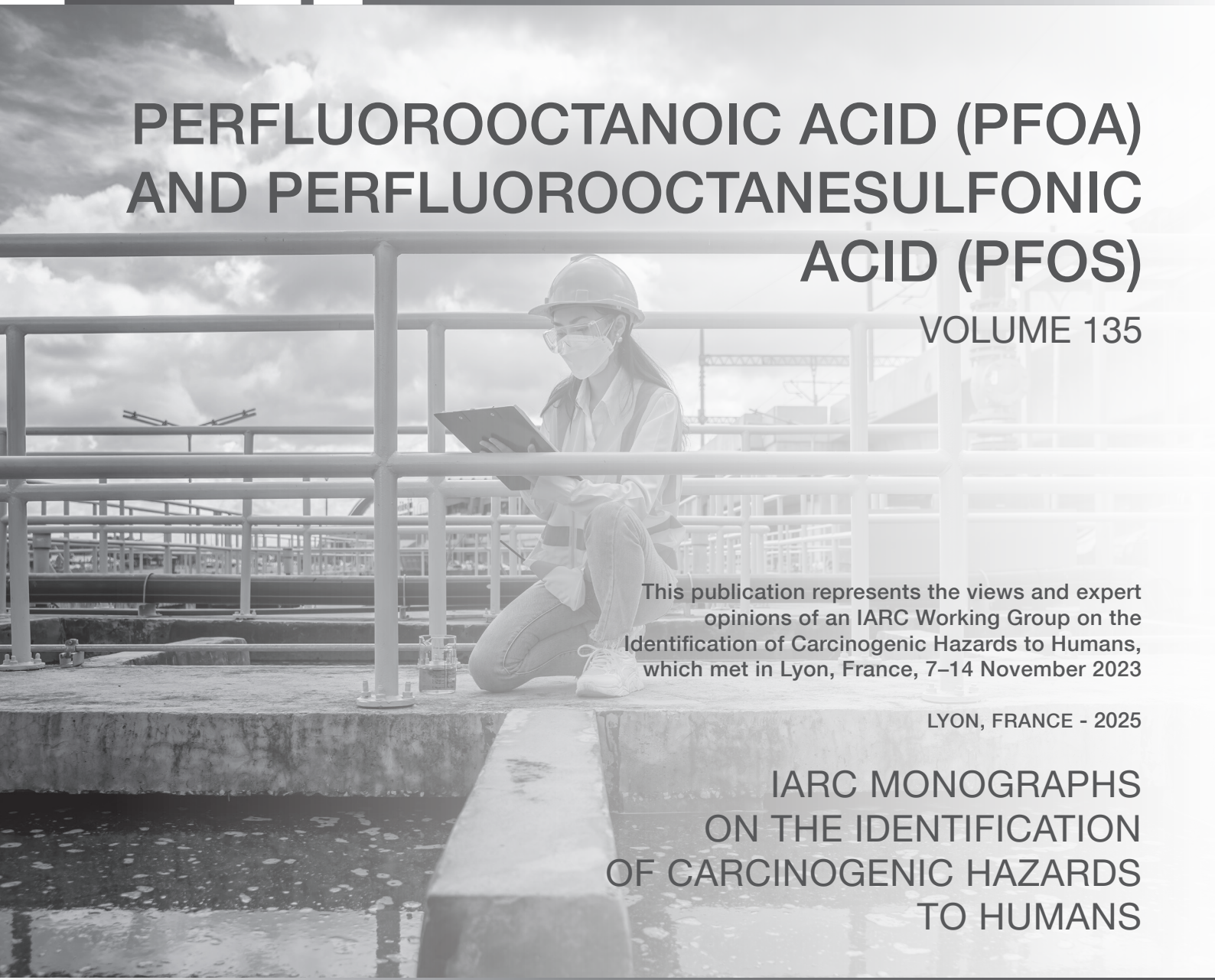
IARC MONOGRAPHS



PERFLUOROOCTANOIC ACID (PFOA) AND PERFLUOROOCTANESULFONIC ACID (PFOS)

VOLUME 135

This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met in Lyon, France, 7–14 November 2023

LYON, FRANCE - 2025

IARC MONOGRAPHS ON THE IDENTIFICATION OF CARCINOGENIC HAZARDS TO HUMANS

International Agency for Research on Cancer

World Health Organization

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
Bonefeld-Jørgensen et al. (2011) Breast cancer	Case–control One hospital in Greenland	Cases (n = 31) were Inuit women admitted to a hospital in Nuuk, Greenland, where all breast cancer cases in Greenland are registered. Controls (n = 115) were Inuit women who were frequency matched with the cases on age and districts. Controls were selected from two cross sectional studies. Serum measurements of all subjects.	Blood collection 2000–2003 at diagnosis (cases) or enrolment (controls).	PFAS measured; PFOS, PFOA, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFHxS, PFOSA Correlations between total perfluoro sulfonic acids (PFSA) and total perfluoro carboxylic acids (PFCA) were high (r = 0.85–0.96, P < 0.05). Type of statistical test was not reported. Correlations between individual compounds not reported.	General population	Single measurement of PFAS for cases and controls. Individual congeners Sum of PFSA (PFHxS, PFOS, PFOSA) Sum of PFCA (PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA) Sum of PFCA+PFSA + polychlorinated biphenyls (PCBs)+ organochlorine pesticides (OCPs) Units: ng/mL	PFAS: LC-MS/MS POPs: GC-ECD Metals: ICP-MS Cotinine: ELISA kit PFAS: LODs from 0.1 to 0.4 ng/mL (details not reported). POPs: LODs were 0.08 ng/mL for p, p'-DDE, p, p'-DDT and b-HCH, and 0.04 ng/mL for other pesticides and PCBs Metals: LODs were not reported Cotinine: LOD was 1 ng/mL Detection frequencies not reported.	Measured: PCBs (PCB 99, PCB 101, PCB 105, PCB 118, PCB 128, PCB 138, PCB 153, PCB 156, PCB 170, PCB 180, PCB 183, PCB 187); β-HCH; Cd; Cotinine (biomarker of tobacco smoking). No information: alcohol consumption, occupation, dioxins and furans exposure. High correlations between PFCA or PFSA and POPs were reported (r = 0.42–0.55, P < 0.05.	Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development.
