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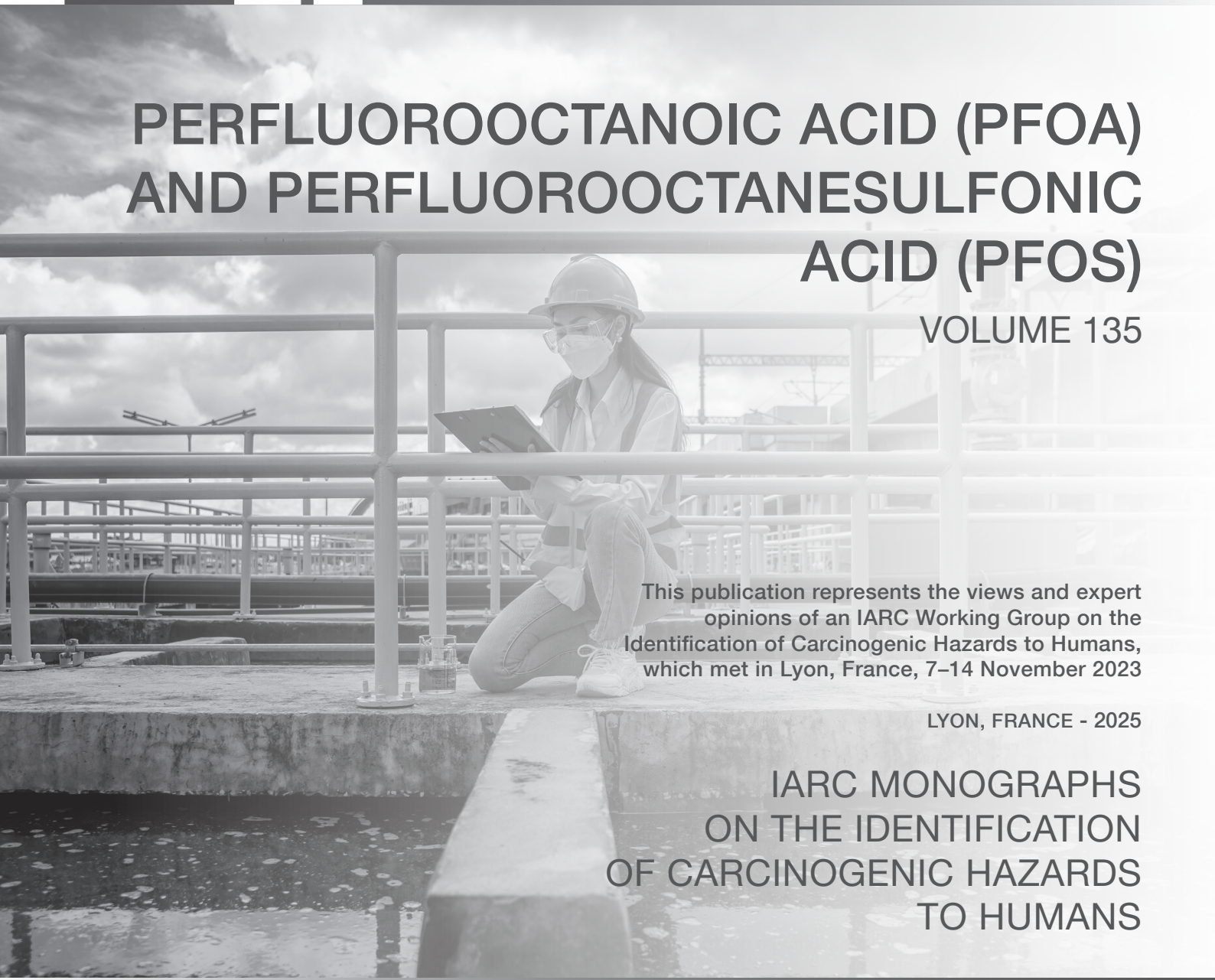

PERFLUOROOCTANOIC ACID (PFOA) AND PERFLUOROOCTANESULFONIC ACID (PFOS)

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International Agency for Research on Cancer

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Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Thyroid hormone pathway (children – adult exposure)							
Thyroid hormone pathway	Blood serum	Ohio, USA Prospective	210, 38 years of age at time of enrolment (median) Female and male	PFOA – 12.7 (median) PFOS – 28.4 (median)	Age, year of measurement, sex, education, income, marital status, and BMI	TSH – no association TT4 – no association ↑ TSH (P = 0.02) TT4 – no association	Blake et al. (2018)
Thyroid hormone pathway	Blood serum	Seoul and Gyeonggi, Republic of Korea Prospective	381 (2 years of age), 569 (4 years of age), 511 (6 years of age) Female and male	PFOA 2 years – 4.4 (median) 4 years – 3.7 (median) 6 years – 3.8 (median) PFOS 2 years – 4.5 (median) 4 years – 4.1 (median) 6 years – 4.0 (median)	Age and sex	↓ TSH (P < 0.05, males only, repeated measures) T3 – no associations ↑ FT4 at 6 years (P < 0.05, driven by males) TSH – no associations (repeated measures) ↑ T3 at 6 years (P < 0.05, driven by males) FT4 – no associations	Kim et al. (2020)
Thyroid hormone pathway	Blood serum	Occupational exposure, Belgium and USA Cross-sectional	506, 21–67 years of age Male	Antwerp facility PFOA – 650 (median) Cottage Grove facility PFOA – 950 (median) Decatur facility PFOA – 1510 (median) Antwerp facility PFOS – 550 (median)	ln age, ln BMI, ln alcohol	TSH – no association TT4 – no association T3 – no association ↓ FT4 (P < 0.002) (FT4 decrease not clinically relevant as within normal reference ranges) Associations with PFOS not tested.	Olsen and Zobel (2007)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				Cottage Grove facility PFOS – 450 (median) Decatur facility PFOS – 1000 (median)			
Thyroid hormone pathway	Blood serum	Occupational exposure, Belgium and USA Cross-sectional	518, 34–53 years of age Female and male	Antwerp facility PFOA – 330 (GM) Decatur facility PFOA – 1130 (GM) Antwerp facility PFOS – 440 (GM) Decatur facility PFOS – 910 (GM)	Age, BMI, alcohol, cigarettes, and location	Associations with PFOA not tested. Female employees TSH – no association T3 – no association TT4, FT4 – no associations Male employees TSH – no association ↑T3 ($P < 0.05$) TT4, FT4 – no associations	Olsen et al. (2003b)
Thyroid hormone pathway	Blood serum	Veneto region, Italy Cross-sectional	10 918 females, 10 906 males, 14–39 years of age	PFOA Female age 14–19 – 0.03 (GM) PFOA Female age 20–39 – 0.02 (GM) PFOA Male age 14–19 – 0.04 (GM) PFOA Male age 20–39 – 0.5 (GM)	Age, BMI, time-lag between the enrolment and the beginning of the study, gender, physical activity, smoking habits, food consumption, country of birth, alcohol consumption, education level and laboratory in	TSH – no associations	Gallo et al. (2022)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				PFOS Female age 14–19 – 0.003 (GM) PFOS Female age 20–39 – 0.003 (GM) PFOS Male age 14–19 – 0.004 (GM) PFOS Male age 20–39 – 0.005 (GM)	charge of the TSH analyses	TSH – no associations	
Thyroid hormone pathway	Blood serum	Mid-Ohio Valley, USA Cross-sectional	10 725, 1–17 years of age Female and male	PFOA – 29.3 (median) PFOS – 20.0 (median)	Age, sex, and month of sampling	TSH – no associations TT4 – no associations TSH – no associations ↑ TT4 (1.1%; 0.6, 1.5)	Lopez-Espinosa et al. (2012)
Thyroid hormone pathway	Blood serum	United Sates, Cross-sectional (NHANES 2007–2008)	1540, > 12 years of age Female and male	PFOA – 0.07 to 104 PFOS – 0.14 to 253	Age, gender, race, smoking status, iodine status, C-reactive protein, BMI, fasting time before blood draw, total calories consumed during the last 24 h	↑ TSH ($P < 0.01$) FT3 – no association ↑ TT3 ($P = 0.01$) FT4 – no association TT4 – no effect No significant associations reported	Jain (2013)
Thyroid hormone pathway	Blood serum	USA, Cross-sectional (NHANES 2007–2008)	1525, > 18 years of age Female and male	PFOA – 4.2 (GM)	Age, log_{10}-transformed serum cotinine, race/ethnicity, sex, parity, pregnancy, and menopause status	In people with high TPOAb and low urinary iodine: ↑ TSH (16.2%; 5.1, 28.5) ↑ FT3 (4.8%; 3.7, 5.8) ↑ TT3 (12.4%; 7, 18.1)	Webster et al. (2016)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						TT4, FT4 – no associations In people with normal TPOAb and iodine: ↑ FT3 (1.2%; 0.1, 2.4) In people with high TPOAb and low urinary iodine: ↑ TSH (17.1%; 6.6, 28.7) ↑ FT3 (4.7%; 3.9, 5.5) ↑ TT3 (12.0%; 6.7, 17.7) ↓FT4 (−4.4%; −7.6, −1.1) TT4– no association	
Thyroid hormone pathway	Blood serum	USA, Cross-sectional (NHANES 2007–2008, 2009–2010)	1181, > 20 years of age Female and male	PFOA – 4.2 (GM) PFOS – 14.2 (GM)	Age, race, drinking, smoking, and natural log-urinary iodine. Also weighted for sampling strategy.	TSH – no association ↑ TT3 ($P = 0.035$, females only) ↑ FT3 ($P \leq 0.04$) TT4, FT4 – no associations TSH – no association TT3, FT3 – no associations TT4, FT4 – no associations	Wen et al. (2013)
Thyroid hormone pathway	Blood serum	USA, Cross-sectional (NHANES 2011–2012)	1325, > 20 years of age Female and male	PFOA – 8.9 (GM) PFOS – 33.5 (GM)	Sex, race/ethnicity, age, BMI, iodine status and smoking status	TSH – no association TT3, FT3 – no associations TT4, FT4 – no associations TSH – no association	van Gerwen et al. (2020)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						TT3, FT3 – no associations TT4 – no association ↑ FT4 (P = 0.003)	
Thyroid hormone pathway	Blood serum	USA, Cross-sectional (NHANES 2011–2012)	1682, 40 years of age (median) Female and males	PFOA Female/Male age 12–19 – 1.5/1.9 (median) PFOA Female/Male age 20–39 – 1.5/2.4 (median) PFOA Female/Male age 40–59 – 1.6/2.3 (median) PFOA Female/Male age 60–80 – 2.6/2.5 (median) PFOS Female/Male age 12–19 – 3.8/4.6 (median) PFOS Female/Male age 20–39 – 4.2/7.8 (median) PFOS Female/Male age 40–59 – 4.9/9.3 (median) PFOS Female/Male age 60–80 – 9.5/11.1 (median)	Age, BMI, poverty income ratio, serum cotinine, and race/ethnicity	Female ↓ TSH (P < 0.05, age 12–19 only) ↑ TT3 (P < 0.05, age 60–80 only) ↑ FT3 (P < 0.05, age 60–80 only) TT4– no association ↑ FT4 (P < 0.05, age 20–39 only) Male TSH – no association TT3, FT3 – no associations TT4, FT4 – no association Female TSH – no association TT3, FT3 – no associations TT4– no association ↑ FT4 (P < 0.05, age 20–39 only) Male ↑ TSH (P < 0.05, age 12–19 only) TT3, FT3 – no associations	Lewis et al. (2015)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Thyroid hormone pathway	Blood serum	Shenyang, China Cross-sectional	1078, Age: 63.5 ± 13.6 (mean ± SD) Female and male	PFOA – 4.7 (GM) PFOS – 24.2 (GM)	Gender, age, BMI, smoking, alcohol drinking, education, occupation, annual income, and seafood consumption	TT4, FT4 – no association ↓ TSH ($P < 0.001$) FT3 – no association ↑ FT4 ($P < 0.001$) ↓ TSH ($P < 0.001$) ↓ FT3 ($P = 0.033$) ↑ FT4 ($P < 0.001$)	Li et al. (2022d)
Thyroid hormone pathway (children – adult exposure)							
Thyroid hormone pathway	Blood plasma	North Carolina, USA Cross-sectional	256, 30–66 years of age Male	PFOA – 9.2 (median) PFOS – 32.3 (median)	Age, duration of abstinence, tobacco use	TSH – no association T3 – no association TT4 – no association TSH – no association ↑ T3 ($P = 0.030$) TT4 – no association	Raymer et al. (2012)
