean PFOA levels 3.16 ng/mL (maternal) and 5.00 ng/mL (paternal) **Linear regression adjustments:** Maternal age, difference between maternal and paternal age, prepregnancy BMI, infant sex, serum cotinine concentration, concentration of other perfluoroalkyls	No significant associations (p>0.05) between maternal or paternal PFOA levels and birth weight, birth length, head circumference, or ponderal index.
Sagiv et al. 2018 Prospective study of 1,645 pregnant women participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFOA 5.8 ng/mL (measured at gestation weeks 5–19) **Statistical adjustments:** Maternal age, race/ethnicity, education, prenatal smoking, parity, history of breastfeeding, prepregnancy BMI, paternal education, household income, child's sex, gestational age at blood draw	No association between maternal PFOA and birth weight for gestational age (β -0.02, 95% CI -0.08–0.03) or gestational length (β -0.05, 95% CI -0.16–0.06). No association between maternal PFOA and preterm births (OR 1.0, 95% CI 0.9–1.3).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Shi et al. 2017 Cross-sectional study of 170 infants in China	**Exposure:** Median cord serum PFOA 1.097 ng/mL (range of 0.363–5.002 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, gestation age, infant sex, maternal height	No associations between cord PFOA and birth weight (β 163.28, 95% CI -127.66–454.23), birth length (β 0.38, 95% CI -0.41–1.17), or ponderal index (β 0.06, 95% CI -0.10–0.22).
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFOA 1.1 ng/mL (measured at 20–34 weeks of gestation); 1st tertile 0.1–0.8 ng/mL, 2nd tertile 0.9–1.4 ng/mL, 3rd tertile 1.4–17.0 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education gestational weight gain, smoking during pregnancy, gravidity, gestational age at blood draw, infant sex, gestational age at birth	Inverse association between maternal PFOA and birth weight (β, 95% CI): 2nd tertile: -15.9 g (-84.9–53.2) 3rd tertile: -92.4 g (-166.2 to -18.5). No association between maternal PFOA and adiposity at birth (β, 95% CI): 2nd tertile: -0.34% fat mass (-1.06–0.38) 3rd tertile: -0.97% fat mass (-0.33–0.49).
Strøm et al. 2014 Prospective study of 876 offspring of women participating in the Danish Fetal Origins 1988 study; neurobehavioral and affective disorders were assessed in the offspring using population-based registry data (20-year follow-up)	**Exposure:** Median maternal serum PFOA (measured during gestation week 30) 3.7 ng/mL **Regression model adjustments:** Maternal age, parity, prepregnancy BMI, maternal education, maternal smoking during pregnancy, offspring sex	No significant associations between maternal serum PFOA and offspring ADHD (trend for 3rd tertile, p=0.45), depression (trend for 3rd tertile p=0.28), or scholastic achievement below the median (trend for 3rd tertile p=0.21).
Vested et al. 2013 Prospective cohort study of 169 males aged 19–21 years in Denmark whose mothers participated in pregnancy cohort study	**Exposure:** Median maternal serum PFOA (measured during gestation week 30) 3.8 ng/mL **Multivariable regression adjustments:** History of reproductive tract disease, BMI, smoking status, maternal smoking during pregnancy, socioeconomic status at birth, abstinence time (sperm parameters)	Significant inverse trend between maternal PFOA levels and sperm concentration (p=0.01) and total sperm count (p=0.001); significant association with LH levels (p=0.03), and FSH levels (p=0.01). No significant association (p>0.05) between maternal PFOA levels and semen volume, percentage progressive spermatozoa, percentage morphologically normal spermatozoa, mean testicular volume, or testosterone, estradiol, inhibin B, SHBG, or FAI levels.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vesterholm Jensen et al. 2014 Nested case-control study of 107 boys with cryptorchidism from Denmark (n=29) or Finland (n=78) and 108 matched controls (30 from Denmark and 78 from Finland)	**Exposure:** Median cord blood serum PFOA 2.6 ng/mL (Denmark cohort) and 2.1 ng/mL (Finland cohort) **Logistic regression adjustments:** Birth weight, gestational age, parity	No significant association between cord serum PFOA and risk of cryptorchidism; OR 0.51 (95% CI 0.21–1.20) for the whole cohort, OR 1.14 (95% CI 0.19–6.95) for the Denmark cohort and OR 0.35 (95% CI 0.12–1.02) for the Finland cohort. When PFOA levels were divided into tertiles, there was a significant inverse trend (p=0.04) in the Finland cohort; OR 0.35 (95% CI 0.12–0.99) for comparisons between the 1st and 3rd tertiles.
Vuong et al. 2016 Prospective study of 256 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 5 and 8 years of age	**Exposure:** Median maternal PFOA (measured at gestation weeks 16 and 26 and within 24 hours of parturition) 5.4 ng/mL (range: 0.5–24.5 ng/mL) **Statistical adjustments:** Maternal age, race, education income, maternal serum cotinine, maternal depression, maternal IQ, a measure of quality and extent of stimulation at home, marital status, child sex	No significant association between maternal PFOA levels and behavioral regulation (β 1.11, 95% CI -1.22–3.44), metacognition (β 0.58, 95% CI -1.77–2.93), or global executive functioning (β 1.06, 95% CI -1.33–3.45).
Vuong et al. 2018 Prospective study of 208 children participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 8 years of age	**Exposure:** geometric mean serum PFOA 2.4 ng/mL in child at 8 years of age **Statistical adjustments:** Maternal age, race/ethnicity, household income, child sex, maternal marijuana use, maternal blood lead, maternal serum cotinine, maternal depression, vitamin use, maternal IQ, marital status, HOME score, breastfeeding	No associations (p>0.05) between child serum PFOA at age 8 years and metacognition index, behavior regulation index, and global executive functioning scores. Association between child serum PFOA and having a BRIEF summary score of ≥60 (defined as being at risk) for metacognition score (OR 3.18, 95% CI 1.17–8.60). No associations between child serum PFOA and having a BRIEF summary score of ≥60 for behavior regulation score (OR 1.56, 95% CI 0.49–4.92) or global executive composite score (OR 2.69, 95% CI 0.92–7.90).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wang et al. 2015b Prospective cohort study of children whose mothers participated in the Taiwan Maternal and Infant Cohort study; full scale IQ, verbal IQ, and performance IQ were assessed when the children were 5 (n=120) and 8 (n=120) years of age	**Exposure:** Median maternal serum PFOA (measured during third trimester) 2.50 ng/mL (5-year-old group) and 2.50 mg/mL (8-year-old group) **Linear regression adjustments:** Child's sex and age at IQ assessment, maternal education, household income, a measure of quality and extent of stimulation at home	No significant association (p>0.05) between maternal PFOA and IQ scores at 5 or 8 years of age.
Wang et al. 2016 Prospective cohort study of 223 children (117 boys and 106 girls) whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at birth and, 2 (n=82 males, 80 females), 5 (n=51 males, 50 females), 8 (n=48 males, 47 females), and 11 (n=48 males, 46 females) years of age	**Exposure:** Median maternal serum PFOA (measured during third trimester) 2.37 ng/mL for male children and 2.34 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	No significant associations (p>0.05) between maternal serum PFOA and birth weight, birth length, head circumference, or SGA among male or female children.
Washino et al. 2009 Prospective cohort study of 428 pregnant Japanese women; infant data obtained from medical records	**Exposure:** Median maternal serum PFOA (measured in second trimester) 1.3 ng/mL (range: ND–5.3 ng/mL) **Regression adjustments:** Maternal age, maternal education level, smoking status during pregnancy, maternal BMI, parity, infant sex, gestational age, blood sampling period	No significant correlations between maternal PFOA and birth weight (p=0.207), birth length (p=0.631), chest circumference (p=0.460), or head circumference (p=0.823).
Whitworth et al. 2012a Cohort study of 901 pregnant women enrolled in the Norwegian Mother and Child Cohort study; birth outcome data taken from Medical Birth Registry of Norway	**Exposure:** Median maternal serum PFOA (measured in around gestation week 17) 2.2 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, weight gain at 17 weeks	No association between maternal PFOA and birth weight (p=0.12). Significant inverse association (p=0.02) between maternal serum PFOA and risk of preterm birth; the OR for serum PFOA levels in the 4th quartile (≥3.04 ng/mL) was 0.1 (95% CI 0.03–0.6). No association between maternal PFOA levels and SGA (p=0.92) or large for gestational age (p=0.33).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wu et al. 2012 Cross-sectional study of 167 pregnant women delivering babies at two hospitals in China; most subjects were recruited as they entered hospital to deliver, some were recruited during prenatal visit	**Exposure:** Mean maternal serum PFOA levels 18.32 ng/mL (range: 5.5–58.5) at one hospital (n=108) and 9.76 ng/mL (4.4–30.0 ng/mL) at second hospital (n=59) **Statistical adjustments:** Gestational age, infant sex, maternal age, education, smoking, husband smoking, catching cold during pregnancy, parity premature delivery history, spontaneous abortion history	Significant differences in serum PFOA levels between women having premature delivery (p=0.003), term low birth weight (<2,500 g and ≥37 weeks gestational age) (p=0.025), and stillbirth (p=<0.001). However, these values have not been adjusted for potential confounders. Multivariant regression analysis found significant inverse associations between maternal serum PFOA (per 10-fold increase in PFOA) and gestational age (β -15.99 g, 95% CI -27.72 to -4.25, p<0.01), birth weight (β -267.30, 95% CI -573.27 to -37.18, p<0.05), birth length (β -1.91, 95% CI -3.31 to -0.52, p<0.01), 5-minute Apgar score (β -1.37, 95% CI -2.42 to -0.32, p<0.05). No association between maternal serum PFOA and ponderal index (β -0.095, 95% CI -0.200–0.389).
Zhang et al. 2018 Prospective study of 167 mother-child pairs participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio	**Exposure:** Median PFOA levels: maternal 5.4 ng/mL (measured at 16 weeks of gestation), 3-year-old child 5.5 ng/mL, 8-year-old child 2.4 ng/mL **Statistical adjustments:** Maternal age, race, education, household income, parity, smoking, maternal IQ, breastfeeding duration	No associations (p>0.05) between maternal PFOA levels and reading scores at age 5 or 8 years. Association (p<0.05) between serum PFOA levels at age 3 years and reading scores at age 5 years, but not at 8 years of age Association (p<0.05) between serum PFOA at age 8 years and reading score (word reading) at 8 years of age.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Grice et al. 2007 A cohort study of 263 current, retired, or former female workers employed for at least 1 year at a PFOS-based fluorochemical manufacturing facility in Decatur, Alabama; 439 singleton pregnancies (421 live births and 14 stillbirths)	**Exposure:** Workers were assigned to an exposure category based on job history; geometric serum PFOS levels were assigned to each category based on monitoring data conducted in 1998 on 186 workers • Group 1: no direct workplace exposure (serum PFOS 110–290 ng/mL) • Group 2: low potential workplace exposure (serum PFOS 390–890 ng/mL) • Group 3: high potential workplace exposure (serum PFOS 1,300–1,970 ng/mL) **Regression model adjustments:** Group 1 was used as a comparison group, estimates adjusted for mother's age, gravidity, smoking habit	Health conditions were self-reported. No significant differences in birth weight were observed between the no exposure group (Group 1) and the ever-exposed group (groups 2 and 3) (p=0.22) or the high-exposure group (group 3) (p=0.15). Birth weight did not correlate with PFOS exposure.
Darrow et al. 2013 Cross-sectional study of 1,330 women participating in the C8 Health Project and giving birth between 2005 and 2010; maternal blood samples collected in 2005–2006; birth outcome data self-reported and taken from Ohio and West Virginia health departments	**Exposure:** Mean and geometric mean serum PFOS were 15.6 and 13.2 ng/mL (range: LOD [0.25]–92.9 ng/mL) • 1st quintile: 0–<8.6 ng/mL • 2nd quintile: 8.6–<12.1 ng/mL • 3rd quintile: 12.1–<15.9 ng/mL • 4th quintile: 15.9–<21.4 ng/mL • 5th quintile: ≥21.4 ng/mL **Logistic regression model adjustments:** Maternal age, educational level, smoking, parity, BMI, self-reported diabetes, time between conception and serum measurement	Nonsignificant trend (p=0.045) across PFOS quintiles for decreased birth weight among full-term infants. The trend was statistically significant (p=0.006) in a subcohort of 783 women whose first pregnancy was conceived after sample collection. No association between PFOS levels and preterm birth or LBW. The ORs (95% CI) for the 5th quintile were: • Preterm birth: 1.07 (0.58–1.95) • LBW: 1.33 (0.60–2.96).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Darrow et al. 2014 Prospective study of 1,129 women participating in the C8 Health Project and reporting pregnancies in follow-up interviews between 2008 and 2011; maternal blood samples collected in 2005–2006; birth outcome data self-reported	**Exposure:** Mean and geometric mean serum PFOS levels were 16.9 and 14.3 ng/mL (range: <0.5–92.9 ng/mL) **Statistical adjustments:** Smoking status, maternal age at time of conception, education, BMI at enrollment, race, self-reported diabetes, time between conception and serum measurement	No significant association between serum PFOS levels and risk of miscarriage was observed, the OR for the 5th quintile (>23.3 ng/mL) was 1.41 (95% CI 0.88–2.26). No associations were found among nulliparous women (OR 2.02, 95% CI 0.83–4.93 for 5th quintile) or parous women (OR 1.12, 95% CI 0.58–2.17 for 5th quintile).
Lopez-Espinosa et al. 2011 Cross-sectional study of 3,076 boys and 2,931 girls aged 8–18 years participating in the C8 Health Project and C8 Science Panel studies	**Exposure:** Median serum PFOS levels in boys and girls were 20 and 18 ng/mL **Logistic regression model adjustments:** Age, time of day for blood sampling (boys only)	Significant association between PFOS levels and the age of puberty in boys (as assessed by total testosterone levels); OR (95% CI): • 2nd quartile: 0.74 (0.46–1.19) • 3rd quartile: 0.58 (0.37–0.90) • 4th quartile: 0.46 (0.29–0.71). The delays in age of puberty were 131 and 190 days, respectively, in boys with serum PFOS levels in the 3rd and 4th quartiles. Significant association between PFOS and age of puberty in girls (as assessed by self-reported menarche or estradiol levels); OR (95% CI) using menarche criteria: • 2nd quartile: 0.72 (0.47–1.10) • 3rd quartile: 0.55 (0.35–0.86) • 4th quartile: 0.55 (0.35–0.87). The delays in the 3rd and 4th quartiles were 141 and 138 days, respectively.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lopez-Espinosa et al. 2016 Cross-sectional study of 1,169 boys and 1,123 girls aged 6–9 years participating in the C8 Health Project study	**Exposure:** Median serum PFOS 22.4 ng/mL in boys and 20.9 ng/mL in girls **Statistical adjustments:** Age, month, and time of sampling	Significant inverse association between serum PFOS and total estradiol in boys (percent difference between 75th and 25th PFOS levels, -4.0, 95% CI -7.7 to -0.1), total testosterone in boys (-5.8, 95% CI -9.4 to -2.0) and girls (-6.6, 95% CI -10.1 to -2.8), and insulin-like growth factor-1 in boys (-5.9, 95% CI -8.3 to -3.3) and girls (-5.6, 95% CI -8.2 to -2.9). No significant associations between serum PFOS and estradiol (-0.3, 95% CI -4.6–4.2) in girls.
Stein et al. 2009 Cross-sectional study of 5,262 pregnancies in Mid-Ohio Valley residents that occurred within the 5 years preceding blood sample collections for the C8 Health Project; self-reported birth outcome	**Exposure:** Mean and median serum PFOS: 14.1 and 12.8 ng/mL (range: 0.25–83.4 ng/mL) • <50th percentile: 0.25–<12.7 ng/mL • 50th–75th percentile:12.7–<17.7 ng/mL • 75th–90th percentile:17.7–<23.2 ng/mL • >90th percentile: 23.2–83.4 ng/mL **Logistic and linear regression model adjustments:** Maternal age, parity, education, smoking status	Increased odds of preterm birth in women with PFOS levels in the >90th percentile (OR 1.4, 95% CI 1.1–1.7). Significant association between serum PFOS levels and odds of LBW for 75th–90th percentile (OR 1.6, 95% CI 1.1–2.3) and >90th percentile (OR 1.8, 95% CI 1.2–2.8). No association between PFOS and miscarriage risk or birth defects risk; OR (95% CI): • Miscarriage: 0.9 (0.7–1.3) • Birth defects: 1.3 (0.8–2.1).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Stein and Savitz 2011 Cross-sectional study of 10,546 non-Hispanic white children aged 5–18 years participating in the C8 Health Project; ADHDs diagnosis and learning problems were reported by parents	**Exposure:** Mean serum PFOS level of 22.9 ng/mL (range: 0.25–202.1 ng/mL) • 1st quartile: 0.25–<14.8 ng/mL • 2nd quartile:14.8–<20.2 ng/mL • 3rd quartile: 20.22–<27.9 ng/mL • 4th quartile: 27.9–202.1 ng/mL **Logistic regression model adjustments:** Age, sex	A significant inverse association between serum PFOS and risk of learning problems; OR (95% CI): 5–18-year-olds • 2nd quartile: 0.83 (0.70–0.98) • 3rd quartile: 0.74 (0.62–0.87) • 4th quartile: 0.85 (0.72–1.00) 12–15-year-olds • 2nd quartile: 0.78 (0.60–1.01) • 3rd quartile: 0.68 (0.52–0.89) • 4th quartile: 0.71 (0.54–0.93). No significant associations between serum PFOS and risk of ADHD diagnosis or ADHD diagnosis with medication, or learning problems. For participants with serum PFOA levels in the 4th quartile, the ORs (95% CI) were 0.99 (0.76–1.30) and 1.32 (0.88–1.99).
Alkhalawi et al. 2016 Retrospective study of 156 mother-child pairs participating in the Duisburg Birth Cohort study in Germany; weight and length recorded at birth and at 1, 4, 6, and 12 months of age.	**Exposure:** Geometric mean maternal serum PFOS 9.04 ng/mL; 1st quartile: 1.70–6.98 ng/mL, 2nd quartile: 7.02–9.31 ng/mL, 3rd quartile: 9.33–11.80 ng/mL, 4th quartile: 11.86–21.93 ng/mL **Statistical adjustments:** Pregnancy duration, maternal BMI before pregnancy, maternal height, maternal blood lead levels, infant sex, mode of delivery, mother place of birth, smoking during pregnancy	Inverse association between maternal PFOS and ponderal index (β -0.355, 95% CI -0.702 to -0.008). No association (p>0.05) between maternal PFOS and birth weight or length.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Apelberg et al. 2007b Cross-sectional study of 341 singleton births in Baltimore Maryland; maternal and neonatal data collected from hospital records	**Exposure:** Median cord blood serum PFOS level 5 ng/mL (range: <LOD [0.2]–34.8 ng/mL) **Linear regression model adjustments:** Gestational age, maternal age, BMI, race, parity, smoking, baby sex, height, net weight gain, diabetes, hypertension, delivery mode (head circumference only)	No significant association (p>0.05) between cord blood serum PFOA levels and gestational age, birth weight, or length. Significant inverse associations between cord blood serum PFOA levels and head circumference and ponderal index.
Ashley-Martin et al. 2016 Cohort study of 1,723 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada; GWG was based on weekly weight gain during the 2nd and 3rd trimesters	**Exposure:** Median serum PFOS (measured during first trimester) and cord blood PFOS: 4.60 and 0.15 ng/mL **Logistic regression adjustments:** Maternal age, prepregnancy BMI	Significant association (p<0.1) between serum PFOS and GWG among subjects with underweight/normal prepregnancy BMI, but not in subjects with overweight or obese BMIs. GWG was significantly associated with increased odds of high cord blood PFOS (>0.30 ng/mL); OR 1.03 (95% CI 1.00–1.05) per 1 kg increase in GWG.
Ashley-Martin et al. 2017 Cross-sectional study of 1,705 mother-infant pairs participating in the Maternal Infant Research on Environmental Chemicals in Canada	**Exposure:** Median maternal plasma PFOS 4.6 ng/mL (measured during first trimester) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, household income, smoking	No association between maternal PFOS and birth weight (β 0.05, 95% CI -0.18–0.29), leptin (β -0.09, 95% CI -0.23–0.04), or adiponectin (β 0.02, 95% CI -0.11–0.07). Similar findings when cord blood PFOS used as biomarker of exposure.
Bach et al. 2016 Cohort study of 1,507 nulliparous women and their children in the Aarhus Birth Cohort in Denmark	**Exposure:** Median serum PFOS levels (measured between gestation week 9 and 20): 8.3 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, maternal education	Lower birth weights were found in women with PFOS levels higher than the 1st quartile; the adjusted difference between the 1st and 4th quartiles was 50 g. No consistent alterations in birth length or head circumference were found in comparisons across serum PFOS quartiles.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Bae et al. 2015 Prospective study of 233 couples from Michigan and Texas participating in the Longitudinal Investigation of Fertility and the Environment Study	**Exposure:** Geometric mean serum PFOS levels 21.7 and 14.5 ng/mL in male and female nulliparous parents and 21.5 and 10.8 ng/mL in male and female parous parents (measured at the time of pregnancy testing) **Logistic regression adjustments:** Age, research site, household income, maternal parity	No significant association between maternal or paternal PFOS levels and the odds of a male birth (maternal: OR 1.16, 95% CI 0.88–1.53; paternal: OR 1.01, 95% CI 0.78–1.33).
Braun et al. 2014 Prospective study of 175 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; social responsiveness scale measures (measurement of autistic behavior) was evaluated when children were 4 and 5 years of age	**Exposure:** Median maternal serum PFOS levels (measured at 16 weeks of gestation): 13 ng/mL **Bayesian regression adjustments:** Maternal age at deliver, race, marital status, education, parity, insurance status, employment, household income, prenatal vitamin use, maternal depressive symptoms, maternal IQ, child sex, caregiving environment, maternal serum cotinine	No association between maternal serum PFOS and scores on the social responsiveness scale.
Buck Louis et al. 2016 Prospective study of 332 couples followed from preconception to 7 weeks post-conception	**Exposure:** Median serum PFOS in women 12.2 ng/mL **Statistical adjustments:** Age, BMI, prior pregnancy loss, alcohol consumption, cigarette smoking during pregnancy	No association between maternal serum PFOS and pregnancy loss (HR 0.81, 95% CI 0.65–1.00).
Callan et al. 2016 Cross-sectional study of 98 pregnant women in Australia	**Exposure:** Median serum PFOS 1.99 ng/mL (range of 0.45–8.1 ng/mL) (measured 2 weeks prior to due date) **Statistical adjustments:** Gestational age, maternal height, prepregnancy BMI, weight gain during pregnancy, infant sex	No association between maternal PFOS and birth weight (β -69 g, 95% CI -231–94), birth length (β -0.22, 95% CI -1.0–0.57), head circumference (β -0.39 95% CI -0.98–0.20), or ponderal index (β -0.03, 95% CI -0.14–0.08).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFOS 1.43 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFOS and birth weight (p=0.84), birth length (p=0.65), or ponderal index (p=0.47).
Chen et al. 2012a Cross-sectional study of 429 infants participating in Taiwan Birth Panel Study	**Exposure:** Geometric mean cord blood PFOS level 5.94 ng/mL **Linear and logistic regression model adjustments:** Maternal age, prepregnancy BMI, education level, type of delivery, parity, infant sex, gestational age (for birth weight, birth length, heard circumference, ponderal index, LBW)	Significant inverse associations between cord blood PFOS and gestational age (p<0.001), birth weight (β -110.2 g (-176.0 to -44.5, p<0.001) per ln PFOS), and head circumference (β -0.25 cm (-0.46–0.05 cm, p<0.05), per ln PFOS). No association (p>0.05) between cord blood PFOS and birth length or ponderal index. Significant association between cord blood PFOS and odds of preterm birth (OR 2.45, 95% CI 1.47–4.08) and SGA (OR 2.27, 95% CI 1.25–4.15). No association with LBW (OR 2.61, 95% CI 0.185–8.03).
Christensen et al. 2011 Case-control study of 448 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; case-control study of girls with early menarche (<11.5 years of age, n=218) and controls (menarche ≥11.5 years, n=230)	**Exposure:** Median maternal (blood samples measured at gestation week 15) serum PFOS 19.8 ng/mL	No significant association between maternal PFOS and odds of earlier age at menarche (OR 0.68, 95% CI 0.40–1.13).
de Cock et al. 2014 Cross-sectional study of 89 mother-infant pairs in the Netherlands; weight, height, and head circumference were measured at 1, 2, 4, 6, 9, and 11 months of age	**Exposure:** Mean and median cord blood plasma PFOS levels were 1.611 and 1.600 ng/mL **Statistical adjustments:** Maternal/ paternal BMI, height, birth weight, gestational age, parity, alcohol, smoking, education, breastfeeding duration	No significant association between cord blood plasma PFOS and infant BMI (p=0.586), weight (p=0.802), height (p=0.975) or head circumference (p=0.649).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Donauer et al. 2015 Prospective study of 349 infants who whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; neurobehavior was evaluated at 5 weeks of age using the Neonatal Intensive Care Unit Network Neurobehavioral Scale	**Exposure:** Geometric mean maternal serum PFOS (most measured at gestation week 16; 10% measured at gestation week 26, and 5% at delivery): 13.25 ng/mL **Statistical adjustments:** Infant sex and age at examination, maternal age, race, household income, marital status, maternal depression, maternal BMI at 13–19 weeks of gestation, alcohol and marijuana use during pregnancy, maternal serum cotinine, infant weight change per month from birth to 5 weeks, maternal blood lead level during pregnancy, variable of high risk infants (gestation age <37 weeks, birth weight <2,500 g and/or stay in NICU after birth)	No significant (p>0.05) associations between maternal serum PFOS levels and neurobehavioral outcomes were found. No significant associations between maternal serum PFOS and the likelihood of infants being categorized as high arousal/difficult (p=0.4678 without statistical adjustments) or hypotonic (p=0.3996 without statistical adjustments), as compared to social/easy going.
Fei et al. 2007, 2008a Cross-sectional study of 1,400 pregnant women participating in Danish National Birth Cohort study; birth outcome data obtained from National Discharge Register at the National Board of Health; body weight, preterm	**Exposure:** Median maternal serum PFOS levels (measured during first trimester) 35.3 ng/mL (range: 6.4–106.7 ng/mL) **Statistical adjustments:** Maternal age, parity, socio-occupational status, prepregnancy BMI, smoking during pregnancy, infant sex, gestational week at blood drawing	No significant associations between maternal PFOS levels and birth weight (β -0.46, 95% CI -2.34–1.41), birth length (β -0.002, 95% CI -0.011–0.006), head (β 0.000, 95% CI -0.006–0.007) or abdominal (β -0.003, 95% CI -0.012–0.005) circumferences, or gestation length (p>0.01). No significant associations between maternal PFOS and risk of preterm birth (OR 1.43, 95% CI 0.50–4.11 for 4th quartile), LBW (OR 4.82, 95% CI 0.56–41.16 for 4th quartile), or SGA (OR 0.98, 95% CI 0.58–1.65 for 4th quartile); maternal serum PFOS levels for the 4th quartile were >43.3 ng/mL.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fei et al. 2008b Cross-sectional study of 1,400 pregnant women participating in Danish National Birth Cohort study; birth outcome data obtained from National Discharge Register at the National Board of Health; infants were examined at birth (Apgar score) and at 5–7 and 18–20 months of age (neurodevelopmental milestones)	**Exposure:** Median maternal serum PFOS levels (measured during first trimester) 35.3 ng/mL (range: 6.4–106.7 ng/mL) **Statistical adjustments:** Maternal age, parity, socio-occupational status, prepregnancy BMI, smoking during pregnancy, infant sex, gestational week at blood drawing	No significant association between maternal PFOS and risk of Apgar scores <10 (assessed 5 minutes after birth); OR 1.20 (95% CI 0.67–2.14). A significant trend for a delay in age of sitting without support was observed (p=0.041), earlier use of word-like sounds to tell what he/she wants (p=0.039), and delays in using sentences of two words (p=0.050). No significant trends (p>0.05) for associations between maternal PFOS levels and other gross motor, fine motor, attention, cognition, or other language developmental milestones assessed at 18 months of age or in motor or mental development at 6 months of age.
Fei and Olsen 2011 Subgroup of the Fei et al. (2007, 2008a, 2008b) cohort consisting of 526–787 children; mothers completed questionnaires regarding behavioral and social development when the children were 7 years of age	**Exposure:** Median maternal serum PFOS levels (measured during first trimester) 34.4 ng/mL (range: 7.3–106.7 ng/mL) **Statistical adjustments:** Parity, maternal age, prepregnancy BMI, smoking and alcohol consumption during pregnancy, socioeconomic status, sex of child, breastfeeding, birth year, home density, gestational age at blood drawing, parental behavioral problem scores during their childhood (not used for developmental coordination disorder analyses)	No significant trends between maternal PFOS levels and the risk of abnormal scores on tests of behavioral health (p>0.39 for trend) or motor coordination (p=0.41 for trend) in children.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Forns et al. 2015 Prospective study of 843 infants of mothers participating in the Norwegian Human Milk Study; neurobehavioral assessment, as measured using the Ages and Stages Questionnaire-II, was conducted at 6 and 24 months of age.	**Exposure:** Median PFOS breast milk level (measured 2 weeks after giving birth) 110 ng/L **Logistic regression adjustments:** Child's age at milk sample collection, fish consumption during pregnancy, maternal age, maternal education, parity, prepregnancy BMI, maternal smoking during pregnancy, interpregnancy interval, duration of total breastfeeding of previous children, child's sex	No alteration in the risk of an abnormal score on neurobehavioral assessment questionnaire at 6 months (OR 0.96, 95% CI 0.76–1.20) or 24 months (OR 0.93, 95% CI 0.74–1.17) of age.
Goudarzi et al. 2016b Prospective study of infants of mothers participating in the Hakkaido Study on Environment and Children's Health in Japan; neurodevelopment was assess using the MDI and PDI tests at age 6 months (n=173) and 18 months (n=133)	**Exposure:** Median maternal serum PFOS levels (measured after second trimester): 5.7 ng/mL for 6-month evaluation group and 5.8 ng/mL for 19-month evaluation group **Statistical adjustments:** Gestational age, maternal age, parity, education, alcohol use, smoking, caffeine during pregnancy, blood sampling period, breastfeeding	No significant associations between serum PFOS and MDI and PDI test scores were found at 6 or 18 months.
Govarts et al. 2016 Cross-sectional study of 202 infants of mothers participating in the Flemish Human Environmental Health Survey in Belgium	**Exposure:** Geometric mean cord blood serum PFOS: 2.63 ng/mL **Linear Regression adjustments:** Gestational age, child's sex, smoking during pregnancy, parity, prepregnancy BMI	No significant association (p=0.798) between cord blood PFOS and birth weight was found.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Govarts et al. 2018 Compilation of data from four birth cohort studies in Europe	**Exposure:** Median cord serum PFOS 1.984 ng/mL; exposure estimate based on measured cord PFOS from one cohort, estimated cord PFOS based on measured breast milk levels from two cohorts; and measured and estimated cord PFOS from one cohort **Statistical adjustments:** Maternal education, age at delivery, height, and prepregnancy BMI, parity, child's sex	Inverse association between cord PFOS and risk of small for gestational age (OR 0.823, 95% CI 0.742–0.913). Among women who smoked during pregnancy, association between cord PFOS and risk of small for gestational age (OR 1.627, 95% CI 1.024–2.588) and inverse association found in nonsmoking women (OR 0.661, 95% CI 0.644–0.717).
Gump et al. 2011 Cross-sectional study of 83 children aged 9–11 years (mean 10.13 years; 36.1% female) living in New York	**Exposure:** Mean and median serum PFOS: 9.90 and 8.79 ng/mL **Statistical adjustments:** Blood lead, sex, body fat, patent's education, family history of high blood pressure, asthma	Serum PFOS was significantly ($p<0.05$) associated with poorer performance on a task requiring behavioral inhibition.
Hamm et al. 2010 Cross-sectional study of 252 pregnant women in Alberta Canada undergoing prenatal screening for Down's syndrome, trisomy 18, and open spina bifida; birth outcome data obtained from medical records	**Exposure:** Mean serum PFOS levels (measured in early second trimester) 9.0 ng/mL (range: <LOD [0.25]–35 ng/mL) **Statistical adjustments:** Maternal age, maternal weight, maternal height, smoking status during pregnancy, infant sex, maternal race, parity	No associations between maternal serum PFOS levels and birth weight (change in birth weight for 3rd tertile of 71.25 (95% CI -54.97–197.48). No significant association between maternal serum PFOS and the risk for preterm delivery; the RR (95% CI) for serum PFOS levels in the 3rd tertile (>10–35 ng/mL) was 1.11 (0.36–3.38). A significant inverse association between serum PFOS and SGA was found (RR 0.26, 95% CI 0.10–0.70 for serum PFOS levels in the 3rd tertile).
Hoffman et al. 2010 Cross-sectional study of 571 children aged 12–15 years participating in NHANES 1999–2000 or 2003–2004	**Exposure:** Median serum PFOS 22.6 ng/mL (range: 2.1–87.2 ng/mL) **Logistic regression model adjustments:** NHANES sample cycle, age, race/ethnicity, sex, environmental tobacco smoke, maternal smoking during pregnancy	Significant association between serum PFOS levels and parent-reported ADHD; the OR for each 1 ng/mL increase in serum PFOS was 1.03 (95% CI 1.01–1.05).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Høyer et al. 2015a Prospective study of 1,106 children of mothers participating in the INUENDO cohort in Greenland, Ukraine, and Poland; parents completed questionnaires when the children were between 5 and 9 years of age to evaluate behavior and motor development	**Exposure:** Median maternal serum PFOS (measured at any time during pregnancy): 10.0 ng/mL **Statistical adjustments:** Maternal cotinine level during pregnancy, alcohol consumption at conception, maternal age at pregnancy, child sex, gestational age at blood sampling	No significant associations between maternal serum PFOS and motor skills were found β -0.1, 95% CI -1.2–1.1). No significant associations between maternal serum PFOS levels and risk of hyperactivity OR 1.4 (95% CI 0.4–4.9) or abnormal behavior OR 1.5 (95% CI 0.5–4.8) for children with maternal serum PFOS levels in the 3rd tertile (16.6–87.3 ng/mL).
Inoue et al. 2004 Cross-sectional study of 15 pregnant Japanese women	**Exposure:** Maternal serum PFOS levels (measured during gestation weeks 38–41) ranged from 4.9 to 7.6 ng/mL; cord blood PFOS levels ranged from 1.6 to 5.3 ng/mL	The investigators noted that there was no apparent correlation between cord blood serum PFOS levels and birth weight or sex or with infant TSH and free T4 levels.
Itoh et al. 2016 Prospective study of 189 infants whose mothers were participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Maternal median serum PFOS levels (measured after the second trimester): 5.2 ng/mL **Linear regression adjustments:** Maternal age, parity, prepregnancy BMI, annual income smoking and caffeine consumption during pregnancy, gestational week of blood sampling, gestational age at birth	Maternal serum PFOS levels were significantly associated (p=0.021) with cord blood estradiol levels in male infants and inversely associated with the ratio of testosterone to estradiol in male infants (p=0.008), progesterone in male (p=0.043) and female (p=0.002) infants, prolactin in female infants (p=0.001), and inhibin B in male infants (p<0.001). Dose-related trends were observed for estradiol (p=0.027), testosterone:estradiol ratio (p=0.015), and inhibin B (p<0.001) levels in male infants and progesterone (p=0.004) and prolactin (p=0.005) in female infants. No significant associations (p>0.05) with estradiol, testosterone, LH, FSH, SHBG, testosterone:SHBG ratio, or insulin-like factor-3 in male and female infants; estradiol, testosterone:estradiol ratio, progesterone, and inhibin B in female infants; or prolactin in male infants.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Jeddy et al. 2017 Prospective study of 432 mother-daughter pairs participating in the Avon Longitudinal Study of Parents and Children in the Great Britain; children were assessed at 15 and 38 months of age	**Exposure:** Maternal median serum PFOS 19.8 ng/mL (measured at 15 weeks of gestation) **Statistical adjustments:** Parity, maternal age, maternal education, maternal smoking status, gestational age at blood sample collection	Associations between maternal PFOS and verbal comprehension scores in 15-month-old children (β 0.03, 95% CI 0.01–0.05), but not for vocabulary comprehension and production, nonverbal communication, or social developmental (p>0.05). When children were categorized by maternal age at delivery, an association between maternal PFOS and vocabulary comprehension and production scores was found in 15-month infants with mothers <25 years of age (β -3.82, 95% CI -6.18 to -1.47). Inverse association between maternal PFOS and intelligibility scores in children 38-months of age (β -0.01, 95% CI -0.01–0.00). When children were categorized by maternal age at delivery, an inverse association between maternal PFOS and intelligibility scores was found in 38-month children with mothers >30 years of age (β -0.01, 95% CI -0.02–0.00) and a positive association was found in mothers <25 years of age (β 0.02, 95% CI 0.01–0.03). No association with maternal PFOS for language or communicative scores in 38-month-old children (p>0.05).
Jensen et al. 2015 Case-control study of 56 women in Denmark having a miscarriage before gestation week 12 and 336 matched controls	**Exposure:** Median maternal serum PFOS levels (measured prior to gestation week 12): 8.10 ng/mL **Logistic regression adjustments:** Age, BMI, parity, and gestational age at serum sampling	No significant association between maternal serum PFOS levels and the risk of miscarriage before gestation week 12; OR 1.16 (95% CI 0.59–1.29).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kim et al. 2011 Cross-sectional study of 44 pregnant women in South Korea; birth outcome data obtained from questionnaires	**Exposure:** Median maternal serum PFOS (mostly measured during the third trimester) 2.93 ng/mL (range: 2.08–4.36 ng/mL); cord blood serum PFOS level 1.26 ng/mL (range: 0.81–1.82 ng/mL) **Statistical adjustments:** Maternal age, gestational age, maternal BMI (T4, TSH, and body weight only)	Serum PFOS levels were significantly ($p<0.01$) higher in than cases than controls. Significant ($p<0.05$) inverse correlation between maternal serum PFOS levels and fetal cord T3 levels. No significant correlations ($p>0.05$) with T4 or TSH levels. No significant correlations ($p>0.05$) between cord blood PFOS and fetal cord T3, T4, or TSH levels. No significant correlations ($p>0.05$) between maternal serum PFOS or cord blood PFOS levels and birth weight.
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFOS: 5.326 ng/mL (cases) and 4.05 ng/mL (controls)	No significant correlation ($p>0.05$) between serum PFOS and TSH, free T4, T3, microsomal antibodies, and thyroid stimulating immunoglobulin.
Kishi et al. 2015 Prospective study of 306 infants whose mothers were participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Mean and median maternal serum PFOS levels (measured after the second trimester): 6.02 and 5.60 ng/mL **Linear regression adjustments:** Maternal age, parity, annual income smoking and alcohol consumption during pregnancy, gestational week of blood sampling	Significant association between maternal serum PFOS and birth weight in female infants ($p=0.031$, unadjusted); no association in male infants ($p=0.187$, unadjusted). Significant inverse associations between maternal serum PFOS and triglyceride ($p=0.032$), palmitic acid ($p=0.004$), palmitoleic acid ($p=0.005$), oleic acid ($p=0.014$), linoleic acid ($p<0.001$), α-linolenic acid ($p<0.001$), arachidonic acid ($p=0.003$), essential fatty acids ($p<0.001$), and omega 6 ($p<0.001$). No association between maternal serum PFOS and stearic acid ($p=0.372$), eicosapentaenoic acid ($p=0.107$), docosahexaenoic acid ($p=0.102$), or omega 3 ($p=0.268$).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kobayashi et al. 2017 Cross-sectional study of 177 mother-infant pairs participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Mean maternal serum PFOS (measured at gestation weeks 24–42) 5.7 ng/mL (range of 1.5–16.2 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, maternal education, maternal smoking during pregnancy, gestational age, infant sex, maternal blood sampling period	Inverse association between maternal PFOS and ponderal index (β -1.07, 95% CI -1.79 to -0.36). No association between maternal PFOS and birth weight (β -56.0, 95% CI -162.8–50.8) or birth length (β 0.32, 95% CI -0.19–0.82).
Kristensen et al. 2013 Prospective study of 343 women whose mothers participated in a Danish pregnancy cohort study	**Exposure:** Median maternal serum PFOS (measured at gestation week 30): 21.1 ng/mL **Statistical adjustments:** Maternal smoking during pregnancy, household income, daughter's BMI, daughter's smoking (menstrual cycle length, reproductive hormones, follicle number), menstrual cycle phase (FSH, LH, estradiol)	No significant association between maternal serum PFOS levels and age of menarche of the daughters (p=0.28). No significant associations (p>0.05) between maternal serum PFOS levels and menstrual cycle length, total testosterone, SHBG, free androgen index, dehydroepiandrosterone sulphate, anti-Müllerian hormone, or number of follicles/ovary in daughters using or not using hormonal contraceptives.
Lauritzen et al. 2017 Case-cohort study of 265 mother-infant pairs participating in a prospective study in Norway	**Exposure:** Median maternal serum PFOS 9.74 ng/mL (range of 0.95–59.6) for Norway cohort (measured in gestation weeks 17–20) **Statistical adjustments:** Maternal age, height, prepregnancy BMI, education, parity, smoking status at conception, interpregnancy interval, child's sex	No association between maternal PFOS and birth weight (p=0.167), birth length (p=0.987), head circumference (p=0.189), or gestational age (p=0.952). No association with risk of SGA (OR 0.71, 95% CI 0.42–1.20).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lauritzen et al. 2017 Case-cohort study of 159 mother-infant pairs participating in a prospective study in Sweden	**Exposure:** Median maternal serum PFOS 16.4 ng/mL (2.28–55.2 ng/mL) (measured in gestation weeks 17–20) **Statistical adjustments:** Maternal age, height, prepregnancy BMI, education, parity, smoking status at conception, interpregnancy interval, child's sex	Inverse association between maternal PFOS and birth weight (β -292, 95% CI -500 to -84; p=0.006), birth length (β -1.2, 95% CI -2.1 to -0.3, p=0.007). No association between maternal PFOA and head circumference (p=0.0.073, or gestational age (p=0.201). No association with risk of SGA and maternal PFOS (OR 2.51, 95% CI 0.93–6.77).
Lee et al. 2013 Cross-sectional study of 59 pregnant women in South Korea; birth outcome data obtained from medical records	**Exposure:** Mean maternal serum PFOS (measured at delivery) 10.77 ng/mL (range: 2.38–35.18 ng/mL). Mean cord blood serum PFOS level 3.44 ng/mL (range: 0.34–9.64 ng/mL) **Logistic regression model adjustments:** Maternal age, gestational age	No significant associations between maternal serum PFOS or cord blood PFOS levels and birth weight (p=0.14, p=0.51), birth length (p=0.23, p=0.68), head circumference (p=0.57, p=0.47), or ponderal index (p=0.15, p=0.98). After adjustments for confounders, there was an inverse association between maternal PFOS levels and ponderal index (OR 0.22, 95% CI 0.05–0.90). No significant associations with birth weight (OR 0.98, 95% CI 0.32–3.03), birth length (OR 0.97, 95% CI 0.29–3.27), or head circumference (OR 1.34, 95% CI 0.20–8.90).
Lee et al. 2016 Cross-sectional study of 85 newborns in South Korea; birth outcome data from medical records	**Exposure:** Mean cord blood serum PFOS: 0.87 ng/mL **Multiple regression adjustments:** Gestational age, maternal age, infant sex, variable to control for sampling bias	No significant association (p>0.05) between cord blood PFOS levels and birth weight.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lenters et al. 2016a, 2016b Prospective study of 1,250 infants whose mothers participated in the INUENDO cohort in Greenland (n=513), Ukraine (n=557), and Poland (n=180)	**Exposure:** Median maternal serum PFOS levels: 20.09 ng/mL for Greenland cohort, 7.81 ng/mL for Poland cohort, and 5.04 ng/mL for Ukraine cohort **Regression model adjustments:** Study population, maternal age, parity, gestational age, infant sex, maternal height, alcohol consumption, cotinine, vitamin D	No significant association (p=0.109) between maternal PFOS levels and term birth weight.
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFOS 3.0 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	Inverse association between cord PFOS and birth weight (β -95.0, 95% CI -154.0 to -36.0). When categorized by sex, association between PFOS and birth weight was found in boys (β -150.6, 95% CI -225.4 to -75.7) but not in girls (β -26.6, 95% CI -125.1–71.8). No association between cord PFOS and gestational age (β 0.11, 95% CI -0.06–0.29); association for boys only (β 0.29, 95% CI 0.05–0.53), but not for girls only (β -0.07, 95% CI -0.35–0.20).
Lien et al. 2016 Prospective study of 282 7-year-old children whose mothers participated in the Taiwan Birth Panel Study or Taiwan Early-Life Cohort; psychometric symptoms related to attention deficit/hyperactivity disorder were assessed using three parent completed questionnaires	**Exposure:** Weighted average cord blood serum PFOS: 4.79 ng/mL **Linear regression (with inverse probability) adjustments:** Child sex, breastfeeding, maternal age, maternal education, parity, maternal environmental tobacco smoke exposure during pregnancy, alcohol consumption during pregnancy, annual income, gestational age, birth weight, cord blood lead, study cohort	No significant associations between cord blood PFOA and scores on tests measuring inattention (p=0.8508), hyperactivity/impulsivity (p=0.6857), oppositional defiant disorder (p=0.6026), internalizing problems (p=0.8848), externalizing problems (p=0.2008), emotional symptoms (p=0.9431), conduct problems (p=0.4938), hyperactivity/inattention (p=0.5226), peer problems (p=0.462), or pro-social behavior (p=0.122).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Liew et al. 2014 Case-control study using data from the Danish National Birth Cohort study; 156 children were diagnosed with congenital cerebral palsy (cases) and 550 randomly selected children served as controls	**Exposure:** Median maternal serum PFOS (86% measured during first trimester and 14% during the second trimester): Cases: • boys 28.90 ng/mL • girls 27.50 ng/mL Controls: • boys 27.60 ng/mL • girls 26.20 ng/mL **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness	Significant association between maternal PFOS levels and risk of congenital cerebral palsy in boys (RR 1.7, 95% CI 1.0–2.8), but not in girls (RR 0.7, 95% CI 0.4–1.4).
Liew et al. 2015 Nested case-control study using data from the Danish National Birth Cohort study; 215 cases of ADHD, 213 cases of autism, and 545 randomly selected children served as controls	**Exposure:** Median maternal serum PFOS (87% measured during first trimester and 13% during the second trimester): 26.80 ng/mL for ADHD cases, 25.40 ng/mL for autism cases, 27.40 ng/mL for controls **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness, gestational week of blood drawn, child's sex, birth year	No significant association between maternal PFOS levels and the risk of ADHD (RR 0.87, 95% CI 0.74–1.02) or autism (RR 0.92, 95% CI 0.69–1.22). When PFOS levels were categorized by quartiles, a significantly lower risk of ADHD (RR 0.79, 95% CI 0.64–0.98) was found for the 4th quartile (PFOS ≥35.61 ng/mL).
Lind et al. 2017a Prospective study of 649 pregnant women participating in the Odense child cohort study in Denmark; infants were examined at 3.5 months of age)	**Exposure:** Median maternal serum PFOS 8.1 ng/mL (measured at gestational weeks 5–12) **Statistical adjustments:** Gestational age, parity, maternal smoking during pregnancy, prepregnancy BMI, maternal ethnicity	No association (p>0.05) between maternal PFOS and birth weight or gestational length. Inverse association between maternal PFOS and anogenital distance in girls (β -0.4, 95% CI -3.8 to -0.7, p<0.01)). No association with anogenital distance in boys (β 0.5, 95% CI -1.2–2.2, p=0.55) or penile width (p=0.67).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Maisonet et al. 2012 Prospective cohort study of 447 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; birth outcome data obtained from medical records; weight and height at age 2 and 20 months were measured	**Exposure:** Median maternal serum PFOS (measured at gestation week 15) 19.6 ng/mL (range: 3.8–112.0 ng/mL) **Linear regression model adjustments:** Maternal smoking during pregnancy (birth weight and length only), maternal prepregnancy BMI, previous live births, gestational age, maternal education (birth length only)	Significant inverse trend between maternal serum PFOS levels and birth weight (β -140.01 g [-238.14 to -41.89 g, p=0.0053 for trend] for the 3rd tertile and birth length (β -0.63 cm [-1.11 to -0.15 cm, p=0.103 for trend] for the 3rd tertile); no significant trend for ponderal index (p=0.1120). Associations between maternal serum PFOS in 3rd tertile and increasing weight at 20 months when adjusted for birth weight (β 438.4 g, 95% CI 71.09–805.65, p=0.0195 for trend), height at 20 months (β 499.84, 95% CI 208.67–791.01, p=0.0008 for trend), or birth weight and height at 20 months (β 579.82, 95% CI 301.40–858.25, p<0.0001 for trend); no significant trend with unadjusted weight at 20 months (p=0.0598).
Maisonet et al. 2015a Prospective cohort study of 72 girls (aged 15 years) participating in Avon Longitudinal Study of Parents and Children in Great Britain.	**Exposure:** Median maternal serum PFOS (measured at gestation week 16) 19.2 ng/mL (range: 7.6–69.2 ng/mL) **Statistical adjustments:** SHBG concentration, maternal education, maternal age at delivery, maternal prepregnancy BMI, maternal smoking during pregnancy, time of day daughter's blood sample obtained, daughter's age at menarche, daughter's BMI at age 15 years	Serum testosterone levels were 0.18 nmol/L (95% CI 0.01–0.35) higher in girls whose maternal serum PFOS levels were in the 3rd tertile (>22.6 ng/mL). No association between serum PFOS and SHBG (3.46, 95% CI -12.06–18.98).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Manzano-Salgado et al. 2017a Prospective study of 1,202 mother-infant pairs participating in the Environment and Childhood Study in Spain	**Exposure:** Mean maternal serum PFOS 6.05 ng/mL (measured during first trimester) **Statistical adjustments:** Maternal age, parity, prepregnancy BMI, fish intake during pregnancy	No association between maternal PFOS and birth weight (β 0.44, 95% CI -32.48–33.36) length (β 0.03, 95% CI -0.12–0.17), head circumference (β -0.00, 95% CI -0.10–0.10), or gestational age (β -0.06, 95% CI -0.19–0.06). No associations between maternal PFOS and risk of small for gestational age (OR 0.92, 95% CI 0.70–1.22), preterm (OR 1.10, 95% CI 0.70–1.74), low birth weight (OR 1.06, 95% CI 0.71–1.58), or low birth weight at term (OR 0.91, 95% CI 0.55–1.50).
Minatoya et al. 2017 Cross-sectional study of 168 mother-infant pairs participating in the Hokkaido Study on Environment and Children's Health in Japan	**Exposure:** Median maternal serum PFOS 5.1 ng/mL (measured at gestation weeks 23–35) **Statistical adjustments:** Maternal BMI, parity, smoking during pregnancy, blood sampling period, gestational age, infant sex	Inverse association between maternal PFOS and ponderal index (β -2.25, 95% CI -4.01 to -0.50, p=0.012); no association with birth weight (β -29, 95% CI -289–232, p=0.828). Association between maternal PFOS and cord blood total adiponectin levels (β 0.12, 95% CI 0.01–0.22, p=0.028). No association with high molecular weight adiponectin levels (p=0.075) or leptin levels (p=0.691).
Monroy et al. 2008 Prospective study of 101 pregnant women participating in the Family Study in Ontario Canada; birth outcome data obtained from medical records	**Exposure:** Median maternal serum PFOS (measured at delivery) 14.54 ng/mL (range: 9.19–20.22 ng/mL); median cord blood PFOS 6.08 ng/mL (range: 3.92–9.11 ng/mL) **Linear regression model adjustments:** Parity, gestational length, maternal BMI, sex, smoking status	No significant correlations (p>0.05) between maternal serum PFOS or cord blood PFOS and birth weight.
Ode et al. 2014 Case-control study of 206 children with ADHD in Sweden and 206 matched controls	**Exposure:** Median cord blood serum level of PFOS 6.92 ng/mL for cases and 6.77 ng/mL for controls **Logistic regression adjustments:** Maternal smoking, parity, gestational age at birth	No significant association between cord blood PFOS and risk of ADHD; OR 0.98 (95% CI 0.92–1.04 for 1 ng/mL increase in cord blood PFOS).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Oulhote et al. 2016 Prospective study of 567 children in the Faroe Islands; 7-year-old child's behavioral development was assessed using a Strengths and Difficulties Questionnaire	**Exposure:** Geometric mean PFOS levels: maternal 27.42 ng/mL (range of 9.4–66.68 ng/mL) (measured at 16 weeks of gestation), 5-year-old child 16.75 ng/mL (range of 6.18–48.23 ng/mL), 7-year-old child 15.27 ng/mL (range of 5.64–35.5 ng/mL) **Statistical adjustments:** Child's age, sex, maternal age, prepregnancy BMI, parity, socio-economic status, alcohol and tobacco use during pregnancy, breastfeeding duration, birth weight	No associations between maternal PFOS levels or 5- and 7-year-old PFOS levels and behavioral development scores.
Quaak et al. 2016 Prospective study of 76 infants whose mothers participated in the Linking Maternal Nutrition to Child Health study in the Netherlands; child behavior was assessed at 18 months of age via a parent completed questionnaire	**Exposure:** Mean and median cord blood plasma PFOS 1.5836 and 1.6000 ng/mL **Linear regression adjustments:** Parental educational level, maternal smoking and alcohol use, family history of ADHD	No significant associations between cord plasma PFOS levels and scores on an ADHD scale (p=0.66 and 0.19 for the 2nd and 3rd tertiles, respectively) or the externalizing problem scale (p=0.62 and 0.31 for 2nd and 3rd tertiles). Stratifying by sex did not alter the scores on the ADHD scale (p=0.35 and p=0.43 for boys and girls in the 3rd tertile, respectively) or the externalizing problem scale (p=0.74 and p=0.31 for boys and girls in the 3rd tertile).
Robledo et al. 2015a, 2015b Cross-sectional study of 234 couples in Michigan and Texas participating in the LIFE study cohort; women reported birth size characteristics after delivery	**Exposure:** Geometric mean PFOS levels 12.44 ng/mL (maternal) and 21.6 ng/mL (paternal) **Linear regression adjustments:** Maternal age, difference between maternal and paternal age, prepregnancy BMI, infant sex, serum cotinine concentration, concentration of other perfluoroalkyls	No significant associations (p>0.05) between maternal or paternal PFOS levels and birth weight, birth length, head circumference, or ponderal index.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Sagiv et al. 2018 Prospective study of 1,645 pregnant women participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFOS 25.7 ng/mL (measured at gestation weeks 5–19); 1st quartile: 0.1–18.8 ng/mL, 2nd quartile: 18.9–25.6 ng/mL, 3rd quartile: 25.7–34.8 ng/mL, 4th quartile: 34.9–185.0 ng/mL **Statistical adjustments:** Maternal age, race/ethnicity, education, prenatal smoking, parity, history of breastfeeding, prepregnancy BMI, paternal education, household income, child's sex, gestational age at blood draw	No association between maternal PFOS and birth weight for gestational age (β -0.04, 95% CI -0.08–0.01) or gestational length (β -0.08, 95% CI -0.17–0.02). Association between maternal PFOS and preterm births (OR, 95% CI): 2nd quartile: 2.0 (1.1–3.7) 3rd quartile: 2.0 (1.1–3.7) 4th quartile: 2.4 (1.3–4.4).
Shi et al. 2017 Cross-sectional study of 170 infants in China	**Exposure:** Median cord serum PFOS 0.974 ng/mL (range of <LOD–6.494 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, gestation age, infant sex, maternal height	No associations between cord PFOS and birth weight (β 160.45, 95% CI -11.85–332.75), birth length (β 0.33, 95% CI -0.14–0.79), or ponderal index (β 0.07, 95% CI -0.03–0.16).
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFOS 2.4 ng/mL (measured at 20–34 weeks of gestation) **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education gestational weight gain, smoking during pregnancy, gravidity, gestational age at blood draw, infant sex, gestational age at birth	No associations between maternal PFOS and birth weight (β -13.8 g, 95% CI -53.8–26.3) or adiposity at birth (β 0.8, 95% CI -0.33–0.49).
Strøm et al. 2014 Prospective study of 876 offspring of women participating in the Danish Fetal Origins 1988 study; neurobehavioral and affective disorders were assessed in the offspring using population-based registry data (20-year follow-up)	**Exposure:** Median maternal serum PFOS (measured during gestation week 30) 21.4 ng/mL **Regression model adjustments:** Maternal age, parity, prepregnancy BMI, maternal education, maternal smoking during pregnancy, offspring sex	No significant associations between maternal serum PFOS and offspring ADHD (trend for 3rd tertile, p=0.38), depression (trend for 3rd tertile p=0.14), or scholastic achievement below the median (trend for 3rd tertile p=0.59).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Toft et al. 2016 Case-control study of 270 cases of cryptorchidism, 75 cases of hypospadias, and 300 controls in Denmark	**Exposure:** Amniotic fluid PFOS • 1st tertile: <0.8 ng/mL • 2nd tertile: 0.8–1.4 ng/mL • 3rd tertile: >1.4 ng/mL **Statistical adjustments:** Gestation age of amniocentesis, maternal age, smoking	No significant associations between amniotic fluid PFOS levels and risk of cryptorchidism (OR 1.01, 95% CI 0.66–1.53 for comparisons between 1st and 3rd tertiles) or hypospadias (OR 0.69, 95% CI 0.35–1.38 for comparisons between 1st and 3rd tertiles). Collapsing across groups, significant associations between amniotic fluid PFOS and testosterone levels (p=0.002), androstenedione (p=0.001), progesterone (p=0.001), and cortisol (p<0.001); there was an inverse association with insulin-like factor 3 (p<0.001). No association with DHEAS (p=0.93).
Vested et al. 2013 Prospective cohort study of 169 males aged 19–21 years in Denmark whose mothers participated in pregnancy cohort study	**Exposure:** Median maternal serum PFOS (measured during gestation week 30) 21.2 ng/mL **Multivariable regression adjustments:** History of reproductive tract disease, BMI, smoking status, maternal smoking during pregnancy, socioeconomic status at birth, abstinence time (sperm parameters)	No significant association (p>0.05) between maternal PFOS levels and sperm concentration, total sperm count, semen volume, percentage progressive spermatozoa, percentage morphologically normal spermatozoa, mean testicular volume, or testosterone, estradiol, LH, FSH, inhibin B, SHBG, or FAI levels.
Vesterholm Jensen et al. 2014 Nested case-control study of 107 boys with cryptorchidism from Denmark (n=29) and Finland (n=78) and 108 matched controls (30 from Denmark and 78 from Finland)	**Exposure:** Median cord blood serum PFOS 9.1 ng/mL (Denmark cohort) and 5.2 ng/mL (Finland cohort) **Logistic regression adjustments:** Birth weight, gestational age, parity	No significant association between cord serum PFOS and risk of cryptorchidism; OR 0.83 (95% CI 0.44–1.58) for the whole cohort, OR 1.30 (95% CI 0.27–6.39) for the Denmark cohort and OR 0.55 (95% CI 0.23–1.32) for the Finland cohort.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vuong et al. 2016 Prospective study of 256 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 5 and 8 years of age	**Exposure:** Median maternal PFOS (measured at gestation weeks 16 and 26 and within 24 hours of parturition) 13.2 ng/mL (range: 0.4–57.2 ng/mL) **Statistical adjustments:** Maternal age, race, education income, maternal serum cotinine, maternal depression, maternal IQ, a measure of quality and extent of stimulation at home, marital status, child sex	Significant association between maternal serum PFOS levels and the risk of a global executive composite score of >60; OR 2.19 (95% CI 1.03–4.66). Associations between maternal PFOS levels and behavioral regulation (β 3.14, 95% CI 0.68–5.61), metacognition (β 3.10, 95% CI 0.62–5.58), or global executive functioning (β 3.38, 95% CI 0.86–5.90).
Vuong et al. 2018 Prospective study of 208 children participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 8 years of age	**Exposure:** Geometric mean serum PFOS 3.9 ng/mL in child at 8 years of age **Statistical adjustments:** Maternal age, race/ethnicity, household income, child sex, maternal marijuana use, maternal blood lead, maternal serum cotinine, maternal depression, vitamin use, maternal IQ, marital status, HOME score, breastfeeding	No associations (p>0.05) between child serum PFOS at age 8 years and metacognition index, behavior regulation index, or global executive functioning scores. No association between child serum PFOS and having a BRIEF summary score of ≥60 (defined as being at risk) for behavior regulation score (OR 0.40, 95% CI 0.14–1.14), metacognition score (OR 1.53, 95% CI 0.67–3.52), or global executive score (OR 1.04, 95% CI 0.41–2.68).
Wang et al. 2015b Prospective cohort study of children whose mothers participated in the Taiwan Maternal and Infant Cohort study; full scale IQ, verbal IQ, and performance IQ were assessed when the children were 5 (n=120) and 8 (n=120) years of age	**Exposure:** Median maternal serum PFOS (measured during third trimester) 13.25 ng/mL (5-year-old group) and 12.28 mg/mL (8-year-old group) **Linear regression adjustments:** Child's sex and age at IQ assessment, maternal education, household income, a measure of quality and extent of stimulation at home	No significant association (p>0.05) between maternal PFOS and IQ scores at 5 or 8 years of age.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Washino et al. 2009 Prospective cohort study of 428 pregnant Japanese women; infant data obtained from medical records	**Exposure:** Median maternal serum PFOS (measured in second trimester) 5.2 ng/mL (range: 1.3–16.2 ng/mL) **Regression adjustments:** Maternal age, maternal education level, smoking status during pregnancy, maternal BMI, parity, infant sex, gestational age, blood sampling period	Significant inverse correlation between maternal serum PFOS and birth weight (β -148.8 g, 95% CI -297.0 to -0.5 g; p=0.049, per log PFOS unit); when analyzed by sex, only significant in females (β -269.4 g, 95% CI -465.7 to -73.0 g, p=0.007 per log PFOS unit), but not in males (p=0.917 for males). No significant correlations between serum PFOS and birth length (p=0.167), chest circumference (p=0.718), or head circumference (p=0.488).
Whitworth et al. 2012a Cohort study of 901 pregnant women enrolled in the Norwegian Mother and Child Cohort study; birth outcome data taken from Medical Birth Registry of Norway	**Exposure:** Median maternal serum PFOS (measured in around gestation week 17) 13.0 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, albumin concentration, maternal education, interpregnancy interval, consumption of lean fish	No association between maternal PFOS and birth weight (p=0.10). Significant inverse association between maternal serum PFOS and risk of preterm birth; OR 0.3 (95% CI 0.1–1.0, p=0.03) for 4th quartile (≥16.59 ng/mL). No association between maternal PFOS levels and SGA (p=0.51) or large for gestational age (p=0.33).
Zhang et al. 2018 Prospective study of 167 mother-child pairs participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio	**Exposure:** Median PFOS levels: maternal 13.0 ng/mL (measured at 16 weeks of gestation), 3-year-old child 6.6 ng/mL, 8-year-old child 3.6 ng/mL **Statistical adjustments:** Maternal age, race, education, household income, parity, smoking, maternal IQ, breastfeeding duration	No associations (p>0.05) between maternal PFOS levels and reading scores at age 5 or 8 years. Association (p<0.05) between serum PFOS levels at age 3 years and reading scores at age 5 years, but not at 8 years of age. Association (p<0.05) between serum PFOS at age 8 years and reading score (word reading) at 8 years of age.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHxS		
Lopez-Espinosa et al. 2016 Cross-sectional study of 1,169 boys and 1,123 girls aged 6–9 years participating in the C8 Health Project study; sexual maturation	**Exposure:** Median serum PFHxS 8.1 ng/mL in boys and 7.0 ng/mL in girls **Statistical adjustments:** Age, month, and time of sampling	No significant associations between serum PFHxS and estradiol (percent difference between 75th and 25th PFHxS levels) in boys (-1.3, 95% CI -5.5–3.1) and in girls (2.1, 95% CI -2.2–6.5), total testosterone in boys (-2.7, 95% CI -6.4–1.2) and in girls (0.2, 95% CI -3.5–4.0), or insulin-like growth factor-1 in boys (-2.5, 95% CI -5.2–0.3) and girls (-2.1, 95% CI -4.8–0.7).
Stein and Savitz 2011 Cross-sectional study of 10,546 non-Hispanic white children aged 5–18 years participating in the C8 Health Project; ADHDs diagnosis and learning problems were reported by parents	**Exposure:** Mean serum PFHxS level of 9.3 ng/mL (range: 0.25–276.4 ng/mL) • 1st quartile: 0.25–<2.9 ng/mL • 2nd quartile:2.9–<5.2 ng/mL • 3rd quartile:5.2–<10.1 ng/mL • 4th quartile: 10.1–276.4 ng/mL **Logistic regression model adjustments:** Age, sex	Significant association between serum PFHxS levels and the risk of ADHD diagnosis; OR (95% CI): 5–18-year-olds • 2nd quartile: 1.27 (1.06–1.52) • 3rd quartile: 1.43 (1.21–1.70) • 4th quartile: 1.53 (1.29–1.83) 12–15-year-olds • 2nd quartile: 1.46 (1.10–1.93) • 3rd quartile: 1.45 (1.10–1.91) • 4th quartile: 1.53 (1.15–2.04) Significant association between serum PFHxS levels and the risk of ADHD diagnosis with medication in 5–18-year-olds; OR (95% CI): 5–18-year-olds • 2nd quartile: 1.44 (1.09–1.90) • 3rd quartile: 1.55 (1.19–2.04) • 4th quartile: 1.53 (1.21–2.08) The association was not significant in 12–15-year-olds; OR 1.42 (95% CI 0.94–2.13) for the 4th quartile. No significant associations between serum PFOS and risk of learning problems. The ORs (95% CI) for the 5–18-year-olds and 12–