Cao et al. (2022) Liver cancer	Case–control One hospital Hangzhou, China	Cases (n = 203) diagnosed with liver cancer, no other diseases Controls (n = 203) were healthy individuals randomly selected from the participants in the Chinese National Breast Cancer Screening Program Serum measurements of all subjects	Blood collection in 2019–2021, Timing of sample collection relative to time point of diagnosis is not reported	PFAS measured; PFOS, PFOA PFHxA, PFHpA, PFNA, PFDA, PFUnA, PFDoA, PFBS, PFHxS, 6:2 Cl⁻PFESA, 8:2 Cl⁻PFESA Spearman's rank correlations between PFOS, PFOA and other PFAS: PFOA: PFNA: 0.63 PFOA: PFDA: 0.10 PFOA: PFBS: 0.51 PFOA: PFHxS: 0.47 PFOA: PFOS:0.25 PFOA: 6:2 cl-PFESA:0.30 PFOS: PFNA: 0.29 PFOS: PFDA: 0.042 PFOS:PFBS: 0.48 PFOS:PFHxS: 0.45 PFOS: 6:2 cl-PFESA: 0.48	General Population	Single measurement of PFASs for cases and controls. Individual congeners Units: ng/mL	LC-MS/MS LODs (ng/mL) were 0.1 for all PFAS measured. Detection frequencies for cases: PFOA, PFNA, PFDA, PFUnDA, PFBS, PFHxS, PFOS and 6:2 Cl⁻PFESA all 100% PFHxA:74% PFHpA:35% PFDoDA:59% 8:2 Cl⁻PFESA:48% Detection frequencies for controls PFOA, PFNA, PFBS, PFHxS, PFOS and 6:2 Cl⁻PFESA all 100% PFHxA:56% PFHpA:61% PFDA:73%, PFUnDA:53% PFDoDA:48%, 8:2 Cl⁻PFESA:58%	Questionnaire: tobacco smoking No information: alcohol consumption, occupation, dioxins, furans and PCB exposure	Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development.
Chen et al. (2023) Retinoblastoma	Case–control California, USA	497 retinoblastoma cases 893 controls, frequency-matched by year of birth Controls were randomly selected from California birth rolls Blood spots measurements of all subjects	Blood collection in newborns in 1983-2011 Average age of diagnosis for unilateral retinoblastoma was 22.1 months, while the average age of diagnosis for bilateral retinoblastoma was 9.3 months	PFAS measured: PFOS, PFOA, PFNA Correlations: weakly correlated (|r| < 0.15).	General population	Single measurement of PFAS for cases and controls. Individual congeners Log 2 transformed intensities	PFASs: LC-HRMS, semi-quantitative, non-targeted method LODs: Not reported Detection frequencies: not reported	No information on potential for co-exposure to other carcinogens	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame. The method used was semi-quantitative
Hardell et al. (2014) Prostate cancer	Case–control One hospital in Sweden	Cases (n = 201) were men with diagnosed prostate cancer admitted to hospital. Two cases were originally enrolled as controls (had not received treatment) Controls (n = 186), healthy non-cancerous, matched on age and geographical area, selected from the Swedish population registry Whole blood measurements of all subjects	Blood collection in 2007–2011, between diagnosis and start of treatment (cases) Blood sampling for cases; same year as diagnosis (n = 123), 1 year after diagnosis (n = 73), 2 years after diagnosis (n = 2), 3 years after diagnosis (n = 1).	PFAS measured; PFOS, PFOA, PFHxA, PFHxS, PFNA, PFDA, PFUnDA, PFDoDA Correlations between PFAS not reported	General Population	Single measurement of PFAS for cases and controls. Individual congeners Units: ng/mL	LC-MS/MS LODs (ng/mL) were 0.01– 01 for PFOS, 0.4–0.7 for PFOA, 0.05–0.1 for PFHxS, 0.05–0.7 for PFNA, 0.06–0.4 for PFDA, and 0.05–0.37 for PFUnDA. Detection frequencies: PFOS: 100% of cases, 100% of controls PFOA 100% of cases, 99,5% of controls PFHxS: 100% of cases, 100% of controls PFNA: 93% of cases, 91% of controls PFDA: 86% of cases, 81% of controls PFUnDA: 80% of cases, 83% of controls	Questionnaire: tobacco smoking No information: alcohol consumption; occupation	Possible differential exposure misclassification if cancer diagnosis impacts whole blood levels of PFASs. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development.