Thyroid hormone pathway	Blood serum	Siheung, Republic of Korea Cross-sectional	633, > 12 years of age Female and male	PFOA – 2.7 (median) PFOS – 8.0 (median)	Age, BMI, sex	TSH – no association TT4 – no association TSH – no association TT4 – no association	Ji et al. (2012)
Thyroid hormone pathway	Blood serum	Quebec, Canada Cross-sectional	186, 3–19 years of age Female and male	PFOA – 0.85 (GM) PFOS – 1.01 (GM)	Centred age, centred age-squared, BMI z-score and studied nation	TSH – no association FT4 – no association TSH – no association	Caron-Beaudoin et al. (2019)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Thyroid hormone pathway	Blood serum	Republic of Korea Cross-sectional	150, 3–18 years of age Female and male	PFOA – 1.9 (median) PFOS – 5.7 (median)	Age, sex, BMI z-score, household income, and second-hand smoking	FT4 – no association TSH – no association FT4 – no association TSH – no association	Kang et al. (2018)
Thyroid hormone pathway	Blood serum	Ohio, USA Cross-sectional	48, 9–12 years of age (obese) Female and male	PFOA – 1 (median) PFOS – 2.8 (median)	Age, sex, and race	FT4 – no association TSH – no association FT4 – no association TSH – no association	Khalil et al. (2018)
Thyroid hormone pathway	Blood serum	Taipei, Taiwan, China Cross-sectional	551, 12–30 years of age Female and male	PFOA – 2.7 (GM) PFOS – 7.8 (GM)	Age, gender, and lifestyle factors (smoking status, drinking status)	FT4 – no association TSH – no association FT4 – no association TSH – no association	Lin et al. (2013)
Thyroid hormone pathway	Blood serum	New York, USA Cross-sectional	31, 31–45 years of age Female and male	PFOA – 1.3 (GM) PFOS – 19.6 (GM)	Not adjusted	FT4 – no association TSH – no association FT4 – no association TSH – no association	Bloom et al. (2010)
Thyroid hormone pathway	Blood serum	New York, USA Cross-sectional	87, 55–74 years of age Female and male	PFOA – 9.3 (median) PFOS – 29.8 (median)	Age, sex, years of education, and serum Σ PCBs	TSH – no association TT3 – no association TT4, FT4 – no associations TSH – no association	Shrestha et al. (2015)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						TT3 – no association ↑ FT4 (P = 0.044) ↑ TT4 (P = 0.001)	
Thyroid hormone pathway	Blood serum	Alaska, USA Cross-sectional	85, 18–45 years of age Female and male	PFOA Female – 0.8 (median) PFOA Male – 1.5 (median) PFOS Female – 3.4 (median) PFOS Male – 6.8 (median)	Age, sex, and smoking habits	↑ TSH (P < 0.005) TT4, FT4 – no associations TT3, FT3 – no associations TSH – no association TT3, FT3 – no associations TT4, FT4 – no associations	Byrne et al. (2018)
Thyroid hormone pathway	Blood serum	North Carolina, USA Cross-sectional	99, 30–44 years of age Females	PFOA – 2.8 (GM) PFOS – 9.3 (GM)	Age	TSH – no association ↑ TT3 (P < 0.05) TT4, FT4 – no associations TSH – no association TT3 – no association TT4, FT4 – no associations	Crawford et al. (2017)
Thyroid hormone pathway	Blood serum	Ronneby, Sweden, Cross-sectional	113 females, 118 males 12–19 years of age	PFOA Female – 5.2 (median) PFOA Male – 6.8 (median) PFOS Female – 91 (median)	Age, sex, BMI	TSH female – no association ↓TSH male (P < 0.04) FT3 – no associations FT4 – no associations TSH female – no association	Li et al. (2021b)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				PFOS Male – 108 (median)		TSH male no associations FT3 – no associations FT4 – no associations	
Thyroid hormone pathway	Blood serum	Shandong Province, China Cross-sectional	185 non-cancer controls, age: 43.9 (± 12.3) (mean (± SD)) Female and male	PFOA – 10.9 (median) PFOS – 7.5 (median)	Age, sex, and diabetes status	↑ TSH ($P < 0.01$) TT3, FT3 – no associations TT4, FT4 – no associations TSH – no association TT3, FT3 – no associations TT4 – no association ↑ FT4 ($P < 0.05$)	Liu et al. (2022b)
Thyroid hormone pathway	Blood serum	Guangdong, Guangxi, Hainan, China Cross-sectional	202, < 1–90 years of age Female and male	PFOA – 1.6 (median) PFOS – 1.3 (median)	Age and sex	TSH – no association FT3 – no association FT4 – no association ↑TSH ($P < 0.05$) ↓ FT3 ($P < 0.01$) ↓ FT4 ($P < 0.01$)	Li et al. (2017c)
Thyroid hormone pathway	Blood serum	Quebec, Canada Cross-sectional	623, ≥ 18 years of age Female and male	PFOS – 18.3 (GM)	Sex, age, BMI, plasma lipids, cigarette consumption, education, fish consumption and alcohol consumption	↓ TSH ($P < 0.05$) ↓ TT3 ($P < 0.05$) ↑ FT4 ($P < 0.05$)	Dallaire et al. (2009)

Thyroid hormone pathway (maternal exposure/maternal hormone status)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Thyroid hormone pathway	Maternal blood serum weeks 3–27 of pregnancy	Sweden, Cross-sectional	2008, Age: 30.9 (± 4.9) (mean (± SD)) Female	PFOA – 1.61 (median) PFOS – 5.29 (median)	maternal age, BMI, parity, smoking status, education level, ethnicity, gestational age at the time of blood sampling, thyroid peroxidase antibodies, thyroglobulin antibodies.	TSH – no association FT3 – no association TT3 – no association ↑ FT4 (P = 0.02) TT4 – no association TSH – no association FT3 – no association ↓ TT3 (P = 0.003) FT4 – no association ↑ TT4 – nonlinear, inverted U (P = 0.03)	Derakhshan et al. (2022)
Thyroid hormone pathway	Maternal blood serum weeks 9–16 of pregnancy	Shanghai, China Cross-sectional	1885, Age: 29 (± 3.4) (mean (± SD)), Female	PFOA – 12.3 (median) PFOS – 9.3 (median)	Pre-pregnancy BMI, maternal education, gestational age at TH measurement, maternal age, fish intake, hospital indicators and difference in gestational week between PFAS and THs measurements	TSH – no association FT3 – no association ↑ FT4 (0.121; 0.015, 0.227) TSH – no association FT3 – no association FT4 – no association	Aimuzi et al. (2020)
Thyroid hormone pathway	Maternal blood serum week 12 of pregnancy (median)	Odense, Denmark Cross-sectional	1007, Age: 30.2 (± 4.5) (mean (± SD)), Female	PFOA – 1.7 (median) PFOS – 7.7 (median)	age, parity status, and educational level	TSH – no association ↑ FT4 (P = 0.02) TSH – no association ↑ FT4 (P < 0.01)	Jensen et al. (2022)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Thyroid hormone pathway	Maternal blood serum weeks 5–19 of pregnancy	Denmark, Cross-sectional	1366, 19–45 years of age Female	PFOA – 4.5 (median) PFOS – 29.5 (median)	maternal age, parental socio-occupational status, pre-pregnancy BMI, parity, maternal smoking, and birth year	TSH – no association FT4 – no association TSH – no association FT4 – no association	Inoue et al. (2019)
Thyroid hormone pathway	Maternal blood serum Week 11.35 (± 3.5) (mean (± SD)) of pregnancy	Sapporo, Hokkaido, Japan Cross-sectional	701, Age: 30.7 (± 4.4) (mean (± SD)), Female	PFOA – 2.0 (median) PFOS – 6.2 (median)	Maternal thyroid status analysis: maternal age at delivery, parity, educational level, pre-pregnancy BMI, alcohol intake during pregnancy and smoking during pregnancy	TSH – no association FT3 – no association FT4 – no association TSH – no association FT3 – no association FT4 – no association	Itoh et al. (2019)
Thyroid hormone pathway	Maternal blood serum Week 10 (± 2.2) (mean (± SD)) of pregnancy	Massachusetts, USA Cross-sectional	732, Age: 32.5 (± 4.7) (mean (± SD)), Female	PFOA – 5.6 (median – all maternal samples) PFOS – 24.0 (median – all maternal samples)	Maternal analysis: maternal age, race/ethnicity, smoking habits, parity, gestational week at blood draw, and fish intake	TSH – no association TT4 – no association TSH – no association (all participants) ↓ TSH (−16.4%; −29.8, −0.38) (TPOAb + participants only) TT4 – no association	Preston et al. (2018)