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		15-year-olds were 1.19 (1.00–1.41) and 1.05 (0.79–1.40), respectively.
Alkhalawi et al. 2016 Retrospective study of 156 mother-child pairs participating in the Duisburg Birth Cohort study in Germany; weight and length recorded at birth and at 1, 4, 6, and 12 months of age	**Exposure:** Geometric mean maternal serum PFHxS 0.62 ng/mL; 1st quartile: <0.2–0.54 ng/mL, 2nd quartile: 0.55–0.76 ng/mL, 3rd quartile: 0.79–0.97 ng/mL, 4th quartile: 0.97–1.72 ng/mL **Statistical adjustments:** Pregnancy duration, maternal BMI before pregnancy, maternal height, maternal blood lead levels, infant sex, mode of delivery, mother place of birth, smoking during pregnancy	No association (p>0.05) between maternal PFHxS and ponderal index, birth weight, or birth length.
Ashley-Martin et al. 2016 Cohort study of 1,723 women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada; GWG was based on weekly weight gain during the 2nd and 3rd trimesters	**Exposure:** Median serum PFHxS (measured during first trimester) and cord blood PFHxS: 1.00 and 0.10 ng/mL **Logistic regression adjustments:** Maternal age, prepregnancy BMI	No significant association (p>0.1) between serum PFHxS and GWG when subjects were stratified by BMI. GWG was not significantly associated with increased odds of high cord blood PFHxS (>0.30 ng/mL); OR 1.01 (95% CI 0.99–1.03) per 1 kg increase in GWG.
Ashley-Martin et al. 2017 Cross-sectional study of 1,705 mother-infant pairs participating in the Maternal Infant Research on Environmental Chemicals in Canada	**Exposure:** Median maternal plasma PFHxS 1.0 ng/mL (measured during first trimester) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, household income, smoking	No association between maternal PFHxS and birth weight (β 0.04, 95% CI -0.12–0.20), leptin (β 0.01, 95% CI -0.08–0.10), or adiponectin (β 0.02, 95% CI -0.08–0.04). Similar findings when cord blood PFHxS used as biomarker of exposure.
Bach et al. 2016 Cohort study of 1,507 nulliparous women and their children in the Aarhus Birth Cohort in Denmark	**Exposure:** Median serum PFHxS levels (measured between gestation week 9 and 20): 0.5 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, maternal education	Lower birth weights were found in women with PFHxS levels higher than the 1st quartile; the adjusted difference between the 1st and 4th quartiles was 49 g. No consistent alterations in birth length or head circumference were found in comparisons across serum PFHxS quartiles.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Braun et al. 2014 Prospective study of 175 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; social responsiveness scale measures (measurement of autistic behavior) was evaluated when children were 4 and 5 years of age	**Exposure:** Median maternal serum PFHxS levels (measured at 16 weeks of gestation): 1.6 ng/mL **Bayesian regression adjustments:** Maternal age at delivery, race, marital status, education, parity, insurance status, employment, household income, prenatal vitamin use, maternal depressive symptoms, maternal IQ, child sex, caregiving environment, maternal serum cotinine	No association between maternal serum PFHxS and scores on the social responsiveness scale.
Braun et al. 2016a, 2016b Prospective study of 204 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; height, weight, waist circumference, and body fat were measured when the children were 8 years of age; height and weight were also measured at ages 2, 3, 4, and 5 years	**Exposure:** Median maternal serum PFHxS levels (measured at 16 weeks of gestation): 1.4 ng/mL **Statistical adjustments:** Maternal age, race, education, marital status, employment, household income, maternal depressive symptoms, maternal BMI at 16 weeks of gestation, parity, maternal serum cotinine, frequency of fruit/vegetable and fish consumption during pregnancy, prenatal vitamin use	No association between maternal serum PFHxS levels and child adiposity scores or changes in BMI scores between 2 and 8 years of age ($p>0.23$). No significant increases in the risk of overweight/obesity at age 8 years were observed; the relative risks for serum PFHxS levels in the 2nd and 3rd tertiles were RR 1.33 (95% CI 0.72–2.48) and RR 1.48 (95% CI 0.75–2.96).
Callan et al. 2016 Cross-sectional study of 98 pregnant women in Australia	**Exposure:** Median serum PFHxS 0.33 ng/mL (range of 0.06–3.3 ng/mL) (measured 2 weeks prior to due date) **Statistical adjustments:** Gestational age, maternal height, prepregnancy BMI, weight gain during pregnancy, infant sex	No association between maternal PFHxS and birth weight (β -103 g, 95% CI -221–15), birth length (β -0.20, 95% CI -0.78–0.38), head circumference (β -0.31, 95% CI -0.74–0.12), or ponderal index (β -0.05, 95% CI -0.13–0.03).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFHxS 0.16 ng/mL; 1st tertile <0.06 ng/mL, 2nd tertile 0.06–0.139 ng/mL, 3rd tertile >0.13 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFHxS and birth weight (p=0.69), birth length (p=0.67), or ponderal index (p=0.85). Association between cord PFHxS and postnatal head circumference (β, 95% CI): 2nd tertile: 1.33 (0.42–2.26) 3rd tertile: 0.90 (0.00–1.81).
Christensen et al. 2011 Case-control study of 448 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; case-control study of girls with early menarche (<11.5 years of age, n=218) and controls (menarche ≥11.5 years, n=230)	**Exposure:** Median maternal (blood samples measured at gestation week 15) serum PFHxS 1.6 ng/mL	No significant association between maternal PFHxS and odds of earlier age at menarche (OR 0.89, 95% CI 0.65–1.22).
Gump et al. 2011 Cross-sectional study of 83 children aged 9–11 years (mean 10.13 years; 36.1% female) living in New York	**Exposure:** Mean and median serum PFHxS: 6.06 and 3.67 ng/mL **Statistical adjustments:** Blood lead, sex, body fat, patent's education, family history of high blood pressure, asthma	Serum PFHxS was significantly (p<0.01) associated with poorer performance on a task requiring behavioral inhibition.
Hamm et al. 2010 Cross-sectional study of 252 pregnant women in Alberta Canada undergoing prenatal screening for Down's syndrome, trisomy 18, and open spina bifida; birth outcome data obtained from medical records	**Exposure:** Mean serum PFHxS levels (measured in early second trimester) 2.1 ng/mL (range: <LOD [0.25]–43 ng/mL) **Statistical adjustments:** Maternal age, maternal weight, maternal height, smoking status during pregnancy, infant sex, maternal race, parity	No associations between maternal serum PFHxS levels and birth weight (change in birth weight for 3rd tertile of 25.99 (95% CI -95.25–147.23). No significant association between maternal serum PFHxS and the risk for SGA; the RR (95% CI) for serum PFHxS levels in the 3rd tertile (>1.4–43 ng/mL) was 2.35 (0.63–8.72). A significant inverse association between serum PFHxS and preterm delivery was found (RR 0.31, 95% CI 0.11–0.90 for serum PFHxS levels in the 3rd tertile).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Hoffman et al. 2010 Cross-sectional study of 571 children aged 12–15 years participating in NHANES 1999–2000 or 2003–2004	**Exposure:** Median serum PFHxS: 2.2 ng/mL (range: ND [0.1]–64.1 ng/mL) **Logistic regression model adjustments:** NHANES sample cycle, age, race/ethnicity, sex, environmental tobacco smoke, and maternal smoking during pregnancy	Significant association between serum PFHxS levels and parent-reported ADHD; the OR for each 1 ng/mL increase in serum PFHxS was 1.06 (95% CI 1.02–1.11).
Jeddy et al. 2017 Prospective study of 432 mother-daughter pairs participating in the Avon Longitudinal Study of Parents and Children in the Great Britain; children were assessed at 15 and 38 months of age	**Exposure:** Maternal median serum PFHxS 1.6 ng/mL (measured at 15 weeks of gestation) **Statistical adjustments:** Parity, maternal age, maternal education, maternal smoking status, gestational age at blood sample collection	No association between maternal PFHxS and verbal comprehension, vocabulary comprehension and production, nonverbal communication, or social developmental scores in 15-month-old children (p>0.05). No associations between maternal PFHxS and language, intelligibility, or communicative scores in 38-month-old children (p>0.05).
Jensen et al. 2015 Case-control study of 56 women in Denmark having a miscarriage before gestation week 12 and 336 matched controls	**Exposure:** Median maternal serum PFHxS levels (measured prior to gestation week 12): 0.298 ng/mL **Logistic regression adjustments:** Age, BMI, parity, and gestational age at serum sampling	No significant association between maternal serum PFHxS levels and the risk of miscarriage before gestation week 12; OR 1.53 (95% CI 0.99–2.38).
Kim et al. 2011 Cross-sectional study of 44 pregnant women in South Korea; birth outcome data obtained from questionnaires	**Exposure:** Median maternal serum PFHxS (mostly measured during the third trimester) 0.55 ng/mL (range: 0.46–0.85 ng/mL); cord blood serum PFHxS level 0.34 ng/mL (range: 0.27–0.51 ng/mL) **Statistical adjustments:** Maternal age, gestational age, maternal BMI (T4, TSH, and body weight only)	No significant correlations (p>0.05) between maternal serum PFHxS or cord blood PFHxS and fetal cord T3, T4, or TSH levels. No significant correlations (p>0.05) between maternal serum PFHxS or cord blood PFHxS levels and birth weight.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFHxS: 1.228 ng/mL (cases) and 1.17 ng/mL (controls)	Significant inverse correlation ($p<0.05$) between serum PFHxS levels and thyroid stimulating immunoglobulin levels in infants with congenital hypothyroidism. No significant correlation ($p>0.05$) between serum PFHxS and TSH, free T4, T3, and microsomal antibodies.
Lee et al. 2013 Cross-sectional study of 59 pregnant women in South Korea; birth outcome data obtained from medical records	**Exposure:** Mean maternal serum PFHxS (measured at delivery) 1.35 ng/mL (range: 0.53–3.67 ng/mL). Mean cord blood serum PFHxS level 0.67 ng/mL (range: 0.22–1.69 ng/mL) **Logistic regression model adjustments:** Maternal age, gestational age	No significant associations between maternal serum PFHxS or cord blood PFHxS levels and birth weight ($p=0.38$, $p=0.92$), birth length ($p=0.42$, $p=0.75$), head circumference ($p=0.65$, $p=0.76$), or ponderal index ($p=0.05$, $p=0.66$). After adjustments for confounders, there were no significant associations between maternal PFOS levels and birth weight (OR 0.57, 95% CI 0.19–1.75), birth length (OR 0.44, 95% CI 0.12–1.58), ponderal index (OR 0.64, 95% CI 0.19–2.23), or head circumference (OR 0.90, 95% CI 0.13–6.13). Inverse association between cord blood PFHxS and birth weight (OR 0.26, 95% CI 0.08–0.85).
Lee et al. 2016 Cross-sectional study of 85 newborns in South Korea; birth outcome data from medical records	**Exposure:** Mean cord blood serum PFHxS: 0.60 ng/mL **Multiple regression adjustments:** Gestational age, maternal age, infant sex, variable to control for sampling bias	No significant association ($p>0.05$) between cord blood PFHxS levels and birth weight.
Lenters et al. 2016a, 2016b Prospective study of 1,250 infants whose mothers participated in the INUENDO cohort in Greenland (n=513), Ukraine (n=557), and Poland (n=180)	**Exposure:** Median maternal serum PFHxS levels: 2.05 ng/mL for Greenland cohort, 2.28 ng/mL for Poland cohort, and 1.56 ng/mL for Ukraine cohort **Regression model adjustments:** Study population, maternal age, parity, gestational age, infant sex, maternal height, alcohol consumption, cotinine, vitamin D	No significant association ($p=0.801$) between maternal PFHxS levels and term birth weight.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFHxS 3.9 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	No associations between cord PFHxS and birth weight (β -30.0, 95% CI -83.4–23.5) or gestational age (β 0.12, 95% CI -0.03–0.27).
Liew et al. 2014 Case-control study using data from the Danish National Birth Cohort study; 156 children were diagnosed with congenital cerebral palsy (cases) and 550 randomly selected children served as controls	**Exposure:** Median maternal serum PFHxS (86% measured during first trimester and 14% during the second trimester): Cases: • boys 0.96 ng/mL • girls 0.90 ng/mL Controls: • boys 0.92 ng/mL • girls 0.92 ng/mL **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness	No significant association between maternal PFHxS levels and risk of congenital cerebral palsy in boys (RR 1.2, 95% CI 0.9–1.7) or girls (RR 1.1, 95% CI 0.6–1.9).
Liew et al. 2015 Nested case-control study using data from the Danish National Birth Cohort study; 215 cases of ADHD, 213 cases of autism, and 545 randomly selected children served as controls	**Exposure:** Median maternal serum PFHxS (87% measured during first trimester and 13% during the second trimester): 0.84 ng/mL for ADHD cases, 0.92 ng/mL for autism cases, 0.92 ng/mL for controls **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness, gestational week of blood drawn, child's sex, birth year	No significant association between maternal PFHxS levels and the risk of ADHD (RR 0.97, 95% CI 0.88–1.08) or autism (RR 1.10, 95% CI 0.92–1.33). When PFHxS levels were categorized by quartiles, a significantly lower risk of ADHD (RR 0.67, 95% CI 0.54–0.83) was found for the 4th quartile (PFHxS ≥1.24 ng/mL).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lind et al. 2017a Prospective study of 649 pregnant women participating in the Odense child cohort study in Denmark; infants were examined at 3.5 months of age	**Exposure:** Median maternal serum PFHxS 0.3 ng/mL (measured at gestational weeks 5–12) **Statistical adjustments:** Gestational age, parity, maternal smoking during pregnancy, prepregnancy BMI, maternal ethnicity	No association (p>0.05) between maternal PFHxS and birth weight or gestational length. No association between maternal PFHxS and anogenital distance in boys (p=0.56) or girls (p=0.10) or penile width (p=0.78).
Maisonet et al. 2012 Prospective cohort study of 447 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain. Birth outcome data obtained from medical records; weight and height at age 2 and 20 months were measured	**Exposure:** Median maternal serum PFHxS (measured at gestation week 15) 1.6 ng/mL (range: 0.2–54.8 ng/mL) **Linear regression model adjustments:** Maternal smoking during pregnancy (birth weight and length only), maternal prepregnancy BMI, previous live births, gestational age, maternal education (birth length only)	Significant inverse trend between maternal serum PFHxS levels and birth weight (p=0.0314) and birth length (p=0.0008); no significant trend for ponderal index (p=0.6802). No significant association between maternal serum PFHxS and weight at 20 months (unadjusted p=0.7511, adjusted by birth weight p=0.2801, adjusted for height at 20 months p=0.9349, or adjusted by height at 20 months and birth weight p=0.4375).
Maisonet et al. 2015a Prospective cohort study of 72 girls (aged 15 years) participating in Avon Longitudinal Study of Parents and Children in Great Britain	**Exposure:** Median maternal serum PFHxS (measured at gestation week 16) 1.6 ng/mL (range: 0.2–54.1 ng/mL) **Statistical adjustments:** SHBG concentration, maternal education, maternal age at delivery, maternal prepregnancy BMI, maternal smoking during pregnancy, time of day daughter's blood sample obtained, daughters age at menarche, daughters BMI at age 15 years	No association between serum PFHxS and testosterone and SHBG; the regression coefficients for the girls whose maternal serum PFHxS levels were in the 3rd tertile (>1.9 ng/mL) were 0.18 (95% CI 0.00–0.35) and -5.31 (95% CI -21.61–11.00).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Manzano-Salgado et al. 2017a Prospective study of 1,202 mother-infant pairs participating in the Environment and Childhood Study in Spain	**Exposure:** Mean maternal serum PFHxS 0.58 ng/mL (measured during first trimester) **Statistical adjustments:** Maternal age, parity, prepregnancy BMI, fish intake during pregnancy	No association between maternal PFHxS and birth weight (β -8.60, 95% CI -32.00–14.80) length (β -0.06, 95% CI -0.17–0.06), head circumference (β -0.01, 95% CI -0.09–0.07), or gestational age (β -0.01, 95% CI -0.10–0.09). No associations between maternal PFHxS and risk of small for gestational age (OR 0.98, 95% CI 0.80–1.19), preterm (OR 0.85, 95% CI 0.63–1.13), low birth weight (OR 0.94, 95% CI 0.71–1.23), or low birth weight at term (OR 0.97, 95% CI 0.68–1.41)
Monroy et al. 2008 Prospective study of 101 pregnant women participating in the Family Study in Ontario Canada; birth outcome data obtained from medical records	**Exposure:** Median maternal serum PFHxS (measured at delivery) 1.62 ng/mL (range: 1.33–2.66 ng/mL); PFHxS was only detected in 47% of samples **Linear regression model adjustments:** Parity, gestational length, maternal BMI, sex, smoking status	No significant correlations (p>0.05) between maternal serum PFHxS and birth weight.
Oulhote et al. 2016 Prospective study of 567 children in the Faroe Islands; 7-year-old child's behavioral development was assessed using a Strengths and Difficulties Questionnaire	**Exposure:** Geometric mean PFHxS levels: maternal 4.43 ng/mL (range of 0.62–26.45 ng/mL) (measured at 16 weeks of gestation), 5-year-old child 0.54 ng/mL (range of 0.08–19.51 ng/mL), 7-year-old child 0.53 ng/mL (range of 0.14–8.93 ng/mL) **Statistical adjustments:** Child's age, sex, maternal age, prepregnancy BMI, parity, socio-economic status, alcohol and tobacco use during pregnancy, breastfeeding duration, birth weight	No associations between maternal PFHxS levels or 5- and 7-year-old PFOS levels and behavioral development scores.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Sagiv et al. 2018 Prospective study of 1,645 pregnant women participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFHxS 2.4 ng/mL (measured at gestation weeks 5–19) **Statistical adjustments:** Maternal age, race/ethnicity, education, prenatal smoking, parity, history of breastfeeding, prepregnancy BMI, paternal education, household income, child's sex, gestational age at blood draw	No association between maternal PFHxS and birth weight for gestational age (β 0.00, 95% CI -0.03–0.02) or gestational length (β 0.02, 95% CI -0.04–0.07). No association between maternal PFHxS and preterm births (OR 1.0, 95% CI 0.9–1.1).
Shi et al. 2017 Cross-sectional study of 170 infants in China	**Exposure:** Median cord serum PFHxS 0.157 ng/mL (range of <LOD-3.048 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, gestation age, infant sex, maternal height	No associations between cord PFHxS and birth weight (β 108.80, 95% CI -53.84–271.45), birth length (β 0.38, 95% CI -0.06–0.82), or ponderal index (β 0.03, 95% CI -0.06–0.12).
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFHxS 0.8 ng/mL (measured at 20–34 weeks of gestation); 1st tertile <LOD–0.5 ng/mL, 2nd tertile 0.6–1.0 ng/mL, 3rd tertile 1.1–10.9 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education gestational weight gain, smoking during pregnancy, gravidity, gestational age at blood draw, infant sex, gestational age at birth	No association between maternal PFHxS and birth weight (β, 95% CI): 2nd tertile: 32.9 g (-36.3–102.0) 3rd tertile: -31.84 g (-105.8–42.2). Inverse association between maternal PFHxS and adiposity at birth (β, 95% CI): 2nd tertile: 0.12% fat mass (-0.59–0.83) 3rd tertile: -0.99% fat mass (-1.75 to -0.23).
Vuong et al. 2016 Prospective study of 256 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 5 and 8 years of age	**Exposure:** Median maternal PFHxS (measured at gestation weeks 16 and 26 and within 24 hours of parturition) 1.5 ng/mL (range: <LOD–32.5 ng/mL) **Statistical adjustments:** Maternal age, race, education income, maternal serum cotinine, maternal depression, maternal IQ, a measure of quality and extent of stimulation at home, marital status, child sex	Significant association between maternal serum PFHxS levels and the risk of a global executive composite score of >60; OR 1.71, 95% CI 1.05–2.77). No significant association between maternal PFHxS levels and behavioral regulation (β 1.19, 95% CI -0.54–5.40), metacognition (β 1.31, 95% CI -0.43–3.04), or global executive functioning (β 1.36, 95% CI -0.41–3.12).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vuong et al. 2018 Prospective study of 208 children participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 8 years of age	**Exposure:** Geometric mean serum PFHxS 1.4 ng/mL in child at 8 years of age **Statistical adjustments:** Maternal age, race/ethnicity, household income, child sex, maternal marijuana use, maternal blood lead, maternal serum cotinine, maternal depression, vitamin use, maternal IQ, marital status, HOME score, breastfeeding	No associations (p>0.05) between child serum PFHxS at age 8 years and metacognition index, behavior regulation index, or global executive functioning scores. No association between child serum PFHxS and having a BRIEF summary score of ≥60 (defined as being at risk) for behavior regulation score (OR 0.54, 95% CI 0.22–1.32), metacognition score (OR 1.10, 95% CI 0.58–2.09), or global executive score (OR 0.65, 95% CI 0.32–1.32).
Wang et al. 2015b Prospective cohort study of children whose mothers participated in the Taiwan Maternal and Infant Cohort study; full scale IQ, verbal IQ, and performance IQ were assessed when the children were 5 (n=120) and 8 (n=120) years of age	**Exposure:** Median maternal serum PFHxS (measured during third trimester) 0.69 ng/mL (5-year-old group) and 0.69 mg/mL (8-year-old group) **Linear regression adjustments:** Child's sex and age at IQ assessment, maternal education, household income, a measure of quality and extent of stimulation at home	No significant association (p>0.05) between maternal PFHxS and IQ scores at 5 or 8 years of age.
Zhang et al. 2018 Prospective study of 167 mother-child pairs participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio	**Exposure:** Median PFHxS levels: maternal 1.5 ng/mL (measured at 16 weeks of gestation), 3-year-old child 1.9 ng/mL, 8-year-old child 1.2 ng/mL **Statistical adjustments:** Maternal age, race, education, household income, parity, smoking, maternal IQ, breastfeeding duration	No associations (p>0.05) between maternal PFHxS levels and reading scores at age 5 or 8 years. No association (p>0.05) between serum PFHxS levels at age 3 years and reading scores at age 5 years or 8 years. No association (p>0.05) between serum PFHxS at age 8 years and reading score at 8 years of age.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFNA		
Lopez-Espinosa et al. 2016 Cross-sectional study of 1,169 boys and 1,123 girls aged 6–9 years participating in the C8 Health Project study; sexual maturation	**Exposure:** Median serum PFNA 1.7 ng/mL in boys and 1.7 ng/mL in girls **Statistical adjustments:** Age, month, and time of sampling	Significant inverse association between serum PFNA and insulin-like growth factor-1 (percent difference between 75th and 25th PFNA levels, -3.5 (95% CI -6.0 to -1.0) in boys and -3.8 (95% CI -6.4 to -1.2) in girls. No significant associations between serum PFNA and estradiol in boys (-2.5, 95% CI -6.2–1.4) and in girls (-2.4, 95% CI -6.3–1.7) or total testosterone in boys (-2.1, 95% CI -5.5–1.3) and in girls (-1.9, 95% CI -5.5–1.9).
Stein and Savitz 2011 Cross-sectional study of 10,546 non-Hispanic white children aged 5–18 years participating in the C8 Health Project; ADHDs diagnosis and learning problems were reported by parents	**Exposure:** Mean serum PFNA level of 1.7 ng//mL (range: 0.25–24.1 ng/mL) • 1st quartile: 0.25–<1.2 ng/mL • 2nd quartile:1.2–<1.5 ng/mL • 3rd quartile: 1.5–<2.0 ng/mL • 4th quartile: 2.0–24.1 ng/mL **Logistic regression model adjustments:** Age, sex	A significant inverse association between serum PFNA and risk of learning problems; OR (95% CI): 5–18-year-olds • 2nd quartile: 0.87 (0.74–1.03) • 3rd quartile: 0.81 (0.69–0.95) • 4th quartile: 0.74 (0.62–0.87) 12–15-year-olds • 2nd quartile: 0.97 (0.74–1.25) • 3rd quartile: 0.86 (0.66–1.11) • 4th quartile: 0.73 (0.55–0.98). No significant associations between serum PFNA and risk of ADHD; the OR (95% CI) for 5–18-year-old participants and 12–15-year-old participants with serum PFNA levels in the 4th quartile (2.0–24.1 ng/mL) were 0.99 (0.84–1.18) and 1.00 (0.75–1.32), respectively.
Bach et al. 2016 Cohort study of 1,507 nulliparous women and their children in the Aarhus Birth Cohort in Denmark	**Exposure:** Median serum PFNA levels (measured between gestation week 9 and 20): 0.8 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, maternal education	No consistent alterations in birth weight, birth length, or head circumference were found in comparisons across serum PFNA quartiles.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Bae et al. 2015 Prospective study of 233 couples from Michigan and Texas participating in the Longitudinal Investigation of Fertility and the Environment Study	**Exposure:** Geometric mean serum PFNA levels 1.60 and 1.37 ng/mL in male and female nulliparous parents and 1.55 and 1.09 ng/mL in male and female parous parents (measured at the time of pregnancy testing) **Logistic regression adjustments:** Age, research site, household income, maternal parity	No significant association between maternal or paternal PFNA levels and the odds of a male birth (maternal: OR 0.94, 95% CI 0.70–1.26; paternal: OR 0.94, 95% CI 0.71–1.24). However, paternal PFNA levels in the 2nd tertile were significantly associated with an increase in female births (OR 0.48, 95% CI 0.25–0.95), but were not significant for the 3rd tertile (OR 0.58, 95% CI 0.28–1.17). When couple PFNA levels were modeled, paternal PFNA was significantly associated with an increase in females only in the group with PFNA levels in the 2nd tertile (OR 0.43, 95% CI 0.21–0.88), but not in the 3rd tertile (OR 0.52, 95% CI 0.23–1.14).
Braun et al. 2014 Prospective study of 175 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; social responsiveness scale measures (measurement of autistic behavior) was evaluated when children were 4 and 5 years of age	**Exposure:** Median maternal serum PFNA levels (measured at 16 weeks of gestation): 0.9 ng/mL **Bayesian regression adjustments:** Maternal age at delivery, race, marital status, education, parity, insurance status, employment, household income, prenatal vitamin use, maternal depressive symptoms, maternal IQ, child sex, caregiving environment, maternal serum cotinine	No association between maternal serum PFNA and scores on the social responsiveness scale.
Buck Louis et al. 2016 Prospective study of 332 couples followed from preconception to 7 weeks post-conception	**Exposure:** Median serum PFNA in women 1.2 ng/mL **Statistical adjustments:** Age, BMI, prior pregnancy loss, alcohol consumption, cigarette smoking during pregnancy	No association between maternal serum PFNA and pregnancy loss (HR 0.86, 95% CI 0.70–1.06).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Callan et al. 2016 Cross-sectional study of 98 pregnant women in Australia	**Exposure:** Median serum PFNA 0.30 ng/mL (range of 0.05–0.1.3 ng/mL) (measured 2 weeks prior to due date) **Statistical adjustments:** Gestational age, maternal height, prepregnancy BMI, weight gain during pregnancy, infant sex	No association between maternal PFNA and birth weight (β 14 g, 95% CI -169–196), birth length (β 0.20, 95% CI -0.68–1.09), head circumference (β -0.14, 95% CI -0.80–0.52), or ponderal index (β -0.03, 95% CI -0.16–0.09).
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFNA 0.13 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFNA and birth weight (p=0.19), birth length (p=0.06), or ponderal index (p=0.91).
Chen et al. 2012a Cross-sectional study of 429 infants participating in Taiwan Birth Panel Study	**Exposure:** Geometric mean cord blood PFNA level 2.36 ng/mL **Linear and logistic regression model adjustments:** Maternal age, prepregnancy BMI, education level, type of delivery, parity, infant sex, gestational age (for birth weight, birth length, head circumference, ponderal index, LBW)	Significant associations between cord blood PFNA and birth length (p<0.01) and inverse association with ponderal index (p<0.05). No significant association (p>0.05) between cord blood PFNA and gestational age, birth weight, or head circumference. No significant associations between cord blood PFNA and odds of preterm birth (OR 0.88, 95% CI 0.71–1.11), LBW (OR 0.76, 95% CI 0.47–1.23), or SGA (OR 0.97, 95% CI 0.74–1.26).
Gump et al. 2011 Cross-sectional study of 83 children aged 9–11 years (mean 10.13 years; 36.1% female) living in New York	**Exposure:** Mean and median serum PFNA: 0.82 and 0.72 ng/mL **Statistical adjustments:** Blood lead, sex, body fat, patent's education, family history of high blood pressure, asthma	Serum PFNA was significantly (p<0.05) associated with poorer performance on a task requiring behavioral inhibition.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Hoffman et al. 2010 Cross-sectional study of 571 children aged 12–15 years participating in NHANES 1999–2000 or 2003–2004	**Exposure:** Median serum PFNA: 0.6 ng/mL (range: ND [0.1]–5.9 ng/mL) **Logistic regression model adjustments:** NHANES sample cycle, age, race/ethnicity, sex, environmental tobacco smoke, and maternal smoking during pregnancy	No significant association between serum PFNA levels and parent-reported ADHD; the OR for each 1 ng/mL increase in serum PFNA was 1.32 (95% CI 0.86–2.02).
Jeddy et al. 2017 Prospective study of 432 mother-daughter pairs participating in the Avon Longitudinal Study of Parents and Children in the Great Britain; children were assessed at 15 and 38 months of age	**Exposure:** Maternal median serum PFNA 0.5 ng/mL (measured at 15 weeks of gestation) **Statistical adjustments:** Parity, maternal age, maternal education, maternal smoking status, gestational age at blood sample collection	No association between maternal PFNA and verbal comprehension, vocabulary comprehension and production, nonverbal communication, or social developmental scores in 15-month-old children (p>0.05). No associations between maternal PFNA and language, intelligibility, or communicative scores in 38-month-old children (p>0.05).
Jensen et al. 2015 Case-control study of 56 women in Denmark having a miscarriage before gestation week 12 and 336 matched controls	**Exposure:** Median maternal serum PFNA levels (measured prior to gestation week 12): 0.72 ng/mL **Logistic regression adjustments:** Age, BMI, parity, and gestational age at serum sampling	Significant associations between maternal serum PFNA levels and the risk of miscarriage before gestation week 12; OR 16.46 (95% CI 7.39–36.62). When participants were categorized by serum PFNA levels, significant associations were found for the 2nd and 3rd tertiles; OR 10.88 (95% CI 4.76–24.84) and OR 16.17 (95% CI 6.88–38.03).
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFNA: 1.931 ng/mL (cases) and 0.633 ng/mL (controls)	Serum PFNA levels were significantly (p<0.001) higher than in cases than controls. No significant correlation (p>0.05) between serum PFNA and TSH, free T4, T3, microsomal antibodies, and thyroid stimulating immunoglobulin.
Lee et al. 2016 Cross-sectional study of 85 newborns in South Korea; birth outcome data from medical records	**Exposure:** Mean cord blood serum PFNA: 0.36 ng/mL **Multiple regression adjustments:** Gestational age, maternal age, infant sex, variable to control for sampling bias	No significant association (p>0.05) between cord blood PFNA levels and birth weight.
Lenters et al. 2016a, 2016b	**Exposure:** Median maternal serum PFNA levels: 0.69 ng/mL for Greenland cohort,	No significant association (p=0.065) between maternal PFNA levels and term birth weight.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Prospective study of 1,250 infants whose mothers participated in the INUENDO cohort in Greenland (n=513), Ukraine (n=557), and Poland (n=180)	0.56 ng/mL for Poland cohort, and 0.61 ng/mL for Ukraine cohort **Regression model adjustments:** Study population, maternal age, parity, gestational age, infant sex, maternal height, alcohol consumption, cotinine, vitamin D	
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFNA 0.2 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	No association between cord PFNA and birth weight (β -45.6, 95% CI -106.9–15.8) or gestational age (β -0.02, 95% CI -0.19–0.10).
Lien et al. 2016 Prospective study of 282 7-year-old children whose mothers participated in the Taiwan Birth Panel Study or Taiwan Early-Life Cohort; psychometric symptoms related to attention deficit/hyperactivity disorder were assessed using three parent completed questionnaires	**Exposure:** Weighted average cord blood serum PFNA: 4.49 ng/mL **Linear regression (with inverse probability) adjustments:** Child sex, breastfeeding, maternal age, maternal education, parity, maternal environmental tobacco smoke exposure during pregnancy, alcohol consumption during pregnancy, annual income, gestational age, birth weight, cord blood lead, study cohort	Significant inverse associations between cord blood PFOA and scores on tests measuring inattention (p=0.0129), oppositional defiant disorder (p=0.0225), and hyperactivity/ inattention (p=0.0484). No associations with hyperactivity/impulsivity (p=0.0588), internalizing problems (p=0.5211), externalizing problems (p=0.3793), emotional symptoms (p=0.1902), conduct problems (p=0.6931), peer problems (p=0.0535), or pro-social behavior (p=0.7493).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Liew et al. 2014 Case-control study using data from the Danish National Birth Cohort study; 156 children were diagnosed with congenital cerebral palsy (cases) and 550 randomly selected children served as controls	**Exposure:** Median maternal serum PFNA (86% measured during first trimester and 14% during the second trimester): Cases: • boys 0.46 ng/mL • girls 0.39 ng/mL Controls: • boys 0.44 ng/mL • girls 0.41 ng/mL **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness	No significant association between maternal PFNA levels and risk of congenital cerebral palsy in boys (RR 1.2, 95% CI 0.6–2.5) or girls (RR 0.6, 95% CI 0.3–1.2).
Liew et al. 2015 Nested case-control study using data from the Danish National Birth Cohort study; 215 cases of ADHD, 213 cases of autism, and 545 randomly selected children served as controls	**Exposure:** Median maternal serum PFNA (87% measured during first trimester and 13% during the second trimester): 0.42 ng/mL for ADHD cases, 0.41 ng/mL for autism cases, 0.43 ng/mL for controls **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness, gestational week of blood drawn, child's sex, birth year	No significant association between maternal PFNA levels and the risk of ADHD (RR 0.80, 95% CI 0.62–1.03) or autism (RR 0.80, 95% CI 0.58–1.11).
Lind et al. 2017a Prospective study of 649 pregnant women participating in the Odense child cohort study in Denmark; infants were examined at 3.5 months of age	**Exposure:** Median maternal serum PFNA 0.7 ng/mL (measured at gestational weeks 5–12) **Statistical adjustments:** Gestational age, parity, maternal smoking during pregnancy, prepregnancy BMI, maternal ethnicity	No association (p>0.05) between maternal PFNA and birth weight or gestational length. Inverse association between maternal PFNA and anogenital distance in girls (β -1.8, 95% CI -3.5 to -0.1, p=0.05). No association with anogenital distance in boys (β -0.5, 95% CI -2.1–1.1, p=0.63) or penile width (p=0.81).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Maisonet et al. 2015a Prospective cohort study of 72 girls (aged 15 years) participating in Avon Longitudinal Study of Parents and Children in Great Britain	**Exposure:** Median maternal serum PFNA (measured at gestation week 16) 0.5 ng/mL (range: 0.2–1.1 ng/mL) **Statistical adjustments:** SHBG concentration, maternal education, maternal age at delivery, maternal prepregnancy BMI, maternal smoking during pregnancy, time of day daughter's blood sample obtained, daughters age at menarche, daughters BMI at age 15 years	No association between serum PFNA and testosterone and SHBG; the regression coefficients for the girls whose maternal serum PFNA levels were in the 3rd tertile (>0.6 ng/mL) were 0.05 (95% CI -0.14–0.24) and 7.91 (95% CI -8.69–24.52).
Manzano-Salgado et al. 2017a Prospective study of 1,202 mother-infant pairs participating in the Environment and Childhood Study in Spain	**Exposure:** Mean maternal serum PFNA 0.66 ng/mL (measured during first trimester) **Statistical adjustments:** Maternal age, parity, prepregnancy BMI, fish intake during pregnancy	No association between maternal PFNA and birth weight (β -10.27, 95% CI -38.14–17.61) length (β -0.00, 95% CI -0.13–0.13), head circumference (β -0.04, 95% CI -0.13–0.05), or gestational age (β -0.00, 95% CI -0.11–0.11). No associations between maternal PFNA and risk of small for gestational age (OR 0.85, 95% CI 0.68–1.07), preterm (OR 0.87, 95% CI 0.62–1.22), low birth weight (OR 0.86, 95% CI 0.63–1.17), or low birth weight at term (OR 0.91, 95% CI 0.60–1.38).
Monroy et al. 2008 Prospective study of 101 pregnant women participating in the Family Study in Ontario Canada; birth outcome data obtained from medical records	**Exposure:** Median maternal serum PFNA (measured at delivery) 0.69 ng/mL (range: 0.542–0.87 ng/mL) **Linear regression model adjustments:** Parity, gestational length, maternal BMI, sex, smoking status	No significant correlations (p>0.05) between maternal serum PFNA and birth weight.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Oulhote et al. 2016 Prospective study of 567 children in the Faroe Islands; 7-year-old child's behavioral development was assessed using a Strengths and Difficulties Questionnaire	**Exposure:** Geometric mean PFNA levels: maternal 0.61 ng/mL (range of 0.12–1.93 ng/mL) (measured at 16 weeks of gestation), 5-year-old child 1.01 ng/mL (range of 0.39–6.16 ng/mL), 7-year-old child 1.2 ng/mL (range of 0.47–9.49 ng/mL) **Statistical adjustments:** Child's age, sex, maternal age, prepregnancy BMI, parity, socio-economic status, alcohol, and tobacco use during pregnancy, breastfeeding duration, birth weight	No associations between maternal PFNA levels and behavioral development scores. Association between child's PFOA levels at age 5 years and total questionnaire score (indicative of higher difficulties) and higher externalizing problems score. No associations between child's PFNA levels at age 7 years and behavioral development scores.
Robledo et al. 2015a, 2015b Cross-sectional study of 234 couples in Michigan and Texas participating in the LIFE study cohort; women reported birth size characteristics after delivery	**Exposure:** Geometric mean PFNA levels 1.211 ng/mL (maternal) and 1.566 ng/mL (paternal) **Linear regression adjustments:** Maternal age, difference between maternal and paternal age, prepregnancy BMI, infant sex, serum cotinine concentration, concentration of other perfluoroalkyls	No significant associations (p>0.05) between maternal or paternal PFNA levels and birth weight, birth length, head circumference, or ponderal index.
Sagiv et al. 2018 Prospective study of 1,645 pregnant women participating in Project Viva in Massachusetts	**Exposure:** Median maternal plasma PFNA 0.7 ng/mL (measured at gestation weeks 5–19); 1st quartile: 0.1–0.4 ng/mL, 2nd quartile: 0.5–0.6 ng/mL, 3rd quartile: 0.7–0.9 ng/mL, 4th quartile: 1.0–6.0 ng/mL **Statistical adjustments:** Maternal age, race/ethnicity, education, prenatal smoking, parity, history of breastfeeding, prepregnancy BMI, paternal education, household income, child's sex, gestational age at blood draw	Inverse association between maternal PFNA and birth weight for gestational age (β, 95% CI): 2nd quartile: -0.03 (-0.17–0.10) 3rd quartile: -0.20 (-0.33 to -0.06) 4th quartile: -0.17 (-0.31 to -0.02). No association between maternal PFNA and gestational length (β -0.07, 95% CI -0.17–0.02). No association between maternal PFNA and preterm births (OR 1.2, 95% CI 1.0–1.4).
Shi et al. 2017 Cross-sectional study of 170 infants in China	**Exposure:** Median cord serum PFNA 0.191 ng/mL (range of 0.039–0.801 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, gestation age, infant sex, maternal height	No associations between cord PFNA and birth weight (β 52.68, 95% CI -206.01–311.36), birth length (β 0.13, 95% CI -0.57–0.83), or ponderal index (β 0.01, 95% CI -0.13–0.15).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFNA 0.4 ng/mL (measured at 20–34 weeks of gestation); 1st half <LOD–0.4 ng/mL, 2nd half 0.5–6.0 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education, gestational weight gain, smoking during pregnancy, gravidity, gestational age at blood draw, infant sex, gestational age at birth	Inverse association between maternal PFNA and birth weight (β, 95% CI): 2nd half: -92.1 g (-150.6 to -33.6). Inverse association between maternal PFNA and adiposity at birth (β, 95% CI): 2nd half: -0.85% fat mass (-1.46 to -0.24).
Vuong et al. 2016 Prospective study of 256 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 5 and 8 years of age	**Exposure:** Median maternal PFNA (measured at gestation weeks 16 and 26 and within 24 hours of parturition) 0.9 ng/mL (range: 0.1–2.9 ng/mL) **Statistical adjustments:** Maternal age, race, education income, maternal serum cotinine, maternal depression, maternal IQ, a measure of quality and extent of stimulation at home, marital status, child sex	No significant association between maternal PFNA levels and behavioral regulation (β 2.57, 95% CI -0.26–5.40), metacognition (β 1.37, 95% CI -1.49–4.23), or global executive functioning (β 2.01, 95% CI -0.89–4.92).
Vuong et al. 2018 Prospective study of 208 children participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 8 years of age	**Exposure:** Geometric mean serum PFNA 0.8 ng/mL in child at 8 years of age **Statistical adjustments:** Maternal age, race/ethnicity, household income, child sex, maternal marijuana use, maternal blood lead, maternal serum cotinine, maternal depression, vitamin use, maternal IQ, marital status, HOME score, breastfeeding	Association between child serum PFNA at age 8 years and poorer metacognition index scores (β 3.4, 95% CI 0.4–6.3, p<0.05) and global executive functioning score (p<0.05). No association with behavior regulation index. When categorized by sex, the associations with behavior regulation index, metacognition index, or global executive functioning score were only observed in the boys. Associations between child serum PFNA and having a BRIEF summary score of ≥60 (defined as being at risk) for behavior regulation score (OR 2.75, 95% CI 1.30–5.79), metacognition score (OR 2.94, 95% CI 1.52–5.69), and global executive score (OR 3.07, 95% CI 1.60–5.90).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wang et al. 2015b Prospective cohort study of children whose mothers participated in the Taiwan Maternal and Infant Cohort study; full scale IQ, verbal IQ, and performance IQ were assessed when the children were 5 (n=120) and 8 (n=120) years of age	**Exposure:** Median maternal serum PFNA (measured during third trimester) 1.59 ng/mL (5-year-old group) and 1.44 mg/mL (8-year-old group) **Linear regression adjustments:** Child's sex and age at IQ assessment, maternal education, household income, a measure of quality and extent of stimulation at home	Significant inverse association between maternal PFNA and visual IQ scores at 8 years of age (β -2.1, 95% CI -3.9 to -0.2). No significant association (p>0.05) between maternal PFNA and IQ scores at 5 years of age.
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age	**Exposure:** Median maternal serum PFNA (measured during third trimester) 1.55 ng/mL for male children and 1.58 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	Significant inverse association (p<0.05) between maternal PFNA levels and birth weight in females; β -0.08 (95% CI -0.16 to -0.00) for 1 ln unit increase in PFNA levels. No significant associations (p>0.05) between maternal serum PFNA and birth weight, birth length, head circumference, or SGA among male children or birth length, head circumference, or SGA in female children.
Zhang et al. 2018 Prospective study of 167 mother-child pairs participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio	**Exposure:** Median PFNA levels: maternal 0.9 ng/mL (measured at 16 weeks of gestation), 3-year-old child 1.2 ng/mL, 8-year-old child 0.7 ng/mL **Statistical adjustments:** Maternal age, race, education, household income, parity, smoking, maternal IQ, breastfeeding duration	No associations (p>0.05) between maternal PFNA levels and reading scores at age 5 or 8 years. Association (p<0.05) between serum PFNA levels at age 3 years and reading scores at age 5 years, but not at 8 years of age. No association (p>0.05) between serum PFNA at age 8 years and reading score at 8 years of age.
PFDA		
Bach et al. 2016 Cohort study of 1,507 nulliparous women and their children in the Aarhus Birth Cohort in Denmark	**Exposure:** Median serum PFDA levels (measured between gestation week 9 and 20): 0.3 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, maternal education	No consistent alterations in birth weight, birth length, or head circumference were found in comparisons across serum PFDA quartiles.
Bae et al. 2015	**Exposure:** Geometric mean serum PFDA levels 0.46 and 0.38 ng/mL in male and	No significant association between maternal or paternal PFDA levels and the odds of a male