Itoh et al. (2021) Breast cancer	Case–control 4 hospitals in Japan	Cases were women with new invasive breast cancer admitted to hospital and healthy (non-cancerous) controls in hospital for medical check-up, matched on age and residential area resulting in 401 matched pairs Serum measurements of all subjects	2001-2005 blood collection, serum collected before chemotherapy. Serum measurements at time of id as case or control No info on date of sampling relative to diagnosis, but cases had to hospitalized with diagnosis. Units: ng/mL	Perfluoroalkyl sulfonic acid (PFSAs) including: linear Perfluorohexanesulfonic acid (n-PFHxS), linear Perfluoroheptane sulfonic acid (n-PFHpS), and linear and branched Perfluorooctane sulfonic acid (n-PFOS, 1 m-PFOS, 3 m-PFOS, 4 m-PFOS, 5 m-PFOS, and 6 m-PFOS), perfluoroalkyl carboxylic acids (PFCAs) including: linear and branched Perfluorooctanoic Acid (n-PFOA and 6 m-PFOA), linear and branched Perfluorononanoic acid, (n-PFNA and 7 m-PFNA), linear and branched Perfluorodecanoic acid (n-PFDA and iso-PFDA), linear and branched perfluoroundecanoic acid (n-PFUnDA and iso- PFUnDA), linear and branched perfluorododecanoic acid (n-PFDoDA and iso-PFDoDA), and linear and branched perfluorotridecanoic acid (n-PFTrDA and isoPFTrDA) Correlation of individual n-PFHXs 0.64-0.96; correlation of individual PFCAs 0.15-0.84; Correlation individual n-PFHXx and individual PFCAs 0.21-0.74	General Population	Single measurement of PFAS for cases and controls. Individual congeners and Total PFHxS, Total PFOS, Total PFOA, Total PFNA, Total FPDA, Total PFUDA, Total PFDoDA, Total PFTrDA, as well as the sum of Perfluoroalkyl sulfonic acids (sum PFSA); and the sum of perfluoroalkyl carboxylic acids (sum PFCA) Units: ng/mL PFAS congeners with measured values below the MQL, were imputed [(1−p) ×MQL], where p=proportion of serum specimens with values < MQL	Gas chromatography-negative chemical ionization-mass spectrometry (GC-NCI-MS) with isotopically labeled internal standards for many isomers. n-PFHxS 96% cases, 97% controls > MQL 0.08ng/mL; nPFHpS 50% cases, 62% controls > MQL 0.09ng/mL; 1m-PFOS 71% cases, 82% controls > MQL 0.12 ng/mL; 6m-PFOS 72% cases, 82% controls > MQL 0.17ng/mL; iso-PFDoDA 81% cases, 86% controls > MQL 0.03ng/mL; isoPFTrDA 44% cases, 53% controls >MQL 0.02ng/mL; all other n-PFHxS's and PFCAs 100-98% > MQL of 0.05-0.68ng/mL Did not include some isomers where 0% > MQL: PFBS, perfluorododecane sulfonate, perfluorohexanoic acid, branched isomer of perfluorotetradecanoic acid, perfluorohexadecanoic acid, 2 m-PFOA, 3 m-PFOA, 5 m-PFOA, 9-chlorohexadecafluoro-3-	Alcoholic beverages (IARC Grp 1) data collected by questionnaire Tobacco Smoking (IARC Group 1) data collected by questionnaire No information: occupation	Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
							oxanonane-1-sulfonate, and 11-chloroeicosafluoro-3-oxaundecane-1-sulfonate Did not include some isomers where < 30.2% of control participants), concentrations were above the MQL: linear isomer of perfluorotetradecanoic acid, perfluoroheptanoic acid, 2m-PFOS, 3,5-perfluorodimethyl-PFOS, 4,5-perfluorodimethyl-PFOS, 1m-PFHxS, 2 m-PFHxS, 3m-PFHxS, 4m-PFHxS, perfluoropentane sulfonate, perfluorodecane sulfonate, perfluoropentadecanoic acid, perfluorononane sulfonate, and perfluoro-4-ethylcyclohexanesulfonate		
Li et al. (2022a) Breast cancer	Case–control One hospital in Tianjin, China	Cases (n = 373) were women diagnosed with breast cancer Controls (n = 657) controls were randomly selected from the participants in the Chinese National Breast Cancer Screening Program (CNBCSP) Plasma measurements of all subjects	Blood collection in 2012–2016 collected after diagnosis but before treatment started (cases), at the screening in the CNBCSP (controls).	PFAS measured; Linear PFOS, linear PFOA, branched isomers of PFOS and PFOA (P1MHpS, P3MHpS, P3MHpA, P4MHpS, P4MHpA, P5MHpS, P5MHpA, P6MHpS, P6MHpA, P55DMHxS, P55DMHxA, P44DMHxS, P44DMHxA, P45DMHxS, P45DMHxA, P35DMHxS, P35DMHxA) PFBS, PFHxS, PFHpS, PFDS, PFBA, PFPeA, PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeDA, 11CL-PF3OUdS, 9CL-PF3ONS, 4:2FTS, 6:2FTS, 8:2FTS Spearman's rank correlations higher than 0.1 between PFOS, PFOA, or their isomers and other PFASs: PFOA: PFNA: 0.62 PFOA: PFDA: 0.42 PFOA: PFUnDA: 0.21 PFOA: PFDoDA: 0.25 PFOA: PFTeDA: 0.11 PFOS: PFHxS: 0.27 PFOS: PFHpS: 0.58 P3MHpS: P4MHpS: 0.92 P3MHpS: P5MHpS: 0.91 P3MHpS: P6MHpS:0.11 P3MHpS: 11CL-PF3OUdS: 0.15 P3MHpS: 9CL-PF3ONS: 0.36 P4MHpS: P5MHpS: 0.98 