Thyroid hormone pathway	Maternal blood serum Week 12.9 (± 1.4) (mean (± SD)) of pregnancy	Spain Cross-sectional	919, Age: 30.6 (± 4.2) (mean (± SD)), Female	PFOA – 2.5 (GM) PFOS – 5.9 (GM)	All analysis: Maternal age, cohort, and country of birth. TSH analysis: educational level and previous breastfeeding.	TSH – no association ↓ TT3 ($P < 0.04$) FT4 – no association TSH – no association TT3 – no association	Sarzo et al. (2021)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
					TT3 analysis: season of blood collection, educational level, smoking habit, and previous breastfeeding. FT4 analysis: season of blood collection	FT4 – no association	
Thyroid hormone pathway	Maternal blood serum weeks < 13–40 of pregnancy	Alberta, Canada Cross-sectional	478, 32 (mean) years of age Female	PFOA – 2.1 (median) PFOS – 4.8 (median)	All analysis: maternal age, ethnicity and history of smoking. FT4 analysis: diagnosed thyroid condition TSH analysis: history of drug and alcohol use	TSH – no association FT3 – no association FT4 – no association ↑ TSH ($P < 0.05$ for ∑ Br-PFOS, 5m-PFOS and ∑3 m + 4 m PFOS) FT3 – no association FT4 – no association	Reardon et al. (2019)
Thyroid hormone pathway	Maternal blood serum weeks 10–34 of pregnancy	Norway Cross-sectional	375, 32 years median age Female	PFOA – 1.5 (median) PFOS – 8.0 (median)	Parity, age, thyroxin binding capacity and BMI	TSH – no association FT3, TT3 – no association FT4, TT4 – no association ↑ TSH ($P < 0.01$) FT3, TT3 – no association FT4, TT4 – no association	Berg et al. (2015)
Thyroid hormone pathway	Maternal blood serum weeks 24–41 of pregnancy	Sapporo, Hokkaido, Japan Cross-sectional	392, Age: 31.1 (± 7.1) (median (± SD)),	PFOA – 1.2 (median) PFOS – 5.2 (median)	Maternal analysis: maternal age at delivery, BMI before pregnancy, parity, educational level,	TSH – no association FT4 – no association ↓ TSH ($P < 0.001$)	Kato et al. (2016)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
			Female		positive for ATG and/or AMC, intake of seaweed more than once a week, blood sampling period for PFOS and PFOA, and the gestational week at which blood sampling for TSH and FT4 was performed.	FT4 – no association	
Thyroid hormone pathway	Maternal blood serum week 34 of pregnancy	Faroe Islands, Denmark Cross-sectional	172, Age: 28.1 (± 5.6) (mean (± SD)), Female	PFOA – 2.4 (GM) PFOS – 20.9 (GM)	Sex of the fetus, gestational age in weeks, maternal education, maternal pre-pregnancy BMI, parity, smoking status during pregnancy, alcohol consumption during pregnancy, maternal hair-mercury. and maternal serum concentrations of the sum of polychlorinated biphenyl	TSH – no association FT3 – no association FT4, TT4 – no associations TSH – no association FT3 – no association FT4, TT4 – no associations	Xiao et al. (2020)
Thyroid hormone pathway	Maternal blood serum weeks 15–18 of pregnancy	Vancouver, British Columbia, Canada Cross-sectional	152, 25–43 years of age Female	PFOA – 1.7 (median) PFOS – 4.8 (median)	week of gestation and TPOAb status (high vs normal)	In women with high TPOAb: ↑ TSH (P = 0.02) FT4 – no association In women with high TPOAb: ↑ TSH (P = 0.02)	Webster et al. (2014)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Thyroid hormone pathway	Neonatal cord blood serum	Sheyang, China Cross-sectional	490 Female and male neonates	PFOA – 3.3 (median) PFOS – 2.0 (median)	Maternal age, maternal education, pre-pregnancy BMI, family annual income, gestational age at delivery, passive smoking during pregnancy, infant's sex, parity, ln-transformed analyte concentration × infant's sex	FT4 – no association TSH – no association FT3, TT3 – no associations FT4 – no association ↑TT4 ($P < 0.05$ TSH – no association FT3, TT3 – no associations ↑ FT4 ($P < 0.05$) ↑ TT4 ($P < 0.05$)	Guo et al. (2021c)
Thyroid hormone pathway	Neonatal cord blood serum	Shanghai, China Cross-sectional	568 Female and male neonates	PFOA – 7.6 (median) PFOS – 2.5 (median)	Maternal age, fish intake, parity, infant sex, gestational age at delivery and maternal pre-pregnancy BMI	TSH – no association ↓FT3 (−0.068; 0.151,0.015 – males only) ↑ FT4 (0.062; 0.024, 0.138 – males only) ↓ TSH (−0.012; −0.019, −0.005) ↑ FT3 (0.059; 0.023, 0.100) ↑FT4 (0.023; −0.035,0.057 – males only)	Aimuzi et al. (2019)
Thyroid hormone pathway	Neonatal cord serum	Seoul, Cheongju and Gumi, Republic of Korea Cross-sectional	43, Female and male neonates	PFOA – 1.2 (median) PFOS – 1.3 (median)	Maternal age and gestational age for T3. Maternal age, gestational age and	TSH – no associations TT3 – no associations TT4 – no associations TSH – no associations	Kim et al. (2011)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
					maternal BMI for T4 and TSH	TT3 – no associations TT4 – no associations	
Thyroid hormone pathway	Maternal blood serum Week 11.35 (± 3.5) (mean (± SD)) of pregnancy	Sapporo, Hokkaido, Japan Cross-sectional	701, Age: 30.7 (± 4.4) (mean (± SD))	PFOA – 2.0 (median, maternal) PFOS – 6.2 (median, maternal)	Neonate TH analysis, maternal age at delivery, parity, educational level, pre-pregnancy BMI (kg/m^2), alcohol intake during pregnancy, smoking during pregnancy, and logFT4	Neonatal cord blood TSH – no association FT3 – no association FT4 – no association Neonatal Cord blood ↑ TSH ($P < 0.05$ – males only) FT3 – no association FT4 – no association	Itoh et al. (2019)
Thyroid hormone pathway	Maternal blood serum weeks 24–41 of pregnancy	Sapporo, Hokkaido, Japan Cross-sectional	392, Age: 31.1 (± 7.1) (median (± SD)), Female	PFOA – 1.2 (median, maternal) PFOS – 5.2 (median, maternal)	Neonatal analysis: maternal factors [maternal age at delivery, parity, positivity for ATG and/or AMC, blood sampling period for PFOS and PFOA, and log 10 values of TSH and FT4] and infant factors [gestational weeks for birth, low birth weight < 2500 g, and born via Caesarean section].	Neonatal heel stick TSH – no association FT4 – no association Neonatal heel stick ↑ TSH ($P = 0.001$) FT4 – no association	Kato et al. (2016)

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End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Thyroid hormone pathway	Maternal blood serum weeks 12–16 of pregnancy	Shanghai-Minhang, China Cross-sectional	300, Age: 27.5 (± 3.5) (median (± SD)), Female	PFOA – 19.4 (median, maternal) PFOS – 10.5 (median, maternal)	Maternal age at delivery, pre-pregnancy BMI, education, parity, gestational age, delivery type, infant' sex, maternal passive smoking during pregnancy, maternal folic acid supplement, and paternal drinking during 3 months before pregnancy	Neonatal Cord Blood TSH – no association ↑ FT3 ($P < 0.05$) ↑ TT3 ($P < 0.05$) FT4, TT4 – no associations Neonatal Cord Blood TSH – no association ↑ FT3 ($P < 0.05$) ↑ TT3 ($P < 0.05$) FT4, TT4 – no associations	Liang et al. (2020)
Thyroid hormone pathway	Maternal blood serum Week 10 (± 2.2) (mean (± SD)) of pregnancy	Massachusetts, USA Cross-sectional	732, Age: 32.5 (± 4.7) (mean (± SD)), Female	PFOA – 5.6 (median – all maternal samples) PFOA – 5.5 (median – mother:neonate pairs) PFOS – 24.0 (median – all maternal samples) PFOS – 23.5 (median – mother:neonate pairs)	Neonate analysis: maternal age, race/ethnicity, smoking habits, parity, gestational week at blood draw, infant sex, age at heel stick, gestational age, and route of delivery	Neonatal Heel Stick TT4 – no association Neonatal Heel Stick TT4 – no association	Preston et al. (2018)