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Prospective study of 233 couples from Michigan and Texas participating in the Longitudinal Investigation of Fertility and the Environment Study	female nulliparous parents and 0.49 and 0.46 ng/mL in male and female parous parents (measured at the time of pregnancy testing) **Logistic regression adjustments:** Age, research site, household income, maternal parity	birth (maternal: OR 1.07, 95% CI 0.81–1.42; paternal: OR 1.02, 95% CI 0.78–1.34).
Buck Louis et al. 2016 Prospective study of 332 couples followed from preconception to 7 weeks post-conception	**Exposure:** Median serum PFDA in women 0.4 ng/mL **Statistical adjustments:** Age, BMI, prior pregnancy loss, alcohol consumption, cigarette smoking during pregnancy	No association between maternal serum PFDA and pregnancy loss (HR 0.83, 95% CI 0.66–1.04.
Callan et al. 2016 Cross-sectional study of 98 pregnant women in Australia	**Exposure:** Median serum PFDA 0.12 ng/mL (range of <0.05–0.39 ng/mL) (measured 2 weeks prior to due date) **Statistical adjustments:** Gestational age, maternal height, prepregnancy BMI, weight gain during pregnancy, infant sex	No association between maternal PFDA and birth weight (β 4 g, 95% CI -161–170), birth length (β 0.36, 95% CI -0.44–1.15), head circumference (β -0.07, 95% CI -0.67–0.53), or ponderal index (β -0.06, 95% CI -0.18–0.05).
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFDA 0.12 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFDA and birth weight (p=0.26), birth length (p=0.24), or ponderal index (p=0.55).
Gump et al. 2011 Cross-sectional study of 83 children aged 9–11 years (mean 10.13 years; 36.1% female) living in New York	**Exposure:** Mean and median serum PFDA: 0.26 and 0.26 ng/mL **Statistical adjustments:** Blood lead, sex, body fat, patent's education, family history of high blood pressure, asthma	Serum PFDA was significantly (p<0.05) associated with poorer performance on a task requiring behavioral inhibition.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Jensen et al. 2015 Case-control study of 56 women in Denmark having a miscarriage before gestation week 12 and 336 matched controls	**Exposure:** Median maternal serum PFDA levels (measured prior to gestation week 12): 0.27 ng/mL **Logistic regression adjustments:** Age, BMI, parity, and gestational age at serum sampling	Significant associations between maternal serum PFDA levels and the risk of miscarriage before gestation week 12; OR 2.30 (95% CI 1.18–4.47). When participants were categorized by serum PFNA levels, a significant association was found for the 3rd tertile OR 2.67 (95% CI 1.31–5.44), but not the 2nd tertile OR 1.86 (95% CI 0.91–3.83).
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFDA: 0.523 ng/mL (cases) and 0.298 ng/mL (controls)	Serum PFDA levels were significantly ($p<0.005$) higher than in cases than controls. No significant correlation ($p>0.05$) between serum PFDA and TSH, free T4, T3, microsomal antibodies, and thyroid stimulating immunoglobulin.
Lee et al. 2016 Cross-sectional study of 85 newborns in South Korea; birth outcome data from medical records	**Exposure:** Mean cord blood serum PFDA: 0.14 ng/mL **Multiple regression adjustments:** Gestational age, maternal age, infant sex, variable to control for sampling bias	No significant association ($p>0.05$) between cord blood PFDA levels and birth weight.
Lenters et al. 2016a, 2016b Prospective study of 1,250 infants whose mothers participated in the INUENDO cohort in Greenland (n=513), Ukraine (n=557), and Poland (n=180)	**Exposure:** Median maternal serum PFDA levels: 0.40 ng/mL for Greenland cohort, 0.22 ng/mL for Poland cohort, and 0.16 ng/mL for Ukraine cohort **Regression model adjustments:** Study population, maternal age, parity, gestational age, infant sex, maternal height, alcohol consumption, cotinine, vitamin D	No significant association ($p=0.158$) between maternal PFDA levels and term birth weight.
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFDA 0.1 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	No association between cord PFDA and birth weight (β -47.3, 95% CI -112.9–18.2) or gestational age (β 0.10, 95% CI -0.09–0.29).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Liew et al. 2014 Case-control study using data from the Danish National Birth Cohort study; 156 children were diagnosed with congenital cerebral palsy (cases) and 550 randomly selected children served as controls	**Exposure:** Median maternal serum PFDA (86% measured during first trimester and 14% during the second trimester): Cases: • boys 0.18 ng/mL • girls 0.16 ng/mL Controls: • boys 0.17 ng/mL • girls 0.16 ng/mL **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness	No significant association between maternal PFDA levels and risk of congenital cerebral palsy in boys (RR 1.1, 95% CI 0.7–1.7) or girls (RR 0.6, 95% CI 0.3–1.1).
Liew et al. 2015 Nested case-control study using data from the Danish National Birth Cohort study; 215 cases of ADHD, 213 cases of autism, and 545 randomly selected children served as controls	**Exposure:** Median maternal serum PFDA (87% measured during first trimester and 13% during the second trimester): 0.15 ng/mL for ADHD cases, 0.15 ng/mL for autism cases, 0.17 ng/mL for controls **Statistical adjustments:** Maternal age, parity, socioeconomic status, maternal smoking and alcohol intake during pregnancy, mother's self-reported psychiatric illness, gestational week of blood drawn, child's sex, birth year	Significant association between maternal PFDA levels and the risk of ADHD (RR 0.76, 95% CI 0.64–0.91). No significant association between maternal PFDA levels and the risk of autism (RR 0.79, 95% CI 0.63–1.01). When PFDA levels were categorized by quartiles, a significantly lower risks of ADHD (RR 0.53, 95% CI 0.43–0.66) and autism (RR 0.52, 95% CI 0.35–0.77) were found for the 4th quartile (PFDA ≥0.24 ng/mL).
Lind et al. 2017a Prospective study of 649 pregnant women participating in the Odense child cohort study in Denmark; infants were examined at 3.5 months of age	**Exposure:** Median maternal serum PFDA 0.3 ng/mL (measured at gestational weeks 5–12) **Statistical adjustments:** Gestational age, parity, maternal smoking during pregnancy, prepregnancy BMI, maternal ethnicity	No association ($p>0.05$) between maternal PFDA and birth weight or gestational length. Inverse association between maternal PFDA and anogenital distance in girls (β -1.3, 95% CI -2.8–0.2, p=0.04). No association with anogenital distance in boys (β -0.6, 95% CI -2.0–0.9, p=0.97) or penile width (p=0.65).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Oulhote et al. 2016 Prospective study of 567 children in the Faroe Islands; 7-year-old child's behavioral development was assessed using a Strengths and Difficulties Questionnaire	**Exposure:** Geometric mean PFDA levels: maternal 0.28 ng/mL (range of 0.03–0.98 ng/mL) (measured at 16 weeks of gestation), 5-year-old child 0.28 ng/mL (range of 0.05–1.2 ng/mL), 7-year-old child 0.36 ng/mL (range of 0.07–2.02 ng/mL) **Statistical adjustments:** Child's age, sex, maternal age, prepregnancy BMI, parity, socio-economic status, alcohol and tobacco use during pregnancy, breastfeeding duration, birth weight	No associations between maternal PFDA levels and behavioral development scores. Association between child's PFDA levels at age 5 years and total questionnaire score (indicative of higher difficulties) and higher externalizing problems, hyperactivity/inattention scores. No associations between child's PFDA levels at age 7 years and behavioral development scores.
Robledo et al. 2015a, 2015b Cross-sectional study of 234 couples in Michigan and Texas participating in the LIFE study cohort; women reported birth size characteristics after delivery	**Exposure:** Geometric mean PFDA levels 0.402 ng/mL (maternal) and 0.458 ng/mL (paternal) **Linear regression adjustments:** Maternal age, difference between maternal and paternal age, prepregnancy BMI, infant sex, serum cotinine concentration, concentration of other perfluoroalkyls	No significant associations ($p>0.05$) between maternal or paternal PFDA levels and birth weight, birth length, head circumference, or ponderal index.
Shi et al. 2017 Cross-sectional study of 170 infants in China	**Exposure:** Median cord serum PFDA 0.075 ng/mL (range of <LOD–0.595 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, gestation age, infant sex, maternal height	No associations between cord PFDA and birth weight (β -3.04, 95% CI -129.67–123.59), birth length (β -0.002, 95% CI -0.354–0.34), or ponderal index (β -0.01, 95% CI -0.08–0.06).
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFDA 0.1 ng/mL (measured at 20–34 weeks of gestation) **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education, gestational weight gain, smoking during pregnancy, gravidity, gestational age at blood draw, infant sex, gestational age at birth	No associations between maternal PFDA and birth weight (β 11.5 g, 95% CI -37.3–60.4) or adiposity at birth (β 0.06, 95% CI -0.45–0.56).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Vuong et al. 2016 Prospective study of 256 children whose mothers participated in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 5 and 8 years of age	**Exposure:** Median maternal PFDA (measured at gestation weeks 16 and 26 and within 24 hours of parturition) 0.2 ng/mL (range: 0.1–1.3 ng/mL) **Statistical adjustments:** Maternal age, race, education income, maternal serum cotinine, maternal depression, maternal IQ, a measure of quality and extent of stimulation at home, marital status, child sex	No significant association between maternal PFDA levels and behavioral regulation (β -0.70, 95% CI -3.31–1.92), metacognition (β -1.24, 95% CI -3.87–1.39), or global executive functioning (β -1.13, 95% CI -3.79–1.54).
Vuong et al. 2018 Prospective study of 208 children participating in the Health Outcomes and Measures of the Environment Study in Cincinnati, Ohio; parents completed a questionnaire to assess executive function when children were 8 years of age	**Exposure:** Not reported **Statistical adjustments:** Maternal age, race/ethnicity, household income, child sex, maternal marijuana use, maternal blood lead, maternal serum cotinine, maternal depression, vitamin use, maternal IQ, marital status, HOME score, breastfeeding	No associations (p>0.05) between child serum PFDA at age 8 years and metacognition index, behavior regulation index, and global executive functioning scores. Associations between child serum PFDA and having a BRIEF summary score of ≥60 (defined as being at risk) for behavior regulation score (OR 1.70, 95% CI 0.59–4.88), metacognition score (OR 2.11, 95% CI 0.83–5.35), or global executive score (OR 2.69, 95% CI 0.95–7.60).
Wang et al. 2015b Prospective cohort study of children whose mothers participated in the Taiwan Maternal and Infant Cohort study; full scale IQ, verbal IQ, and performance IQ were assessed when the children were 5 (n=120) and 8 (n=120) years of age	**Exposure:** Median maternal serum PFDA (measured during third trimester) 0.44 ng/mL (5-year-old group) and 0.44 mg/mL (8-year-old group) **Linear regression adjustments:** Child's sex and age at IQ assessment, maternal education, household income, a measure of quality and extent of stimulation at home	No significant association (p>0.05) between maternal PFDA and IQ scores at 5 or 8 years of age.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age	**Exposure:** Median maternal serum PFDA (measured during third trimester) 0.46 ng/mL for male children and 0.43 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	Significant inverse association ($p<0.05$) between maternal PFDA levels and birth weight in females; β -0.14 (95% CI -0.26 to -0.02) for 1 ln unit increase in PFDA levels. Significant increase ($p<0.05$) in risk of SGA among females; OR 3.14 (95% CI 1.07–9.19). No significant associations ($p>0.05$) between maternal serum PFDA and birth weight, birth length, head circumference, or SGA among male children or birth length or head circumference in male children.
PFUnA		
Bach et al. 2016 Cohort study of 1,507 nulliparous women and their children in the Aarhus Birth Cohort in Denmark	**Exposure:** Median serum PFUnA levels (measured between gestation week 9 and 20): 0.3 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, maternal education	No consistent alterations in birth weight, birth length, or head circumference were found in comparisons across serum PFUnA quartiles.
Callan et al. 2016 Cross-sectional study of 98 pregnant women in Australia	**Exposure:** Median serum PFUnA 0.08 ng/mL (range of <0.06–0.36 ng/mL) (measured 2 weeks prior to due date) **Statistical adjustments:** Gestational age, maternal height, prepregnancy BMI, weight gain during pregnancy, infant sex	No association between maternal PFUnA and birth weight (β 102 g, 95% CI -41–245), birth length (β 0.32, 95% CI -0.37–1.02), head circumference (β -0.29, 95% CI -0.81–0.24), or ponderal index (β 0.01, 95% CI -0.09–0.11). Association between maternal PFUnA and proportion of optimal body weight (β 5.3, 95% CI 1.2–9.3).
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFUnA 0.10 ng/mL; 1st tertile <0.06 ng/mL, 2nd tertile 0.06–0.11 ng/mL, 3rd tertile >0.11 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	Association between cord PFUnA and birth length (β, 95% CI): 2nd tertile: 0.33 (-0.17–0.67) 3rd tertile: 0.41 (0.06–0.77). No association between cord PFUnA and birth weight ($p=0.08$) or ponderal index ($p=0.56$).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Chen et al. 2012a Cross-sectional study of 429 infants participating in Taiwan Birth Panel Study	**Exposure:** Geometric mean cord blood PFUnA level 10.26 ng/mL **Linear and logistic regression model adjustments:** Maternal age, prepregnancy BMI, education level, type of delivery, parity, infant sex, gestational age (for birth weight, birth length, head circumference, ponderal index, LBW)	No significant associations (p>0.05) between cord blood PFUnA and gestational age, birth weight, birth length, head circumference, or ponderal index. No significant association between cord blood PFOA and odds of preterm birth (OR 0.87, 95% CI 0.64–1.16), LBW (OR 1.01, 95% CI 0.53–1.91), or SGA (OR 0.93, 95% CI 0.65–1.33).
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFUnA: 0.982 ng/mL (cases) and 0.438 ng/mL (controls)	Serum PFUnA levels were significantly (p<0.005) higher than in cases than controls. No significant correlation (p>0.05) between serum PFUnA and TSH, free T4, T3, microsomal antibodies, and thyroid stimulating immunoglobulin.
Lee et al. 2016 Cross-sectional study of 85 newborns in South Korea; birth outcome data from medical records	**Exposure:** Mean cord blood serum PFUnA: 0.22 ng/mL **Multiple regression adjustments:** Gestational age, maternal age, infant sex, variable to control for sampling bias	No significant association (p>0.05) between cord blood PFUnA levels and birth weight.
Lenters et al. 2016a, 2016b Prospective study of 1,250 infants whose mothers participated in the INUENDO cohort in Greenland (n=513), Ukraine (n=557), and Poland (n=180)	**Exposure:** Median maternal serum PFUnA levels: 0.70 ng/mL for Greenland cohort, 0.13 ng/mL for Poland cohort, and 0.16 ng/mL for Ukraine cohort **Regression model adjustments:** Study population, maternal age, parity, gestational age, infant sex, maternal height, alcohol consumption, cotinine, vitamin D	No significant association (p=0.275) between maternal PFUnA levels and term birth weight.
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFUnA 0.1 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	No association between cord PFUnA and birth weight (β -29.7, 95% CI -85.7–26.3) or gestational age (β 0.09, 95% CI -0.07–0.25).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lien et al. 2016 Prospective study of 282 7-year-old children whose mothers participated in the Taiwan Birth Panel Study or Taiwan Early-Life Cohort; psychometric symptoms related to attention deficit/hyperactivity disorder were assessed using three parent completed questionnaires	**Exposure:** Weighted average cord blood serum PFUnA: 7.96 ng/mL **Linear regression (with inverse probability) adjustments:** Child sex, breastfeeding, maternal age, maternal education, parity, maternal environmental tobacco smoke exposure during pregnancy, alcohol consumption during pregnancy, annual income, gestational age, birth weight, cord blood lead, study cohort	No significant associations between cord blood PFOA and scores on tests measuring inattention (p=0.6177), hyperactivity/impulsivity (p=0.3642), oppositional defiant disorder (p=0.2198), internalizing problems (p=0.6953), externalizing problems (p=0.6319), emotional symptoms (p=0.0517), conduct problems (p=0.1207), hyperactivity/inattention (p=0.9991), peer problems (p=0.9606), or pro-social behavior (p=0.6193).
Shi et al. 2017 Cross-sectional study of 170 infants in China	**Exposure:** Median cord serum PFUnA 0.063 ng/mL (range of <LOD–0.699 ng/mL) **Statistical adjustments:** Maternal age, prepregnancy BMI, parity, gestation age, infant sex, maternal height	No associations between cord PFUnA and birth weight (β -28.87, 95% CI -128.16–70.42), birth length (β -0.20, 95% CI -0.47–0.07), or ponderal index (β 0.01, 95% CI -0.04–0.06).
Wang et al. 2015b Prospective cohort study of children whose mothers participated in the Taiwan Maternal and Infant Cohort study; full scale IQ, verbal IQ, and performance IQ were assessed when the children were 5 (n=120) and 8 (n=120) years of age	**Exposure:** Median maternal serum PFUnA (measured during third trimester) 3.42 ng/mL (5-year-old group) and 3.13 mg/mL (8-year-old group) **Linear regression adjustments:** Child's sex and age at IQ assessment, maternal education, household income, a measure of quality and extent of stimulation at home	Significant inverse association (p<0.05) between maternal serum PFUnA and performance IQ scores in 5-year-old children (β -1.6, 95% CI -3.0 to -0.2).
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age	**Exposure:** Median maternal serum PFUnA (measured during third trimester) 3.52 ng/mL for male children and 3.31 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	Significant inverse association (p<0.05) between maternal PFUnA levels and birth weight in females; β -0.06 (95% CI -0.11 to -0.01) for 1 ln unit increase in PFUnA levels. Significant increase (p<0.05) in risk of SGA among females; OR 1.83 (95% CI 1.01–3.32). No significant associations (p>0.05) between maternal serum PFUnA and birth weight, birth length, head circumference, or SGA among male children or birth length or head circumference in male children.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHpA		
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFHpA: 0.284 ng/mL (cases) and 0.0.324 ng/mL (controls)	No significant difference (p>0.05) between serum PFHpA levels in cases and controls. No significant correlation (p>0.05) between serum PFHpA and TSH, free T4, T3, microsomal antibodies, and thyroid stimulating immunoglobulin.
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFHpA 0.1 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	No associations between cord PFHpA and birth weight (β -103.7, 95% CI -211.3–3.8) or gestational age (β 0.14, 95% CI -0.17–0.45). When categorized by sex, inverse association between PFHpA and birth weight was found in boys (β -266.6, 95% CI -426.8 to -106.3) but not in girls (β 15.5, 95% CI -134.1–165.1).
PFBA		
Kim et al. 2016a Case-control study of 27 infants with congenital hypothyroidism and 13 matched controls living in South Korea	**Exposure:** Mean serum PFBA: 0.464 ng/mL (cases) and 0.220 ng/mL (controls)	No significant correlation (p>0.05) between serum PFBA and TSH, free T4, T3, microsomal antibodies, and thyroid stimulating immunoglobulin.
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFBA 0.1 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	No association between cord PFBA and birth weight (β -46.2, 95% CI -111.3–19.0) or gestational age (β 0.01, 95% CI -0.18–0.20).