P4MHpS: P6MHpS: 0.13 P4MHpS: 11CL-PF3OUdS: 0.14 P4MHpS: 9CL-PF3ONS: 0.38 P5MHpS: P6MHpS: 0.13 P5MHpS: 11CL-PF3OUdS: 0.14 P5MHpS: 9CL-PF3ONS: 0.38 P6MHpS: P45DMHxS: 0.14 P6MHpS: 9CL-PF3ONS: 0.19	General Population	Single measurement of PFASs for cases and controls. Individual congeners Sum of PFCAs included PFOA, PFNA, PFDA, PFUdA, PFDoA, PFTrDA, and PFTeDA. Sum of PFSAs included PFHxS, PFHpS, and PFOS. Sum of PFSA isomers included P3MHpS, P4MHpS, P5MHpS, P6MHpS, P45DMHxS, 11CL-PF3OUdS, and 9CL-PF3ONS Units: ng/mL	LC-MS/MS LOQs (ng/mL) were 0.969 for PFOS, 0.116 for PFOA, 0.081 for P1MHpS, 0.043 for P3MHpS, 0.101 for P3MHpA, 0.211 for P4MHpS, 0.058 for P4MHpA, 0.120P5MHpS, 0.025 for P5MHpA, 0.076 for P6MHpS, 0.023 for P6MHpA, 0.006 for P55DMHxS, 0.017 for P55DMHxA, 0.006 for P44DMHxS, 0.169 for P44DMHxA, not reported for P45DMHxS, not reported for P45DMHxA, 0.026 for P35DMHxS, 0.173 for P35DMHxA, 0.010 for PFBS, 0.012 for PFHxS, 0.03 for PFHpS, 0.013 for PFDS, 0.795 for PFBA, 0.519 for PFPeA, not reported for PFHxA, 0.060 for PFHpA, 0.220 for PFNA, 0.010 for PFDA, 0.009 for PFUnDA, 0.010 for PFDoDA, 0.028 for PFTrDA, 0.008 for PFTeDA, 0.00 111 for CL-PF3OUdS, 0.0079 for CL-PF3ONS, 0.490 for 4:2FTS, 0.549 for 6:2FTS, 0.113 for 8:2FTS Detection frequencies: PFOA, PFHxS, PFDA and 9CL-PF3ONS all 100% PFOS:99% PFBS:40% PFHpS:98% PFDS:4% PFBA:1% PFHpA:2% PFNA:97% PFUnDA:99% PFDoDA:97% PFTrDA:94% PFTeDA:81% P3MHpS:93% P4MHpS:93% P5MHpS:97% P6MHpS:86% P6MHpA:18% 11CL- P44DMHxS:85% PF3OUdS:99% P55DMHxS, P55DMHxA, P44DMHxA, P35DMHxS, P35DMHxA, P1MHpS, P3MHpA, P4MHpA, P5MHpA, 4:2FTS, 6:2FTS, 8:2FTS and PFPeA all 0% PFHxA, P45DMHxS and P45DMHxA were not reported	Questionnaire: tobacco smoking, alcohol consumption, use of estrogen or estrogen replacement therapy, consumption of red meat No information: occupation	Possible differential exposure misclassification if cancer diagnosis impacts plasma levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development.
Lin et al. (2020) Paediatric germ cell tumours (GCT)	Case–control One hospital in Shanghai, China	Cases (n = 42), were children 11–47 months of age pathologically diagnosed with a GCT (including immature teratoma, yolk sac tumour, or germinoma) Controls (n = 42) children 13–48 months of age with mycoplasma/bacterial pneumonia and asthma Serum measurements of all subjects	Blood collection 2014–2017 collected one week following the pathological identification (cases) or on the day of discharge from the hospital (controls)	PFAS measured; PFOS, PFOA, PFBS, PFHpA, PFHxS, PFNA, PFDA, PFUnDA, PFOSA, PFDoDA Correlations between PFASs not reported	General Population	Single measurement of PFASs for cases and controls. Individual congeners Units: ng/mL	LC-MS/MS LODs (ng/mL) were 0.009 for PFBS,0.03 for PFHpA, 0.02 for PFHxS, 0.09 for PFOA, 0.09 for PFOS, 0.02 for PFNA, 0.02 for PFDA, 0.02 for PFUnDA, 0.12 for PFOSA and 0.05 for PFDoDA Detection frequencies for PFBS, PFHpA, PFHxS, PFOA, PFOS, PFNA, PFDA and PFUnDA all 100% PFOSA:46%	Excluded: cohabitation with tobacco smokers within the family Questionnaire: barbeque during pregnancy, history of hair dye usage during pregnancy No information: alcohol consumption in pregnancy	Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development.

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
Tsai et al. (2020) Breast cancer	Case–control One hospital in Taiwan, China	Cases (*n* = 120), were women with breast cancer Controls (*n* = 119) were recruited through advertisements at the hospital and in the community, without any history of malignancy Plasma measurements of all subjects	Blood collection in 2014 −2016, collected between time of diagnosis and start of treatment (cases)	The following additional PFASs were measured; PFHxS, PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA Correlations between PFAS not reported	General Population	Single measurement of PFASs for cases and controls. Individual congeners Units: ng/mL	PFDoDA:99% LC-MS/MS LOQs (ng/mL) were 0.2 for PFHxA, 0.4 for PFHpA, 0.2 for PFHxS, 0.1 for PFOS, 0.5 for PFOA, 0.2 for PFNA, 0.2 for PFDA, 0.2 for PFUnDA, 0.1 for PFDoDA, and 0.1 for PFTrDA. Detection frequencies for PFHxA:39% PFHpA:10% PFHxS:79% PFOS:100% PFOA:94% PFNA:99% PFDA:88% PFUnDA:97% PFDoDA:68% PFTrDA:80%	Questionnaire: tobacco smoking, alcohol consumption No information: occupation	Possible differential exposure misclassification if cancer diagnosis impacts plasma levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development.