Thyroid hormone pathway	Maternal blood serum week 34 of pregnancy	Faroe Islands, Denmark Cross-sectional	172, Age: 28.1 (± 5.6) (mean (± SD)), Female	PFOA – 2.4 (GM, maternal)	Sex of the fetus, gestational age in weeks, maternal education, maternal pre-pregnancy BMI, parity,	Neonatal Cord Blood ↑ TSH (40% (95% CI: 8–81%)) FT3 – no association FT4, TT4 – no associations	Xiao et al. (2020)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				PFOS – 20.9 (GM, maternal)	smoking status during pregnancy, alcohol consumption during pregnancy, maternal hair-mercury. and maternal serum concentrations of the sum of polychlorinated biphenyl	Neonatal Cord Blood ↑ TSH (53% (95% CI: 18–99%)) FT3 – no association FT4, TT4 – no associations	
Thyroid hormone pathway	Maternal and neonatal cord blood serum weeks 12–16 of pregnancy	Ohio, USA Cross-sectional	256 (cord), 185 (maternal), 25–35 years of age Female adults Female and male neonates	PFOA – 5.5 (median – maternal) PFOA – 5.6 (median – cord) PFOS – 14.3 (median – maternal) PFOS – 14.3 (median – cord)	Maternal age at delivery, race/ethnicity, marital status at baseline, maternal education level, household income, mean log_{10}-transformed cotinine, maternal alcohol usage during pregnancy, nulliparity, maternal BMI based on pre-pregnancy weight in pounds, the neonate's sex, gestational week at blood draw for PFAS measurement, and delivery mode	Neonatal Cord Blood TSH – no association FT3, TT3 – no associations↓ FT4 ($P < 0.05$, only in those with high maternal TPOAb) TT4 – no association but ↓ TT4 for PFOA+high TPOAb ($P < 0.05$) Neonatal Cord Blood TSH – no association FT3, TT3 – no associations ↓ FT4 ($P < 0.05$, only in those with high maternal TPOAb) TT4 – no association	Lebeaux et al. (2020)
Thyroid hormone pathway	Neonatal cord blood serum	Zwolle, Netherlands Cross-sectional	83, Age: 33.0 (± 4.9) (mean (± SD)),	PFOA – 0.9 (median)	Health problems related to the thyroid gland, use of thyroid medication,	Neonatal Heel Stick ↑ TT4 ($P < 0.05$, females in highest quartile of exposure only)	de Cock et al. (2014)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
			Female and male neonates	PFOS – 1.6 (median)	birth weight, Caesarean section, gestational weight gain, gestational age, parity, smoking, alcohol, maternal BMI, and maternal age at birth	Neonatal Heel Stick TT4 – no association	
Thyroid hormone pathway	Neonatal heel stick blood spot	California, United States Cross-sectional	18 Neonate Female – 9 Male – 9	PFOA – 0.85 PFOS – 0.74	Not adjusted	↑ T4 (0.59 Spearman correlation) ↓ TSH (−0.40 Spearman correlation) ↑ T4 (0.49 Spearman correlation) ↓ TSH (−0.70 Spearman correlation)	Rosen Vollmar et al. (2023)
Androgen/estrogen pathway (child-adult exposure)							
Androgen/estrogen pathway	Blood plasma	San Francisco, California and Cincinnati, OH, United States Longitudinal	704, 6–8 years of age at recruitment Female	PFOA – 6.4 (median, measured at recruitment) PFOS – 13.1 (median, measured at recruitment)	Race, BMI at closest visit before pubertal event, and site	Six months before thelarche Estradiol – no association ↓ Estrone ($P = 0.04$) ↓ Testosterone ($P = 0.03$) ↓ DHEAS ($P < 0.01$) No associations were observed at thelarche or at 6 months or 12 months past thelarche Estradiol – no associations Estrone – no associations Testosterone – no associations DHEAS – no associations	Pinney et al. (2023)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Androgen/estrogen pathway	Blood plasma	Denmark Cross-sectional	1041, 18–21 years of age Male	PFOA – 1.2 (median) PFOS – 3.9 (median)	BMI, smoking status, maternal smoking and family occupational status during pregnancy	LH – no association Estradiol – no association Calculated Free and Total Testosterone – no association LH – no association Estradiol – no association Calculated Free and Total Testosterone – no association	Petersen et al. (2022)
Androgen/estrogen pathway	Blood serum	Shanghai, China Cross-sectional	902, Age: 31.3 (± 3.8) (mean (± SD)), years of age Male	n-PFOA – 24.9 (median) n-PFOS – 13.7 (median)	Age, BMI, education level, family annual income, smoking and drinking status, time of blood collection and whether impregnant before	LH – no association Estradiol – no association Total Testosterone – no association LH – no association ↓ Estradiol ($P < 0.05$) Total Testosterone – no association	Luo et al. (2021)
Androgen/estrogen pathway	Blood serum	Mid-Ohio Valley, USA Cross-sectional	2292, 6–9 years of age Female and male	PFOA – 34.8 (median, male) PFOA – 30.1 (median, female) PFOS – 22.4 (median, male) PFOS – 20.9 (median, female)	Age, month, and time of sampling	Estradiol – no associations ↓ Total Testosterone (−4.9% (−8.7, −0.8) – males only) ↓ Estradiol (−4.0% (−7.7, −0.1) – males only) ↓ Total Testosterone (−5.8% (−9.4, −2.0) – males; −6.6% (−10.1, −2.8) – females)	Lopez-Espinosa et al. (2016)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Androgen/estrogen pathway	Blood serum	Mid-Ohio Valley, USA Cross-sectional	29 957 18–65 years of age Female	PFOA – 17.6 (median, 18 ≤ 42 yr) PFOA – 23.4 (median, > 42 ≤ 51 yr) PFOA – 32.5 (median, > 51 ≤ 65 yr) PFOS – 15.0 (median, 18 ≤ 42 yr) PFOS – 16.2 (median, > 42 ≤ 51 yr) PFOS – 21.5 (median, > 51 ≤ 65 yr)	Age, BMI, alcohol consumption, smoking, and exercise	Estradiol – no associations ↓ Estradiol ($P < 0.0001$, > 42 ≤ 51 yr; $P = 0.007$, > 51 ≤ 65 yr)	Knox et al. (2011)
Androgen/estrogen pathway	Blood serum	Faroe Islands, Denmark	263, 24–26 years of age Male	PFOA – 2.8 (median) PFOS – 19.5 (median)	Age, BMI groups, current smoking, time of sampling (not for LH)	LH – no association Total testosterone – no association Free testosterone – no association Estradiol – no association ↑ LH ($P = 0.04$) Total testosterone – no association Free testosterone – no association Estradiol – no association	Petersen et al. (2018)
Androgen/estrogen pathway	Blood serum	United States, Cross-sectional (NHANES 2011–2012)	1682, 41 years of age (median)	PFOA Female/Male age 12–19 – 1.5/1.9 (median) PFOA Female/Male age 20–39 – 1.5/2.4 (median)	Age, BMI, poverty income ratio, serum cotinine, and race/ethnicity	Female Total testosterone – no association Male	Lewis et al. (2015)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
			Female and males	PFOA Female/Male age 40–59 – 1.6/2.3 (median) PFOA Female/Male age 60–80 – 2.6/2.5 (median) PFOS Female/Male age 12–19 – 3.8/4.6 (median) PFOS Female/Male age 20–39 – 4.2/7.8 (median) PFOS Female/Male age 40–59 – 5.0/9.3 (median) PFOS Female/Male age 60–80 – 9.5/11.1 (median)		Total testosterone – no association Female Total testosterone – no association Male Total testosterone – no association	