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFDoDA		
Cao et al. 2018 Cross-sectional study of 337 newborns in China; children examined at birth and at approximately 19 months (mean) of age	**Exposure:** Mean umbilical cord serum PFDoDA 0.04 ng/mL; 1st tertile <0.02 ng/mL, 2nd tertile 0.02–0.04 ng/mL, 3rd tertile >0.04 ng/mL **Statistical adjustments:** Maternal age, education, household income, parity, paternal smoking, paternal drinking, infant's sex	No association between cord PFDoDA and birth weight (p=0.94), birth length (p=0.51), or ponderal index (p=0.60). Association between cord PFDoDA and postnatal length (β, 95% CI): 2nd tertile: 0.14 (-1.80–1.98) 3rd tertile: 2.03 (0.21–3.85).
Lee et al. 2016 Cross-sectional study of 85 newborns in South Korea; birth outcome data from medical records	**Exposure:** Mean cord blood serum PFDoDA: 0.14 ng/mL **Multiple regression adjustments:** Gestational age, maternal age, infant sex, variable to control for sampling bias	No significant association (p>0.05) between cord blood PFDoDA levels and birth weight.
Lenters et al. 2016a, 2016b Prospective study of 1,250 infants whose mothers participated in the INUENDO cohort in Greenland (n=513), Ukraine (n=557), and Poland (n=180)	**Exposure:** Median maternal serum PFDoDA levels: 0.13 ng/mL for Greenland cohort, 0.05 ng/mL for Poland cohort, and 0.04 ng/mL for Ukraine cohort **Regression model adjustments:** Study population, maternal age, parity, gestational age, infant sex, maternal height, alcohol consumption, cotinine, vitamin D	No significant association (p=0.440) between maternal PFDoDA levels and term birth weight.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Li et al. 2017 Cross-sectional study of 321 mother-infant pairs participating in the Guangzhou Birth Cohort study in China	**Exposure:** Median cord serum PFDoDA 0.1 ng/mL **Statistical adjustments:** Gestational age, delivery education, parity, infant sex, maternal age, pregnancy-induced hypertension, gestational diabetes, anemia	No association between cord PFDoDA and birth weight (β -46.86, 95% CI -122.0–28.4) or gestational age (β 0.07, 95% CI -0.24–0.39). When categorized by sex, inverse association between PFDoDA and birth weight was found in girls (β -130.4, 95% CI -239.1 to -21.7) but not in boys (β 18.4, 95% CI -86.8–123.5).
Wang et al. 2015b Prospective cohort study of children whose mothers participated in the Taiwan Maternal and Infant Cohort study; full scale IQ, verbal IQ, and performance IQ were assessed when the children were 5 (n=120) and 8 (n=120) years of age	**Exposure:** Median maternal serum PFDoDA (measured during third trimester) 0.38 ng/mL (5-year-old group) and 0.37 mg/mL (8-year-old group) **Linear regression adjustments:** Child's sex and age at IQ assessment, maternal education, household income, a measure of quality and extent of stimulation at home	No significant association (p>0.05) between maternal PFDoDA and IQ scores at 5 or 8 years of age.
Wang et al. 2016 Prospective cohort study of 223 children whose mothers participated in the Taiwan Maternal and Infant Cohort Study; growth assessments were conducted at 2, 5, 8, and 11 years of age.	**Exposure:** Median maternal serum PFDoDA (measured during third trimester) 0.37 ng/mL for male children and 0.37 ng/mL for female children **Regression adjustments:** Maternal age at delivery, education, previous live births self-reported prepregnancy BMI, family income	Significant inverse association (p<0.05) between maternal PFDoDA levels and birth weight in females; β -0.12 (95% CI -0.21 to -0.02) for 1 ln unit increase in PFDoDA levels. Significant inverse association (p<0.05) between maternal PFDoDA levels and head circumference; β -0.38 (95% CI -0.74 to -0.02) for 1 ln unit increase in PFDoDA levels. No significant associations (p>0.05) between maternal serum PFDoDA and birth weight, birth length, head circumference, or SGA among male children or birth length or SGA in male children.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
FOSA		
Bae et al. 2015 Prospective study of 233 couples from Michigan and Texas participating in the Longitudinal Investigation of Fertility and the Environment Study	**Exposure:** Geometric mean serum FOSA levels 0.11 and 0.10 ng/mL in male and female nulliparous parents and 0.10 and 0.12 ng/mL in male and female parous parents (measured at the time of pregnancy testing) **Logistic regression adjustments:** Age, research site, household income, maternal parity	No significant association between maternal or paternal FOSA levels and the odds of a male birth (maternal: OR 1.07, 95% CI 0.81–1.41; paternal: OR 1.14, 95% CI 0.86–1.51).
Christensen et al. 2011 Case-control study of 448 girls participating in Avon Longitudinal Study of Parents and Children in Great Britain; case-control study of girls with early menarche (<11.5 years of age, n=218) and controls (menarche ≥11.5 years, n=230)	**Exposure:** Median maternal (blood samples measured at gestation week 15) serum FOSA 0.2 ng/mL	No significant association between maternal FOSA and odds of earlier age at menarche (OR 0.91, 95% CI 0.67–1.24).
Gump et al. 2011 Cross-sectional study of 83 children aged 9–11 years (mean 10.13 years; 36.1% female) living in New York	**Exposure:** Mean and median serum FOSA: 0.75 and 0.61 ng/mL **Statistical adjustments:** Blood lead, sex, body fat, patent's education, family history of high blood pressure, asthma	Serum FOSA was significantly ($p<0.05$) associated with poorer performance on a task requiring behavioral inhibition.
Halldorsson et al. 2012 Prospective cohort study of 665 offspring of women participating in a birth cohort study in Denmark; the offspring were examined at 20 years of age	**Exposure:** Median maternal serum FOSA level (measured at gestation week 30) 1.1 ng/mL **Statistical adjustments:** Maternal age, maternal education, maternal prepregnancy BMI, smoking during pregnancy, parity, infant birth weight, and offspring age at follow-up	No significant associations ($p>0.56$) between maternal serum FOSA and offspring BMI and waist circumference were found.

Table 13. Developmental Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Robledo et al. 2015a, 2015b Cross-sectional study of 234 couples in Michigan and Texas participating in the LIFE study cohort; women reported birth size characteristics after delivery	**Exposure:** Geometric mean FOSA levels 0.112 ng/mL (maternal) and 0.114 ng/mL (paternal) **Linear regression adjustments:** Maternal age, difference between maternal and paternal age, prepregnancy BMI, infant sex, serum cotinine concentration, concentration of other perfluoroalkyls	Mean birth weight of infant boys was inversely associated with maternal FOSA levels ($p<0.05$) No significant associations ($p>0.05$) between maternal or paternal FOSA levels and birth length, head circumference, or ponderal index.

ADHD = attention deficit hyperactivity disorder; BMI = body mass index; CI = confidence interval; FAI = free androgen index (testosterone/SHBG); FOSA = perfluorooctane sulfonamide; FSH = follicle stimulating hormone; GWG = gestational weight gain; IQ = intelligence quotient; LBW = low birth weight; LH = luteinizing hormone; LHWA = Little Hocking Water Authority; LLOQ = lower limit of quantification; LOD = limit of detection; MDI = Mental Developmental Index; NHANES = National Health and Nutrition Examination Survey; NICU = neonatal intensive care unit; OR = odds ratio; PBPK = physiologically based pharmacokinetic; PDI = Psychomotor Developmental Index; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; RR = relative risk; SGA = small for gestational age; SHBG = sex hormone binding globulin; T3 = triiodothyronine; T4 = thyroxine; TSH = thyroid stimulating hormone

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Leonard 2006 Retrospective cohort mortality study of 6,027 (80% males) workers at a fluoropolymers production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between January 1, 1948 (plant start-up) and December 31, 2002	**Exposure:** Based on the results of a cross-sectional study (Sakr et al. 2007b), serum PFOA levels ranged from 5 to 9,550 ng/mL. Workers divided into three exposure categories: no APFO use jobs (serum PFOA levels 250 ng/mL); APFO-use jobs with median serum level of between <250 and ≤750 ng/mL; and APFO jobs with median serum levels of >750 ng/mL. Cumulative exposure was calculated for each worker by multiplying time in various jobs categories by an intensity factor (210, 430, or 1,690 ng/mL, respectively). **Reference populations:** Three comparisons groups were used: U.S. general population, West Virginia population, and population of DuPont workers residing in West Virginia and seven neighboring states (excluding workers at Washington Works)	Significant increase in deaths from diabetes mellitus (SMR 183, 95% CI 112–283) in males when DuPont worker population used as a reference. No significant association (SMRs <100 when the United States and West Virginia populations used as references). SMRs were not calculated for females since only two deaths from diabetes were found.
Leonard et al. 2008 Retrospective cohort mortality study 6,027 (80% males) workers at a fluoropolymers production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between January 1, 1948 (plant start-up) and December 31, 2002	**Exposure:** Not reported **Reference populations:** Three comparisons groups were used: U.S. general population, West Virginia population, and population of DuPont workers residing in West Virginia and seven neighboring states (excluding workers at Washington Works)	Significant increase in the risk of diabetes mellitus (SMR 197, 95% CI 123–298) when compared to the DuPont reference population, but not when compared to the United States (SMR 85, 95% CI 53–129) or West Virginia (SMR 70, 95% CI 43–106) reference populations.
Lundin et al. 2009 Cohort mortality study of 3,993 (80% male) workers at an APFO manufacturing facility (Cottage Grove); 807 workers died during the follow-up period; cohort consisted of workers employed for at least 365 days prior to December 31, 1997	**Exposure:** Workers were divided into three exposure classifications: • Definite occupational exposure, workers were exposed on a regular basis with potential high exposure (group 1) • Probable occupational exposure, jobs in other chemical division where APFO exposure was possible, but likely lower or transient (group 2)	Significant increases in deaths from diabetes mellitus in the probable exposure group; SMRs (95% CI): • Definite exposure: no deaths from diabetes • Probable exposure: 2.0 (1.2–3.2) • No or minimal exposure: 0.5 (0.2–1.2). In time-dependent Cox regression analysis, there was a significant increase in diabetes

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	• No or minimal occupational exposure (group 3) Serum PFOA levels measured in 2000 from 131 current workers ranged from 2,600 to 5,200 ng/mL in definite exposure jobs and from 300 to 1,500 ng/mL in the probable exposure jobs; no data were available for the no exposure jobs. **Reference population and adjustments:** Mortality rates were compared to rates from Minnesota general population; statistical models were adjusted for sex, year of birth, age at entry into the cohort, smoking status, and wage type; Cox regression analyses were done with an internal referent population	mellitus deaths among workers with moderate exposure (defined as ever working in a job with probable exposure or <6 months of definite exposure), HR 3.7 (95% CI 1.4–10.1); there were no deaths from diabetes among worker with definite exposure for ≥6 months.
Raleigh et al. 2014 Retrospective cohort mortality study of 9,027 workers (84% male) at two 3M facilities in Minnesota; 4,668 workers at an APFO facility in Cottage Grove (3,993 of these workers were included in the Lundin et al. 2009 cohort) and 4,359 workers at a non-APFO facility in St. Paul; cohort consisted of workers employed for at least 1 year; the Cottage Grove cohort included workers in a non-chemical division without exposure to APFO	**Exposure:** Work history and industrial monitoring were used to estimate PFOA exposure. Cumulative exposure in the Cottage Grove workers was divided into quartiles: • 1st quartile: >2.9x10^{-5} µg/m^3 • 2nd quartile: ≤1.5x10^{-4} µg/m^3 • 3rd quartile: ≤7.9x10^{-4} µg/m^3 • 4th quartile: >7.9x10^{-4} µg/m^3 **Reference population:** Mortality rates were compared to rates from Minnesota general population; Cottage Grove cohort was also compared to the St. Paul cohort	As compared to the Minnesota population, no significant alteration in deaths from diabetes mellitus (SMR 0.76, 95% CI 0.50–1.11) in the Cottage Grove cohort. As compared to the St. Paul cohort, no significant alteration in the risk of death from diabetes mellitus (HR 0.72, 95% CI 0.34–1.52) in workers in the 4th quartile.

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was estimated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum PFOA levels in 2005–2006 were 325 and 113 ng/mL in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	No significant associations between estimated cumulative serum PFOA and risk of type 2 diabetes (p=0.66 and 0.94 for trend with no lag or 10-year lag). The RRs (95% CI) were 1.10 (0.77–1.57) for no lag and 1.12 (95% CI 0.76–1.66) for 10-year lag.
Steenland and Woskie 2012 Retrospective cohort mortality study of 1,084 deceased workers at a fluoropolymers production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between 1948 and 2002; deaths were obtained through 2008; this is an extension of the Leonard (2006) study	**Exposure:** Cumulative exposure was estimated using serum PFOA levels of workers measured between 1979 and 2004 (median of 580 ng/mL with a range of 160–2,880 ng/mL). Exposures over time were estimated for eight job categories. The mean estimated cumulative exposure was 7,800 ng/mL-years (median of 4,300 ng/mL-years) and an estimated average annual serum PFOA concentration of 350 ng/mL (median 230 ng/mL. **Reference population:** Population, of DuPont workers residing in West Virginia and seven neighboring states (excluding workers at Washington Works)	Significant increase in deaths from diabetes was observed for all workers combined the SMR 1.90 (95% CI 1.35–2.61), but not in the highest exposure (4th quartile) (SMR 1.90, 95% CI 0.98–3.32). Analyzing with a 10- or 20-year lag did not result in increased risks (SMR 1.90, 95% CI 0.98–3.33 for 10-year lag and SMR 1.73, 95% CI 0.83–3.18 for 20-year lag).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Anderson-Mahoney et al. 2008 Cross-sectional study of 566 adult residents (mean age of 49.9 years) living near a Teflon manufacturing facility in West Virginia for at least 1 year; most subjects were exposed to PFOA in drinking water provided by Lubeck Public Service District (37%) or Little Hocking water district (27%); some subjects also worked at the facility	**Exposure:** Individual biomonitoring data were not provided; reported PFOA levels in the Lubeck and Little Hocking water districts were 0.4–3.9 and 1.7–4.3 µg/L, respectively. **Reference population:** SPRs were estimated using NHANES data; statistical analyses were adjusted for age and sex	Significantly increased risks of self-reported diabetes (SPR 1.54; 95% CI 1.16–2.05).
Conway et al. 2016 Cross-sectional study of 6,460 participants in the C8 Health Project with type 1 diabetes (n=820), type 2 diabetes (n=4,291) uncategorized diabetes (n=1,349) or no diabetes (n=60,439)	**Exposure:** Mean serum PFOA 68.4 ng/mL in type 1 diabetics, 92.8 ng/mL in type 2 diabetics, 86.5 ng/mL in uncategorized diabetics, and 82.3 ng/mL in the no diabetes group **Statistical adjustments:** Age, sex	Inverse association between serum PFOA and type 1 diabetes (OR 0.69, 95% CI 0.65–0.74), type 2 diabetes (OR 0.87, 95% CI 0.89–0.91), or uncategorized diabetes (OR 0.92, 95% CI 0.88–0.97). When subjects were categorized by age, inverse associations were observed in adults (≥20 years of age) between serum PFOA and type 1 diabetes (OR 0.74, 95% CI 0.70–0.79), type 2 diabetes (OR 0.91, 95% CI 0.89–0.94), or uncategorized diabetes (OR 0.92, 95% CI 0.88–0.96). In children and adolescents (<20 years of age), inverse association found for type 1 diabetes (OR 0.72, 95% CI 0.54–0.97), but no associations for type 2 diabetes (OR 1.13, 95% CI 0.82–1.56) or uncategorized diabetes (OR 1.18, 95% CI 0.90–1.55).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Karnes et al. 2014 Retrospective and prospective study of 32,254 participants in the C8 Health Project and a cohort of 3,713 workers at a DuPont Washington Works facility who worked at the plant between 1948 and 2002	**Exposure:** Serum PFOA levels based on estimated environmental levels on a fate and transport model to estimate PFOA levels in in water and air per year since production began in 1951 and PBPK model using standard assumptions about water intake, body weight, and PFOA half-life. Exposures of workers were estimated using a job history matrix. **Cox proportional hazards model adjustments:** Sex, non-white race, education, smoking, alcohol consumption, BMI, use of cholesterol and blood pressure lowering medication	No significant association between estimated cumulative serum PFOA and the risk of self-reported type II diabetes in retrospective and prospective analyses. The HRs (95% CI) in the retrospective and prospective analyses (per unit increase in estimated cumulative PFOA) were 1.00 (0.99–1.00, p=0.60) and 1.00 (1.00–1.01, p=0.31), respectively. No significant association (p>0.05) between estimated cumulative serum PFOA and fasting glucose levels in non-diabetic participants.
MacNeil et al. 2009 Case-control study of 13,922 adults (1,055 cases of type II diabetes) participating in the C8 Health Project	**Exposure:** Mean and median serum PFOA in cases were 122.7 and 48.5 ng/mL **Statistical adjustments:** Age, sex, family history, race, use of cholesterol-lowering and blood pressure medication	No significant association between serum PFOA levels and validated type II diabetes; the OR for subjects having serum PFOA levels in the 10th decile (>191.2 ng/mL) was 0.72 (95% CI 0.52–1.00). No significant associations (P>0.05) between serum PFOA and serum fasting glucose levels.
Cardenas et al. 2017 Cross-sectional study of 957 participants in the Diabetes Prevention Program in the U.S. Participants were at high risk of developing type 2 diabetes (BMI of 24 kg/m^2, fasting glucose of 95–125 mg/dL and glucose of 140–199 mg/dL 2 hours after a 75-g oral glucose load); participants were in the intensive lifestyle intervention or placebo-treated control groups of the study	**Exposure:** Geometric mean serum PFOA 4.82 ng/mL **Statistical adjustments:** Sex, race/ethnicity, BMI, age, marital status, education, smoking history	Doubling PFOA concentration was associated with increases (p<0.05) in HOMA-IR, fasting insulin, 30-minute insulin, fasting proinsulin, HOMA-β, insulinogenic index, fasting glucose, HbA1c, and adiponectin. However, these associations were not found in longitudinal analyses. No association between serum PFOA and risk of developing diabetes (HR 1.06, 95% CI 0.89–1.28, p=0.50).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Domazet et al. 2016 Prospective study of 501 Danish children participating in the European Youth Heart Study; subjects were evaluated at 9, 15, and 21 years of age	**Exposure:** Median serum PFOA in males and females at age 9 years 9.7 and 9.0 ng/mL, respectively, and 3.7 and 3.4 ng/mL at age 15 years, respectively **Statistical adjustments:** Sex, age, ethnicity, maternal parity, maternal income	Inverse association between serum PFOA at 9 years of age and HOMA-β at 15 years of age (β -11.10, 95% CI -20.28 to -1.01). No associations for glucose (β 1.87, 95% CI -1.19–4.93), insulin (β -12.99, 95% CI -25.95–2.23), or HOMA-IR (β -12.54, 95% CI -25.59–2.77) at 15 years of age. No association between serum PFOA at 9 years of age and glucose (β -1.01, 95% CI -14.62–30.07), insulin (β -13.98, 95% CI -36.23–16.00), HOMA-β (β -7.82, 95% CI -22.44–9.66), or HOMA-IR (β -14.16, 95% CI -36.60–16.28) at age 21. No association between serum PFOA at 15 years of age and glucose (β 5.83, 95% CI -3.70–16.92), insulin (β -0.59, 95% CI -44.76–79.43), HOMA-β (β -11.70, 95% CI -37.16–24.67), or HOMA-IR (β 0.93, 95% CI -44.45–83.55) at age 21.
Fisher et al. 2013 Cross-sectional study of 2,700 adult (aged 18–74 years) participants in the Canadian Health Measures Survey (2007–2009)	**Exposure:** Geometric mean serum PFOA 2.46 ng/mL **Linear regression model adjustments:** Age, sex, education, BMI	No significant associations between serum PFOA levels and insulin (p=0.12), glucose (p=0.17), or HOMA-IR (p=0.10).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Fleisch et al. 2017 Prospective study of 665 mother-child pairs participating in the Project Viva in Boston Massachusetts; children were evaluated at 7.7 (median) years of age	**Exposure:** Geometric mean maternal PFOA 5.3 ng/mL (measured at 9.6 weeks of gestation) and childhood serum PFOA 4.2 ng/mL **Statistical adjustments:** Child's age, sex, and race/ethnicity; maternal age, education, parity, and smoking during pregnancy; neighborhood median household income and percentage below poverty level; pregnancy hematodynamics	No associations (per interquartile range increment) between maternal PFOA and child's adiponectin (β -1.2, 95% CI -7.2–5.2) and HOMA-IR (β -0.7, 95% CI -9.8–9.4) levels. Inverse association (per interquartile range increment) between child's PFOA and child's HOMA-IR (β -10.1, 95% CI -17.3 to -2.3) levels. No association (per interquartile range increment) between child's PFOA and child's adiponectin (β 1.0, 95% CI -4.9–5.2) levels.
He et al. 2018 Cross-sectional study of 7,904 adult participants in 2003–2012 NHANES	**Exposure:** Mean serum PFOA in males and females 4.50 and 3.46 ng/mL. Serum PFOA for 1st, 2nd, 3rd, and 4th quartiles: <2.1, 2.1–3.34, 3.34–5.1, and >5.1 ng/mL, respectively **Statistical adjustments:** Age, race, BMI, education, energy intake, serum cotinine, alcohol consumption, PIR, time in front of television, video game, and computer	Association between serum PFOA and diabetes prevalence in males (p=0.001 for trend), OR (95% CI): 2nd quartile: 2.13 (1.30–3.46) 3rd quartile: 2.44 (1.49–3.98) 4th quartile: 2.67 (1.63–4.38) No association between serum PFOA and diabetes prevalence in females (p=0.737 for trend), OR (95% CI): 2nd quartile: 1.38 (0.87–2.19) 3rd quartile: 1.57 (0.95–2.61) 4th quartile: 1.47 (0.87–2.48).
Jensen et al. 2018 Prospective study of 158 pregnant women participating in the Odense Child Cohort study in Denmark	**Exposure:** Maternal median serum PFOA 1.67 ng/mL (measured at gestational week 11) **Statistical adjustments:** Age, parity, educational level, prepregnancy BMI	In women with a high risk of gestational diabetes mellitus, a 2-fold increase in serum PFOA was not associated with changes (β, 95% CI) in fasting glucose (-1.3, -3.0–0.5), fasting insulin (-4.0, -12.2–5.0), 2-hour glucose -2.6, -6.9–1.8), HOMA-IR (-5.2, -14.2–4.7), HOMA-β (-0.4, -8.0–8.0), or insulin sensitivity (6.1, -4.5–17.8) in response to an oral glucose tolerance test performed at gestational week 28.

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFOA 1.88 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFOA and fasting blood glucose (β 1.262, 95% CI -1.108–3.633, p=0.294).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOA 1.81 ng/mL (WTCHR group) and 1.39 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFOA and HOMA-IR (β -0.05, 95% CI -0.21–0.12, p=0.58).
Lin et al. 2009 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 474 adolescents (12–20 years old) and 969 adult (>20 years of age) participants	**Exposure:** Mean log serum PFOA was 1.51 and 1.48 ng/mL in adolescents and adults **Statistical adjustments:** Age, sex, race, smoking, alcohol intake, household income	Significant correlations (p<0.05) between serum PFOA and insulin levels and β -cell function were found in adults; these associations were not significant (p>0.05) in adolescents. No significant associations (p>0.05) between serum PFOA and fasting glucose or HOMA-IR were found in adults or adolescents.
Lind et al. 2014 Cross-sectional study of 1,016 men and women participating in the Prospective Investigation of the Vasculature in Uppsala Seniors in Sweden; diabetes was defined as a fasting glucose of >7 mmol/L or use of hypoglycemic medication; 114 participants had diabetes	**Exposure:** Median serum PFOA level 3.3 ng/mL **Linear regression model adjustments:** Sex, serum cholesterol and triacylglycerol, BMI, smoking, exercise habits, energy and alcohol intakes, and education level; quadratic terms of perfluorinated compounds were included in the models to search for nonlinear effects	No significant relationship between serum PFOA and the prevalence of diabetes; OR 0.97 (95% CI 0.61–1.53; p=0.88). There was a significant inverse association between serum PFOA and proinsulin/insulin ratio, OR 0.071 (95% CI 0.001–0.014; p=0.48); no association with HOMA-IR (p=0.20).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Liu et al. 2018b Cross-sectional study utilizing 2013–2014 NHANES data for 1,871 adults	**Exposure:** Geometric mean serum PFOA 1.86 ng/mL **Statistical adjustments:** Age, sex, ethnicity, smoking status, alcohol intake, household income, waist circumference, medications (anti-hypertensive, anti-hyperglycemic, anti-lipidemic)	Associations between serum PFOA and HbA1C (β 0.12, p<0.05) and β cell function (β 0.12, p<0.05). No associations between serum PFOA and fasting glucose (β 5.32, p>0.05), glucose levels 2-hour after glucose tolerance test (β -0.87, p>0.05), insulin levels (β 0.06, p>0.05), or HOMA-IR (β 0.03, p>0.05).
Melzer et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,966 adults (≥20 years of age)	**Exposure:** Mean serum PFOA levels were 5.23 ng/mL (0.1–45.9 ng/mL) in men and 4.25 ng/mL (0.1–123.0 ng/mL) in women Mean levels in each quartile: • 1st quartile: M 2.47 ng/mL; F 1.71 ng/mL • 2nd quartile: M 4.42 ng/mL; F 3.32 ng/mL • 3rd quartile: M 6.12 ng/mL; F 4.79 ng/mL • 4th quartile: M 10.39 ng/mL; F 9.47 ng/mL **Logistic regression model adjustments:** Age, ethnicity, study year, BMI, smoking status, alcohol consumption	No association between self-reported diabetes and serum PFOA levels were found; the OR (95% CI) for the 4th quartile was 0.69 (0.41–1.16, p=0.158).
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 306 adolescents (12–19 years of age and 524 adults (20–80 years of age)	**Exposure:** Serum mean and median PFOA levels were 4.6 and 3.9 ng/mL (range: 0.1–37.3 ng/mL **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	No significant association between serum PFOA and HOMA were found in adults (p>0.05), male adolescents (p=0.16) or female adolescents (p=0.11).
Predieri et al. 2015 Case-control study of 25 Italian children and adolescents with type I diabetes and 19 healthy controls	**Exposure:** Levels of PFOA in blood Non-parametric statistical analysis performed to assess differences in biochemical parameters between children with diabetes and healthy controls	No significant (p=0.160) difference in serum levels of PFOA between the two groups.