van Gerwen et al. (2023) Thyroid cancer	Nested Case control 88 cases 88 controls pair-matched on sex, age (±5 years), race/ethnicity, body mass index, smoking status, and year of sample collection Mt Sinai Icahn School of Medicine Bio*Me* medical record linked biobased.	Plasma samples were drawn and stored 2008-2021 analysed for 18 PFAS using untargeted method	PFAS samples were drawn and stored 2008-2021. Time between sample collection and thyroid cancer diagnosis was 0–8.47 years with cases diagnosed at least 1 yr after collection averaging 3.99 years (n = 62 longitudinal) and those diagnosed less than 1 year after collection averaging 0.08 years (n=114 cross-sectional).	Ten out of 18 PFAS were excluded due to non-detected intensities for more than 40% of plasma samples Eight PFAS included: linear perfluorohexanesulfonic acid (n-PFHxS), perfluorooctanoic acid (PFOA), perfluoroheptanesulfonic acid (PFHpS), perfluorooctylphosphonic acid (PFOPA), branched and linear perfluorooctane sulfonic acid (Sb-PFOS and n-PFOS), perfluorononanoic acid (PFNA), and n-ethylperfluoro-octanesulfonamido-acetic acid (N-MeFOSAA PFOA correlated ≥ 0.7 with PFHpS, PFOPA, sbPFOS, PFNA, nPFOS sbPFOS correlated ≥ 0.8 nPFHxS, PFOA, PFHpS, PFOPA, nPFOS nPFOS correlated ≥ 0.7 nPFHxS, PFOA, PFHpS, PFOPA, sbPFOS MeFOSAA was not significantly correlated with any PFAS	General population	Single point untargeted measurement of each PFAS peak (shown to have high concordance with validated quantitative concentration measurements and their quantiles) (intraclass correlation coefficient: 0.91 for PFOS deciles) Note: Using certified reference material, the estimated median PFHxS, PFOS, PFOA, and PFNA concentrations in the study population (n = 176) was 1.1, 5.2, 2.9, and 0.7 ng/mL, Analysis used 8 individual PFAS as log2 untargeted intensities or IQR intensities Did not sum branched and linear PFOS, did not report branched and linear PFOA isomers	Liquid chromatography-high resolution mass spectrometry (LC-HRMS) LODs not reported All PFAS reported > 60% detectable but no additional information	No information on alcohol, smoking or occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method however a single measurement may not reliably reflect relevant dose during cancer development. Possible differential exposure misclassification due to thyroid development impacting serum levels of PFAS since 65% samples collected < 1 year from diagnosis,
Velarde et al. (2022) Breast cancer	Case–control 1 hospital in Philippines 75 breast cancer cases and 75 controls	Cases are women with breast cancer in outpatient clinic and healthy (non-cancerous) controls recruited by advertising. Serum measurements of all subjects	2018 breast cancer patients not undergoing chemotherapy Random community controls Serum measurements at time of id as case or control Units: ng/mL	12 PFAS: [perfluorobutanoic acid (PFBA), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), per- fluorododecanoic acid (PFDoA), perfluorobutane sulfonic acid (PFBuS), perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), and perfluorooctane sulfonamide (PFOSA)]. No info on correlation of PFAS with each other.	General Population	Single measurement of PFAS for cases and controls. Quartiles of each individual PFAS used for ORs Units: ng/mL Samples with concentrations below the limit of detection (LOD) were imputed as LOD/√2	Liquid chromatography-tandem mass spectrometry (LC-MS/MS) with deconjugation and solid phase extraction. Use of isotope dilution of labeled internal reference standards LOD from Trowbridge et al. (2020). All LOD 0.02 ng/mL except PFNA 0.05 ng/mL. 100-98% detectable for PFHxA; PFNA; PFDA; PFUnDA, PFOS;PFHpA 90%; detectable PFDoA 97% detectable ; PFBuS 2% detectable; PFHxS 93% detectable ; PFOSA 21% detectable	No info on alcohol or smoking both IARC Group 1 No information: occupation 11 phthalate urine metabolites measured :[monoethyl phthalate (MEP), monobutyl phthalate (MBP), mono (2-ethylhexyl) phthalate (MEHP), mono (2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono (2-ethyl-5-carboxypentyl) phthalate (MECPP), monobenzyl phthalate (MBzP), monocyclohexyl phthalate (MCHP), monoisononyl phthalate (MiNP), monoisodecyl phthalate (MiDP), monopentyl phthalate (MPP), monohexyl phthalate (MHxP)),Di-(2-ethylhexyl)pthalate IARC Group 2B 8 urinary phenols measured: methyl paraben, ethyl paraben, propyl paraben, butyl paraben, benzophenone-1, benzophenone-3, pentachlorophenol, triclosan, Benzophenone IARC Group 2B 10 urinary bisphenols measured:bisphenol A (BPA), bisphenol AF (BPAF), bisphenol AP (BPAP), bisphenol B (BPB), bisphenol C (BPC), bisphenol E (BPE), bisphenol F (BPF), bisphenol P (BPP), bisphenol S (BPS), bisphenol Z (BPZ)]Bisphenol A diglycidyl ether IARC Group 3 No info on correlation of other exposures with PFAS	Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development
Wielsøe et al. (2017) Breast cancer	Case–control One hospital in Greenland	Samples collected 2000–2003: Cases (n = 31) were Inuit women with breast cancer (same individuals as in Bonefeld-Jørgensen et al, 2011) Controls (n = 115, but only 31 included in the statistical analyses) were Inuit women from two cross-sectional studies on healthy persons with serum measurements on persistent organic pollutant (POP) collected during the same time period, frequency matched on age and geographical living area	Blood collection in 2000 −2003 and 2011 −2014 Collected after diagnosis but before treatment started (Cases)	PFAS measured in all samples; PFOS, PFOA, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFHxS, PFOSA Further, the following PFAS were measured in the samples collected in 2011–2014: PFHxA, PFPeA, PFTeDA, PFBS, PFHpS, PFDS Correlations not reported.	General population	Single measurement of PFAS for cases and controls. Individual congeners Sum of PFCA included: PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA Sum of PFSAs included: PFHxS, PFOS and PFOSA Sum of PFAA included: sum PFCA + sum PFSA.	PFASs: LC-MS/MS POPs: GC-ECD Cotinine: ELISA kit LOQs (ng/mL) in 2000–03 and 2011–14, respectively: 0.1/0.09 for PFOS 0.4/0.07 for PFOA x (not measured)/0.02 for PFBS , 0.4/0.03 for PFHxS, x/0.04 for PFHpS, x/0.12 for PFDS,	Measured: PCBs (PCB 28, PCB 52, PCB 99, PCB 101, PCB 105, PCB 118, PCB 128, PCB 138, PCB 153, PCB 156, PCB 170, PCB 180, PCB 183, PCB 187), β-HCH, cotinine (biomarker of tobacco smoking) Questionnaire: smoking No information: alcohol consumption, occupation,	Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