Androgen/estrogen pathway	Blood serum	United States NHANES (2015–2016) Cross-sectional	1886, 17.50% (n = 330) between 12–19, 41.62% (n = 785) between 20–49 40.88% (n = 771) ≥ 50 years old Female and male	PFOA Female/Male age 12–19 – 1.0/1.3 (median) PFOA Female/Male age 20–49 – 1.0/1.8 (median) PFOA Female/Male, age ≥ 50 – 1.8/2.1 (median) PFOS Female/Male age 12–19 – 1.7/2.4 (median) PFOS Female/Male age 20–49 – 2.0/3.7 (median) PFOS Female/Male age ≥ 50 – 4.0/5.6 (median)	Age, race, BMI, education, ratio of family income to poverty, cotinine, age at menarche, and use of contraceptives	Estradiol ↓ (P = 0.027, Females, age 20–49) Free and Total Testosterone – no associations Estradiol ↑ (P = 0.049, in Q2 only in females age 20–49) ↑ Free and Total Testosterone (P = 0.01, P = 0.001 – males only)	Xie et al. (2021)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Androgen/estrogen pathway	Blood serum	United States Cross-sectional	1371, 47–52 years of age Female	n-PFOA – 4.1 (median) Total PFOS – 24.9 (median)	Age, site, race/ethnicity, smoking status, menopausal status, parity, and BMI.	Estradiol – no association Total Testosterone – no association Estradiol – no association Total Testosterone – no association	Harlow et al. (2021)
Androgen/estrogen pathway	Blood serum	Taipei, Taiwan, China Cross-sectional	225, 13–15 years of age Female and male	PFOA – 0.5 (median, male) PFOA – 0.5 (median, female) PFOS – 29.9 (median, male) PFOS – 28.8 (median, female)	Age, sex, BMI, environmental tobacco smoke exposure, parental education, regular exercise, and month of survey.	↑ Estradiol (0.09 pmol/L (0.02, 0.17) – males only) Total Testosterone – no associations Estradiol – no associations ↓ Total Testosterone (−0.003 nmol/L (−0.006, −0.0003) – males only)	Zhou et al. (2016)
Androgen/estrogen pathway	Blood serum	Taipei, Taiwan, China Cross-sectional	456, 10–15 years of age Female and male (cohort overlaps with Zhou et al., 2016)	PFOA – 1.2 (median, with asthma) PFOA – 0.5 (median, without asthma) PFOS – 33.9 (median, with asthma) PFOS – 28.9 (median, without asthma)	Age, sex, BMI, parental education, environmental tobacco smoke exposure, physical activity, and month of survey	↑ Estradiol (0.05 pmol/L (0.02, 0.09) –adolescents with asthma only) ↓ Total Testosterone (−0.04 nmol/L (−0.07, −0.001) – adolescents with asthma only ↑ Estradiol (0.001 pmol/L (0.000, 0.003) –adolescents with asthma only) ↓ Total Testosterone (−0.004 nmol/L (−0.005, −0.003) – adolescents with asthma only	Zhou et al. (2017)
Androgen/estrogen pathway	Blood plasma	Taipei, Taiwan, China	540,	PFOA – 2.7 (GM)	Age, gender, BMI, and high fat diet	LH – no associations	Tsai et al. (2015)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
		Cross-sectional	12–30 years of age Female and male	PFOS – 7.8 (GM)		Estradiol – no associations Free and Testosterone – no associations LH – no associations Estradiol – no associations ↓ Total Testosterone ($P < 0.05$ – Females age 12–17 only) Free Testosterone – no association	
Androgen/estrogen pathway	Blood serum	Nanjing, China Cross-sectional	651, Age: 29.4 (± 5.4) (mean (± SD)), Male	PFOA – 8.6 (median) PFOS – 9.9 (median)	Age, BMI, smoking status, blood sampling time, and fasting status	LH – no association Estradiol – no association ↓ Free and Total Testosterone ($P = 0.015$, $P = 0.008$) LH – no association Estradiol – no association ↓ Total Testosterone ($P = 0.04$) Free Testosterone – no association	Cui et al. (2020)
Androgen/estrogen pathway	Blood serum	Denmark Cross-sectional	247, Age: 19.6 (± 1.4) (mean (± SD)), Male	PFOA – 3.0 (median) PFOS – 7.8 (median)	BMI and smoking	LH – no association Estradiol – no association Calculated Free and Total Testosterone – no association LH – no association Estradiol – no association	Joensen et al. (2013)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Androgen/estrogen pathway	Blood plasma	North Carolina, USA Cross-sectional	250, 30–66 years of age Male	PFOA – 9.2 (median) PFOS – 32.3 (median)	Not adjusted	↓ Calculated Free and Total Testosterone ($P < 0.05$, $P < 0.05$) ↑ LH ($P = 0.011$) ↑ Free Testosterone ($P = 0.015$) Total Testosterone – no association Estradiol – no association LH – no association Free Testosterone – no association Total Testosterone – no association Estradiol – no association	Raymer et al. (2012)
Androgen/estrogen pathway	Blood serum	Denmark Cross-sectional	105, 18–25 years of age Male	PFOA – 4.9 (median) PFOS – 24.5 (median)	Time of blood sampling	LH – no association Estradiol – no association Calculated Free and Total Testosterone – no association LH – no association Estradiol – no association Calculated Free and Total Testosterone – no association	Joensen et al. (2009)
Androgen/ estrogen pathway	Blood serum	Hull, United Kingdom Cross-sectional	59, Age: 32.9 (± 4.6) (mean (± SD)), Female	PFOA – 2.4 (median, controls) PFOA – 2.4 (median, PCOS cases)	Serum albumin	Estradiol – no association ↑ Total Testosterone ($P < 0.01$) Androstenedione – no association	Heffernan et al. (2018)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				PFOS – 3.1 (median, controls) PFOS – 3.9 (median, PCOS cases)		Estradiol – no association Total Testosterone – no association Androstenedione – no association	
Androgen/ estrogen pathway	Blood serum	United States NHANES (2013–2016) Cross-sectional	706, 63 (median) years of age Female (post-menopause)	n-PFOA – 2.0 (median) n-PFOS – 4.2 (median) Sm-PFOS – 1.9 (median)	Age, race/ethnicity, BMI, education level, smoking, drinking, serum albumin, parity, time since menopause, type of menopause, NHANES survey cycle	Estradiol – no association ↑ Free and Total Testosterone ($P < 0.05$, $P < 0.05$) Estradiol – no association ↑ Free and Total Testosterone ($P < 0.05$, $P < 0.05$)	Wang et al. (2021b)
Androgen/estrogen pathway	Blood serum	Tromsø, Norway, Cross-sectional	178, 25–35 years of age Female	PFOA – 3.4 (median, nulliparous) PFOA – 2.0 (median, parous) PFOS – 14.8 (median, nulliparous) PFOS – 12.7 (median, parous)	Age, marital status, parity (parous/nulliparous), BMI, physical activity, history of hormonal contraceptive use, alcohol use, and smoking	Saliva Follicular estradiol – no association Saliva Follicular estradiol – no association	Barrett et al. (2015)
Androgen/estrogen pathway	Blood serum	Italy Cross-sectional	111, 18–40 years of age Female	PFOA – levels not reported PFOS – levels not reported	Not applied	White blood cells (mRNA expression level) Estrogen receptors α/β – no association Androgen receptor – no association White blood cells (mRNA expression level)	Caserta et al. (2013)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						Estrogen receptors α/β – no association ↑ Androgen receptor ($P < 0.05$, infertile)	
Androgen/estrogen pathway	Blood serum	Italy Cross-sectional	153, 27–40 years of age Male	PFOA – < 0.4 (median, fertile and infertile) PFOS – < 0.4 (median, fertile and infertile)	Not applied	White blood cells (mRNA expression level) ↓ Estrogen receptors α/β ($P < 0.05$, fertile and infertile) ↓ Androgen receptor ($P < 0.05$, fertile and infertile) White blood cells (mRNA expression level) Estrogen receptors α/β – no association Androgen receptor – no association	La Rocca et al. (2015)
Androgen/estrogen pathway	Maternal amniotic fluid weeks 14–18 of pregnancy	Denmark Cross-sectional	545, Age: 32.6 (± 5.3) (mean (± SD)), Maternal: Female Child: Male	PFOS – 1.1 (median, maternal)	Gestational age of amniocentesis, maternal age, smoking (cotinine groups), and case or control status	Amniotic fluid ↑ Total Testosterone ($P = 0.002$) ↑ Androstenedione ($P = 0.001$) ↑ Progesterone ($P = 0.001$) ↑ 17-Hydroxyprogesterone ($P < 0.001$)	Toft et al. (2016)