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Shapiro et al. 2016 Cross-sectional study of 1,274 pregnant women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Geometric mean plasma PFOA levels (measured during the first trimester) were 1.68 ng/mL in participants with normal glucose levels (n=1,167), 1.70 ng/mL in participants with impaired glucose tolerance (n=48), and 1.64 ng/mL in participants with gestational diabetes (n=59) **Logistic regression model adjustments:** Age at delivery, prepregnancy BMI, parity, household income, education, race, smoking status	There were no significant associations between plasma PFOA levels and the risk of gestational diabetes (p=0.86 for trend), impaired glucose tolerance (p=0.36 for trend) or gestational diabetes or impaired glucose intolerance (p=0.44).
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFOA 1.1 ng/mL (measured at 20–34 weeks of gestation); 1st tertile 0.1–0.8 ng/mL, 2nd tertile 0.9–1.4 ng/mL, 3rd tertile 1.4–17.0 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education smoking during pregnancy, gravidity, gestational age at blood draw	Inverse association between maternal PFOA and maternal glucose levels (β, 95% CI): 2nd tertile: -0.014 (-0.034–0.006) 3rd tertile: -0.025 (-0.046 to -0.004).
Su et al. 2016 Cross-sectional study of 571 Taiwanese adults, 39 of whom had diabetes.	**Exposure:** Median plasma level of PFOA 8.0 ng/mL • 1st quartile: <5.8 ng/mL • 2nd quartile: 5.8–8.0 ng/mL • 3rd quartile: 8.0–10.5 ng/mL • 4th quartile: >10.5 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, education, smoking status, alcohol use, BMI, hypertension, total cholesterol, regular exercise	Significant inverse association between plasma PFOA levels and risk of diabetes (p<0.01 for trend). ORs (95% CI): • 2nd quartile: 0.39 (0.16–0.96) • 3rd quartile: 0.20 (0.07–0.58) • 4th quartile: 0.16 (0.05–0.50). Significant inverse associations between plasma PFOA and fasting blood glucose levels (p<0.01 for trend), glucose levels in response to an oral glucose tolerance test (p<0.01 for trend), and glycated hemoglobin level (p=0.04 for trend).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Sun et al. 2018 Prospective nested case-control study of participants in the Nurses' Health Study II (n=793 females of self-reported type 2 diabetes validated with supplemental questionnaire on glucose levels, treatment with medication, or diabetic symptoms and 793 female controls)	**Exposure:** Mean serum PFOA 4.96 ng/mL (cases) and 4.57 ng/mL (controls) • 2nd tertile: 3.76–5.48 ng/mL • 3rd tertile: 5.48–112 ng/mL **Statistical adjustments:** Age, ethnicity, time of blood draw, fasting status, state of residence, family history of diabetes, menopausal status and postmenopausal hormone use, oral contraceptive use, breastfeeding duration, number of children delivered after 1993, BMI, alternative health eating index	Association between serum PFOA and type 2 diabetes risk (p=0.03, trend OR (95% CI): • 2nd tertile: 1.27 (0.87–1.86) • 3rd tertile: 1.54 (1.04–2.28).
Wang et al. 2018 Prospective study of 385 pregnant women in China	**Exposure:** Median serum PFOA 7.3 ng/mL (range of 1.2–77.7 ng/mL) (measured in early pregnancy); • 2nd tertile: 5.4–10.1 ng/mL • 3rd tertile: ≥10.1 ng/mL **Statistical adjustments:** Maternal age; diabetes mellitus family history; husband smoking status; family income; child's sex; meat, vegetable, and seafood intake; physical activity, energy intake; prepregnant BMI	No associations between serum PFOA and glycemic parameters measured during early, middle, and late pregnancy: fasting blood glucose (β -0.005, 95% CI -0.018–0.008, p=0.465), fasting insulin (β 0.069, 95% CI -0.005–0.143, p=0.068), HOMA-IR (β 0.074, 95% CI -0.011–0.158, p=0.087), or averaged 1 and 2- hour blood glucose levels in response to oral glucose tolerance test (β 0.014, 95% CI -0.013–0.041, p=0.305). No association between serum PFOA and prevalence of gestation diabetes mellitus (HR 2.11, 95% CI 0.76–5.86, p=0.151) for the 3rd tertile.
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFOA 1.90 ng/mL (range of 0.6–5.0 ng/mL) **Statistical adjustments:** Age	No association between serum PFOA and fasting blood glucose levels (β 0.545, 95% CI -1.8–2.887).
Zhang et al. 2015a Prospective study of 258 women living in Michigan or Texas and participating in the Longitudinal Investigation of Fertility and the Environment Study; women self-reported a physician diagnosis of gestational diabetes	**Exposure:** Geometric mean serum PFOA levels were 3.07 and 3.94 ng/mL in women with or without gestational diabetes **Statistical adjustments:** Age, BMI, parity conditional on gravidity, race/ethnicity, smoking	Significant association between serum PFOA levels and risk of gestational diabetes; OR 1.86 (95% CI 1.14–3.02).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Conway et al. 2016 Cross-sectional study of 6,460 participants in the C8 Health Project with type 1 diabetes (n=820), type 2 diabetes (n=4,291) uncategorized diabetes n=1,349) or no diabetes (n=60,439)	**Exposure:** Mean serum PFOS 21.8 ng/mL in type 1 diabetics, 25.2 ng/mL in type 2 diabetics, 25.1 ng/mL in uncategorized diabetics, and 23.1 ng/mL in the no diabetes group. **Statistical adjustments:** Age, sex	Inverse association between serum PFOS and type 1 diabetes (OR 0.65, 95% CI 0.61–0.70) and type 2 diabetes (OR 0.86, 95% CI 0.82–0.90). No association for uncategorized diabetes (OR 0.93, 95% CI 0.86–1.03).
Cardenas et al. 2017 Cross-sectional study of 957 participants in the Diabetes Prevention Program in the U.S. Participants were at high risk of developing type 2 diabetes (BMI of 24 kg/m^2, fasting glucose of 95–125 mg/dL and glucose of 140–199 mg/dL 2 hours after a 75-g oral glucose load); participants were in the intensive lifestyle intervention or placebo-treated control groups of the study	**Exposure:** Geometric mean serum PFOS 26.38 ng/mL **Statistical adjustments:** Sex, race/ethnicity, BMI, age, marital status, education, smoking history	Doubling PFOS concentration was associated with increases ($p<0.05$) in HOMA-IR, fasting insulin, 30-minute insulin, fasting proinsulin, HOMA-β, fasting glucose, and HbA1c. However, these associations were not found in longitudinal analyses. No association between serum PFOS and risk of developing diabetes (HR 0.87, 95% CI 0.74–1.02, p=0.08).
Domazet et al. 2016 Prospective study of 501 Danish children participating in the European Youth Heart Study; subjects were evaluated at 9, 15, and 21 years of age	**Exposure:** Median serum PFOS in males and females at age 9 years 44.5 and 39.9 ng/mL, respectively, and 22.3 and 20.8 ng/mL at age 15 years **Statistical adjustments:** Sex, age, ethnicity, maternal parity, maternal income	Association between serum PFOS at 9 years of age and glucose (β 0.88, 95% CI 0.07–1.60) at 15 years of age. No associations between serum PFOS at 9 years of age and insulin (β -0.29, 95% CI -4.26–3.67), HOMA-β (β -0.47, 95% CI -3.09–2.23), or HOMA-IR (β -0.29, 95% CI -4.17–3.76) at 15 years of age. No association between serum PFOS at 9 years of age and glucose (β 0.64, 95% CI -0.55–1.84), insulin (β -1.01, 95% CI -8.00–6.62), HOMA-β (β -1.66, 95% CI -5.70–2.67), or HOMA-IR (β -0.83, 95% CI -7.91–6.71) at age 21. No association between serum PFOS at 15 years of age and glucose (β 0.81, 95% CI -1.27–2.72), insulin (β 4.78, 95% CI -6.82–17.77), HOMA-β (β 1.81, 95%

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		CI -4.77–9.09), or HOMA-IR (β 4.74, 95% CI -6.69–17.91) at age 21.
Fisher et al. 2013 Cross-sectional study of 2,700 adult (aged 18–74 years) participants in the Canadian Health Measures Survey (2007–2009)	**Exposure:** Geometric mean serum PFOS 8.40 ng/mL **Linear regression model adjustments:** Age, sex, education, BMI	No significant associations between serum PFOS levels and insulin (p=0.88), glucose (p=0.96), or HOMA-IR (p=0.25).
Fleisch et al. 2017 Prospective study of 665 mother-child pairs participating in the Project Viva in Boston Massachusetts; children were evaluated at 7.7 (median) years of age	**Exposure:** Geometric mean maternal PFOS 24.4 ng/mL (measured at 9.6 weeks of gestation) and childhood serum PFOS 6.2 ng/mL **Statistical adjustments:** Child's age, sex, and race/ethnicity; maternal age, education, parity, and smoking during pregnancy; neighborhood median household income and percentage below poverty level; pregnancy hematodynamics	No associations (per interquartile range increment) between maternal PFOS and child's adiponectin (β 1.1, 95% CI -3.8–6.2) and HOMA-IR (β -0.6, 95% CI -8.2–7.6) levels. Inverse association (per interquartile range increment) between child's PFOS and child's HOMA-IR (β -10.1, 95% CI -16.4 to -3.3) levels. No association (per interquartile range increment) between child's PFOS and child's adiponectin (β -0.5, 95% CI -5.1–4.3) levels.
He et al. 2018 Cross-sectional study of 7,904 adult participants in 2003–2012 NHANES	**Exposure:** Mean serum PFOS in males and females 20.80 and 14.51 ng/mL. Serum PFOS for 2nd, 3rd, and 4th quartiles: <7.305, 7.305–13.1, 13.1–25.5, and >25.5 ng/mL, respectively **Statistical adjustments:** Age, race, BMI, education, energy intake, serum cotinine, alcohol consumption, PIR, time in front of television, video game, and computer	No association between serum PFOS and diabetes prevalence in males (p=0.305 for trend), OR (95% CI): 2nd quartile: 1.32 (0.71–2.45) 3rd quartile: 1.64 (0.92–2.93) 4th quartile: 1.75 (1.00–3.04). No association between serum PFOS and diabetes prevalence in females (p=0.829 for trend), OR (95% CI): 2nd quartile: 1.11 (0.66–1.88) 3rd quartile: 1.06 (0.63–1.78) 4th quartile: 1.41 (0.82–2.41).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Jensen et al. 2018 Prospective study of 158 pregnant women participating in the Odense Child Cohort study in Denmark; oral glucose tolerance tests at gestational week 28	**Exposure:** Maternal median serum PFOS 8.37 ng/mL (measured at gestational week 11) **Statistical adjustments:** Age, parity, educational level, prepregnancy BMI	In women with a high risk of gestational diabetes mellitus, a 2-fold increase in serum PFOS was not associated with changes (β, 95% CI) in fasting glucose (-0.1, -2.3–2.2), fasting insulin (2.7, -8.5–15.2), 2-hour glucose (2.9, -2.8–8.9), HOMA-IR (-2.6, -9.7–16.6), HOMA-β (-2.9, -7.1–14.1), or insulin sensitivity (-1.9, -14.3–12.3) in response to an oral glucose tolerance test performed at gestational week 28.
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFOS 5.68 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFOS and fasting blood glucose (β 0.707, 95% CI -1.921–3.336, p=0.595).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFOS 3.72 ng/mL (WTCHR group) and 2.78 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFOS and HOMA-IR (β -0.06, 95% CI -0.18–0.06, p=0.31).
Lin et al. 2009 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 474 adolescents (12–20 years old) and 969 adult (>20 years of age) participants	**Exposure:** Mean log serum PFOS levels were 3.11 and 3.19 ng/mL in adolescents and adults, respectively **Statistical adjustments:** Age, sex, race, smoking, alcohol intake, household income	Significant correlations (p<0.05) between serum PFOS and insulin levels, HOMA-IR, and β -cell function were found in adults; these associations were not significant (p>0.05) in adolescents. No significant associations (p>0.05) between serum PFOS and fasting glucose were found in adults or adolescents.

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lind et al. 2014 Cross-sectional study of 1,016 men and women participating in the Prospective Investigation of the Vasculature in Uppsala Seniors in Sweden; diabetes was defined as a fasting glucose of >7 mmol/L or use of hypoglycemic medication; 114 participants had diabetes	**Exposure:** Median serum PFOS level was 13.2 ng/mL **Linear regression model adjustments:** Sex, serum cholesterol and triacylglycerol, BMI, smoking, exercise habits, energy and alcohol intakes, and education level; quadratic terms of perfluorinated compounds were included in the models to search for nonlinear effects	No significant relationship between serum PFOS and the prevalence of diabetes; OR 1.43 (95% CI 0.94–22.16; p=0.09). No significant associations between serum PFOS and proinsulin/insulin ratio (p=0.46) or HOMA-IR (p=0.51).
Liu et al. 2018b Cross-sectional study utilizing 2013–2014 NHANES data for 1,871 adults	**Exposure:** Geometric mean serum PFOS 5.28 ng/mL **Statistical adjustments:** Age, sex, ethnicity, smoking status, alcohol intake, household income, waist circumference, medications (anti-hypertensive, anti-hyperglycemic, anti-lipidemic)	Association between serum PFOS and fasting glucose (β -1.96, p<0.05). No associations between serum PFOS and glucose levels 2-hour after glucose tolerance test (β -1.75, p>0.05), HbA1C (β -0.04, p>0.05), insulin levels (β 0.03, p>0.05), HOMA-IR (β 0.01, p>0.05) or β cell function (β 0.06, p<0.05).
Melzer et al. 2010 Cross-sectional study utilizing 1999–2000 and 2003–2006 NHANES data for 3,966 adults (≥20 years of age)	**Exposure:** Mean serum PFOS levels were 29.57 ng/mL (0.3–435.0 ng/mL) in men and 23.24 ng/mL (0.14–406.0 ng/mL) in women. Mean levels in each quartile: • 1st quartile: M 12.29 ng/mL; F 8.13 ng/mL • 2nd quartile: M 21.82 ng/mL; F 15.75 ng/mL • 3rd quartile: M 30.81 ng/mL; F 24.21 ng/mL • 4th quartile: M 57.73 ng/mL; F 50.96 ng/mL **Logistic regression model adjustments:** Age, ethnicity, study year, BMI, smoking status, alcohol consumption	No association between self-reported diabetes and serum PFOS levels were found; the OR (95% CI) for the 4th quartile was 0.87 (0.57–1.31, p=0.491).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 306 adolescents (12–19 years of age and 524 adults (20–80 years of age)	**Exposure:** Serum mean and median PFOS levels were 25.3 and 21.0 ng/mL (range: 1.4–392.0 ng/mL **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	No significant association between serum PFOS and HOMA were found in adults ($p>0.05$), male adolescents ($p=0.18$), or female adolescents ($p=0.22$).
Predieri et al. 2015 Case-control study of 25 Italian children and adolescents with type I diabetes and 19 healthy controls	**Exposure:** Levels of PFOS in blood Non-parametric statistical analysis performed to assess differences in biochemical parameters between children with diabetes and healthy controls	Significantly ($p<0.001$) higher mean PFOS in diabetics (1.53 ng/mL) than in controls (0.56 ng/mL).
Shapiro et al. 2016 Cross-sectional study of 1,274 pregnant women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada	**Exposure:** Geometric mean plasma PFOS levels (measured during the first trimester) were 4.58 ng/mL in participants with normal glucose levels (n=1,167), 4.29 ng/mL in participants with impaired glucose tolerance (n=48), and 4.74 ng/mL in participants with gestational diabetes (n=59) **Logistic regression model adjustments:** Age at delivery, prepregnancy BMI, parity, household income, education, race, smoking status	There were no significant associations between plasma PFOS levels and the risk of gestational diabetes ($p=0.70$ for trend), impaired glucose tolerance ($p=0.74$ for trend), or gestational diabetes or impaired glucose intolerance ($p=0.59$).
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFOS 2.4 ng/mL (measured at 20–34 weeks of gestation) **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education, smoking during pregnancy, gravidity, gestational age at blood draw	No association between maternal PFOS and maternal glucose levels (β -0.009 g, 95% CI -0.020–0.003).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Su et al. 2016 Cross-sectional study of 571 Taiwanese adults, 39 of whom had diabetes.	**Exposure:** Median plasma level of PFOS 3.2 ng/mL • 1st quartile: <2.4 ng/mL • 2nd quartile: 2.44–3.2 ng/mL • 3rd quartile: 3.2–4.8 ng/mL • 4th quartile: >4.8 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, education, smoking status, alcohol use, BMI, hypertension, total cholesterol, regular exercise	Significant association between plasma PFOS levels and risk of diabetes ($p<0.01$) for trend). The risk was significant increased for participants in the 4th quartile; OR 3.37 (95% CI 1.18–9.65). Significant associations between plasma PFOS and fasting blood glucose levels ($p<0.01$ for trend), glucose levels in response to an oral glucose tolerance test ($p<0.01$ for trend), and glycated hemoglobin level ($p=0.04$ for trend). The ORs (95% CI) for participants with plasma PFOS levels in the 4th quartile were 1.05 (1.02–1.09), 1.12 (1.06–1.09), and 1.02 (0.99–1.05), respectively.
Sun et al. 2018 Prospective nested case-control study of participants in the Nurses' Health Study II (n=793 females of self-reported type 2 diabetes validated with supplemental questionnaire on glucose levels, treatment with medication, or diabetic symptoms and 793 female controls)	**Exposure:** Mean serum PFOS 35.7 ng/mL (cases) and 33.1 ng/mL (controls) • 1st tertile: 6.04–26.3 ng/mL • 2nd tertile: 26.3–41.4 ng/mL • 3rd tertile: 41.4–421 ng/mL **Statistical adjustments:** Age, ethnicity, time of blood draw, fasting status, state of residence, family history of diabetes, menopausal status and postmenopausal hormone use, oral contraceptive use, breastfeeding duration, number of children delivered after 1993, BMI, alternative health eating index	Association between serum PFOS and type 2 diabetes risk ($p=0.02$, trend OR (95% CI): • 2nd tertile: 1.63 (1.25–2.12) • 3rd tertile: 1.62 (1.09–2.41).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Wang et al. 2018 Prospective study of 385 pregnant women in China	**Exposure:** Median serum PFOS 5.4 ng/mL (range of 0.8–114.6 ng/mL) (measured in early pregnancy); serum PFOS levels in 3rd tertile ≥7.3 ng/mL **Statistical adjustments:** Maternal age; diabetes mellitus family history; husband smoking status; family income; child's sex; meat, vegetable, and seafood intake; physical activity, energy intake; prepregnant BMI	No associations between serum PFOS and glycemic parameters measured during early, middle, and late pregnancy: fasting blood glucose (β -0.009, 95% CI -0.019–0.002, p=0.108), fasting insulin (β 0.013, 95% CI -0.048–0.074, p=0.672), HOMA-IR (β 0.005, 95% CI -0.064–0.073, p=0.896), or averaged 1- and 2-hour blood glucose levels in response to oral glucose tolerance test (β 0.006, 95% CI -0.015–0.028, p=0.562). No association between serum PFOS and prevalence of gestation diabetes mellitus (HR 2.11, 95% CI 0.76–8.56, p=0.151) for the 3rd tertile.
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFOS 3.00 ng/mL (range of 0.3–14.6 ng/mL) **Statistical adjustments:** Age	No association between serum PFOS and fasting blood glucose levels (β -1.237, 95% CI -2.63–1.59).
Zhang et al. 2015a Prospective study of 258 women living in Michigan or Texas and participating in the Longitudinal Investigation of Fertility and the Environment Study; women self-reported a physician diagnosis of gestational diabetes	**Exposure:** Geometric median serum PFOS levels were 13.10 and 12.04 ng/mL in women with or without gestational diabetes **Statistical adjustments:** Age, BMI, parity conditional on gravidity, race/ethnicity, smoking	No significant association between serum PFOS levels and risk of gestational diabetes; OR 1.13 (95% CI 0.75–1.72).
PFHxS		
Conway et al. 2016 Cross-sectional study of 6,460 participants in the C8 Health Project with type 1 diabetes (n=820), type 2 diabetes (n=4,291), uncategorized diabetes n=1,349), or no diabetes (n=60,439)	**Exposure:** Mean serum PFHxS 3.4 ng/mL in type 1 diabetics, 3.8 ng/mL in type 2 diabetics, 4.2 ng/mL in uncategorized diabetics, and 5.2 ng/mL in the no diabetes group **Statistical adjustments:** Age, sex	Inverse association between serum PFHxS and type 1 diabetes (OR 0.59, 95% CI 0.54–0.64), type 2 diabetes (OR 0.74, 95% CI 0.71–0.77), or uncategorized diabetes (OR 0.84, 95% CI 0.78–0.90).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cardenas et al. 2017 Cross-sectional study of 957 participants in the Diabetes Prevention Program in the United States. Participants were at high risk of developing type 2 diabetes (BMI of 24 kg/m^2, fasting glucose of 95–125 mg/dL and glucose of 140–199 mg/dL 2 hours after a 75-g oral glucose load); participants were in the intensive lifestyle intervention or placebo-treated control groups of the study.	**Exposure:** Geometric mean serum PFHxS 2.41 ng/mL **Statistical adjustments:** Sex, race/ethnicity, BMI, age, marital status, education, smoking history	Doubling PFHxS concentration was associated with increases ($p<0.05$) in HOMA-IR, fasting insulin, 30-minute insulin, fasting proinsulin, HOMA-β, and insulinogenic index. However, these associations were not found in longitudinal analyses. No association between serum PFHxS and risk of developing diabetes (HR 0.98, 95% CI 0.86–1.12, p=0.79).
Fisher et al. 2013 Cross-sectional study of 2,700 adult (aged 18–74 years) participants in the Canadian Health Measures Survey (2007–2009)	**Exposure:** Geometric mean serum PFHxS was 2.18 ng/mL **Linear regression model adjustments:** Age, sex, education, BMI	No significant associations between serum PFHxS levels and insulin (p=0.89), glucose (p=0.98), or HOMA-IR (p=0.20).
Fleisch et al. 2017 Prospective study of 665 mother-child pairs participating in the Project Viva in Boston Massachusetts; children were evaluated at 7.7 (median) years of age	**Exposure:** Geometric mean maternal PFHxS 2.5 ng/mL (measured at 9.6 weeks of gestation) and childhood serum PFHxS 2.2 ng/mL **Statistical adjustments:** Child's age, sex, and race/ethnicity; maternal age, education, parity, and smoking during pregnancy; neighborhood median household income and percentage below poverty level; pregnancy hematodynamics	No associations (per interquartile range increment) between maternal PFHxS and child's adiponectin (β 0.6, 95% CI -2.4–3.6) and HOMA-IR (β -2.07, 95% CI -5.9–2.0) levels. No associations (per interquartile range increment) between child's PFOA and child's adiponectin (β 0.3, 95% CI -1.4–1.9) and HOMA-IR (β -1.7, 95% CI -3.8–0.5) levels.

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
He et al. 2018 Cross-sectional study of 7,904 adult participants in 2003–2012 NHANES	**Exposure:** Mean serum PFHxS in males and females 2.88 and 1.94 ng/mL; serum PFHxS for 1st, 2nd, 3rd, and 4th quartiles: <0.9, 0.9–1.64, 1.64–2.9, and >2.9 ng/mL, respectively **Statistical adjustments:** Age, race, BMI, education, energy intake, serum cotinine, alcohol consumption, PIR, time in front of television, video game, and computer	Association between serum PFHxS and diabetes prevalence in males (p=0.071 for trend), OR (95% CI): 2nd quartile: 1.99 (1.19–3.33) 3rd quartile: 1.87 (1.15–3.05) 4th quartile: 2.31 (1.37–3.91). No association between serum PFHxS and diabetes prevalence in females (p=0.056 for trend), OR (95% CI): 2nd quartile: 0.65 (0.41–1.03) 3rd quartile: 0.87 (0.52–1.43) 4th quartile: 1.22 (0.71–2.11).
Jensen et al. 2018 Prospective study of 158 pregnant women participating in the Odense Child Cohort study in Denmark; oral glucose tolerance tests at gestational week 28	**Exposure:** Maternal median serum PFHxS 0.31 ng/mL (measured at gestational week 11 **Statistical adjustments:** Age, parity, educational level, prepregnancy BMI	In women with a high risk of gestational diabetes mellitus, a 2-fold increase in serum PFHxS was associated with changes (β, 95% CI) in fasting glucose (1.7, 0.2–3.2), fasting insulin (7.7, 0.1–15.9), and HOMA-IR (9.5, 1.0–18.8) in response to an oral glucose tolerance test performed at gestational week 28. No associations with 2-hour glucose (2.9, -0.8–6.8), HOMA-β 2.3, -4.3–9.4), or insulin sensitivity (-7.1, -14.8–1.3).
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFHxS 0.793 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFHxS and fasting blood glucose (β 0.925, 95% CI -1.779–2.164, p=0.500).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFHxS 0.67 ng/mL (WTCHR group) and 0.53 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	Association between serum PFHxS and HOMA-IR (β -0.09, 95% CI -0.18–0.003, p=0.04).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lin et al. 2009 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 474 adolescents (12–20 years old) and 969 adult (>20 years of age) participants	**Exposure:** Mean log serum PFHxS levels were 0.95 and 0.60 ng/mL in adolescents and adults, respectively **Statistical adjustments:** Age, sex, race, smoking, alcohol intake, household income	No significant associations (p>0.05) between serum PFHxS and fasting glucose, insulin, HOMA-IR, or β -cell function were found in adults or adolescents.
Lind et al. 2014 Cross-sectional study of 1,016 men and women participating in the Prospective Investigation of the Vasculature in Uppsala Seniors in Sweden Diabetes was defined as a fasting glucose of >7 mmol/L or use of hypoglycemic medication; 114 participants had diabetes	**Exposure:** Median plasm PFHxS level 2.1 ng/mL **Linear regression model adjustments:** Sex, serum cholesterol and triacylglycerol, BMI, smoking, exercise habits, energy and alcohol intakes, and education level; quadratic terms of perfluorinated compounds were included in the models to search for nonlinear effects	No significant relationship between serum PFHxS and the prevalence of diabetes; OR 1.00 (95% CI 0.74–1.35; p=0.98). No significant associations between serum PFHxS and proinsulin/insulin ratio (p=0.20) or HOMA-IR (p=0.29).
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 306 adolescents (12–19 years of age and 524 adults (20–80 years of age)	**Exposure:** Serum mean and median PFHxS levels were 2.6 and 1.8 ng/mL (range: 0.2–27.1 ng/mL **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	No significant association between serum PFHxS and HOMA were found in adults (p>0.05) or male adolescents (p=0.20). A significant inverse association between PFHxS and HOMA was found in female adolescents (p=0.001).
Shapiro et al. 2016 Cross-sectional study of 1,274 pregnant women participating in the Maternal-Infant Research on Environmental Chemicals Study in Canada.	**Exposure:** Geometric mean plasma PFHxS levels (measured during the first trimester) were 1.02 ng/mL in participants with normal glucose levels (n=1,167), 1.00 ng/mL in participants with impaired glucose tolerance (n=48), and 1.05 ng/mL in participants with gestational diabetes (n=59) **Logistic regression model adjustments:** Age at delivery, prepregnancy BMI, parity, household income, education, race, smoking status	There were no significant associations between plasma PFHxS levels and the risk of gestational diabetes (p=0.73 for trend), impaired glucose tolerance (p=0.44 for trend) or gestational diabetes or impaired glucose intolerance (p=0.47). However, there was a significant association between plasma PFHxS and risk of impaired glucose intolerance for participants with plasma PFHxS levels in the 2nd quartile (0.67–1 ng/mL) (OR 3.5, 95% CI 1.4–8.8), but not in participants with plasma PFHxS levels in the 3rd or 4th quartiles.

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFHxS 0.8 ng/mL (measured at 20–34 weeks of gestation); 1st tertile <LOD–0.5 ng/mL, 2nd tertile 0.6–1.0 ng/mL, 3rd tertile 1.1–10.9 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education smoking during pregnancy, gravidity, gestational age at blood draw	Inverse association between maternal PFHxS and maternal glucose levels (β, 95% CI): 2nd tertile: -0.009 g (-0.029–0.010) 3rd tertile: -0.023 g (-0.044 to -0.002).
Sun et al. 2018 Prospective nested case-control study of participants in the Nurses' Health Study II (n=793 females of self-reported type 2 diabetes validated with supplemental questionnaire on glucose levels, treatment with medication, or diabetic symptoms and 793 female controls)	**Exposure:** Mean serum PFHxS 2.15 ng/mL (cases) and 2.01 ng/mL (controls) **Statistical adjustments:** Age, ethnicity, time of blood draw, fasting status, state of residence, family history of diabetes, menopausal status and postmenopausal hormone use, oral contraceptive use, breastfeeding duration, number of children delivered after 1993, BMI, alternative health eating index	No association between serum PFHxS and type 2 diabetes risk (p=0.24, trend OR (95% CI): • 2nd tertile: 1.15 (0.79–1.67) • 3rd tertile: 1.26 (0.86–1.86).
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFHxS 3.80 ng/mL (range of 0.1–9.8 ng/mL) **Statistical adjustments:** Age	No association between serum PFHxS and fasting blood glucose levels (β -0.29, 95% CI -1.9–1.32).
PFNA		
Conway et al. 2016 Cross-sectional study of 6,460 participants in the C8 Health Project with type 1 diabetes (n=820), type 2 diabetes (n=4,291), uncategorized diabetes n=1,349), or no diabetes (n=60,439)	**Exposure:** Mean serum PFNA 1.4 ng/mL in type 1 diabetics, 1.5 ng/mL in type 2 diabetics, 1.5 ng/mL in uncategorized diabetics, and 1.6 ng/mL in the no diabetes group **Statistical adjustments:** Age, sex	Inverse association between serum PFNA and type 1 diabetes (OR 0.65, 95% CI 0.57–0.74). No associations for type 2 diabetes (OR 0.94, 95% CI 0.88–1.00) or uncategorized diabetes (OR 0.95, 95% CI 0.85–1.06).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Cardenas et al. 2017 Cross-sectional study of 957 participants in the Diabetes Prevention Program in the U.S. Participants were at high risk of developing type 2 diabetes (BMI of 24 kg/m^2, fasting glucose of 95–125 mg/dL and glucose of 140–199 mg/dL 2 hours after a 75-g oral glucose load); participants were in the intensive lifestyle intervention or placebo-treated control groups of the study	**Exposure:** Geometric mean serum PFNA 0.53 ng/mL **Statistical adjustments:** Sex, race/ethnicity, BMI, age, marital status, education, smoking history	Doubling PFNA concentration was associated with increases ($p<0.05$) in fasting proinsulin and fasting glucose. However, these associations were not found in longitudinal analyses. No association between serum PFNA and risk of developing diabetes (HR 0.99, 95% CI 0.87–1.12, p=0.82).
Fleisch et al. 2017 Prospective study of 665 mother-child pairs participating in the Project Viva in Boston Massachusetts; children were evaluated at 7.7 (median) years of age	**Exposure:** Geometric mean maternal PFNA 0.6 ng/mL (measured at 9.6 weeks of gestation) and childhood serum PFNA 1.7 ng/mL **Statistical adjustments:** Child's age, sex, and race/ethnicity; maternal age, education, parity, and smoking during pregnancy; neighborhood median household income and percentage below poverty level; pregnancy hematodynamics	No associations (per interquartile range increment) between maternal PFNA and child's adiponectin (β -5.5, 95% CI -11.3–0.6) and HOMA-IR (β 1.4, 95% CI -8–11.7) levels. No associations (per interquartile range increment) between child's PFHxS and child's adiponectin (β 0.3, 95% CI -1.4–1.9) and HOMA-IR (β -0.6, 95% CI -3.2–2.6) levels.
He et al. 2018 Cross-sectional study of 7,904 adult participants in 2003–2012 NHANES	**Exposure:** Mean serum PFNA in males and females 1.52 and 1.30 ng/mL, respectively. Serum PFNA for 1st, 2nd, 3rd, and 4th quartiles: <0.738, 0.738–1.07, 1.07–1.64, and >1.64 ng/mL, respectively **Statistical adjustments:** Age, race, BMI, education, energy intake, serum cotinine, alcohol consumption, PIR, time in front of television, video game, and computer	No association between serum PFNA and diabetes prevalence in males (p=0.457 for trend), OR (95% CI): 2nd quartile: 1.25 (0.77–2.04) 3rd quartile: 1.17 (0.74–1.87) 4th quartile: 1.19 (0.73–1.95). No association between serum PFNA and diabetes prevalence in females (p=0.250 for trend), OR (95% CI): 2nd quartile: 0.98 (0.63–1.54) 3rd quartile: 1.50 (0.88–2.57) 4th quartile: 1.01 (0.62–1.65).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Jensen et al. 2018 Prospective study of 158 pregnant women participating in the Odense Child Cohort study in Denmark; oral glucose tolerance tests at gestational week 28	**Exposure:** Maternal median serum PFNA 0.65 ng/mL (measured at gestational week 11 **Statistical adjustments:** Age, parity, educational level, prepregnancy BMI	In women with a high risk of gestational diabetes mellitus, a 2-fold increase in serum PFNA was associated with changes (β, 95% CI) in fasting insulin (12.1, 0.7–24.8), HOMA-β (12.4, 2.2–23.7) in response to an oral glucose tolerance test performed at gestational week 28. No associations with fasting glucose (0.03, -2.1–2.2), 2-hour glucose (-1.3, -6.5–4.2), HOMA-IR (12.2, -0.5–26.4), or insulin sensitivity (-5.4, -16.7–7.5).
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFNA 0.938 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFNA and fasting blood glucose (β 0.428, 95% CI -1.785–2.641, p=0.703).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFNA 0.61 ng/mL (WTCHR group) and 0.49 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFNA and HOMA-IR (β 0.01, 95% CI -0.13–0.14, p=0.89).
Lin et al. 2009 Cross-sectional study utilizing 1999–2000 and 2003–2004 NHANES data for 474 adolescents (12–20 years old) and 969 adult (>20 years of age) participants	**Exposure:** Mean log serum PFNA levels were -0.35 and -0.21 ng/mL in adolescents and adults, respectively **Statistical adjustments:** Age, sex, race, smoking, alcohol intake, household income	Significant inverse correlations ($p<0.05$) between serum PFNA and insulin levels and β -cell function were found in adolescents; these associations were not significant ($p>0.05$) in adults. No significant associations ($p>0.05$) between serum fasting glucose or HOMA-IR were found in adults or adolescents.