		Samples collected 2011–2014: Cases (n = 66), were Inuit women with breast cancer Controls (n = 62) controls were Inuit women which were patients with non-malignant diagnoses at the hospital, and frequency matched on age and geographical living area Serum measurements of all subjects				Units: ng/mL	0.2/0.4 for PFOSA, x/0.06 for PFPeA, x/0.01 for PFHxA, 0.1/0.02 for PFHpA, 0.5//0.09 for PFNA, 0.1/0.03 for PFDA, 0.2/0.05 for PFUnDA, 0.3/0.14 for PFDoDA. 0.3/0.14 for PFTrDA, x/0.14 for PFTeDA, x/0.01 for Aldrin, 0.04/0.005 for Cis-Nonachlor, 0.04/0.01 for Trans-Nonachlor, 0.04/0.04 for HCB, 0.04/0.01 for Mirex, 0.01/0.005 for Oxychlordane, x/0.01 for Alpha-chlordane, x/0.005 for Gamma-chlordane, 0.08/0.09 for p,p'-DDE, 0.08/0.05 for p,p'- DDT, 0.08/0.01 for β-HCH, x/0.03 for PBB 153, x/0.03 for PBDE 15, x/0.03 for PBDE 17, x/0.03 for PBDE 25, x/0.03 for PBDE 28, x/0.03 for PBDE 33, x/0.03 for PBDE 47, x/0.02 for PBDE 99, x/0.02 for PBDE 100, x/0.03 for PBDE 153, x/0.05 for PCB 28, x/0.3 for PCB 52, 0.04/0.03 for PCB 99, 0.04/0.03 for PCB 101, 0.04/0.01 for PCB 105, not reported for PCB 118, x/0.01 for PCB128, 0.04/0.01 for PCB 138, 0.04/0.01 for PCB 153, 0.04/0.01 for PCB 156, 0.04/0.01 for PCB 170, 0.04/0.01 for PCB 180, 0.04/0.01 for PCB 183, 0.04/0.01 for PCB 187 Detection frequencies: PFOS, HCB, Oxychlordane, PCB 138, PCB 153, PCB 170, PCB 180, PCB 187 and p,p'-DDE all 100% PFOA:97% PFHxS:99% PFHpS:95% PFDS:2% PFOSA:27% PFHpA:72% PFNA:96% PFDA:99% PFUnDA:98% PFDoDA:57% PFTrDA:35% Cis-Nonachlor:99% Trans-Nonachlor:99% Mirex:95% Alpha-chlordane:2% p,p'- DDT:69% β-HCH:99% PBB 153:17% PBDE 33:3% PBDE 47:7% PBDE 99:0% PBDE 100:1% PBDE 153:8% PCB 28:9% PCB 99:97% PCB 101:54% PCB 105:92% PCB128:49% PCB 156:98% PCB 183:98% PFBS, PFPeA, PFHxA, PFTeDA,		

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
							Aldrin, Gamma-chlordane, PBDE 15, PBDE 17, PBDE 25, PBDE 28 and PCB 52 all 0%		
Occupational cohort studies									
Alexander et al. (2003) Mortality from Cancers and non-malignant causes	Cohort Study of plant that produces perfluorooctanesulfonyl fluoride (POSF) based compounds 3M Decatur AL film and chemical plant 145 deaths were identified in the 2083 cohort members.	Olsen et al. (2003) measured 186 serum samples (126 chemical plant and 60 film plant) in 1998. Did not use measured values in Exposure Matrix. Exposure assigned based on job title.	Serum samples collected 2003. Work histories 1961-1997 Production processes have remained constant over time. Chemical plant jobs were classified into eight categories. Most film plant jobs have no direct workplace exposure to fluorochemicals. Their serum levels are thought to be due to environmental exposure in proximity to the chemical plant	Olsen et al. (2003) measured serum Perfluorooctane sulfonic acid (PFOS); N-ethyl perfluorooctanesulfonamidoacetate (PFOSAA), N-methyl perfluorooctanesulfonamidoacetate (M570);Perfluorooctanesulfonamidoacetate (M556); perfluorooctanesulfonylamide (PFOSA); perfluorooctanoate (PFOA) ;perfluorohexanesulfonate (PFHS/PFHxS). Units in ppm No info on correlation of measurements.	Occupational exposures	A simple exposure matrix (EM) assigned each job/department to 1 of 3 exposure categories based on job category serum PFOS levels: No POSF exposure (film plant jobs); Low exposure (non-production jobs in chemical plant); High exposure (production jobs in chemical plant EM was combined with job history to categorize workers as: Ever in a high exposure job Ever in a low exposure job but not in a high job, Only in No POSF job At least 1 year in high exposure job	Serum samples were extracted using an ion pairing extraction procedure and were quantitatively analysed for serum PFOS using high pressure liquid chromatography/electrospray tandem mass spectrometry methods. Standard curves used either extracted rabbit sera or human sera No data on LOD/MQL but PFOSA levels were not reported because only 15% of the samples were detectable	Exposure to other fluorochemicals was possible because although POSF was the major sulfonate fluorochemical manufactured, it was used as the precursor to production of a variety of perfluorinated amides, alcohols, acrylates,and other fluorochemical polymers produced as protective and performance chemicals. Until 1998, PFOA was not manufactured at this facility but was a by-product or emulsifier in production. Olsen et al. (2003) reported measurable levels of PFOSAA, N-methyl perfluorooctanesulfonamidoacetate (M570), perfluorooctanesulfonamidoacetate (M556), PFHS and PFOA in all chemical plant jobs. Although observed at slightly lower levels, the serum PFOA levels correlated with serum PFOS levels. Company records were examined of use of any of 45 potential bladder carcinogens. Five had been used at the plant. Four were part of a former inactive process (4,4-methylene-dianiline, orthotoluidine, benzidine salts, and butyl benzyl phthalate). The use of these materials ended in the 1960s and 1970s. Melamine was in use during the study period in the chemical plant in epoxy capsule manufacturing. Chloroprene was also used in several manufacturing processes in the chemical plant in the 1960s and 1970s. No info on alcohol or smoking both IARC Group 1 No information: occupation	Exposure misclassification likely due to comparisons based on categorization of subjects as “ever” in a high or low exposure job