Androgen/estrogen pathway	Maternal blood serum	Shandong, China Cross-sectional	349, Age: 28.4 (± 4.1) (mean (± SD))	PFOA – 42.8 (median, maternal)	Maternal age, maternal education, maternal BMI before pregnancy, parity for maternal	Neonatal cord blood ↑ Estradiol ($P < 0.05$) Total Testosterone – no association	Yao et al. (2021)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
	3 days before delivery			PFOS – 4.6 (median, maternal)	PFAS associations, and paternal age, paternal education, paternal BMI	Neonatal cord blood Estradiol – no association Total Testosterone – no association	
Androgen/estrogen pathway	Maternal blood serum 30–37 weeks of pregnancy	Sapporo, Hokkaido, Japan Cross-sectional	224, Age: 30.0 (± 4.8) (mean (± SD))	PFOA – 1.4 (median, maternal) PFOS – 5.0 (median, maternal)	Maternal age, maternal smoking during the third trimester, maternal alcohol consumption during pregnancy, annual household income, parity, infant sex, maternal blood sampling periods, and infant birth weight	Neonatal cord blood Estradiol – no association Total Testosterone – no association DHEA – no association Androstenedione – no association Neonatal cord blood ↑ Estradiol (P = 0.04) Total Testosterone – no association ↑ DHEA (P < 0.001) Androstenedione – no association	Kobayashi et al. (2021b)
Androgen/estrogen pathway	Neonatal cord blood serum	Hubei, China Cross-sectional	942, Age: 28.1 (± 3.3) (mean (± SD)), Female and male neonates	PFOA – 1.6 (median) PFOS – 4.1 (median)	Maternal age, pre-pregnancy BMI, maternal education, annual household income, parity, passive smoking during pregnancy, neonatal sex.	Neonatal cord blood ↑ Estrone (P = 0.003) ↑ Estradiol (P = 0.0001) ↑ Estriol (P = 0.003) Neonatal cord blood ↑ Estrone (P = 0.005) ↑ Estradiol (P = 0.002) Estriol – no association	Liu et al. (2021)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Androgen/estrogen pathway	Neonatal cord blood serum	Hebei, China Cross-sectional	424, 20–40 years of age Female and male neonates	PFOA – 2.0 (median) PFOS – 0.7 (median)	Pregnant age, family income, maternal education level, maternal career, husband's smoking, energy daily intake, daily physical activity, gestational age, parity, pre-pregnancy maternal BMI, gestational diabetes mellitus, infant sex, delivery mode, and gestational weight gain	Neonatal cord blood ↑ Estrone (P = 0.051) Estradiol – no association Estriol – no association Neonatal cord blood ↑ Estrone (P = 0.006) Estradiol – no association ↑ Estriol (P < 0.001)	Wang et al. (2019)
Androgen/estrogen pathway	Neonatal cord blood serum	Shandong, China Cross-sectional	351, Age: 28.4 (± 4.2) (mean (± SD)), Female and male neonates	PFOA – 34.7 (median) PFOS – 1.4 (median)	Maternal age, pre-pregnancy BMI, parity, infant gender, mode of delivery, passive smoking during pregnancy, gestational age and household income level	Neonatal cord blood Total testosterone – no association ↑ Estradiol (P < 0.01) Neonatal cord blood ↑ Total testosterone (P < 0.01) Estradiol – no association	Yao et al. (2019)
Androgen/estrogen pathway (Pre-natal Exposure)							
Androgen/estrogen pathway	Maternal blood serum After 2nd trimester	Sapporo, Hokkaido, Japan Cross-sectional	185, Age: 29.7 (± 4.7) (mean (± SD)), Maternal: Female Neonates: Female and male	PFOA – 1.4 (median – maternal) PFOS – 5.2 (median – maternal)	Gestational age, maternal age, parity, smoking and caffeine intake during pregnancy, maternal educational level, and blood sampling period	Neonatal Cord Blood ↓ DHEA (P = 0.010) Androstenedione – no association Neonatal Cord Blood ↑ DHEA (P = 0.004)	Goudarzi et al. (2017b)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						Androstenedione – no association	
Androgen/estrogen pathway	Maternal blood serum 25–41 weeks of pregnancy	Hokkaido, Japan Cross-sectional	1024, Age: 31.1 (± 4.2) (mean (± SD))	PFOA – 2.0 (median, maternal)	Sex, birth weight, maternal age, parity, alcohol consumption, and smoking in the first trimester	Neonate ↑ 2 digit:4 digit length ($P < 0.05$, males only) an indicator of estrogenic exposure with 2D:4D being higher in females	Nishimura et al. (2022)
				PFOS – 6.1 (median, maternal)		Neonate 2D:4D – no association	
Androgen/estrogen pathway	Maternal blood plasma < Week 12 of pregnancy	Canada Cross-sectional	403, Age: 31.3 (± 4.8) (mean (± SD)), Maternal: Female Neonates: Female and male	PFOA – 1.7 (geometric mean, maternal)	Household income, active smoking status during pregnancy and gestational age	Neonate Anogenital distance – no associations An indicator of androgen exposures with AGD being longer in males	Arbuckle et al. (2020)
				PFOS – 4.4 (geometric mean, maternal)		Neonate Anogenital distance – no associations	
Androgen/estrogen pathway	Maternal blood serum weeks 10–15 of pregnancy	Odense, Denmark Cross-sectional	373, Age: 30.1 (± 4.4) (mean (± SD)), Maternal: Female Child: Female and male	PFOA – 1.7 (median – female, maternal) PFOA – 1.6 (median – male, maternal)	Age of the child at examination time, maternal parity, and sex of the child	Child serum (4 months of age) LH – no association DHEA- no association Androstenedione – no association DHEAS – no association 17-Hydroxyprogesterone – no association	Jensen et al. (2020)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				PFOS – 8.1 (median – female, maternal) PFOS – 8.3 (median – male, maternal)		Child serum (4 months of age) LH – no association DHEA- no association Androstenedione – no association DHEAS – no association 17-Hydroxyprogesterone – no association	
Androgen/estrogen pathway	Maternal blood serum 11–28 weeks of pregnancy	Avon, United Kingdom Cross-sectional	72, 15 years of age Female (daughters)	PFOA – 3.6 (median, maternal) PFOS – 19.2 (median, maternal)	SHBG concentration, maternal education, maternal age at delivery, maternal pre-pregnancy BMI, maternal smoking during pregnancy, time of day daughter's blood sample was obtained, daughter's age at menarche, and daughter's BMI at 15 years	Adolescent daughter ↑ Total Testosterone (0.24 nmol/L; 0.05, 0.43) Adolescent daughter ↑ Total Testosterone (0.18 nmol/L; 0.01, 0.35)	Maisonet et al. (2015)
Androgen/estrogen pathway	Maternal blood serum 30 weeks of pregnancy	Aarhus, Denmark Cross-sectional	343, 19–20 years of age Female (daughters)	PFOA – 3.6 (median, maternal)	Smoking during pregnancy, social class, daughter's BMI and daughter's smoking. LH and estradiol were additionally adjusted for menstrual cycle phase	Young adult daughter (using or not using hormonal contraception) LH – no association Total Testosterone – no association DHEAS – no association Estradiol – no association	Kristensen et al. (2013)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				PFOS – 21.1 (median, maternal)		Young adult daughter (using or not using hormonal contraception) LH – no association Total Testosterone – no association DHEAS – no association Estradiol – no association	
Androgen/estrogen pathway	Maternal blood serum Weeks 30 of pregnancy	Aarhus, Denmark Cross-sectional	169, 19–21 years of age Male	PFOA – 3.8 (median, maternal) PFOS – 21.2 (median, maternal)	History of reproductive tract disease, son's BMI, son's smoking status, maternal smoking during pregnancy, and socioeconomic status	Young adult son ↑ LH (P = 0.03) Estradiol – no association Testosterone – no association Young adult son LH – no association Estradiol – no association Testosterone – no association	Vested et al. (2013)