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Lind et al. 2014 Cross-sectional study of 1,016 men and women participating in the Prospective Investigation of the Vasculature in Uppsala Seniors in Sweden; diabetes was defined as a fasting glucose of >7 mmol/L or use of hypoglycemic medication; 114 participants had diabetes.	**Exposure:** Median serum PFNA level 0.7 ng/mL **Linear regression model adjustments:** Sex, serum cholesterol and triacylglycerol, BMI, smoking, exercise habits, energy and alcohol intakes, and education level; quadratic terms of perfluorinated compounds were included in the models to search for nonlinear effects	No significant relationship between serum PFNA and the prevalence of diabetes; OR 1.30 (95% CI 0.85–1.97; p=0.22). However, inclusion of quadratic terms showed a non-linear positive association with serum PFNA, OR 1.96 (95% CI 1.19–3.22; p=0.008) for the linear term and OR 1.25(95% CI 1.08–1.44; p=0.002) for the quadratic term. No significant associations between serum PFNA and proinsulin/insulin ratio (p=0.15) or HOMA-IR (p=0.90).
Nelson et al. 2010 Cross-sectional study utilizing 2003–2004 NHANES data for 306 adolescents (12–19 years of age and 524 adults (20–80 years of age)	**Exposure:** Serum mean and median PFNA levels were 1.3 and 1.0 ng/mL (range: 0.1–10.3 ng/mL) **Regression model adjustments:** Age, sex, race/ethnicity, BMI (cholesterol analysis only), socioeconomic status, exercise, time in front of television or computer, alcohol consumption, smoking	No significant associations between serum PFNA and HOMA were found in adults (p>0.05), male adolescents (p=0.83), or female adolescents (p=0.20). In females aged 20–59 years, a significant association (p=0.05) was found between PFNA and HOMA; however, no significant associations were found in other male or female subgroups.
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFNA 0.4 ng/mL (measured at 20–34 weeks of gestation); 1st half <LOD–0.4 ng/mL, 2nd half 0.5–6.0 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education smoking during pregnancy, gravidity, gestational age at blood draw	Inverse association between maternal PFNA and maternal glucose levels (β, 95% CI) 2nd half: -0.025 g (-0.042 to -0.009).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Su et al. 2016 Cross-sectional study of 571 Taiwanese adults, 39 of whom had diabetes	**Exposure:** Median plasma levels of PFNA 3.8 ng/mL • 1st quartile: <2.6 ng/mL • 2nd quartile: 2.6–3.8 ng/mL • 3rd quartile: 3.8–5.1 ng/mL • 4th quartile: >5.1 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, education, smoking status, alcohol use, BMI, hypertension, total cholesterol, regular exercise	Significant inverse association between plasma PFNA levels and risk of diabetes (p=0.05 for trend). The association was significant in participants with PFNA levels in the 4th quartile; OR 0.31 (95% CI 0.11–0.88). Significant inverse association between plasma PFNA and glucose levels in response to an oral glucose tolerance test (p<0.01 for trend). No significant associations between serum PFNA and fasting blood glucose (p=0.10 for trend) and glycated hemoglobin level (p=0.11 for trend).
Sun et al. 2018 Prospective nested case-control study of participants in the Nurses' Health Study II (n=793 females of self-reported type 2 diabetes validated with supplemental questionnaire on glucose levels, treatment with medication, or diabetic symptoms and 793 female controls)	**Exposure:** Mean serum PFNA 0.60 ng/mL (cases) and 0.61 ng/mL (controls) **Statistical adjustments:** Age, ethnicity, time of blood draw, fasting status, state of residence, family history of diabetes, menopausal status and postmenopausal hormone use, oral contraceptive use, breastfeeding duration, number of children delivered after 1993, BMI, alternative health eating index	No association between serum PFNA and type 2 diabetes risk (p=0.97, trend OR (95% CI): • 2nd tertile: 1.08 (0.75–1.56) • 3rd tertile: 0.99 (0.67–1.48).
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFNA 0.50 ng/mL (range of 0.1–1.1 ng/mL) **Statistical adjustments:** Age	No association between serum PFNA and fasting blood glucose levels (β -0.627, 95% CI -2.54–1.29).
Zhang et al. 2015a Prospective study of 258 women living in Michigan or Texas and participating in the Longitudinal Investigation of Fertility and the Environment Study; women self-reported a physician diagnosis of gestational diabetes	**Exposure:** Geometric median serum PFNA levels were 1.23 and 1.20 ng/mL in women with or without gestational diabetes **Statistical adjustments:** Age, BMI, parity conditional on gravidity, race/ethnicity, smoking	No significant association between serum PFNA levels and risk of gestational diabetes; OR 1.06 (95% CI 0.70–1.60).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFDA		
Fleisch et al. 2017 Prospective study of 665 mother-child pairs participating in the Project Viva in Boston Massachusetts; children were evaluated at 7.7 (median) years of age	**Exposure:** Geometric mean childhood serum PFDA 0.3 ng/mL **Statistical adjustments:** Child's age, sex, and race/ethnicity; maternal age, education, parity, and smoking during pregnancy; neighborhood median household income and percentage below poverty level; pregnancy hematodynamics	Inverse association (per interquartile range increment) between child's PFDA and child's HOMA-IR (β -14.7, 95% CI -22.1 to -6.5) levels. No associations (per interquartile range increment) between child's PFDA and child's adiponectin (β 5.1, 95% CI -1.7–12.3) levels.
Jensen et al. 2018 Prospective study of 158 pregnant women participating in the Odense Child Cohort study in Denmark; oral glucose tolerance tests at gestational week 28	**Exposure:** Maternal median serum PFDA 0.26 ng/mL (measured at gestational week 11 **Statistical adjustments:** Age, parity, educational level, prepregnancy BMI	In women with a high risk of gestational diabetes mellitus, a 2-fold increase in serum PFDA was not associated with changes (β, 95% CI) in fasting glucose (-1.3, -3.6–1.0), fasting insulin (-0.2, -11.2–12.1), 2-hour glucose (-3.3, -8.7–2.5), HOMA-IR (-1.5, -13.5–12.1), HOMA-β (3.9, -6.4–15.2), or insulin sensitivity (5.6, -7.9–21.1) in response to an oral glucose tolerance test performed at gestational week 28.
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFDA 0.0592 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFDA and fasting blood glucose (β -0.201, 95% CI -1.280–0.878, p=0.713).
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFDA 0.14 ng/mL (WTCHR group) and 0.11 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFDA and HOMA-IR (β -0.04, 95% CI -0.11–0.03, p=0.26).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Starling et al. 2017 Prospective study of 604 mother-infant pairs participating in the Healthy Start cohort study in Colorado	**Exposure:** Median maternal serum PFDA 0.1 ng/mL (measured at 20–34 weeks of gestation); 1st half ≤0.1 ng/mL, 2nd half 0.2–3.5 ng/mL **Statistical adjustments:** Maternal age, prepregnancy BMI, race/ethnicity, education, smoking during pregnancy, gravidity, gestational age at blood draw	Inverse association between maternal PFDA and maternal glucose levels (β, 95% CI) 2nd half: -0.024 g (-0.041 to -0.007).
Sun et al. 2018 Prospective nested case-control study of participants in the Nurses' Health Study II (n=793 females of self-reported type 2 diabetes validated with supplemental questionnaire on glucose levels, treatment with medication, or diabetic symptoms and 793 female controls)	**Exposure:** Mean serum PFDA 0.13 ng/mL (cases) and 0.16 ng/mL (controls) **Statistical adjustments:** Age, ethnicity, time of blood draw, fasting status, state of residence, family history of diabetes, menopausal status and postmenopausal hormone use, oral contraceptive use, breastfeeding duration, number of children delivered after 1993, BMI, alternative health eating index	No association between serum PFDA and type 2 diabetes risk (p=0.09, trend OR (95% CI): • 2nd tertile: 0.91 (0.64–1.32) • 3rd tertile: 0.71 (0.48–1.05).
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFDA 0.40 ng/mL (range of 0.1–1.1 ng/mL) **Statistical adjustments:** Age	Inverse association between serum PFDA and fasting blood glucose levels (β -2.543, 95% CI -4.65 to -0.44).
Zhang et al. 2015a Prospective study of 258 women living in Michigan or Texas and participating in the Longitudinal Investigation of Fertility and the Environment Study; women self-reported a physician diagnosis of gestational diabetes	**Exposure:** Geometric median serum PFDA level 0.41 and 0.40 ng/mL in women with or without gestational diabetes **Statistical adjustments:** Age, BMI, parity conditional on gravidity, race/ethnicity, smoking	No significant association between serum PFDA levels and risk of gestational diabetes; OR 1.04 (95% CI 0.70–1.53).
PFUnA		
Kang et al. 2018 Cross-sectional study of 150 children (ages 3–18 years) in Korea	**Exposure:** Median serum PFUnA 0.652 ng/mL **Statistical adjustments:** Age, sex, BMI, household income, second-hand smoking	No association between serum PFUnA and fasting blood glucose (β 1.350, 95% CI -0.020–2.721, p=0.053).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Koshy et al. 2017 Cross-sectional study of 180 children enrolled in the WTCHR and a matched comparison group of 222 children	**Exposure:** Median serum PFUnA 0.12 ng/mL (WTCHR group) and 0.04 ng/mL (comparison group) **Statistical adjustments:** Sex, race, caloric intake, physical activity, smoke exposure, BMI	No association between serum PFUnA and HOMA-IR (β -0.04, 95% CI -0.10–0.02, p=0.21).
Lind et al. 2014 Cross-sectional study of 1,016 men and women participating in the Prospective Investigation of the Vasculature in Uppsala Seniors in Sweden Diabetes was defined as a fasting glucose of >7 mmol/L or use of hypoglycemic medication; 114 participants had diabetes	**Exposure:** Median serum PFUnA level 0.3 ng/mL **Linear regression model adjustments:** Sex, serum cholesterol and triacylglycerol, BMI, smoking, exercise habits, energy and alcohol intakes, and education level; quadratic terms of perfluorinated compounds were included in the models to search for nonlinear effects	No significant relationship between serum PFUnA and the prevalence of diabetes; OR 0.95 (95% CI 0.59–1.52; p=0.81). No significant associations between serum PFUnA and proinsulin/insulin ratio (p=0.49) or HOMA-IR (p=0.32).
Su et al. 2016 Cross-sectional study of 571 Taiwanese adults, 39 of whom had diabetes	**Exposure:** Median plasma levels of PFUnA 6.4 ng/mL • 1st quartile: <3.6 ng/mL • 2nd quartile: 3.6–6.4 ng/mL • 3rd quartile: 6.4–9.2 ng/mL • 4th quartile: >9.2 ng/mL **Multivariable logistic regression model adjustments:** Age, sex, education, smoking status, alcohol use, BMI, hypertension, total cholesterol, regular exercise	Significant inverse association between plasma PFUnA levels and risk of diabetes (p<0.01 for trend). ORs (95% CI): • 3rd quartile: 0.24 (0.08–0.78) • 4th quartile: 0.23 (0.08–0.64) Significant inverse associations between plasma PFUnA and fasting blood glucose levels (p<0.01 for trend) and glucose levels in response to an oral glucose tolerance test (p<0.01 for trend). No significant association with glycated hemoglobin level (p=0.17 for trend).
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFUnA 0.30 ng/mL (range of 0.1–0.8 ng/mL) **Statistical adjustments:** Age	Inverse association between serum PFUnA and fasting blood glucose levels (β -1.821, 95% CI -3.45 to -0.189).

Table 14. Health Outcomes Related to Diabetes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFHpA		
Lind et al. 2014 Cross-sectional study of 1,016 men and women participating in the Prospective Investigation of the Vasculature in Uppsala Seniors in Sweden; diabetes was defined as a fasting glucose of >7 mmol/L or use of hypoglycemic medication; 114 participants had diabetes	**Exposure:** Median serum PFHpA level 0.05 ng/mL **Linear regression model adjustments:** Sex, serum cholesterol and triacylglycerol, BMI, smoking, exercise habits, energy and alcohol intakes, and education level; quadratic terms of perfluorinated compounds were included in the models to search for nonlinear effects	No significant relationship between serum PFHpA and the prevalence of diabetes; OR 1.02 (95% CI 0.77–1.34; p=0.90). No significant associations between serum PFHpA and proinsulin/insulin ratio (p=0.39) or HOMA-IR (p=0.56).
Yang et al. 2018 Cross-sectional study of 148 men in China (81 diagnosed with metabolic syndrome)	**Exposure:** Median serum PFHpA 0.20 ng/mL (range of 0.1–0.4 ng/mL) **Statistical adjustments:** Age	No association between serum PFHpA and fasting blood glucose levels (β -1.101, 95% CI -5.54–3.34).
FOSA		
Lind et al. 2014 Cross-sectional study of 1,016 men and women participating in the Prospective Investigation of the Vasculature in Uppsala Seniors in Sweden; diabetes was defined as a fasting glucose of >7 mmol/L or use of hypoglycemic medication; 114 participants had diabetes	**Exposure:** Median serum FOSA level 0.11 ng/mL **Linear regression model adjustments:** Sex, serum cholesterol and triacylglycerol, BMI, smoking, exercise habits, energy and alcohol intakes, and education level; quadratic terms of perfluorinated compounds were included in the models to search for nonlinear effects	No significant relationship between serum FOSA and the prevalence of diabetes; OR 1.07 (95% CI 0.75–1.53; p=0.71). No significant associations between serum FOSA and proinsulin/insulin ratio (p=0.094) or HOMA-IR (p=0.070).

APFO = ammonium perfluorooctanoate; BMI = body mass index; CI = confidence interval; F = female(s); FOSA = perfluorooctane sulfonamide; HOMA = homeostatic model assessment; HR = hazard ratio; IR = insulin resistance; M = male(s); NHANES = National Health and Nutrition Examination Survey; OR = odds ratio; PFDA = perfluorodecanoic acid; PFHpA = perfluoroheptanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; PIR = poverty income ratio; RR = relative risk; SMR = standardized mortality ratio; SPR = standardized prevalence ratio; WTCHR = World Trade Center Health Registry

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOA		
Gilliland and Mandel 1993 Retrospective cohort mortality study of 3,537 (79% male) workers (398 deaths) employed at a PFOA production facility for at least 6 months between January 1, 1947 and December 31, 1983	**Exposure:** Workers were considered exposed to PFOA if they were employed for at least 1 month in the Chemical Division of the facility **Reference population:** Minnesota general population	No significant increases in deaths from all cancer types or specific cancer types were found (SMR 0.86, 95% CI 0.72–1.01 for males and SMR 0.75, 95% CI 0.56–0.99 for females). The SMR (95% CI) for prostate cancer was 2.03 (0.55–4.59) among men in the Chemical Division. The length of employment in the Chemical Division was significantly associated with prostate cancer risk; the RR (95% CI) for a 1-year increase in employment time was 1.13 (1.01–1.27). The RR for a 10-year employment in the Chemical Division was 3.3 (1.02–10.6).
Leonard 2006 Retrospective cohort mortality study of 6,027 (80% males) (806 deceased) workers at a fluoropolymers production plant (Washington Works); cohort consisted of all individuals who had ever worked at the plant at any time between January 1, 1948 (plant start-up) and December 31, 2002; these data are also reported in Leonard et al. (2008)	**Exposure:** Based on the results of a cross-sectional study (Sakr et al. 2007b), serum PFOA levels ranged from 5 to 9,550 ng/mL Workers divided into three exposure categories: • No APFO use jobs (serum PFOA levels 250 ng/mL) • APFO-use jobs with median serum level of between <250 and ≤750 ng/mL • APFO jobs with median serum levels of >750 ng/mL Cumulative exposure was calculated for each worker by multiplying time in various jobs categories by an intensity factor (210, 430, or 1,690 ng/mL, respectively). **Reference populations:** Three comparisons groups were used: U.S. general population, West Virginia population, and population of DuPont workers residing in West Virginia and seven	No increases in deaths from all malignant neoplasms, as compared to U.S. (M: SMR 74, 95% CI 64–84; F: SMR 87, 95% CI 45–151), West Virginia (M: SMR 68, 95% CI 60–78; F: SMR 79, 95% CI 41–139), or DuPont worker (M: SMR 100, 95% CI 88–114; F: 149, 95% CI 77–260) populations. No increases in deaths from kidney cancer in males (there were no reported cases of kidney cancer in females) compared to the U.S. (SMR 156, 95% CI 80–272), West Virginia (SMR 155, 95% CI 80–272), or DuPont (SMR 185, 95% CI 95–323) populations. The investigators noted that the small number of kidney cancer deaths (12) did not have sufficient statistical power to fit Cox proportional hazard models for assessing outcome with exposure category and noted that only half of the cases had ever worked in the APFO-use divisions. No increases in deaths from biliary passages and liver cancer (SMR 133, 95% CI 53–274), pancreatic cancer (SMR 100, 95% CI 50–180), bladder or other urinary organ cancer (SMR

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
	neighboring states (excluding workers at Washington Works)	131, 95% CI 53–269), prostate cancer (SMR 65, 95% CI 34–114), or bronchus, trachea, and lung cancers (SMR 81, 95% CI 63–104) when the DuPont worker population was used as a reference. Cancer site-specific analyses were not conducted in females since 0 or 1 cases were found for each site. Lower SMRs were found for these cancers when the United States or West Virginia general populations were used as comparison groups.
Lundin et al. 2009 Cohort mortality study of 3,993 (80% male) workers at a APFO manufacturing facility (Cottage Grove); 807 workers died during the follow-up period; cohort consisted of workers employed for at least 365 days prior to December 31, 1997	**Exposure:** Workers were divided into three exposure classifications: • Definite occupational exposure, workers were exposed on a regular basis with potential high exposure (group 1) • Probable occupational exposure, jobs in other chemical division where APFO exposure was possible, but likely lower or transient (group 2) • No or minimal occupational exposure (group 3) Serum PFOA levels measured in 2000 from 131 current workers ranged from 2,600 to 5,200 ng/mL in definite exposure jobs, 300 to 1,500 ng/mL in the probable exposure jobs; no data were available for the no exposure jobs **Reference population and adjustments:** Mortality rates were compared to rates from Minnesota general population; statistical models were adjusted for sex, year of birth, age at entry into the cohort, smoking status, and wage type; Cox regression analyses were done with an internal referent population	No significant increases in deaths from all cancers; pancreas; trachea, bronchus, and lung; and prostate; the respective SMRs (95% CI) were: • Group 1: 0.9 (0.5–1.4), 0.9 (0.0–4.7), 1.2 (0.5–2.3), 2.1 (0.4–6.1) • Group 2: 0.9 (0.8–1.1), 1.0 (0.4–2.1), 1.0 (0.7–1.4), 0.9 (0.4–1.8) • Group 3: 0.8 (0.6–1.0), 0.7 (0.2–1.6), 0.8 (0.5–1.1), 0.4 (0.1–0.9) In time-dependent Cox regression analysis, there was a significant increase in prostate cancer deaths and among workers with high exposure (defined as definite exposure for ≥6 months), HR 6.6 (95% CI 1.1–37.7), as compared to workers in the low exposure category. Increase in risk was also found in workers with definite exposure for ≥5 years HR 3.7 (95% CI 1.3–10.4), as compared to workers with definite exposure for <1 year.

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Raleigh et al. 2014 Retrospective cohort mortality study of 9,027 workers (84% male) at 2 3M facilities in Minnesota; 4,668 workers at an APFO facility in Cottage Grove (3,993 of these workers were included in the Lundin et al. 2009 cohort) and 4,359 workers at a non-APFO facility in St. Paul; cohort consisted of workers employed for at least 1 year; the Cottage Grove cohort included workers in a non-chemical division without exposure to APFO	**Exposure:** Work history and industrial monitoring were used to estimate PFOA exposure Cumulative exposure in the Cottage Grove workers was divided into quartiles: • 1st quartile: >2.9×10^{-5} µg/m^3 • 2nd quartile: ≤1.5×10^{-4} µg/m^3 • 3rd quartile: ≤7.9×10^{-4} µg/m^3 • 4th quartile: >7.9×10^{-4} µg/m^3 **Reference population:** Mortality rates were compared to rates from Minnesota general population; Cottage Grove cohort was also compared to the St. Paul cohort	As compared to the Minnesota population, significantly lower deaths from all causes (SMR 0.85, 95% CI 0.80–0.90) and all cancers (SMR 0.87, 95% CI 0.78–0.97) were found in the Cottage Grove cohort. No significant alterations in deaths from pancreatic cancer (SMR 0.85, 95% CI 0.50–1.34), prostate cancer (SMR 0.83, 95% CI 0.53–1.23), kidney cancer (SMR 0.53, 95% CI 0.20–1.16), liver cancer (SMR 0.81, 95% CI 0.35–1.59), breast cancer (SMR 0.82, 95% CI 0.41–1.47), or bladder cancer (SMR 0.89, 95% CI 0.38–1.76) were observed in the Cottage Grove cohort. As compared to the St. Paul cohort, no signification alterations in the risk of death from pancreatic cancer (HR 1.23, 95% CI 0.50–3.00) in workers in the combined 3rd or 4th quartile, prostate cancer (HR 1.32, 95% CI 0.61–2.84) for the 4th quartile, kidney cancer (HR 0.39 (95% CI 0.11–1.32) for 3rd and 4th quartiles combined, bladder cancer (HR 1.96, 95% CI 0.63–6.15) in workers in the combined 3rd or 4th quartiles, liver cancer (HR 0.67, 95% CI 0.14–3.27) in workers in the combined 3rd or 4th quartiles, or breast cancer (HR 0.54, 95% CI 0.15–1.94) in workers in the combined 3rd or 4th quartiles. As compared to the St. Paul cohort, no signification alterations in the risk of pancreatic cancer (HR 1.36, 95% CI 0.59–3.11) in workers in the combined 3rd or 4th quartiles, prostate cancer (HR 1.11, 95% CI 0.82–1.49) for 4th quartile, kidney cancer (HR 0.73, 95% CI 0.21–2.48) for 4th quartile, bladder cancer (HR 1.66, 95% CI 0.86–3.18) in workers in the 4th quartile, or breast cancer (HR 1.27, 95% CI 0.70–2.31) in workers in the 4th quartile.

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Steenland et al. 2015 Retrospective study of 3,713 workers (80% male) at the DuPont Washington Works facility employed for at least 1 day between 1948 and 2002 (these workers were also examined in the Steenland et al. 2013 study); 1,881 of the workers also participated in the C8 Health Project	**Exposure:** Serum PFOA levels were estimated based on job history and combined with residential exposure. Residential exposure was estimated based on the amount of PFOA released from the DuPont facility, wind patterns, river flow, groundwater flow, and residential address history. Cumulative exposure was calculated as the sum of yearly exposure estimates from birth to a given year. The mean and median measured serum PFOA levels in 2005–2006 were 325 and 113 ng/mL in the workers also participating in the C8 study. **Statistical adjustments:** Sex, race, education, smoking, BMI, alcohol consumption	Significant inverse association between estimated cumulative serum PFOA and risk of bladder cancer (p=0.04 and 0.06 for trend with no lag or 10-year lag). The RR for workers with estimated cumulative exposure in the 4th quartile was 0.23 (95% CI 0.05–0.93) with no lag. No significant associations between estimated cumulative serum PFOA and risk of colorectal cancer (p=0.91 and 0.86 for trend with no lag or 10-year lag), prostate cancer (p=0.83 and 0.91 for trend with no lag or 10-year lag), or melanoma (p=0.16 and 0.55 for trend with no lag or 10-year lag).
Steenland and Woskie 2012 Retrospective cohort mortality study of 1,084 deceased workers at a fluoropolymers production plant (Washington Works). Cohort consisted of all individuals who had ever worked at the plant at any time between 1948 and 2002; deaths were obtained through 2008; this is an extension of the Leonard (2006) study	**Exposure:** Cumulative exposure was estimated using serum PFOA levels of workers measured between 1979 and 2004 (median of 7,800 ng/mL-years). Exposures over time were estimated for eight job categories. The mean estimated cumulative exposure was 7,800 ng/mL-years (median of 4,300 ng/mL-years) and an estimated average annual serum PFOA concentration of 350 ng/mL (median 230 ng/mL). **Reference population:** Population, of DuPont workers residing in West Virginia and seven neighboring states (excluding workers at Washington Works)	No significant increase in deaths from all cancers or specific (pancreatic, lung, prostate, bladder, and non-Hodgkin's lymphoma); the SMRs for the 4th exposure quartile (highest exposure) were <1.0. A significant increase in kidney cancer deaths (SMR 2.66, 95% CI 1.15–5.24), and mesothelioma deaths (SMR 6.27, 95% CI 2.04–14.63) were significantly increased for workers with the highest exposure (4th quartile). Analyzing with a 10- or 20-year lag increased the SMRs for kidney cancer (2.82, 1.13–5.81 and 3.67, 1.48–7.57 with 10- and 20-year lags).

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Barry et al. 2013 Cohort study of 32,254 adults participating in the C8 Health Project and C8 Health Panel or who ever worked at the DuPont facility (11% of the cohort); cancer incidence data obtained from questionnaires and cancer diagnosis verified through review of medical records or Ohio/West Virginia cancer registry	**Exposure:** Measured (2005–2006) median serum PFOA levels • Community members: 24.2 ng/mL (0.25–4,752 ng/mL) • Workers: 112.7 ng/mL (0.25–22,412 ng/mL) Estimated median annual exposure (based on historical data of amount of PFOA emitted from facility, wind patterns, river flow, groundwater flow, residential history, drinking water source, tap water consumption, workplace water consumption, and PFOA PBPK model) • Community members: 19.4 ng/mL (2.8–9,217 ng/mL) • Workers: 174.4 ng/mL (5.2–3,683 ng/mL) **Regression adjustments:** Smoking, alcohol consumption, sex, education, birth year	Significant increase in risk of testicular cancer with increasing estimated cumulative PFOA concentration; HR 1.34 (95% CI 1.00–1.79, p=0.05) with no lag and 1.28 (95% CI 0.95–1.73, p=0.10) with a 10-year lag. An increased risk of kidney cancer was observed, although the CIs included unity; HR 1.10 (95% CI 0.98–1.24) for continuous exposure and HR 1.58 (95% CI 0.88–2.84, p=0.18 for trend). A decreased risk of breast cancer was observed; HR 0.94 (95% CI 0.89–1.00, p=0.05) with no lag and HR 0.93 (95% CI 0.88–0.99, p=0.03) with 10-year lag. No significant increases (p>0.05) in risk were identified for other cancer types.
Ducatman et al. 2015a, 2015b Cross-sectional study of 25,412 men (≥20 years of age) participating in the C8 Health Study	**Exposure:** Mean serum PFOA level 40.22 ng/mL **Statistical adjustments:** Age, smoking status, alcohol intake, BMI	No significant association (p>0.05) between serum PFOA and PSA levels were observed in men 20–49 or 50–69 years of age.

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Innes et al. 2014 Cross-sectional study of residents in Ohio and West Virginia living near Washington Works facility participating in the C8 Health Study Project; 208 cases of colorectal cancer and 47,359 cancer-free adults; diagnosis of cancer and cancer-type was verified via medical records	**Exposure:** Mean and median serum PFOA levels 86.6 and 27.9 ng/mL (range: <0.5–22,412 ng/mL) • 1st quartile: 0.25–13.4 ng/mL • 2nd quartile: 13.5–27.8 ng/mL • 3rd quartile: 27.9–71.2 ng/mL • 4th quartile: ≥71.3 ng/mL **Logistic regression adjustments:** Age, sex, race/ethnicity, marital status, socioeconomic status, participation in regular exercise program, vegetarian diet, smoking, current alcohol consumption, menopausal status, use of hormone replacement therapy (women), BMI, medical comorbidity	Significant inverse association between serum PFOA levels and risk of colorectal cancer; OR (95% CI): • 2nd quartile: 0.47 (0.31–0.74) • 3rd quartile: 0.49 (0.33–0.74) • 4th quartile: 0.61 (0.42–0.89). The inverse association between serum PFOA and colorectal cancer was stronger in males than females and in lean adults than in obese adults.
MDH 2007 Cross-sectional study of residents of Washington and Dakota Counties, Minnesota living near a PFOA facility; cancer incidence data obtained from the Minnesota Cancer Surveillance System (1988–2002) and compared to expected rates taken from statewide averages	**Exposure:** No exposure information provided Data were analyzed on a county basis and zip code/city basis for eight communities within these counties: Washington county (Oakdale, Lake Elmo, Cottage Grove, Newport, St. Paul Park, Woodbury), Dakota county (Hastings, South St. Paul)	The ratio of actual to expected cancers were significantly different from 1.00 ($p<0.05$) for the following cancer types: Less than 1.00: • All cancers in males in Washington and Dakota counties and Woodbury • All cancers in females in Hastings • lung and bronchus cancer in males in Washington and Dakota counties and Woodbury • larynx cancer in males in Dakota county • breast cancer in females in Hastings • Hodgkin lymphoma in females in Washington county • total leukemias in females in Washington county. Greater than 1.00: • all cancers (ratio of 1.08) in males in South St. Paul • liver cancer in females in Dakota county (ratio 1.47) and St. Paul Park (ratio of 5.77)

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
		• breast cancer (ratio of 1.05) in females in Dakota county • lung and bronchus cancer in females in Oakdale (ratio of 1.33) and South St. Paul (ratio of 1.33) and males in South St. Paul (ratio of 1.29) • oral cancers (ratio of 2.20) in males in Lake Elmo • kidney cancer (ratio of 1.64) in males in Cottage Grove.
Vieira et al. 2013 Case-control study of 25,107 residents in Ohio and West Virginia living near Washington Works facility; controls comprised all other cancers in the study data set except kidney, pancreatic, testicular, and liver cancers	**Exposure:** Residents were grouped by water district; estimated median PFOA concentrations in the water in 1995 were 125, 65.8, 23.9, 18.7, 10.7, and 5.3 µg/L in the Little Hocking, Lubeck, Tupper Plains, Belpre, Pomeroy, and Mason water districts, respectively. Serum PFOA levels were estimated based on residential history, facility releases, fate and transport characteristics of PFOA, hydrogeology properties, and PBPK models. **Regression model adjustments:** Age, sex, diagnosis year, smoking status, insurance provider	Significant increases in testicular cancer were found in the Little Hocking area residents (OR 5.1, 95% CI 1.6–15.6), kidney cancer in the Tupper Plains residents (OR 2.0, 95% CI 1.3–3.1), and lung cancer in the Mason residents (OR 1.3, 95% CI 1.1–1.5). When analyzed by estimated serum PFOA levels, significant increases in kidney cancer were found in residents with high serum PFOA levels (30.8–109 ng/mL); OR 2.0 (95% CI 1.3–3.2); in the very high PFOA group (110–655 ng/mL), the 95% CI included the null value (OR 2.0, 95% CI 1.0–3.9). Elevated risks of testes, prostate, and breast (females only) cancers were also observed, although the confidence limits included unity; the ORs (95% CI) were 2.8 (0.8–9.2), 1.5 (0.9–2.5), and 1.4 (0.9–2.3), respectively, in the very high exposure group.
Bonefeld-Jorgensen et al. 2011 Case-control study of 31 breast cancer cases among Inuit women in Greenland and 115 matched controls	**Exposure:** Median serum PFOA levels in the cases and controls: 2.5 and 1.6 ng/mL **Logistic regression adjustments:** Age, BMI, total number of full-term pregnancies, breastfeeding, menopausal status, serum cotinine	Serum PFOA levels were significantly higher in the cases (p=0.04). No significant association between serum PFOA levels and the risk of breast cancer was found; OR 1.20 (95% CI 0.77–1.88, p=0.43).

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Bonefeld-Jorgensen et al. 2014 Case-control study of 250 breast cancer cases and 233 matched controls among women participating in the Danish National Birth Cohort study	**Exposure:** Mean serum PFOA level 5.2 ng/mL **Statistical adjustments:** Age, BMI before pregnancy, gravidity, oral contraceptive use, menarche age, smoking during pregnancy, alcohol intake, education, physical activity	No significant association between serum PFOA and risk of breast cancer (RR 1.00, 95% CI 0.90–1.11).
Eriksen et al. 2009 Prospective cohort study of 1,240 Danish men and women with prostate (n=713), bladder (n=332), pancreatic (n=128), or liver (n=67) cancer; comparison group was 772 men and women without cancer	**Exposure:** Median serum PFOA levels were 6.8 and 6.0 ng/mL in male and female cancer patients and 6.9 and 5.4 ng/mL in males and females in the comparison group **Statistical adjustments:** Education (prostate, pancreas, liver), BMI (prostate), dietary fat intake (prostate, pancreas), fruit and vegetable intake (prostate, pancreas), smoking status (bladder, pancreas, liver), occupation (bladder, liver), alcohol consumption (liver)	No significant associations between serum PFOA levels and prostate, bladder, pancreas, or liver cancer; the IRR (95% CI) for serum PFOA levels in the 4th quartile: • Prostate: 1.18 (0.84–1.65) • Bladder: 0.81 (0.53–1.24) • Pancreas: 1.55 (0.85–2.80) • Liver: 0.60 (0.26–1.37).
Hardell et al. 2014 Case-control study of 201 cases of prostate cancer and 186 controls living in Sweden	**Exposure:** Mean and median serum PFOA levels were 2.3 and 2.0 ng/mL in cases and 2.0 and 1.9 ng/mL in controls **Logistic regression adjustments:** Age, BMI, year of sampling	No significant association between serum PFOA and risk of prostate cancer; OR 1.1 (95% CI 0.7–1.7). Among subjects with a heredity risk (first degree relative with prostate cancer) and with a serum PFOA level above the median, there was a significant increase in the risk of prostate cancer; OR 2.6 (95% CI 1.2–6.0).
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFOA 2.08 ng/mL (range of 0.20–9.52 ng/mL) in cases and 1.48 ng/mL (range 0.20–6.29 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFOA and risk of breast cancer, OR (95% CI): Continuous 1.26 (1.01–1.58, p=0.039) 2nd tertile: 1.86 (0.80–4.31, p=0.149) 3rd tertile: 2.64 (1.17–5.97, p=0.019).

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFOS		
Alexander et al. 2003 Retrospective cohort mortality study of 2,083 workers (145 deaths) employed for at least 1 year by December 31, 1997 at a PFOS manufacturing facility in Decatur, Alabama	**Exposure:** Workers were assigned to an exposure category based on job history; geometric serum PFOS levels were assigned to each category based on monitoring data conducted in 1998 on 186 workers • Group 1: no direct workplace exposure • Group 2: low potential workplace exposure • Group 3: high potential workplace exposure **Reference population:** Alabama general population	The all cancer deaths were fewer than expected (SMRs<1) for the whole and for the specific exposure groups (SMR 0.84, 95% CI 0.50–1.32 for Group 3). Increase in risk of bladder and other urinary organ cancer; the SMR (95% CI) were 4.81 (0.99–14.06) for the whole cohort, 12.77 (2.63–37.35) for group 3, and 16.12 (3.32–47.14) for workers with at least 1 year of high potential exposure. The SMRs were calculated based on three cases of bladder cancer.
Alexander and Olsen 2007 This is a follow-up of Alexander et al. 2003 Retrospective cohort study of current and former workers (n=1,895) and deceased workers (n=188) at a PFOS manufacturing facility who had worked for at least 1 year prior to 1998	**Exposure:** Workers were assigned to an exposure category based on job history; geometric serum PFOS levels were assigned to each category based on monitoring data conducted in 1998 on 186 workers • Group 1: no direct workplace exposure • Group 2: low potential workplace exposure • Group 3: high potential workplace exposure **Reference population:** Alabama general population	Eleven cases of bladder cancer were identified; two were self-reported and confirmed with medical records. Four other self-reported bladder cancers were not confirmed and were included in the analyses. For the whole cohort, no significant increase in bladder cancer was found (SIR 1.28, 95% CI 0.64–2.29). Categorizing the cohort by exposure category or duration of cumulative exposure did not result in significant associations. The SIRs (95% CI) in the high exposure group and ≥10-year exposure group were 1.74 (0.64–3.79) and 1.43 (0.16–5.15), respectively. Using the cohort as an internal referent population, no increases in the risk of bladder cancer were observed in workers with 1–<5 years (RR 0.83, 95% CI 0.15–4.65), 5–<10 years (RR 1.92, 95% CI 0.30–12.06), or ≥10 years (RR 1.52, 95% CI 0.21–10.99) cumulative exposure, as compared to workers with 0–<1-year cumulative exposure.

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Grice et al. 2007 A cohort study of 1,400 (81% males) current, retired, or former workers employed for at least 1 year at a PFOS-based fluorochemical manufacturing facility in Decatur, Alabama	**Exposure:** Workers were assigned to an exposure category based on job history; geometric serum PFOS levels were assigned to each category based on monitoring data conducted in 1998 on 186 workers • Group 1: no direct workplace exposure (serum PFOS 110 ng/mL) • Group 2: low potential workplace exposure (serum PFOS 390–890 ng/mL) • Group 3: high potential workplace exposure (serum PFOS 1,300–1,970 ng/mL) **Logistic regression model adjustments:** Group 1 was used as a comparison group, ORs were adjusted for age and sex	Health conditions were self-reported. No significant associations between exposure to PFOS and colon cancer, melanoma, or prostate cancer were found. The ORs (95% CI) in the ever exposed group (groups 2 and 3) and the high exposure group (group 3) were: Colon cancer • Groups 2 and 3: 1.21 (0.51–2.87) • Group 3: 1.69 (0.68–4.17) Melanoma • Groups 2 and 3: 1.08 (0.31–3.72) • Group 3: 1.01 (0.25–4.11) Prostate cancer • Groups 2 and 3: 1.34 (0.62–2.91) • Group 3:1.08 (0.44–2.69).
Olsen et al. 2004a Cross-sectional study examining episodes of care among current or retired workers employed for at least 1 year between 1993–1998 at a PFOS-based fluorochemical manufacturing facility in Decatur, Alabama	**Exposure:** Workers working at the chemical plant (n=652) were considered exposed to PFOS; these workers were divided into low and high potential subgroups. Workers at the film plant (n=659) were not considered exposed to PFOS and served as the comparison group. **Statistical analysis:** Ratio of two indirect standardization methods was used to calculate RRE_pC, which was adjusted for age and sex	An increased RRE_pC was calculated for malignant melanoma of the skin (12, 95% CI 1.0–>100) and malignant neoplasm of the colon in which the CI included unity (5.4, 95% CI 0.5–>100). Among long-term workers (>10 years) with high potential for exposure, the RRE_pC was 10 (95% CI 0.7–>100) for malignant melanoma of the skin and 12 (95% CI 0.8–>100) for malignant colon neoplasms.
Ducatman et al. 2015a, 2015b Cross-sectional study of 25,412 men (≥20 years of age) participating in the C8 Health Study	**Exposure:** Mean serum PFOS level 22.18 ng/mL **Statistical adjustments:** Age, smoking status, alcohol intake, BMI	No significant association (p>0.05) between serum PFOS and PSA levels were observed in men 20–49 years of age or 50–69 years of age.

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Innes et al. 2014 Case-control study of residents in Ohio and West Virginia living near Washington Works facility participating in the C8 Health Study Project; 208 cases of colorectal cancer and 47,359 cancer-free adults; diagnosis of cancer and cancer-type was verified via medical records	**Exposure:** Mean and median serum PFOS levels 23.4 and 20.2 ng/mL (range: <0.5–759.2 ng/mL) • 1st quartile: 0.25–13.5 ng/mL • 2nd quartile: 13.6–20.1 ng/mL • 3rd quartile: 20.2–29.1 ng/mL • 4th quartile: ≥29.2 ng/mL **Logistic regression adjustments:** Age, sex, race/ethnicity, marital status, socioeconomic status, participation in regular exercise program, vegetarian diet, smoking, current alcohol consumption, menopausal status, use of hormone replacement therapy (women), BMI, medical comorbidity, current treatment for hypertension or hyperlipidemia	Significant inverse association between serum PFOS levels and risk of colorectal cancer; OR (95% CI): • 2nd quartile: 0.35 (0.24–0.53) • 3rd quartile: 0.30 (0.20–0.45) • 4th quartile: 0.23 (0.15–0.34).
Bonefeld-Jorgensen et al. 2011 Case-control study of 31 breast cancer cases among Inuit women in Greenland and 115 matched controls	**Exposure:** Median serum PFOS levels in the cases and controls: 45.6 and 21.9 ng/mL **Logistic regression adjustments:** Age, BMI, total number of full-term pregnancies, breastfeeding, menopausal status, serum cotinine	Serum PFOS levels were significantly higher in the cases ($p<0.0001$). Significant association between serum PFOS levels and the risk of breast cancer; OR 1.03 (95% CI 1.001–1.07, $p=0.05$).
Bonefeld-Jorgensen et al. 2014 Case-control study of 250 breast cancer cases and 233 matched controls among women participating in the Danish National Birth Cohort study	**Exposure:** Mean serum PFOS level 30.6 ng/mL **Statistical adjustments:** Age, BMI before pregnancy, gravidity, oral contraceptive use, menarche age, smoking during pregnancy, alcohol intake, education, physical activity	No significant association between serum PFOS and risk of breast cancer (RR 0.99, 95% CI 0.98–1.01).