Alexander & Olsen (2007) Bladder cancer	Cohort Study of plant that produces perfluorooctanesulfonyl fluoride (POSF) 3M Decatur AL film and chemical plant 1895 current and former employees of plant. 188 death certificates	Olsen et al. (2003) measured 186 serum samples (126 chemical plant and 60 film plant) in 1998.	Serum samples collected 2003. Work histories 1961-1997 Production processes have remained constant over time. Chemical plant jobs were classified into eight categories. Most film plant jobs have no direct workplace exposure to fluorochemicals. Their serum levels are thought to be due to environmental exposure in proximity to the chemical plant.	Olsen et al. (2003) measured serum Perfluorooctane sulfonic acid (PFOS); N-ethyl perfluorooctanesulfonamidoacetate (PFOSAA), N-methyl perfluorooctanesulfonamidoacetate (M570); Perfluorooctanesulfonamidoacetate (M556); perfluorooctanesulfonylamide (PFOSA); perfluorooctanoate (PFOA); perfluorohexanesulfonate (PFHS/PFHxS) Units in ppm No info on correlation of measurements.	Occupational exposures	a simple exposure matrix (EM) assigned each job/department to 1 of 3 exposure categories based on job category serum PFOS levels: No POSF exposure (film plant jobs); Low exposure (non-production jobs in chemical plant); High exposure (production jobs in chemical plant These POSF job exposure categories (no, low, high) were assigned an exposure value of 1, 3, 10 respectively based on biomonitoring data Cumulative exposure was calculated as years in a POSF job category multiplied by the relevant exposure weight.	Serum samples were extracted using an ion pairing extraction procedure and were quantitatively analysed for serum PFOS using high pressure liquid chromatography/electrospray tandem mass spectrometry methods. Standard curves used either extracted rabbit sera or human sera No data on LOD/MQL but PFOSA levels were not reported because only 15% of the samples were detectable	Exposure to other fluorochemicals was possible. Until 1998, PFOA was not manufactured at this facility but was a by-product or emulsifier in production. Olsen et al. (2003) reported measurable levels of PFOSAA, M570, M556, PFHS and PFOA in all chemical plant jobs. Although observed at slightly lower levels, the serum PFOA levels correlated with serum PFOS levels. Although observed at slightly lower levels, the serum PFOA levels correlated with serum PFOS levels. Company records were examined of use of any of 45 potential bladder carcinogens. Five had been used at the plant. Four were part of a former inactive process (4,4 methylene-dianiline, orthotoluidine, benzidine salts, and butyl benzyl phthalate). The use of these materials ended in the 1960s and 1970s. Melamine was in use during the study period in the chemical plant in epoxy capsule manufacturing. Chloroprene was also used in several manufacturing processes in the chemical plant in the 1960s and 1970s. No info on alcohol or smoking both IARC Group 1	Exposure misclassification likely due to comparisons based on categorization of subjects as “ever” in a high or low exposure job
Consonni et al. (2013) All cancers (deaths)	Cohort mortality study 5879 workers, 4773 exposed to TFE 775 deaths	The job-exposure matrix provided yearly semiquantitative estimates (in arbitrary units) of TFE and APFO exposure for relevant job titles at each production site, from the start of TFE production to 2002. (Sleeuwenhoek and Cherrie, 2012) No measured values Main analysis focuses on TFE	Workers in TFE production manufacturing facilities in US and Europe (6 facilities). At least 1 job period from start of TFE production until 2002. TFE and PFOA	Semiquantitative JEM, no measured exposure data. Exposure reconstruction led to JEM with yearly semiquantitative estimates in arbitrary units for both TFE and PFOA	Occupation	Cumulative exposure (Low, Medium, High) Also ever worked at plant (compared workers to national death rates)	NA	Main analysis focused on TFE. Majority of cohort exposed to both TFE and PFOA (88.1%), 11.9% never exposed to PFOA; no workers exposed to PFOA only. Ran analysis where people with no PFOA exposure were analysed separately. Results similar for PFOA and FTE, so unable to distinguish separate associations. Information on co-exposures to vinyl chloride and asbestos were collected on a facility level.	Differential classification is unlikely with respect to disease. Non-differential classification is unlikely.
Girardi & Merler (2019) Mortality inc cancers	Cohort study Rimar-Miteni (RM) Factory Italy 462 employees (107 deaths)	Serum measurements modelled into historical serum estimates: 696 blood samples analysed for PFOA 2000-2013 among 120 workers in plant. 74 chemical operators, 15 maintenance workers, 11 lab techs, 10 clerks, 2 warehouse workers, 8 other tasks. Most recruited after 1990 with average employment 17 years.	Cohort worked at factory 1960-2008 more than 6 months. Follow-up was 1970-2018 Cumulative serum levels estimated for each worker’s history 1970-2008 based on modelled serum levels for 3 job categories using 2000-2013 data	Factory produced perfluorinated alkylated substances (PFASs), fluoroaromatics (FA), and benzotrifluorides (BTF) in three separate buildings, Subjects working at the PFAS plant were simultaneously exposed to PFOA and PFOS during the years both were in production. PFOA was the primary, but not the only PFAS produced at this facility; however, PFAS other than PFOA and PFOS were never bio-monitored. In this study cumulative exposure to PFOS was not conducted due to low number of	Occupational exposure	Jobs categorized into: 1) “Ever PFAS” operators that were at the PFAS production plant, and those who subsequently moved to other production areas; 2) “Never PFAS” workers, who were not engaged in the PFAS plant, but involved in production of BTF or FA, or warehousemen, laboratory	HPLC-Electrospray-Tandem Mass Spectrometry. 2000-2004 by lab described by Olsen et al. (2005) LOD 1.9 ng/mL PFOA; 2004+ by another lab LOD 0.05 ng/mL. Correlation of 5 samples by 2 labs = 0.9 No info on % detectable levels PFOA or how handle < LOD values.	The FA production process within the RM factory included a diazotation step to convert aniline (IARC Grp 2A) and ortho-toluidine (IARC Grp 1) to fluorine toluenes and fluorine benzenes which were then transformed into a orthofluorobenzoyl chloride product Regional mortality rates used for SMR. No accounting for water source or occupation. Also used a reference group from nearby OGR workplace who may have been exposed to asbestos	Non-differential exposure misclassification possible since measurements via 2 labs over time and different job categories had different amounts of data available to use for modelling.