Progesterone pathway (pregnancy and pre-natal exposures)							
Progesterone	Blood serum	Tromsø, Norway, Cross-sectional	178, 25–35 years of age Female	PFOA – 3.4 (median, nulliparous) PFOA – 2.0 (median, parous) PFOS – 14.8 (median, nulliparous) PFOS – 12.7 (median, parous)	Age, marital status, parity (parous/nulliparous), BMI, physical activity, history of hormonal contraceptive use, alcohol use, and smoking	Saliva Luteal progesterone – no association Saliva ↓ Luteal progesterone	Barrett et al. (2015)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						(β, 0.472, 95% CI; 0.043, 0.987) (nulliparous women only) (P = 0.04)	
Progesterone	Maternal amniotic fluid Weeks 14–18 of pregnancy	Denmark Cross-sectional	545, Age: 32.6 (± 5.3) (mean (± SD)), Maternal: Female Child: Male	PFOS – 1.1 (median)	Gestational age of amniocentesis, maternal age, smoking (cotinine groups), and case or control status	Amniotic Fluid ↑ Progesterone (P = 0.001)	Toft et al. (2016)
Progesterone	Maternal blood serum 33.2 (± 3.7) (mean (± SD) weeks of pregnancy	Sapporo, Hokkaido, Japan Cross-sectional	224, Age: 30.0 (± 4.8) (mean (± SD))	PFOA – 1.4 (median, maternal) PFOS – 5.0 (median, maternal)	Maternal age, maternal smoking during the third trimester, maternal alcohol consumption during pregnancy, annual household income, parity, infant sex, maternal blood sampling periods, and infant birth weight	Neonatal cord blood Progesterone – no association Neonatal cord blood ↓ Progesterone (P < 0.001)	Kobayashi et al. (2021b)
Progesterone	Maternal blood serum 3rd trimester	Sapporo, Hokkaido, Japan Cross-sectional	189, Age: 29.3 (± 4.8) (mean (± SD)), Maternal: Female Neonate: Female and male	PFOA – 1.7 (median – primiparous) PFOA – 1.0 (median – multiparous) PFOS – 5.7 (median – primiparous)	Maternal factors (age, parity, BMI before pregnancy, annual income, smoking during pregnancy, caffeine consumption during pregnancy, and gestational weeks of blood sampling for	Neonatal cord blood ↓ Progesterone (P = 0.002, females) (P = 0.043, males) Neonatal cord blood Progesterone – no associations	Itoh et al. (2016)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
				PFOS – 4.8 (median – multiparous)	PFOS/PFOA measurement) and infant factors (gestational age at birth)		
Progesterone	Neonatal cord blood serum	Wuhan, China Cross-sectional	374, Age: 27.6 (± 2.9) (mean (± SD)), Female and male neonates	PFOA – 1.7 (median) PFOS – 4.2 (median)	Maternal age at delivery, pre-pregnancy BMI, maternal education status, passive smoking during pregnancy, parity, neonatal gender, gestational weeks and sample-collecting time	Neonatal cord blood Progesterone – no association 17-Hydroxyprogesterone – no association Neonatal cord blood Progesterone – no association 17-Hydroxyprogesterone – no association	Liu et al. (2020b)
Progesterone	Neonatal cord blood plasma	Flanders, Belgium Cross-sectional	170, Age 30 (average) Female and male neonates	PFOA – 1.6 (median) PFOS – 2.7 (median)	Not applied	White blood cells ↑ in progesterone receptor-mediated gene expression White blood cells ↑ in progesterone receptor-mediated gene expression	Remy et al. (2016)
Glucocorticoid pathway (pregnancy and pre-natal exposures)							
Glucocorticoid	Maternal blood serum 1st trimester	Odense, Sweden Cross-sectional	1048, Age: 30.2 (± 4.5) (mean (± SD)), Female	PFOA – 1.6 (median, maternal) PFOS – 7.6 (median, maternal)	Age, parity, and offspring sex	Urine collected at GW 27–28 Cortisol – no association Cortisone – no association Cortisol – no association ↓ Cortisone ($P < 0.01$)	Dreyer et al. (2020)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Glucocorticoid	Maternal amniotic fluid Weeks 14–18 of pregnancy	Denmark Cross-sectional	545, Age: 32.6 (± 5.3) (mean (± SD)), Maternal: Female Fetus: Male	PFOS – 1.1 (median)	Gestational age of amniocentesis, maternal age, smoking (cotinine groups), and case or control status	Amniotic Fluid ↑ Cortisol ($P < 0.001$)	Toft et al. (2016)
Glucocorticoid	Maternal blood serum After the 2nd trimester	Sapporo, Hokkaido, Japan Cross-sectional	185, Age: 29.7 (± 4.7) (mean (± SD)), Maternal: Female Neonate: Female and male	PFOA – 1.4 (median – maternal) PFOS – 5.2 (median – maternal)	Gestational age, maternal age, parity, smoking and caffeine intake during pregnancy, maternal educational level, and blood sampling period	Neonatal Cord Blood Cortisol – no association Cortisone – no association Cortisol/Cortisone – no association Neonatal Cord Blood ↓ Cortisol ($P < 0.001$) ↓ Cortisone ($P < 0.001$) ↓ Cortisol/Cortisone ($P = 0.03$)	Goudarzi et al. (2017b)
Glucocorticoid	Neonatal cord blood serum	Wuhan, China Cross-sectional	374, Age: 27.6 (± 2.9) (mean (± SD)), Female and male neonates	PFOA – 1.7 (median, maternal) PFOS – 4.2 (median, maternal)	maternal age at delivery, pre-pregnancy BMI, maternal education status, passive smoking during pregnancy, parity, neonatal gender, gestational weeks and sample-collecting time	Neonatal cord blood ↑ 11-Deoxycortisol ($P < 0.01$) Cortisol – no association Cortisone – no association Neonatal cord blood ↑ 11-Deoxycortisol ($P = 0.03$) Cortisol – no association Cortisone – no association	Liu et al. (2020b)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
Other nuclear receptors (all exposures)							
Vitamin D receptor	Blood serum	United States NHANES (2003–2010) Cross-sectional	7040, Age 12–19 – 14% Age 20–59 – 67% Age 60+ – 20% Female and male	PFOA – 3.9 (median) PFOS – 15.1 (median)	gender, age, race/ethnicity, family income to poverty ratio category, BMI category, vitamin D supplement use, smoking status, and six-month examination period	Total serum 25-hydroxyvitamin D – no association ↓ Total serum 25-hydroxyvitamin D (−0.9 nmol/L; −1.5, −0.2)	Etzel et al. (2019)
Vitamin D receptor	Blood serum	Ohio, USA Cross-sectional	48, 8–12 years of age Female and male	PFOA – 1 (median) PFOS – 2.8 (median)	Age, sex, and race	Total serum 25-hydroxyvitamin D – no association Total serum 25-hydroxyvitamin D – no association	Khalil et al. (2018)
Vitamin D receptor	Pregnancy blood serum 1st trimester: 8–14 weeks of pregnancy 2nd trimester: 24–30 weeks of pregnancy	Georgia, United States Cross-sectional	442, 18–40 years of age Female	PFOA – 0.7 (median) PFOS – 2.2 (median)	Maternal age, education, BMI, parity, fetal sex, tobacco use, marijuana use, and season of sample collection for 25(OH)D, and PFAS × fetal sex interaction	1st trimester Total serum 25-hydroxyvitamin D – no associations Free serum 25-hydroxyvitamin D – no associations 2nd trimester ↑ Total serum 25-hydroxyvitamin D (P < 0.01, male pregnancies only) ↑ Free serum 25-hydroxyvitamin D (P = 0.03, male pregnancies only) 1st trimester ↑ Total serum 25-hydroxyvitamin D (P < 0.01, all pregnancies)	Chang et al. (2021)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						Free serum 25-hydroxyvitamin D – no associations 2nd trimester ↑ Total serum 25-hydroxyvitamin D ($P \leq 0.01$, all pregnancies) ↑ Free serum 25-hydroxyvitamin D ($P = 0.02$, male pregnancies only)	
Vitamin D receptor	Neonatal cord blood serum	Wuhan, China Cross-sectional	992, Age: 28.2 (± 3.3) (mean (± SD)), Female and male neonates	PFOA – 1.6 (median) PFOS – 4.0 (median)	Maternal age at delivery, pre-pregnancy BMI, maternal education status, annual household income, parity, passive smoking, hypertensive disorders of pregnancy, gestational diabetes mellitus, neonatal sex and birth seasons	Total serum 25-hydroxyvitamin D – no association ↑ Total serum 25-hydroxyvitamin D ($P < 0.05$)	Liu et al. (2023c)