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Eriksen et al. 2009 Prospective cohort study of 1,240 Danish men and women with prostate (n=713), bladder (n=332), pancreatic (n=128), or liver (n=67) cancer; comparison group was 772 men and women without cancer	**Exposure:** Median serum PFOS levels 35.1 and 32.1 ng/mL in male and female cancer patients and 35.0 and 29.3 ng/mL in males and females in the comparison group **Statistical adjustments:** Education (prostate, pancreas, liver), BMI (prostate), dietary fat intake (prostate, pancreas), fruit and vegetable intake (prostate, pancreas), smoking status (bladder, pancreas, liver), occupation (bladder, liver), alcohol consumption (liver)	No significant associations between serum PFOS levels and prostate, bladder, pancreas, or liver cancer; IRR (95% CI) for serum PFOA levels in the 4th quartile: • Prostate: 1.05 (0.97–1.14) • Bladder: 0.93 (0.83–1.03) • Pancreas: 0.99 (0.86–1.14) • Liver: 0.59 (0.27–1.27).
Hardell et al. 2014 Case-control study of 201 cases of prostate cancer and 186 controls living in Sweden	**Exposure:** Mean and median serum PFOS levels were 11 and 9.0 ng/mL in cases and 10 and 8.3 ng/mL in controls **Logistic regression adjustments:** Age, BMI, year of sampling	No significant association between serum PFOS and risk of prostate cancer; OR 1.0 (95% CI 0.6–1.5). Among subjects with a heredity risk (first degree relative with prostate cancer) and with a serum PFOS level above the median, there was a significant increase in the risk of prostate cancer; OR 2.7 (95% CI 1.04–6.8).
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFOS 35.50 ng/mL (range of 4.23–187.00 ng/mL) in cases and 18.2 ng/mL (range 1.70–133.00 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFOS and risk of breast cancer, OR (95% CI): Continuous 1.02 (1.01–1.03, p=0.005) 2nd tertile: 3.13 (1.20–8.15, p=0.020) 3rd tertile: 5.50 (2.19–13.54, p<0.001).
PFHxS		
Ducatman et al. 2015a, 2015b Cross-sectional study of 25,412 men (≥20 years of age) participating in the C8 Health Study	**Exposure:** Mean serum PFHxS level 3.58 ng/mL **Statistical adjustments:** Age, smoking status, alcohol intake, BMI	No significant association (p>0.05) between serum PFHxS and PSA levels were observed in men 20–49 or 50–69 years of age.

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Bonefeld-Jorgensen et al. 2014 Case-control study of 250 breast cancer cases and 233 matched controls among women participating in the Danish National Birth Cohort study.	**Exposure:** Mean serum PFHxS level 1.2 ng/mL **Statistical adjustments:** Age, BMI before pregnancy, gravidity, oral contraceptive use, menarche age, smoking during pregnancy, alcohol intake, education, physical activity	Significant inverse association between serum PFHxS levels and risk of breast cancer (RR 0.66, 95% CI 0.47–0.94). When stratified by age, the significant inverse associations were only found in women ≤40 years of age.
Hardell et al. 2014 Case-control study of 201 cases of prostate cancer and 186 controls living in Sweden	**Exposure:** Mean and median serum PFHxS levels were 1.1 and 0.909 ng/mL in cases and 0.940 and 0.865 ng/mL in controls **Logistic regression adjustments**: Age, BMI, year of sampling	No significant association between serum PFHxS and risk of prostate cancer; OR 1.3 (95% CI 0.8–1.9). Among subjects with a heredity risk (first-degree relative with prostate cancer) and with a serum PFHxS level above the median, there was a significant increase in the risk of prostate cancer; OR 4.4 (95% CI 1.7–12).
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFHxS 2.52 ng/mL (range of 0.19–23.40 ng/mL) in cases and 1.14 ng/mL (range 0.16–13.90 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFHxS and risk of breast cancer, OR (95% CI): Continuous 1.16 (1.02–1.32, p=0.029) 2nd tertile: 3.13 (0.48–2.66, p=0.788) 3rd tertile: 2.69 (1.23–5.88, p=0.013).
PFNA		
Ducatman et al. 2015a, 2015b Cross-sectional study of 25,412 men (≥20 years of age) participating in the C8 Health Study	**Exposure:** Mean serum PFNA level 1.47 ng/mL **Statistical adjustments:** Age, smoking status, alcohol intake, BMI	No significant association (p>0.05) between serum PFNA and PSA levels were observed in men 20–49 or 50–69 years of age.
Bonefeld-Jorgensen et al. 2014 Case-control study of 250 breast cancer cases and 233 matched controls among women participating in the Danish National Birth Cohort study	**Exposure:** Mean serum PFNA level 0.5 ng/mL **Statistical adjustments:** Age, BMI before pregnancy, gravidity, oral contraceptive use, menarche age, smoking during pregnancy, alcohol intake, education, physical activity	No significant association between serum PFNA and risk of breast cancer (RR 0.76, 95% CI 0.30–1.94).

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
Hardell et al. 2014 Case-control study of 201 cases of prostate cancer and 186 controls living in Sweden	**Exposure:** Mean and median serum PFNA levels were 0.679 and 0.612 ng/mL in cases and 0.631 and 0.572 ng/mL in controls **Logistic regression adjustments:** Age, BMI, year of sampling	No significant association between serum PFNA and risk of prostate cancer; OR 1.2 (95% CI 0.8–1.8) Among subjects with a heredity risk (first degree relative with prostate cancer) and with a serum PFNA level above the median, there was no significant increase in the risk of prostate cancer; OR 2.1 (95% CI 0.9–4.8).
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFNA 3.28 ng/mL (range of 0.30–38.60 ng/mL) in cases and 1.83 ng/mL (range 0.25–12.50 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFNA and risk of breast cancer, OR (95% CI): Continuous 1.07 (0.98–1.17, p=0.116) 2nd tertile: 2.43 (1.07–5.51, p=0.034) 3rd tertile: 2.07 (0.90–4.76, p=0.056).
PFDA		
Hardell et al. 2014 Case-control study of 201 cases of prostate cancer and 186 controls living in Sweden	**Exposure:** Mean and median serum PFDA levels were 0.338 and 0.301 ng/mL in cases and 0.291 and 0.269 ng/mL in controls **Logistic regression adjustments:** Age, BMI, year of sampling	No significant association between serum PFDA and risk of prostate cancer; OR 1.4 (95% CI 0.9–2.1). Among subjects with a heredity risk (first degree relative with prostate cancer) and with a serum PFDA level above the median, there was a significant increase in the risk of prostate cancer; OR 2.6 (95% CI 1.1–6.1).
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFDA 1.30 ng/mL (range of 0.20–11.10 ng/mL) in cases and 1.01 ng/mL (range 0.05–6.41 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFDA and risk of breast cancer, OR (95% CI): Continuous 1.17 (0.97–1.40, p=0.094) 2nd tertile: 2.14 (0.94–4.91, p=0.072) 3rd tertile: 2.36 (1.04–5.36, p=0.041).

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
PFUnA		
Hardell et al. 2014 Case-control study of 201 cases of prostate cancer and 186 controls living in Sweden	**Exposure:** Mean and median serum PFUnA levels were 0.308 and 0.264 ng/mL in cases and 0.285 and 0.254 ng/mL in controls **Logistic regression adjustments:** Age, BMI, year of sampling	No significant association between serum PFUnA and risk of prostate cancer; OR 1.2 (95% CI 0.8–1.9). Among subjects with a heredity risk (first-degree relative with prostate cancer) and with a serum PFUnA level above the median, there was a significant increase in the risk of prostate cancer; OR 2.6 (95% CI 1.1–5.9).
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFUnA 2.23 ng/mL (range of 0.20–24.90 ng/mL) in cases and 2.02 ng/mL (range 0.03–20.0 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFUnA and risk of breast cancer, OR (95% CI): Continuous 1.06 (0.97–1.15, p=0.207) 2nd tertile: 2.13 (0.95–4.81, p=0.068) 3rd tertile: 2.00 (0.88–4.53, p=0.019).
PFHpA		
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFHpA 0.11 ng/mL (range of 0.03–1.55 ng/mL) in cases and 0.08 ng/mL (range 0.03–0.59 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFHpA and risk of breast cancer, OR (95% CI): Continuous 6.98 (0.61–80.0, p=0.119) 2nd tertile: 1.13 (0.40–3.20, p=0.816) 3rd tertile: 1.52 (0.54–4.24, p=0.425).
PFDoDA		
Wielsøe et al. 2017 Case-control study of Inuit women from Greenland (77 cases and 84 controls)	**Exposure:** Median serum PFDoDA 0.40 ng/mL (range of 0.21–5.71 ng/mL) in cases and 0.21 ng/mL (range 0.15–6.49 ng/mL) in controls **Statistical adjustments:** Age, BMI, cotinine levels, parity, breastfeeding	Association between serum PFDoDA and risk of breast cancer, OR (95% CI): Continuous 1.03 (1.01–1.06, p=0.447) 2nd tertile: 1.67 (0.72–3.84, p=0.232) 3rd tertile: 0.93 (0.45–1.91, p=0.839).

Table 15. Cancer Outcomes in Humans Exposed to Perfluoroalkyls

Reference and study population	Exposure	Outcomes
FOSA		
Bonefeld-Jorgensen et al. 2014 Case-control study of 250 breast cancer cases and 233 matched controls among women participating in the Danish National Birth Cohort study	**Exposure:** Mean serum FOSA level 3.5 ng/mL **Statistical adjustments:** Age, BMI before pregnancy, gravidity, oral contraceptive use, menarche age, smoking during pregnancy, alcohol intake, education, physical activity	Significant association between serum FOSA levels and risk of breast cancer among women with serum FOSA levels of >5.75 ng/mL (RR 1.89, 95% CI 1.01–3.54). When stratified by age, the association was only significant in women ≤40 years of age.

APFO = ammonium perfluorooctanoate; BMI = body mass index; CI = confidence interval; FOSA = perfluorooctane sulfonamide; HR = hazard ratio; IRR = incidence rate ratio; NR = not reported; OR = odds ratio; PBPK = physiologically based pharmacokinetic; PFDA = perfluorodecanoic acid; PFDoDA = perfluorododecanoic acid; PFHpA = perfluoroheptanoic acid; PFHxS = perfluorohexane sulfonic acid; PFNA = perfluorononanoic acid; PFOA = perfluorooctanoic acid; PFOS = perfluorooctane sulfonic acid; PFUnA = perfluoroundecanoic acid; PIR = poverty-income ratio; PSA = prostate-specific antigen; RR = relative risk; RRE_pC = risk ratio episodes of care; SIR = standardized incidence ratio; SMR = standardized mortality ratio

REFERENCES

Alexander BH, Olsen GW. 2007. Bladder cancer in perfluorooctanesulfonyl fluoride manufacturing workers. Ann Epidemiol 17(6):471-478.

Alexander BH, Olsen GW, Burris JM, et al. 2003. Mortality of employees of a perfluorooctanesulphonyl fluoride manufacturing facility. Occup Environ Med 60:722-729.

Alkhalawi E, Kasper-Sonnenberg M, Wilhelm M, et al. 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(22-23):1041-1049. http://doi.org/10.1080/15287394.2016.1219552.

Andersen CS, Fei C, Gamborg M, et al. 2010. Prenatal exposures to perfluorinated chemicals and anthropometric measures in infancy. Am J Epidemiol 172(11):1230-1237.

Andersen CS, Fei C, Gamborg M, et al. 2013. Prenatal exposures to perfluorinated chemicals and anthropometry at 7 years of age. Am J Epidemiol 178(6):921-927.

Anderson-Mahoney P, Kotlerman J, Takhar H, et al. 2008. Self-reported health effects among community residents exposed to perfluorooctanoate. New Solut 18(2):129-143.

Apelberg FJ, Witter FR, Herbstman JB, et al. 2007b. Cord serum concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in relation to weight and size at birth. Environ Health Perspect 115:1670-1676.

Ashley-Martin J, Dodds L, Arbuckle TE, et al. 2016. Maternal and neonatal levels of perfluoroalkyl substances in relation to gestational weight gain. Int J Environ Res Public Health 13(1):146. 10.3390/ijerph13010146.

Ashley-Martin J, Dodds L, Arbuckle TE, et al. 2017. Maternal concentrations of perfluoroalkyl substances and fetal markers of metabolic function and birth weight. Am J Epidemiol 185(3):185-193. http://doi.org/10.1093/aje/kww213.

Ashley-Martin J, Dodds L, Levy AR. 2015. Prenatal exposure to phthalates, bisphenol A and perfluoroalkyl substances and cord blood levels of IgE, TSLP and IL-33. Environ Res 140:360-368.

Bach CC, Bech BH, Nohr EA, et al. 2016. Perfluoroalkyl acids in maternal serum and indices of fetal growth: The Aarhus Birth Cohort. Environ Health Perspect 10.1289/ehp.1510046.

Bach CC, Bech BH, Nohr EA, et al. 2015a. Serum perfluoroalkyl acids and time to pregnancy in nulliparous women. Environ Res 142:535-541. 10.1016/j.envres.2015.08.007.

Bach CC, Liew Z, Bech BH, et al. 2015c. Perfluoroalkyl acids and time to pregnancy revisited: An update from the Danish National Birth Cohort. Environ Health 14:59. 10.1186/s12940-015-0040-9.

Bach CC, Liew Z, Bech BH, et al. 2015d. Additional file to perfluoroalkyl acids and time to pregnancy revisited: An update from the Danish National Birth Cohort [Environ Health 14:59]. Environ Health 10.1186/s12940-015-0040-9.

Bae J, Kim S, Schisterman EF, et al. 2015. Maternal and paternal serum concentrations of perfluoroalkyl and polyfluoroalkyl substances and the secondary sex ratio. Chemosphere 133:31-40. 10.1016/j.chemosphere.2015.03.015.

Bao WW, Qian ZM, Geiger SD, et al. 2017. Gender-specific associations between serum isomers of perfluoroalkyl substances and blood pressure among Chinese: Isomers of C8 Health Project in China. Sci Total Environ 607-608:1304-1312. http://doi.org/10.1016/j.scitotenv.2017.07.124.

Barrett ES, Chen C, Thurston SW, et al. 2015. Perfluoroalkyl substances and ovarian hormone concentrations in naturally cycling women. Fertil Steril 103(5):1261-1270 e1263. 10.1016/j.fertnstert.2015.02.001.

Barry V, Darrow LA, Klein M, et al. 2014. Early life perfluorooctanoic acid (PFOA) exposure and overweight and obesity risk in adulthood in a community with elevated exposure. Environ Res 132:62-69.

Barry V, Winquist A, Steenland K. 2013. Perfluorooctanoic acid (PFOA) exposures and incident cancers among adults living near a chemical plant. Environ Health Perspect 121(11-12):1313-1318.

REFERENCES

Berg V, Nost TH, Hansen S, et al. 2015. Assessing the relationship between perfluoroalkyl substances, thyroid hormones and binding proteins in pregnant women; a longitudinal mixed effects approach. Environ Int 77:63-69. 10.1016/j.envint.2015.01.007.

Berg V, Nost TH, Pettersen RD, et al. 2017. Persistent organic pollutants and the association with maternal and infant thyroid homeostasis: A multipollutant assessment. Environ Health Perspect 125(1):127-133. http://doi.org/10.1289/ehp152.

Bloom MS, Kannan K, Spliethoff HM, et al. 2010. Exploratory assessment of perfluorinated compounds and human thyroid function. Physiol Behav 99(2):240-245.

Bonefeld-Jorgensen EC, Long M, Bossi R, et al. 2011. Perfluorinated compounds are related to breast cancer risk in Greenlandic Inuit: A case control study. Environ Health 10:88. 10.1186/1476-069X-10-88.

Bonefeld-Jorgensen EC, Long M, Fredslund SO, et al. 2014. Breast cancer risk after exposure to perfluorinated compounds in Danish women: A case-control study nested in the Danish National Birth Cohort. Cancer Causes Control 25(11):1439-1448. 10.1007/s10552-014-0446-7.

Braun JM, Chen A, Romano ME, et al. 2016a. Prenatal perfluoroalkyl substance exposure and child adiposity at 8 years of age: The HOME study. Obesity (Silver Spring, Md.) 24(1):231-237. 10.1002/oby.21258.

Braun JM, Chen A, Romano ME, et al. 2016b. Supplemental material for: Prenatal perfluoroalkyl substance exposure and child adiposity at 8 years of age: The HOME study. [Obesity 24(1):231-237]. Obesity (Silver Spring, Md.) 24(1):231-237. http://onlinelibrary.wiley.com/store/10.1002/oby.21258/asset/supinfo/oby21258-sup-0001-suppinfo01.docx?v=1&s=cac722d8275d428f198a62d78041881f25813e38.

Braun JM, Kalkbrenner AE, Just AC, et al. 2014. Gestational exposure to endocrine-disrupting chemicals and reciprocal social, repetitive, and stereotypic behaviors in 4- and 5-year-old children: The HOME study. Environ Health Perspect 122(5):513-520. 10.1289/ehp.1307261.

Buck Louis GM, Chen Z, Schisterman EF, et al. 2015. Perfluorochemicals and human semen quality: The LIFE study. Environ Health Perspect 123(1):57-63. 10.1289/ehp.1307621.

Buck Louis GM, Peterson CM, Chen Z, et al. 2012. Perfluorochemicals and endometriosis. The ENDO study. Epidemiology 23(6):799-805.

Buck Louis GM, Sapra KJ, Barr DB, et al. 2016. Preconception perfluoroalkyl and polyfluoroalkyl substances and incident pregnancy loss, LIFE Study. Reprod Toxicol 65:11-17. http://doi.org/10.1016/j.reprotox.2016.06.011.

Buck Louis GM, Sundaram R, Schisterman EF, et al. 2013. Persistent environmental pollutants and couple fecundity: The LIFE Study. Environ Health Perspect 121:231-236.

Buser MC, Scinicariello F. 2016. Perfluoroalkyl substances and food allergies in adolescents. Environ Int 88:74-79. 10.1016/j.envint.2015.12.020.

Callan AC, Rotander A, Thompson K, et al. 2016. Maternal exposure to perfluoroalkyl acids measured in whole blood and birth outcomes in offspring. Sci Total Environ 569-570:1107-1113. http://doi.org/10.1016/j.scitotenv.2016.06.177.

Campbell S, Raza M, Pollack AZ. 2016. Perfluoroalkyl substances and endometriosis in US women in NHANES 2003-2006. Reprod Toxicol 65:230-235. http://doi.org/10.1016/j.reprotox.2016.08.009.

Cao W, Liu X, Liu X, et al. 2018. Perfluoroalkyl substances in umbilical cord serum and gestational and postnatal growth in a Chinese birth cohort. Environ Int 116:197-205. http://doi.org/10/1016/j.envint.2018.04.015.

Cardenas A, Gold DR, Hauser R, et al. 2017. Plasma concentrations of per- and polyfluoroalkyl substances at baseline and associations with glycemic indicators and diabetes incidence among high-risk adults in the diabetes prevention program trial. Environ Health Perspect 125(10):107001. http://doi.org/10.1289/ehp1612.

Chan E, Burstyn I, Cherry N, et al. 2011. Perfluorinated acids and hypothyroxinemia in pregnant women. Environ Res 111(4):559-564.

REFERENCES

Château-Degat ML, Pereg D, Dallaire R, et al. 2010. Effects of perfluorooctanesulfonate exposure on plasma lipid levels in the Inuit population of Nunavik (Northern Quebec). Environ Res 110(7):710-717.

Chen MH, Ha EH, Liao HF, et al. 2013. Perfluorinated compound levels in cord blood and neurodevelopment at 2 years of age. Epidemiology 24(6):800-808. 10.1097/EDE.0b013e3182a6dd46.

Chen MH, Ha EH, Wen TW, et al. 2012a. Perfluorinated compounds in umbilical cord blood and adverse birth outcomes. PLoS ONE 7(8):e42474.

Christensen KY, Maisonet M, Rubin C, et al. 2011. Exposure to polyfluoroalkyl chemicals during pregnancy is not associated with offspring age at menarche in a contemporary British cohort. Environ Int 37(1):129-135.

Conway B, Innes KE, Long D. 2016. Perfluoroalkyl substances and beta cell deficient diabetes. J Diabetes Complications 30(6):993-998. http://doi.org/10.1016/j.jdiacomp.2016.05.001.

Costa G. 2004. Report on the meeting held on Friday 20th and Saturday 21st 2004 at the Inn at Montchanin Village (Wilmington, USA) with 3M and DuPont delegations. DuPont. Submitted to the U.S. Environmental Protection Agency. AR226-1866.

Costa G, Sartori S, Consonni D. 2009. Thirty years of medical surveillance in perfluooctanoic acid production workers. J Occup Environ Med 51(3):364-372.

Crawford NM, Fenton SE, Strynar M, et al. 2017. Effects of perfluorinated chemicals on thyroid function, markers of ovarian reserve, and natural fertility. Reprod Toxicol 69:53-59. http://doi.org/10.1016/j.reprotox.2017.01.006.

Dallaire R, Ayotte P, Pereg D, et al. 2009. Determinants of plasma concentrations of perfluorooctanesulfonate and brominated organic compounds in Nunavik Inuit adults (Canada). Environ Sci Technol 43(13):5130-5136.

Dalsager L, Christensen N, Husby S, et al. 2016. Association between prenatal exposure to perfluorinated compounds and symptoms of infections at age 1-4 years among 359 children in the Odense Child Cohort. Environ Int 96:58-64.

Darrow LA, Groth AC, Winquist A, et al. 2016. Modeled perfluorooctanoic acid (PFOA) exposure and liver function in a mid-Ohio Valley community. Environ Health Perspect [Advance publication]. 10.1289/ehp.1510391.

Darrow LA, Howards PP, Winquist A, et al. 2014. PFOA and PFOS serum levels and miscarriage risk. Epidemiology 25(4):505-512. 10.1097/ede.0000000000000103.

Darrow LA, Stein CR, Steenland K. 2013. Serum perfluorooctanoic acid and perfluorooctane sulfonate concentrations in relation to birth outcomes in the Mid-Ohio Valley, 2005-2010. Environ Health Perspect 121(10):1207-1213.

de Cock M, de Boer MR, Lamoree M, et al. 2014. First year growth in relation to prenatal exposure to endocrine disruptors - a Dutch prospective cohort study. Int J Environ Res Public Health 11(7):7001-7021. 10.3390/ijerph110707001.

Dhingra R, Darrow LA, Klein M, et al. 2016a. Perfluorooctanoic acid exposure and natural menopause: A longitudinal study in a community cohort. Environ Res 146:323-330. 10.1016/j.envres.2015.12.037.

Dhingra R, Lally C, Darrow LA, et al. 2016b. Perfluorooctanoic acid and chronic kidney disease: Longitudinal analysis of a Mid-Ohio Valley community. Environ Res 145:85-92. 10.1016/j.envres.2015.11.018.

Domazet SL, Grontved A, Timmermann AG, et al. 2016. Longitudinal associations of exposure to perfluoroalkylated substances in childhood and adolescence and indicators of adiposity and glucose metabolism 6 and 12 years later: The European youth heart study. Diabetes Care 39(10):1745-1751. http://doi.org/10.2337/dc16-0269.

Donauer S, Chen A, Xu Y, et al. 2015. Prenatal exposure to polybrominated diphenyl ethers and polyfluoroalkyl chemicals and infant neurobehavior. J Pediatr 166(3):736-742. 10.1016/j.jpeds.2014.11.021.

REFERENCES

Dong GH, Tung KY, Tsai CH, et al. 2013. Serum polyfluoroalkyl concentrations, asthma outcomes, and immunological markers in a case-control study of Taiwanese children. Environ Health Perspect 121(4):507-513.

Ducatman AM, Zhang J, Fan H. 2015a. Letter to the editor. (Prostate-specific antigen and perfluoroalkyl acids in the C8 health study population. J Occup Environ Med 57(1):111-114). J Occup Environ Med 57(6):e61. 10.1097/jom.0000000000000470.

Ducatman A, Zhang J, Fan H. 2015b. Prostate-specific antigen and perfluoroalkyl acids in the C8 health study population. J Occup Environ Med 57(1):111-114. 10.1097/jom.0000000000000319.

Dufour P, Pirard C, Seghaye MC, et al. 2018. Association between organohalogenated pollutants in cord blood and thyroid function in newborns and mothers from Belgian population. Environ Pollut 238:389-396. http://doi.org/10.1016/j.envpol.2018.03.058.

Emmett EA, Zhang H, Shofer FS, et al. 2006b. Community exposure to perfluorooctanoate: Relationships between serum levels and certain health parameters. J Occup Environ Med 48(8):771-779.

Eriksen KT, Raaschou-Nielsen O, McLaughlin JK, et al. 2013. Association between plasma PFOA and PFOS levels and total cholesterol in a middle-aged Danish population. PLoS ONE 8(2):e56969.

Eriksen KT, Sorensen M, McLaughlin JK, et al. 2009. Perfluorooctanoate and perfluorooctanesulfonate plasma levels and risk of cancer in the general Danish population. J Natl Cancer Inst 101(8):605-609.

Fei C, Olsen J. 2011. Prenatal exposure to perfluorinated chemicals and behavioral or coordination problems at age 7 years. Environ Health Perspect 119(4):573-578.

Fei C, McLaughlin JK, Lipworth L, et al. 2009. Maternal levels of perfluorinated chemicals and subfecundity. Hum Reprod 24(5):1200-1205.

Fei C, McLaughlin JK, Lipworth L, et al. 2008b. Prenatal exposure to perfluorooctanoate (PFOA) and perfluorooctanesulfonate (PFOS) and maternally reported developmental milestones in infancy. Environ Health Perspect 116(10):1391-1395.

Fei C, McLaughlin JK, Tarone RE, et al. 2007. Perfluorinated chemicals and fetal growth: A study within the Danish National Birth Cohort. Environ Health Perspect 115:1677-1682.

Fei C, McLaughlin JK, Tarone RE, et al. 2008a. Fetal growth indicators and perfluorinated chemicals: A study in the Danish National Birth Cohort. Am J Epidemiol 168(1):66-72.

Fei C, McLaughlin JK, Lipworth L, et al. 2010. Prenatal exposure to PFOA and PFOS and risk of hospitalization for infectious diseases in early childhood. Environ Res 110(8):773-777. 10.1016/j.envres.2010.08.004.

Fei C, Weinberg CR, Olsen J. 2012. Commentary: Perfluorinated chemicals and time to pregnancy: A link based on reverse causation? Epidemiology 23(2):264-266.

Fisher M, Arbuckle TE, Wade M, et al. 2013. Do perfluoroalkyl substances affect metabolic function and plasma lipids? Analysis of the 2007-2009, Canadian Health Measures Survey (CHMS) Cycle 1. Environ Res 121:95-103.

Fitz-Simon N, Fletcher T, Luster MI, et al. 2013. Reductions in serum lipids with a 4-year decline in serum perfluorooctanoic acid and perfluorooctanesulfonic acid. Epidemiology 24(4):569-576.

Fleisch AF, Rifas-Shiman SL, Mora AM, et al. 2017. Early-life exposure to perfluoroalkyl substances and childhood metabolic function. Environ Health Perspect 125(3):481-487. http://doi.org/10.1289/ehp303.

Forns J, Iszatt N, White RA, et al. 2015. Perfluoroalkyl substances measured in breast milk and child neuropsychological development in a Norwegian birth cohort study. Environ Int 83:176-182.

Frisbee SJ, Shankar A, Knox SS, et al. 2010. Perfluorooctanoic acid, perfluorooctanesulfonate, and serum lipids in children and adolescents: Results from the C8 Health Project. Arch Pediatr Adolesc Med 164(9):860-869.

Fu Y, Wang T, Fu Q, et al. 2014a. Associations between serum concentrations of perfluoroalkyl acids and serum lipid levels in a Chinese population. Ecotoxicol Environ Saf 106:246-252. 10.1016/j.ecoenv.2014.04.039.

REFERENCES

Gallo V, Leonardi G, Brayne C, et al. 2013. Serum perfluoroalkyl acids concentrations and memory impairment in a large cross-sectional study. BMJ Open 3(6):e002414.

Gallo V, Leonardi G, Genser B, et al. 2012. Serum perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) concentrations and liver function biomarkers in a population with elevated PFOA exposure. Environ Health Perspect 120(5):655-660.

Geiger SD, Xiao J, Shankar A. 2014a. No association between perfluoroalkyl chemicals and hypertension in children. Integrated blood pressure control 7:1-7. 10.2147/ibpc.s47660.

Geiger SD, Xiao J, Ducatman A, et al. 2014b. The association between PFOA, PFOS and serum lipid levels in adolescents. Chemosphere 98:78-83. 10.1016/j.chemosphere.2013.10.005.

Geiger SD, Xiao J, Shankar A. 2013. Positive association between perfluoroalkyl chemicals and hyperuricemia in children. Am J Epidemiol 177(11):1255-1262.

Gilliland FD. 1992. Fluorocarbons and human health: Studies in an occupational cohort: A thesis. University of Minnesota, 29-229.

Gilliland FD, Mandel JS. 1993. Mortality among employees of a perfluorooctanoic acid production plant. J Occup Med 35(9):950-954.

Gilliland FD, Mandel JS. 1996. Serum perfluorooctanoic acid and hepatic enzymes, lipoproteins, and cholesterol: A study of occupationally exposed men. Am J Ind Med 29(5):560-568.

Gleason JA, Post GB, Fagliano JA. 2015. Associations of perfluorinated chemical serum concentrations and biomarkers of liver function and uric acid in the US population (NHANES), 2007-2010. Environ Res 136:8-14. 10.1016/j.envres.2014.10.004.

Goudarzi H, Araki A, Itoh S, et al. 2017b. The association of prenatal exposure to perfluorinated chemicals with glucocorticoid and androgenic hormones in cord blood samples: The Hokkaido Study. Environ Health Perspect 125(1):111-118. http://doi.org/10.1289/ehp142.

Goudarzi H, Miyashita C, Okada E, et al. 2016a. Effects of prenatal exposure to perfluoroalkyl acids on prevalence of allergic diseases among 4-year-old children. Environ Int 94:124-132. http://doi.org/10.1016/j.envint.2016.05.020.

Goudarzi H, Nakajima S, Ikeno T, et al. 2016b. Prenatal exposure to perfluorinated chemicals and neurodevelopment in early infancy: The Hokkaido Study. Sci Total Environ 541:1002-1010. 10.1016/j.scitotenv.2015.10.017.

Govarts E, Remy S, Bruckers L, et al. 2016. Combined effects of prenatal exposures to environmental chemicals on birth weight. Int J Environ Res Public Health 13(5) 10.3390/ijerph13050495.

Govarts E, Iszatt N, Trnovec T, et al. 2018. Prenatal exposure to endocrine disrupting chemicals and risk of being born small for gestational age: Pooled analysis of seven European birth cohorts. Environ Int 115:267-278. http://doi.org/10/1016/jenvint.2018.03.017.

Grandjean P, Andersen EW, Budtz-Jorgensen E, et al. 2012. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. J Am Med Assoc 307(4):391-397.

Grandjean P, Heilmann C, Weihe P, et al. 2017. Serum vaccine antibody concentrations in adolescents exposed to perfluorinated compounds. Environ Health Perspect. 10.1289/EHP275.

Granum B, Haug LS, Namork E, et al. 2013. Pre-natal exposure to perfluoroalkyl substances may be associated with altered vaccine antibody levels and immune-related health outcomes in early childhood. J Immunotoxicol 10(4):373-379.

Grice MM, Alexander BH, Hoffbeck R, et al. 2007. Self-reported medical conditions in perfluorooctanesulfonyl fluoride manufacturing workers. J Occup Environ Med 49(7):722-729.

Gump BB, Wu Q, Dumas AK, et al. 2011. Perfluorochemical (PFC) exposure in children: Associations with impaired response inhibition. Environ Sci Technol 45(19):8151-8159.

Halldorsson TI, Rytter D, Haug LS, et al. 2012. Prenatal exposure to perfluorooctanoate and risk of overweight at 20 years of age: A prospective cohort study. Environ Health Perspect 120(5):668-673.

Hamm MP, Cherry NM, Chan E, et al. 2010. Maternal exposure to perfluorinated acids and fetal growth. J Expo Sci Environ Epidemiol 20(7):589-597.

REFERENCES

Hardell E, Karrman A, van Bavel B, et al. 2014. Case-control study on perfluorinated alkyl acids (PFAAs) and the risk of prostate cancer. Environ Int 63:35-39.

Hartman TJ, Calafat AM, Holmes AK, et al. 2017. Prenatal exposure to perfluoroalkyl substances and body fatness in girls. Childhood obesity (Print) 13(3):222-230. http://doi.org/10.1089/chi.2016.0126.

He X, Liu Y, Xu B, et al. 2018. PFOA is associated with diabetes and metabolic alteration in US men: National Health and Nutrition Examination Survey 2003-2012. Sci Total Environ 625:566-574. http://doi.org/10.1016/jscutitebv,2917.12.186.

Hoffman K, Webster TF, Weisskopf MG, et al. 2010. Exposure to polyfluoroalkyl chemicals and attention deficit/hyperactivity disorder in U.S. children 12-15 years of age. Environ Health Perspect 118(12):1762-1767.

Høyer BB, Ramlau-Hansen CH, Obel C, et al. 2015a. Pregnancy serum concentrations of perfluorinated alkyl substances and offspring behaviour and motor development at age 5-9 years--a prospective study. Environ Health 14:2. 10.1186/1476-069x-14-2.

Høyer BB, Ramlau-Hansen CH, Vrijheid M, et al. 2015b. Anthropometry in 5- to 9-Year-Old Greenlandic and Ukrainian Children in Relation to Prenatal Exposure to Perfluorinated Alkyl Substances. Environ Health Perspect 123(8):841-846. 10.1289/ehp.1408881.

Huang M, Jiao J, Zhuang P, et al. 2018. Serum polyfluoroalkyl chemicals are associated with risk of cardiovascular diseases in national US population. Environ Int 119:37-46. http://doi.org/10.1016/j.envint.2018.05.051.

Humblet O, Dias-Ramirez LG, Balmes JR, et al. 2014. Perfluoroalkyl chemicals and asthma among children 12-19 years of age: NHANES (1999-2008). Environ Health Perspect 122(10):1129-1133.

Impinen A, Nygaard UC, Lodrup Carlsen KC, et al. 2018. Prenatal exposure to perfluoralkyl substances (PFASs) associated with respiratory tract infections but not allergy- and asthma-related health outcomes in childhood. Environ Res 160:518-523. http://doi.org/10.1016/j.envres.2017.10.012.

Innes KE, Ducatman AM, Luster MI, et al. 2011. Association of osteoarthritis with serum levels of the environmental contaminants perfluorooctanoate and perfluorooctane sulfonate in a large Appalachian population. Am J Epidemiol 174(4):440-450.

Innes KE, Wimsatt JH, Frisbee S, et al. 2014. Inverse association of colorectal cancer prevalence to serum levels of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) in a large Appalachian population. BMC Cancer[electronic resource]. http://www.bilomedcentral.com/1471/14/45. December 10, 2011.

Inoue K, Okada F, Ito R, et al. 2004. Perfluorooctane sulfonate (PFOS) and related perfluorinated compounds in human maternal and cord blood samples: Assessment of PFOS exposure in a susceptible population during pregnancy. Environ Health Perspect 112:1204-1207.

Itoh S, Araki A, Mitsui T, et al. 2016. Association of perfluoroalkyl substances exposure *in utero* with reproductive hormone levels in cord blood in the Hokkaido Study on Environment and Children's Health. Environ Int 94:51-59. 10.1016/j.envint.2016.05.011.

Jain RB. 2013. Association between thyroid profile and perfluoroalkyl acids: Data from NHANES 2007-2008. Environ Res 126:51-59. 10.1016/j.envres.2013.08.006.

Jeddy Z, Hartman TJ, Taylor EV, et al. 2017. Prenatal concentrations of perfluoroalkyl substances and early communication development in British girls. Early Hum Dev 109:15-20. http://doi.org/10.1016/j.earlhumdev.2017.04.004.

Jensen TK, Andersen LB, Kyhl HB, et al. 2015. Association between perfluorinated compound exposure and miscarriage in Danish pregnant women. PLoS ONE 10(4):e0123496. 10.1371/journal.pone.0123496.

Jensen RC, Glintborg D, Gade Timmermann CA, et al. 2018. Perfluoroalkyl substances and glycemic status in pregnant Danish women: The Odense Child Cohort. Environ Int 116:101-107. http://doi.org/10.1016/j.envint.2018.04.010.

REFERENCES

Ji K, Kim S, Kho Y, et al. 2012. Serum concentrations of major perfluorinated compounds among the general population in Korea: Dietary sources and potential impact on thyroid hormones. Environ Int 45:78-85.

Joensen UN, Bossi R, Leffers H, et al. 2009. Do perfluoroalkyl compounds impair human semen quality? Environ Health Perspect 117(6):923-927.

Joensen UN, Veyrand B, Antignac JP, et al. 2013. PFOS (perfluorooctanesulfonate) in serum is negatively associated with testosterone levels, but not with semen quality, in healthy men. Hum Reprod 28(3):599-608.

Jørgensen KT, Specht IO, Lenters V, et al. 2014a. Perfluoroalkyl substances and time to pregnancy in couples from Greenland, Poland and Ukraine. Environ Health 13:116. 10.1186/1476-069x-13-116.

Jørgensen KT, Specht IO, Lenters V, et al. 2014b. Supplemental files to "Perfluoroalkyl substances and time to pregnancy in couples from Greenland, Poland and Ukraine" [Environ Health 13:116. 10.1186/1476-069x-13-116]. Environ Health 10.1186/1476-069x-13-116.

Kang H, Lee H, Moon HB, et al. 2018. Perfluoroalkyl acids in serum of Korean children: Occurrences, related sources, and associated health outcomes. Sci Total Environ 645:958-965. http://doi.org/10.1016/j.scitotenv.2018.07.177.

Karlsen M, Grandjean P, Weihe P, et al. 2017. Early-life exposures to persistent organic pollutants in relation to overweight in preschool children. Reprod Toxicol 68:145-153. http://doi.org/10.1016/j.reprotox.2016.08.002.

Karnes C, Winquist A, Steenland K. 2014. Incidence of type II diabetes in a cohort with substantial exposure to perfluorooctanoic acid. Environ Res 128:78-83. 10.1016/j.envres.2013.11.003.

Kataria A, Trachtman H, Malaga-Dieguez L, et al. 2015. Association between perfluoroalkyl acids and kidney function in a cross-sectional study of adolescents. Environ Health 14:89. 10.1186/s12940-015-0077-9.

Khalil N, Chen A, Lee M, et al. 2016. Association of perfluoroalkyl substances, bone mineral density, and osteoporosis in the U.S. Population in NHANES 2009-2010. Environ Health Perspect 124(1):81-87. 10.1289/ehp.1307909.