Other nuclear receptors	Blood serum	Italy Cross-sectional	154 (111 infertile + 44 fertile) 18–40 years of age Female	PFOA – levels not reported PFOS – levels not reported	Not applied	White blood cells (mRNA expression level) ↓ Pregnane X receptor ($P < 0.05$, fertile) PPARγ – no association ↓ Aryl Hydrocarbon receptor ($P < 0.05$, infertile) White blood cells (mRNA expression level)	Caserta et al. (2013)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
						↑ Pregnane X receptor ($P < 0.05$, infertile)	
						PPARγ – no association	
						Aryl Hydrocarbon receptor – no association	
Other nuclear receptors	Blood serum	Italy Cross-sectional	153, 27–40 years of age Male	PFOA – < 0.4 (median, fertile and infertile)	Not applied	White blood cells (mRNA expression level)	La Rocca et al. (2015)
						↓ Pregnane X receptor ($P < 0.05$, fertile and infertile)	
						PPARγ – no association	
						↓ Aryl Hydrocarbon receptor ($P < 0.05$, fertile and infertile)	
				PFOS – < 0.4 (median, fertile and infertile)		White blood cells (mRNA expression level)	
						Pregnane X receptor – no association	
						PPARγ – no association	
						Aryl Hydrocarbon – no association	
Other nuclear receptors	Blood serum	Mid-Ohio Valley, USA Cross-sectional	290, Age (female): 43.7 (± 11.3) (mean (± SD)), Age (male): 44.5 (± 10.9) (mean (± SD)),	PFOA – 25.5 (geomean, female) PFOA – 40.9 (geomean, male)	Age, sex, socioeconomic status as measured by average household income, BMI and smoking status,	White blood cells (mRNA expression level)	Fletcher et al. (2013)
						Liver X Receptor α – no association	
						↓ Liver X Receptor β ($P = 0.002$)	
						PPARα – no association	
						PPAR β/δ – no association	

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
			Female and Male			PPAR γ – no association	
				PFOS – 5.5 (geomean, female)		White blood cells (mRNA expression level)	
				PFOS – 8.3 (geomean, male)		↓ Liver X Receptor α (P = 0.04)	
						Liver X Receptor β – no association	
						PPARα – no association	
						PPAR β/δ – no association	
						PPAR γ – no association	
Not informative studies							
PPARs: PPARγC1A and PPARδ	Maternal blood serum 2nd trimester	Sapporo, Hokkaido, Japan Cross-sectional	504, Age: 30.4 (± 4.9) (mean (± SD)), Female	PFOA – 1.4 (median)	Maternal age, maternal smoking during the 3rd trimester, maternal alcohol consumption during pregnancy, annual household income, parity, and sampling period	Serum fatty acids (Palmitic acid, Palmitoleic acid, Steric acid, Oleic acid, Linoleic acid) – no associations	Kobayashi et al. (2021a)
				PFOS – 5.4 (median)		↓ Palmitic acid (P < 0.001)	
						↓ Palmitoleic acid (P < 0.001)	
						Steric acid – no association	
						↓ Oleic acid (P < 0.001)	
						Linoleic acid – no association	
						* interaction with the *PPARD* allele (A > G; rs2267668) and reductions in palmitic and oleic acid	
Parathyroid hormone receptor	Blood serum	Mid-Ohio Valley, USA	189,	PFOA – 24.6 (geomean)	Age, sex, BMI, average household family	White blood cells (mRNA expression level)	Galloway et al. (2015)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
		Cross-sectional	38 years of age (geomean) Female	PFOS – 5.5 (geomean)	income and smoking status ("ever" smokers versus "never" smokers).	↓ *PTH2R (P = 0.017)* White blood cells (mRNA expression level) ↓ *PTH2R (P = 0.006)*	
Thyroid hormone pathway	Blood serum	Liege, Belgium Case–control	78 17–74 years of age Female and male	PFOA – 1.6 (median)	Age, sex, smoking status, BMI, and delay (in months) between sampling and start of the recruitment	↓ risk of hyperthyroidism (OR – 0.19) ↓ risk of hypothyroidism (OR – 0.18)	Dufour et al. (2020)
				PFOS – 3.6 (median)	Age, sex, smoking status, BMI, and delay (in months) between sampling and start of the recruitment	↓ risk of hyperthyroidism (OR – 0.19) Hypothyroidism – no relationship	
Thyroid hormone pathway	Blood serum	Seoul, Republic of Korea Cross-sectional	40 (27 infants with congenital hypothyroidism + 13 control group infants) 1–3 months of age Sex not indicated	PFOA (mean) Control group infants: 2.1 infants with congenital hypothyroidism: 5.4 PFOS (mean) Control group infants: 4.1 Infants with congenital hypothyroidism: 5.3	No adjustments reported	↓ in thyroid stimulating immunoglobulin in infants with congenital hypothyroidism. No associations with TSH, TT3, or FT4 PFOS did not appear in the analytical table	Kim et al. (2016c)
Androgen/estrogen pathway	Blood serum	Nanjing, China Cross-sectional	240 (120 healthy + 120 with premature ovarian insufficiency)	PFOA (median) POI: 11.1 Control group: 8.4	Age, BMI, education, income, sleep, and parity	Women with POI: ↑ PRL ($P < 0.05$) T – no association	Zhang et al. (2018)

Table S4.23 End-points relevant to modulation of receptor-mediated effects in humans exposed to PFOA or PFOS

End-point	Biosample type	Location, setting/study design	Study participants	Geometric Mean/Median PFAS Concentration (ng/mL)	Covariates adjusted for	Associations	Reference
			20–40 years of age			The control group did not show an association with sexual hormones	
				PFOS (median)		Women with POI:	
				POI: 8.2		↑ PRL ($P < 0.05$)	
				Control group: 6.0		↓ E2 ($P < 0.05$)	
						↑ FSH ($P < 0.05$)	
						T – No association	
						The control group did not show an association with sexual hormones	
Androgen/estrogen pathway	Maternal blood serum 21(± 1.8) (mean ((± SD)) weeks of pregnancy	New York, USA Cross-sectional	285, Age: 29.5 (± 5) (mean (± SD))	PFOA – 0.6 (median)	Maternal age, race, parity, education, pre pregnancy BMI, and gestational age at sample collection	Longitudinal analysis of sex hormones (total T, free T, E1, E2, E3) all crossed the null. No p values reported.	Rivera-Núñez et al. (2023)
				PFOS – 2.5 (median)		Longitudinal analysis of sex hormones (total T, free T, E1, E2, E3) all crossed the null. No p values reported.	

AR, androgen receptor; ARE, antioxidant responsive element; AMC, antimicrosomal antibody; ATG, antithyroglobulin antibody; BMI, body mass index; DHEA, dehydroepiandrosterone; DHEAS, dihydroepiandrosterone sulfate; E1, estrone; E2, estradiol; E3, estriol; EC_{20}, 20% effective concentration; EC_{50}, half-maximal effective concentration; GM, geometric mean; IC_{50}, half-maximal inhibitory concentration; LEC, lowest effective concentration; LH, luteinizing hormone; NHANES, National Health and Nutrition Examination Survey; NA, not applicable; 25(OH)D, 25-hydroxy vitamin D; OH, Ohio; PCB, polychlorinated biphenyl, PFAS, per- and polyfluoroalkyl substances; PFOA, perfluorooctanoic acid; PFOS, perfluorooctanesulfonic acid; POI, premature ovarian insufficiency; PPAR, peroxisome proliferator-activated receptor; PRL, prolactin; SD, standard deviation; SHBG, sex hormone-binding globulin; T, testosterone; TH, thyroid hormone; TPOAb, thyroid peroxidase antibodies; TSH, thyroid-stimulating hormone; FT3, free triiodothyronine; FT4, free thyroxine; TT4, total thyroxine; T3, triiodothyronine; UK, United Kingdom; USA, United States of America.

[a] ↓, decrease; ↑, increase. No association is defined as no statistically significant association ($P > 0.05$). When P-values were not reported, β estimates with confidence intervals are provided (β estimate; CI).