Khalil N, Ebert JR, Honda M, et al. 2018. Perfluoroalkyl substances, bone density, and cardio-metabolic risk factors in obese 8-12 year old children: A pilot study. Environ Res 160:314-321. http://doi.org/10.1016/j.envres.2017.10.014.

Kielsen K, Shamin Z, Ryder LP, et al. 2016. Antibody response to booster vaccination with tetanus and diphtheria in adults exposed to perfluorinated alkylates. J Immunotoxicol 13(2):270-273.

Kim DH, Kim UJ, Kim HY, et al. 2016a. Perfluoroalkyl substances in serum from South Korean infants with congenital hypothyroidism and healthy infants - Its relationship with thyroid hormones. Environ Res 147:399-404. 10.1016/j.envres.2016.02.037.

Kim SK, Lee KT, Kang CS, et al. 2011. Distribution of perfluorochemicals between sera and milk from the same mothers and implications for prenatal and postnatal exposures. Environ Pollut 159(1):169-174.

Kishi R, Nakajima T, Goudarzi H, et al. 2015. The association of prenatal exposure to perfluorinated chemicals with maternal essential and long-chain polyunsaturated fatty acids during pregnancy and the birth weight of their offspring: The Hokkaido Study. Environ Health Perspect 123(10):1038-1045. 10.1289/ehp.1408834.

Knox SS, Jackson T, Frisbee SJ, et al. 2011a. Perfluorocarbon exposure, gender and thyroid function in the C8 Health Project. J Toxicol Sci 36(4):403-410.

Knox SS, Jackson T, Javins B, et al. 2011b. Implications of early menopause in women exposed to perfluorocarbons. J Clin Endocrinol Metab 96(6):1747-1753. I 10.1210/jc.2010-2401.

Kobayashi S, Azumi K, Goudarzi H, et al. 2017. Effects of prenatal perfluoroalkyl acid exposure on cord blood IGF2/H19 methylation and ponderal index: The Hokkaido Study. J Expo Sci Environ Epidemiol 27(3):251-259. http://doi.org/10.1038/jes.2016.50.

REFERENCES

Koshy TT, Attina TM, Ghassabian A, et al. 2017. Serum perfluoroalkyl substances and cardiometabolic consequences in adolescents exposed to the World Trade Center disaster and a matched comparison group. Environ Int 109:128-135. http://doi.org/10.1016/j.envint.2017.08.003.

Kristensen SL, Ramlau-Hansen CH, Ernst E, et al. 2013. Long-term effects of prenatal exposure to perfluoroalkyl substances on female reproduction. Hum Reprod 28(12):3337-3348. 10.1093/humrep/det382.

Kvist L, Giwercman YL, Jonsson BA, et al. 2012. Serum levels of perfluorinated compounds and sperm Y:X chromosome ratio in two European populations and in Inuit from Greenland. Reprod Toxicol 34(4):644-650.

Lauritzen HB, Larose TL, Oien T, et al. 2017. Maternal serum levels of perfluoroalkyl substances and organochlorines and indices of fetal growth: A Scandinavian case-cohort study. Pediatr Res 81(1-1):33-42. http://doi.org/10.1038/pr.2016.187.

Lee ES, Han S, Oh JE. 2016. Association between perfluorinated compound concentrations in cord serum and birth weight using multiple regression models. Reprod Toxicol 59:53-59. 10.1016/j.reprotox.2015.10.020.

Lee YJ, Kim M-K, Bae J, et al. 2013. Concentrations of perfluoroalkyl compounds in maternal and umbilical cord sera and birth outcomes in Korea. Chemosphere 90(5):1603-1609.

Lenters V, Portengen L, Rignell-Hydbom A, et al. 2016a. Prenatal phthalate, perfluoroalkyl acid, and organochlorine exposures and term birth weight in three birth cohorts: Multi-pollutant models based on elastic net regression. Environ Health Perspect 124(3):365-372. 10.1289/ehp.1408933.

Lenters V, Portengen L, Rignell-Hydbom A, et al. 2016b. Supplemental material to prenatal phthalate, perfluoroalkyl acid, and organochlorine exposures and term birth weight in three birth cohorts: Multi-pollutant models based on elastic net regression. [Environ Health Perspect 124(3):365-372]. 10.1289/ehp.1408933.

Leonard RC. 2006. Ammonium perfluorooctanoate: Phase II. Retrospective cohort mortality analyses related to a serum biomarker of exposure in a polymer production plant. Wilmington, DE: E.I. du pont de Nemours and Company.

Leonard RC, Kreckmann KH, Sakr CJ, et al. 2008. Retrospective cohort mortality study of workers in a polymer production plant including a reference population of regional workers. Ann Epidemiol 18:15-22.

Lewis RC, Johns LE, Meeker JD. 2015. Serum biomarkers of exposure to perfluoroalkyl substances in relation to serum testosterone and measures of thyroid function among adults and adolescents from NHANES 2011-2012. Int J Environ Res Public Health 12(6):6098-6114.

Li M, Zeng XW, Qian ZM, et al. 2017. Isomers of perfluorooctanesulfonate (PFOS) in cord serum and birth outcomes in China: Guangzhou Birth Cohort Study. Environ Int 102:1-8. http://doi.org/10.1016/j.envint.2017.03.006.

Lien GW, Huang CC, Shiu JS, et al. 2016. Perfluoroalkyl substances in cord blood and attention deficit/hyperactivity disorder symptoms in seven-year-old children. Chemosphere 156:118-127. 10.1016/j.chemosphere.2016.04.102.

Liew Z, Ritz B, Bonefeld-Jorgensen EC, et al. 2014. Prenatal exposure to perfluoroalkyl substances and the risk of congenital cerebral palsy in children. Am J Epidemiol 180(6):574-581. 10.1093/aje/kwu179.

Liew Z, Ritz B, von Ehrenstein OS, et al. 2015. Attention deficit/hyperactivity disorder and childhood autism in association with prenatal exposure to perfluoroalkyl substances: A nested case-control study in the Danish National Birth Cohort. Environ Health Perspect 123(4):367-373. 10.1289/ehp.1408412.

Lin CY, Chen PC, Lin YC, et al. 2009. Association among serum perfluoroalkyl chemicals, glucose homeostasis, and metabolic syndrome in adolescents and adults. Diabetes Care 32(4):702-707.

Lin CY, Lin LY, Chiang CK, et al. 2010. Investigation of the associations between low-dose serum perfluorinated chemicals and liver enzymes in US adults. Am J Gastroenterol 105(6):1354-1363.

REFERENCES

Lin CY, Lin LY, Wen TW, et al. 2013a. Association between levels of serum perfluorooctane sulfate and carotid artery intima-media thickness in adolescents and young adults. Int J Cardiol 168(4):3309-3316. 10.1016/j.ijcard.2013.04.042.

Lin CY, Lin LY, Wen TW, et al. 2013b. Supplemental material: Association between levels of serum perfluoroctane sulfate and carotid artery intima-media thickness in adolescents and young adults. Int J Cardiol 168:3309-3316.

Lin LY, Wen LL, Su TC, et al. 2014. Negative association between serum perfluorooctane sulfate concentration and bone mineral density in US premenopausal women: NHANES, 2005-2008. The Journal of clinical endocrinology and metabolism 99(6):2173-2180. 10.1210/jc.2013-3409.

Lind DV, Priskorn L, Lassen TH, et al. 2017a. Prenatal exposure to perfluoroalkyl substances and anogenital distance at 3 months of age in a Danish mother-child cohort. Reprod Toxicol 68:200-206. http://doi.org/10.1016/j.reprotox.2016.08.019.

Lind PM, Salihovic S, van Bavel B, et al. 2017b. Circulating levels of perfluoroalkyl substances (PFASs) and carotid artery atherosclerosis. Environ Res 152:157-164. http://doi.org/10.1016/j.envres.2016.10.002.

Lind L, Zethelius B, Salihovic S, et al. 2014. Circulating levels of perfluoroalkyl substances and prevalent diabetes in the elderly. Diabetologia 57(3):473-479. 10.1007/s00125-013-3126-3.

Liu G, Dhana K, Furtado JD, et al. 2018a. Perfluoroalkyl substances and changes in body weight and resting metabolic rate in response to weight-loss diets: A prospective study. PLoS Med 15(2):e1002501. http://doi.org/10.1371/journal.pmed.1002502.

Liu HS, Wen LL, Chu PL, et al. 2018b. Association among total serum isomers of perfluorinated chemicals, glucose homeostasis, lipid profiles, serum protein and metabolic syndrome in adults: NHANES, 2013-2014. Environ Pollut 232:73-79. http://doi.org/10.1016/j.envpol.2017.09.019.

Looker C, Luster MI, Calafat AM, et al. 2014. Influenza vaccine response in adults exposed to perfluorooctanoate and perfluorooctanesulfonate. Toxicol Sci 138(1):76-88.

Lopez-Espinosa MJ, Fletcher T, Armstrong B, et al. 2011. Association of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) with age of puberty among children living near a chemical plant. Environ Sci Technol 45(19):8160-8166.

Lopez-Espinosa MJ, Mondal D, Armstrong B, et al. 2012. Thyroid function and perfluoroalkyl acids in children living near a chemical plant. Environ Health Perspect 120(7):1036-1041. 10.1289/ehp.1104370.

Lopez-Espinosa MJ, Mondal D, Armstrong BG, et al. 2016. Perfluoroalkyl substances, sex hormones, and insulin-like growth factor-1 at 6-9 years of age: A Cross-sectional analysis within the C8 Health Project. Environ Health Perspect 124:1269-1275. 10.1289/ehp.1509869.

Lum KJ, Sundaram R, Barr DB, et al. 2017. Perfluoroalkyl chemicals, menstrual cycle length, and fecundity: Findings from a prospective pregnancy study. Epidemiology 28(1):90-98. http://doi.org/10.1097/ede.0000000000000552.

Lundin JI, Alexander BH, Olsen GW, et al. 2009. Ammonium perfluorooctanoate production and occupational mortality. Epidemiology 20(6):921-928.

Lyngsø J, Ramlau-Hansen CH, Hoyer BB, et al. 2014. Menstrual cycle characteristics in fertile women from Greenland, Poland and Ukraine exposed to perfluorinated chemicals: A cross-sectional study. Hum Reprod 29(2):359-367. 10.1093/humrep/det390.

MacNeil J, Steenland NK, Shankar A, et al. 2009. A cross-sectional analysis of type II diabetes in a community with exposure to perfluorooctanoic acid (PFOA). Environ Res 109(8):997-1003.

Maisonet M, Terrell ML, McGeehin MA, et al. 2012. Maternal concentrations of polyfluoroalkyl compounds during pregnancy and fetal and postnatal growth in British girls. Environ Health Perspect 120(10):1432-1437.

Maisonet M, Calafat AM, Marcus M, et al. 2015a. Prenatal exposure to perfluoroalkyl acids and serum testosterone concentrations at 15 years of age in female ALSPAC study participants. Environ Health Perspect 123(12):1325-1330. 10.1289/ehp.1408847.

Maisonet M, Nayha S, Lawlor DA, et al. 2015b. Prenatal exposures to perfluoroalkyl acids and serum lipids at ages 7 and 15 in females. Environ Int 82:49-60. 10.1016/j.envint.2015.05.001.

Manzano-Salgado CB, Casas M, Lopez-Espinosa MJ, et al. 2017a. Prenatal exposure to perfluoroalkyl substances and birth outcomes in a Spanish birth cohort. Environ Int 108:278-284. http://doi.org/10.1016/j.envint.2017.09.006.

Manzano-Salgado CB, Casas M, Lopez-Espinosa MJ, et al. 2017b. Prenatal exposure to perfluoroalkyl substances and cardiometabolic risk in children from the Spanish INMA birth cohort study. Environ Health Perspect 125(9):097018. http://doi.org/10.1289/ehp1330.

Mattsson K, Rignell-Hydbom A, Holmberg S, et al. 2015. Levels of perfluoroalkyl substances and risk of coronary heart disease: Findings from a population-based longitudinal study. Environ Res 142:148-154. 10.1016/j.envres.2015.06.033.

MDH. 2007. Groundwater health risk limits. St. Paul, MN: Minnesota Department of Health. http://www.health.state.mn.us/divs/eh/groundwater/hrltable.html. July 1, 2008.

Melzer D, Rice N, Depledge MH, et al. 2010. Association between serum perfluorooctanoic acid (PFOA) and thyroid disease in the U.S. National Health and Nutrition Examination Survey. Environ Health Perspect 118(5):686-692.

Min JY, Lee KJ, Park JB, et al. 2012. Perfluorooctanoic acid exposure is associated with elevated homocysteine and hypertension in US adults. Occup Environ Med 69(9):658-662.

Minatoya M, Itoh S, Miyashita C, et al. 2017. Association of prenatal exposure to perfluoroalkyl substances with cord blood adipokines and birth size: The Hokkaido Study on environment and children's health. Environ Res 156:175-182. http://doi.org/10.1016/j.envres.2017.03.033.

Mogensen UB, Grandjean P, Heilmann C, et al. 2015a. Structural equation modeling of immunotoxicity associated with exposure to perfluorinated alkylates. Environ Health 14:47 10.1186/s12940-015-0032-9.

Monroy R, Morrison K, Teo K, et al. 2008. Serum levels of perfluoroalkyl compounds in human maternal and umbilical cord blood samples. Environ Res 108:56-62.

Mora AM, Oken E, Rifas-Shiman SL, et al. 2017. Prenatal Exposure to perfluoroalkyl substances and adiposity in early and mid-childhood. Environ Health Perspect 125(3):467-473. http://doi.org/10.1289/ehp246.

Mundt DJ, Mundt KA, Luippold RS, et al. 2007. Clinical epidemiological study of employees exposed to surfactant blend containing perfluorononanoic acid. Occup Environ Med 64:589-594.

Nelson JW, Hatch EE, Webster TF. 2010. Exposure to polyfluoroalkyl chemicals and cholesterol, body weight, and insulin resistance in the general U.S. population. Environ Health Perspect 118(2):197-202.

Nolan LA, Nolan JM, Shofer FS, et al. 2009. The relationship between birth weight, gestational age and perfluorooctanoic acid (PFOA)-contaminated public drinking water. Reprod Toxicol 27:231-238.

Nolan LA, Nolan JM, Shofer FS, et al. 2010. Congenital anomalies, labor/delivery complications, maternal risk factors and their relationship with perfluorooctanoic acid (PFOA)-contaminated public drinking water. Reprod Toxicol 29(2):147-155.

Ode A, Kallen K, Gustafsson P, et al. 2014. Fetal exposure to perfluorinated compounds and attention deficit hyperactivity disorder in childhood. PLoS ONE 9(4):e95891. 10.1371/journal.pone.0095891.

Okada E, Sasaki S, Saijo Y, et al. 2012. Prenatal exposure to perfluorinated chemicals and relationship with allergies and infectious diseases in infants. Environ Res 112:118-125.

Okada E, Sasaki S, Kashino I, et al. 2014. Prenatal exposure to perfluoroalkyl acids and allergic diseases in early childhood. Environ Int 65:127-134. 10.1016/j.envint.2014.01.007.

Olsen GW, Zobel LR. 2007. Assessment of lipid, hepatic, and thyroid parameters with serum perfluorooctanoate (PFOA) concentrations in fluorochemical production workers. Int Arch Occup Environ Health 81:231-246.

Olsen GW, Burlew MM, Marshall JC, et al. 2004a. Analysis of episodes of care in a perfluorooctanesulfonyl fluoride production facility. J Occup Environ Hyg 46(8):837-846.

REFERENCES

Olsen GW, Burris JM, Burlew MM, et al. 2003a. Epidemiologic assessment of worker serum perfluorooctanesulfonate (PFOS) and perfluorooctanoate (PFOA) concentrations and medical surveillance examinations. J Occup Environ Med 45(3):260-270.

Olsen GW, Burris JM, Burlew MM, et al. 2000. Plasma cholecystokinin and hepatic enzymes, cholesterol and lipoproteins in ammonium perfluorooctanoate production workers. Drug Chem Toxicol 23(4):603-620.

Olsen GW, Burris JM, Mandel JH, et al. 1998a. An epidemiologic investigation of clinical chemistries, hematology and hormones in relation to serum levels of perfluorooctane sulfonate in male fluorochemical production employees. St. Paul, MN: 3M Company. AR226-0030.

Olsen GW, Burris JM, Mandel JH, et al. 1999. Serum perfluorooctane sulfonate and hepatic and lipid clinical chemistry tests in fluorochemical production employees. J Occup Environ Med 41(9):799-806.

Olsen GW, Ehresman DJ, Buehrer BD, et al. 2012. Longitudinal assessment of lipid and hepatic clinical parameters in workers involved with the demolition of perfluoroalkyl manufacturing facilities. J Occup Environ Med 54(8):974-983.

Olsen GW, Gilliland FD, Burlew MM, et al. 1998b. An epidemiologic investigation of reproductive hormones in men with occupational exposure to perfluorooctanoic acid. J Occup Environ Med 40(7):614-622.

Osuna CE, Grandjean P, Weihe P, et al. 2014. Autoantibodies associated with prenatal and childhood exposure to environmental chemicals in Faroese children. Toxicol Sci 142(1):158-166. 10.1093/toxsci/kfu163.

Oulhote Y, Steuerwald U, Debes F, et al. 2016. Behavioral difficulties in 7-year old children in relation to developmental exposure to perfluorinated alkyl substances. Environ Int 97:237-245. http://doi.org/10.1016/j.envint.2016.09.015.

Power MC, Webster TF, Baccarelli AA, et al. 2013. Cross-sectional association between polyfluoroalkyl chemicals and cognitive limitation in the National Health and Nutrition Examination Survey. Neuroepidemiology 40(2):125-132.

Predieri B, Iughetti L, Guerranti C, et al. 2015. High levels of perfluorooctane sulfonate in children at the onset of diabetes. Int J Endocrinol 2015:234358. 10.1155/2015/234358.

Preston EV, Webster TF, Oken E, et al. 2018. Maternal plasma per- and polyfluoroalkyl substance concentrations in early pregnancy and maternal and neonatal thyroid function in a prospective birth cohort: Project Viva (USA). Environ Health Perspect 126(2):027013. http://doi.org/10.1289/EHP2534.

Qin XD, Qian ZM, Dharmage SC, et al. 2017. Association of perfluoroalkyl substances exposure with impaired lung function in children. Environ Res 155:15-21. http://doi.org/10.1016/j.envres.2017.01.025.

Qin XD, Qian Z, Vaughn MG, et al. 2016. Positive associations of serum perfluoroalkyl substances with uric acid and hyperuricemia in children from Taiwan. Environ Pollut 212:519-524. 10.1016/j.envpol.2016.02.050.

Quaak I, de Cock M, de Boer M, et al. 2016. Prenatal exposure to perfluoroalkyl substances and behavioral development in children. Int J Environ Res Public Health 13(5). 10.3390/ijerph13050511.

Raleigh KK, Alexander BH, Olsen GW, et al. 2014. Mortality and cancer incidence in ammonium perfluorooctanoate production workers. Occup Environ Med 71(7):500-506. 10.1136/oemed-2014-102109.

Raymer JH, Michael LC, Studabaker WB, et al. 2012. Concentrations of perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) and their associations with human semen quality measurements. Reprod Toxicol 33(4):419-427.

Robledo CA, Yeung E, Mendola P, et al. 2015a. Preconception maternal and paternal exposure to persistent organic pollutants and birth size: The LIFE study. Environ Health Perspect 123(1):88-94. 10.1289/ehp.1308016.

REFERENCES

Robledo CA, Yeung E, Mendola P, et al. 2015b. Supplemental material to preconception maternal and paternal exposure to persistent organic pollutants and birth size: The LIFE study. [Environ Health Perspect 123(1):88-94]. Environ Health Perspect 10.1289/ehp.1308016.

Romano ME, Xu Y, Calafat AM, et al. 2016. Maternal serum perfluoroalkyl substances during pregnancy and duration of breastfeeding. Environ Res 10.1016/j.envres.2016.04.034.

Sagiv SK, Rifas-Shiman SL, Fleisch AF, et al. 2018. Early-pregnancy plasma concentrations of perfluoroalkyl substances and birth outcomes in Project Viva: Confounded by pregnancy hemodynamics? Am J Epidemiol 187(4):793-802.

Sakr CJ, Kreckmann KH, Green JW, et al. 2007b. Cross-sectional study of lipids and liver enzymes related to a serum biomarker of exposure (ammonium perfluorooctanoate or APFO) as part of a general health survey in a cohort of occupationally exposed workers. J Occup Environ Med 49:1086-1096.

Sakr CJ, Leonard RC, Kreckmann KH, et al. 2007a. Longitudinal study of serum lipids and liver enzymes in workers with occupational exposure to ammonium perfluorooctanoate. J Occup Environ Med 49:872-879.

Sakr CJ, Symons JM, Kreckmann KH, et al. 2009. Ischaemic heart disease mortality study among workers with occupational exposure to ammonium perfluorooctanoate. Occup Environ Med 66:699-703.

Savitz DA, Stein CR, Bartell SM, et al. 2012a. Perfluorooctanoic acid exposure and pregnancy outcome in a highly exposed community. Epidemiology 23(3):386-392.

Savitz DA, Stein CR, Elston B, et al. 2012b. Relationship of perfluorooctanoic acid exposure to pregnancy outcome based on birth records in the Mid-Ohio Valley. Environ Health Perspect 120(8):1201-1207.

Shah-Kulkarni S, Kim BM, Hong YC, et al. 2016. Prenatal exposure to perfluorinated compounds affects thyroid hormone levels in newborn girls. Environ Int 94:607-613. http://doi.org/10.1016/j.envint.2016.06.024.

Shankar A, Xiao J, Ducatman A. 2011a. Perfluoroalkyl chemicals and chronic kidney disease in US adults. Am J Epidemiol 174(8):893-900.

Shankar A, Xiao J, Ducatman A. 2011b. Perfluoroalkyl chemicals and elevated serum uric acid in US adults. Clin Epidemiol 3:251-258.

Shankar A, Xiao J, Ducatman A. 2012. Perfluorooctanoic acid and cardiovascular disease in US adults. Arch Intern Med 172(18):1397-1403.

Shapiro GD, Dodds L, Arbuckle TE, et al. 2016. Exposure to organophosphorus and organochlorine pesticides, perfluoroalkyl substances, and polychlorinated biphenyls in pregnancy and the association with impaired glucose tolerance and gestational diabetes mellitus: The MIREC Study. Environ Res 147:71-81. 10.1016/j.envres.2016.01.040.

Shi Y, Yang L, Li J, et al. 2017. Occurrence of perfluoroalkyl substances in cord serum and association with growth indicators in newborns from Beijing. Chemosphere 169:396-402. http://doi.org/10.1016/j.chemosphere.2016.11.050.

Shrestha S, Bloom MS, Yucel R, et al. 2015. Perfluoroalkyl substances and thyroid function in older adults. Environ Int 75:206-214. 10.1016/j.envint.2014.11.018.

Shrestha S, Bloom MS, Yucel R, et al. 2017. Perfluoroalkyl substances, thyroid hormones, and neuropsychological status in older adults. Int J Hyg Environ Health 220(4):679-685. http://doi.org/10.1016/j.ijheh.2016.12.013.

Simpson C, Winquist A, Lally C, et al. 2013. Relation between perfluorooctanoic acid exposure and strokes in a large cohort living near a chemical plant. Environ Res 127:22-28. 10.1016/j.envres.2013.10.002.

Skuladottir M, Ramel A, Rytter D, et al. 2015. Examining confounding by diet in the association between perfluoroalkyl acids and serum cholesterol in pregnancy. Environ Res 143(Pt A):33-38. 10.1016/j.envres.2015.09.001.

REFERENCES

Smit LA, Lenters V, Hoyer BB, et al. 2015. Prenatal exposure to environmental chemical contaminants and asthma and eczema in school-age children. Allergy 70(6):653-660. 10.1111/all.12605.

Specht IO, Hougaard KS, Spano D, et al. 2012. Sperm DNA integrity in relation to exposure to environmental perfluoroalkyl substances. A study of spouses of pregnant women in three geographical regions. Reprod Toxicol 33:577-583.

Starling AP, Adgate JL, Hamman RF, et al. 2017. Perfluoroalkyl substances during pregnancy and offspring weight and adiposity at birth: examining mediation by maternal fasting glucose in the Healthy Start Study. Environ Health Perspect 125(6):067016. http://doi.org/10.1289/ehp641.

Starling AP, Engel SM, Richardson DB, et al. 2014b. Perfluoroalkyl substances during pregnancy and validated preeclampsia among nulliparous women in the Norwegian Mother and Child Cohort Study. Am J Epidemiol 179(7):824-833. 10.1093/aje/kwt432.

Starling AP, Engel SM, Whitworth KW, et al. 2014a. Perfluoroalkyl substances and lipid concentrations in plasma during pregnancy among women in the Norwegian Mother and Child Cohort Study. Environ Int 62:104-112. 10.1016/j.envint.2013.10.004.

Steenland K, Woskie S. 2012. Cohort mortality study of workers exposed to perfluorooctanoic acid. Am J Epidemiol 176(10):909-917.

Steenland K, Tinker S, Frisbee S, et al. 2009b. Association of perfluorooctanoic acid and perfluorooctane sulfonate with serum lipids among adults living near a chemical plant. Am J Epidemiol 170(10):1268-1278.

Steenland K, Tinker S, Shankar A, et al. 2010b. Association of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) with uric acid among adults with elevated community exposure to PFOA. Environ Health Perspect 118(2):229-233.

Steenland K, Zhao L, Winquist A, et al. 2013. Ulcerative colitis and perfluorooctanoic acid (PFOA) in a highly exposed population of community residents and workers in the Mid-Ohio Valley. Environ Health Perspect 121(8):900-905.

Steenland K, Zhao L, Winquist A. 2015. A cohort incidence study of workers exposed to perfluorooctanoic acid (PFOA). Occup Environ Med 72(5):373-380. 10.1136/oemed-2014-102364.

Stein CR, Savitz DA. 2011. Serum perfluorinated compound concentration and attention deficit/hyperactivity disorder in children 5-18 years of age. Environ Health Perspect 119(10):1466-1471.

Stein CR, McGovern KJ, Pajak AM, et al. 2016a. Perfluoroalkyl and polyfluoroalkyl substances and indicators of immune function in children aged 12-19 y: National Health and Nutrition Examination Survey. Pediatr Res 79(2):348-357. 10.1038/pr.2015.213.

Stein CR, Ge Y, Wolff MS, et al. 2016b. Perfluoroalkyl substance serum concentrations and immune response to FluMist vaccination among healthy adults. Environ Res 149:171-178. 10.1016/j.envres.2016.05.020.

Stein CR, Savitz DA, Bellinger DC. 2013. Perfluorooctanoate and neuropsychological outcomes in children. Epidemiology 24(4):590-599.

Stein CR, Savitz DA, Bellinger DC. 2014a. Perfluorooctanoate exposure in a highly exposed community and parent and teacher reports of behaviour in 6-12-year-old children. Paediatr Perinat Epidemiol 28(2):146-156. 10.1111/ppe.12097.

Stein CR, Savitz DA, Bellinger DC. 2014b. Supporting information to perfluorooctanoate exposure in a highly exposed community and parent and teacher reports of behaviour in 6-12-year-old children. Paediatr Perinat Epidemiol 10.1111/ppe.12097.

Stein CR, Savitz DA, Elston B, et al. 2014c. Perfluorooctanoate exposure and major birth defects. Reprod Toxicol 47:15-20. 10.1016/j.reprotox.2014.04.006.

Stein CR, Savitz DA, Dougan M. 2009. Serum levels of perfluorooctanoic acid and perfluorooctane sulfonate and pregnancy outcome. Am J Epidemiol 170(7):837-846.

Strøm M, Hansen S, Olsen SF, et al. 2014. Persistent organic pollutants measured in maternal serum and offspring neurodevelopmental outcomes--a prospective study with long-term follow-up. Environ Int 68:41-48. 10.1016/j.envint.2014.03.002.

REFERENCES

Su TC, Kuo CC, Hwang JJ, et al. 2016. Serum perfluorinated chemicals, glucose homeostasis and the risk of diabetes in working-aged Taiwanese adults. Environ Int 88:15-22. 10.1016/j.envint.2015.11.016.

Sun Q, Zong G, Valvi D, et al. 2018. Plasma concentrations of perfluoroalkyl substances and risk of type 2 diabetes: A prospective investigation among U.S. women. Environ Health Perspect 126(3):037001. http://doi.org/10.1289/ehp2619.

Taylor KW, Hoffman K, Thayer KA, et al. 2014. Polyfluoroalkyl chemicals and menopause among women 20-65 years of age (NHANES). Environ Health Perspect 122(2):145-150. 10.1289/ehp.1306707.

Timmermann CAG, Budtz-Jorgensen E, Petersen MS, et al. 2017. Shorter duration of breastfeeding at elevated exposures to perfluoroalkyl substances. Reprod Toxicol 68:164-170. http://doi.org/10.1016/j.reprotox.2016.07.010.

Timmermann CA, Rossing LI, Grontved A, et al. 2014. Adiposity and glycemic control in children exposed to perfluorinated compounds. J Clin Endocrinol Metab 99(4):E608-614. 10.1210/jc.2013-3460.

Toft G, Jonsson BA, Bonde JP, et al. 2016. Perfluorooctane sulfonate concentrations in amniotic fluid, biomarkers of fetal Leydig Cell Function, and cryptorchidism and hypospadias in Danish boys (1980-1996). Environ Health Perspect 124(1):151-156. 10.1289/ehp.1409288.

Toft G, Jonsson BA, Lindh CH, et al. 2012. Exposure to perfluorinated compounds and human semen quality in Arctic and European populations. Hum Reprod 27(8):2532-2540.

Tsai MS, Lin CC, Chen MH, et al. 2017. Perfluoroalkyl substances and thyroid hormones in cord blood. Environ Pollut 222:543-548. http://doi.org/10.1016/j.envpol.2016.11.027.

Tsai MS, Lin CY, Lin CC, et al. 2015. Association between perfluoroalkyl substances and reproductive hormones in adolescents and young adults. Int J Hyg Environ Health 218(5):437-443. 10.1016/j.ijheh.2015.03.008.

Uhl SA, James-Todd T, Bell ML. 2013. Association of osteoarthritis with perfluorooctanoate and perfluorooctane sulfonate in NHANES 2003-2008. Environ Health Perspect 121(4):447-452.

Vagi SJ, Azziz-Baumgartner E, Sjodin A, et al. 2014. Exploring the potential association between brominated diphenyl ethers, polychlorinated biphenyls, organochlorine pesticides, perfluorinated compounds, phthalates, and bisphenol A in polycystic ovary syndrome: A case-control study. BMC Endoc Disord 14:86. 10.1186/1472-6823-14-86.

Vélez MP, Arbuckle TE, Fraser WD. 2015. Maternal exposure to perfluorinated chemicals and reduced fecundity: The MIREC study. Hum Reprod 30(3):701-709. 10.1093/humrep/deu350.

Vested A, Ramlau-Hansen CH, Olsen SF, et al. 2013. Associations of *in utero* exposure to perfluorinated alkyl acids with human semen quality and reproductive hormones in adult men. Environ Health Perspect 121(4):453-458.

Vestergaard S, Nielsen F, Andersson AM, et al. 2012. Association between perfluorinated compounds and time to pregnancy in a prospective cohort of Danish couples attempting to conceive. Hum Reprod 27(3):873-880.

Vesterholm Jensen D, Christensen J, Virtanen HE, et al. 2014. No association between exposure to perfluorinated compounds and congenital cryptorchidism: A nested case-control study among 215 boys from Denmark and Finland. Reproduction 147(4):411-417.

Vieira VM, Hoffman K, Shin M, et al. 2013. Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: A geographic analysis. Environ Health Perspect 121(3):318-323.

Vuong AM, Yolton K, Wang Z, et al. 2018. Childhood perfluoroalkyl substance exposure and executive function in children at 8 years. Environ Int 119:212-219. http://doi.org/10.1016/j.envint.2018.06.028.

Vuong AM, Yolton K, Webster GM, et al. 2016. Prenatal polybrominated diphenyl ether and perfluoroalkyl substance exposures and executive function in school-age children. Environ Res 147:556-564. 10.1016/j.envres.2016.01.008.

REFERENCES

Wang IJ, Hsieh W-S, Chen C-Y, et al. 2011. The effect of prenatal perfluorinated chemicals exposures on pediatric atopy. Environ Res 111(6):785-791.

Wang J, Zhang Y, Zhang W, et al. 2012. Association of perfluorooctanoic acid with HDL cholesterol and circulating miR-26b and miR-199-3p in workers of a fluorochemical plant and nearby residents. Environ Sci Technol 46(17):9274-9281.

Wang Y, Adgent M, Su PH, et al. 2016. Prenatal exposure to perfluorocarboxylic acids (PFCAs) and fetal and postnatal growth in the Taiwan maternal and infant cohort study. Environ Health Perspect 10.1289/ehp.1509998.

Wang Y, Rogan WJ, Chen PC, et al. 2014. Association between maternal serum perfluoroalkyl substances during pregnancy and maternal and cord thyroid hormones: Taiwan maternal and infant cohort study. Environ Health Perspect 122(5):529-534. 10.1289/ehp.1306925.

Wang Y, Rogan WJ, Chen HY, et al. 2015b. Prenatal exposure to perfluoroalkyl substances and children's IQ: The Taiwan maternal and infant cohort study. Int J Hyg Environ Health 218(7):639-644. 10.1016/j.ijheh.2015.07.002.

Wang Y, Starling AP, Haug LS, et al. 2013a. Association between perfluoroalkyl substances and thyroid stimulating hormone among pregnant women: A cross-sectional study. Environ Health 12(1):76. 10.1186/1476-069x-12-76

Wang Z, Boucher JM, Scheringer M, et al. 2017. Toward a comprehensive global emission inventory of C4-C10 perfluoroalkanesulfonic acids (PFSAs) and related precursors: Focus on the life cycle of C8-based products and ongoing industrial transition. Environ Sci Technol 51(8):4482-4493. http://doi.org/10.1021/acs.est.6b06191.

Washino N, Saijo Y, Sasaki S, et al. 2009. Correlations between prenatal exposure to perfluorinated chemicals and reduced fetal growth. Environ Health Perspect 117:660-667.

Watkins DJ, Josson J, Elston B, et al. 2013. Exposure to perfluoroalkyl acids and markers of kidney function among children and adolescents living near a chemical plant. Environ Health Perspect 121(5):625-630.

Webster GM, Rauch SA, Marie NS, et al. 2016. Cross-sectional associations of serum perfluoroalkyl acids and thyroid hormones in U.S. adults: Variation according to TPOAb and iodine status (NHANES 2007-2008). Environ Health Perspect 124(7):935-942. 10.1289/ehp.1409589.

Wen LL, Lin LY, Su TC, et al. 2013. Association between serum perfluorinated chemicals and thyroid function in U.S. adults: The national health and nutrition examination survey 2007-2010. J Clin Endocrinol Metab 98(9):E1456-1464. 10.1210/jc.2013-1282.

Whitworth KW, Haug LS, Baird DD, et al. 2012a. Perfluorinated compounds in relation to birth weight in the Norwegian Mother and Child Cohort Study. Am J Epidemiol 175(12):1209-1216.

Whitworth KW, Haug LS, Baird DD, et al. 2012b. Perfluorinated compounds and subfecundity in pregnant women. Epidemiology 23(2):257-263.

Whitworth KW, Haug LS, Sabaredzovic A, et al. 2016. Brief report: Plasma concentrations of perfluorooctane sulfonamide and time-to-pregnancy among primiparous women. Epidemiology 27(5):712-715. http://doi.org/10.1097/ede.0000000000000524.

Wielsoe M, Kern P, Bonefeld-Jorgensen EC. 2017. Serum levels of environmental pollutants is a risk factor for breast cancer in Inuit: A case control study. Environ Health 16(1):56. http://doi.org/10.1186/s12940-017-0269-6.

Winquist A, Steenland K. 2014a. Modeled PFOA exposure and coronary artery disease, hypertension, and high cholesterol in community and worker cohorts. Environ Health Perspect 122(12):1299-1305. 10.1289/ehp.1307943.

Winquist A, Steenland K. 2014b. Perfluorooctanoic acid exposure and thyroid disease in community and worker cohorts. Epidemiology 25(2):255-264. 10.1097/ede.0000000000000040.

Wu K, Xu X, Peng L, et al. 2012. Association between maternal exposure to perfluorooctanoic acid (PFOA) from electronic waste recycling and neonatal outcomes. Environ Int 48:1-8.

Yamaguchi M, Arisawa K, Uemura H, et al. 2013. Consumption of seafood, serum liver enzymes, and blood levels of PFOS and PFOA in the Japanese population. J Occup Health 55(3):184-194.

REFERENCES

Yang Q, Guo X, Sun P, et al. 2018. Association of serum levels of perfluoroalkyl substances (PFASs) with the metabolic syndrome (MetS) in Chinese male adults: A cross-sectional study. Sci Total Environ 621:1542-1549. http://doi.org/10.1016/j.scitotenv.2017.10.074.

Yang L, Li J, Lai J, et al. 2016a. Placental transfer of perfluoroalkyl substances and associations with thyroid hormones: Beijing prenatal exposure study. Sci Rep 6:21699. 10.1038/srep21699.

Zeng XW, Qian Z, Emo B. 2015. The association between perfluoroalkyl chemicals and serum lipid levels in children. Sci Total Environ 512-513:364-370

Zhang C, Sundaram R, Maisog J, et al. 2015a. A prospective study of prepregnancy serum concentrations of perfluorochemicals and the risk of gestational diabetes. Fertil Steril 103(1):184-189.

Zhang H, Yolton K, Webster GM, et al. 2018. Prenatal and childhood perfluoroalkyl substances exposures and children's reading skills at ages 5 and 8 years. Environ Int 111:224-231. http://doi.org/10.1016/j.envint.2017.11.031.

Zhou Y, Hu LW, Qian ZM, et al. 2016. Association of perfluoroalkyl substances exposure with reproductive hormone levels in adolescents: By sex status. Environ Int 94:189-195. http://doi.org/10.1016/j.envint.2016.05.018.

Zhou Y, Hu LW, Qian ZM, et al. 2017. Interaction effects of polyfluoroalkyl substances and sex steroid hormones on asthma among children. Scientific Reports 7(1):899. http://doi.org/10.1038/s41598-017-01140-5.

Zhu Y, Qin XD, Zeng XW, et al. 2016. Associations of serum perfluoroalkyl acid levels with T-helper cell-specific cytokines in children: By gender and asthma status. Sci Total Environ 559:166-173. 10.1016/j.scitotenv.2016.03.187.