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
				serum measurements and lack of production data. Production ceased in 2005. In addition to PFOA & PFOS ammonia perfluorooctanoate (APFO), and perfluorobutyl-sulfonyl fluoride (trade name RM60) were also produced (1968–2005). Considered whether each worker lived in area served by PFAS contaminated drinking water (Red Zone)		technicians, maintainers, and operators at the pilot plant 3) "Office", subjects e.g., clerks, draughtsman, receptionists, or office cleaners Using PFOA serum samples from 2000-2013 for operators of PFAS and then in 2012 for other tasks, regression models for the 3 categories of exposure above were developed to estimate 1970-2013 serum levels (Cat 1 500 measurements, 56 workers); Cat 2 177 measurements, 60 workers, Cat 3 19 measurements, 8 workers). A mixed regression model was adopted with random subject intercept and a repeated-measures covariance structure to estimate the coefficients. The fixed effects included: Employment at PFASs department < 1975 (0/1), Employment date > 2005 (0/1) Years at the PFASs department, Annual PFOA produced (x 100 tons), Years in departments other than PFASs, Years since the end of work at the PFASs department, Maintenance activity (0/1), Occasional work at PFASs department (0/1), Years in office work. To address process changes between 2000 and 2013, a long-term effect was included, modelled by cubic spline. For the period before 2000 the earlier years the level was fixed at 2001. If a worker left employment, the serum levels at retirement were set to decline at 0.816 each subsequent year (assuming half-life of 3.4 years). Cumulative exposure was estimated by utilizing work histories assigned annually to category 1-3 level and summed. Producing ng/mL-years metric.		insulation (IARC Grp 1) welding, welding fumes (IARC Grp 1) and paint (Painters IARC Grp 1). OGR workplace not in Red Zone for water contamination and workers home location evaluated relative to Red zone like for PFOA workers No info on Alcoholic beverages IARC Grp 1 or Tobacco Smoking IARC Grp 1	
Lundin et al. (2009) Cancer mortality liver, pancreatic or testicular cancer	Cohort Study 3993 workers 68 deaths	Exposure reconstruction based on job history. Jobs classified as definite, probable, and no or minimal occupational PFOA exposure. Then further classified each job for individual as 1) definite exposure >6 months (high exposure), 2) definite exposure <6 months or never definite but ever probable (moderate), 3) working jobs with no fluorochemical exposure (low exposure). Then cumulative exposure based on time at those exposure levels. Biomonitoring showed that definite exposure PFOA levels ranged from 2.6-5.2 µg/mL; probable exposure jobs had 0.3 to 1.5 µg/mL. Using this data, weights were assigned for each job: 1=no exposure 30 = probable exposure 100 = definite exposure Cumulative exposure = weighted exposure level x days exposed	Occupational exposure All exposures evaluated prior to outcome	Only PFOA evaluated	Occupational exposure to PFOA	Cumulative exposure to PFOA based on weighted exposure duration. Exposure-intensity days	NA … all participants had levels assigned	Smoking history available for some participants	Differential and non-differential misclassification is unlikely
Raleigh et al. (2014) Cancer of liver, pancreas, testes, prostate, kidney, bladder, breast, and thyroid	Cohort study 3M Cottage Grove APFO Production Plant Total 9027 in cohort (4668 exposed facility) with 2979 deaths (1145 in exposed facility)	Environmental air measurements in APFO production areas (205 personal samples and 659 area samples). For a reference group at another non APFO using 3M plant workers were assigned a background level (1×10^{-9}–1×10^{-7} mg/m^3) to reflect exposures in the general population equivalent to an exposure range one order of magnitude	Air samples 1997-2000. Production processes prior to 1977 similar but exposures assumed lower due to lower production volume Units: µg/m^3	Ammonium perfluorooctanoate APFO (ammonium salt of PFOA)	Occupational Air 8-hour TWA Exposure levels	A TWA was calculated for each combination of department, job title, work area, equipment, task and year to create an exposure matrix (EM) that contained 23 departments and 45 job titles within the Chemical Division (1947–2002).	No info on method of sample analysis or LOD or sample results	Tetrafluoroethylene (TFE) IARC Group 2A) use infrequent and low volume 1979-1981 and 1983-1990 (fewer than 4 workers with minimal exposure). In 1982 up to 12 workers potentially exposed for short duration tasks. Full-shift TWA TFE exposures were below 0.02 ppm for the highest volume production year (1982) and 0.002 ppm other years with low production.	Potential of non-differential exposure misclassification due to methods used in developing EM and inability to account for episodic peak exposures

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
		lower than the Cottage Grove Non-Chemical Division workers.				However expert judgement was used to estimate TWAs for non-APFO production areas in the Chemical Division and the entire Non-Chemical Division based on relative proximity to the APFO production area. Exposure Matrix (EM) was combined with job history to produce cumulative estimates in µg/m^3-years of APFO (units).		No info on alcohol or smoking both IARC Group 1	
Steenland et al. (2015) All cancers incidence	Cohort study 3713 workers Workers at the Dupont Washington Works Plant in Parkersburg, WV.	Cumulative PFOA serum concentrations estimated based on JEMs and residential history. Estimated historical PFOA serum levels via a job-exposure matrix based on over 2000 serum measurements. Non-occupational exposure from drinking water was also estimated. Lifetime serum cumulative dose (combining occupational and non-occupational exposure) was our exposure metric. Estimates for occupational exposures was based on Woskie et al. (2012); estimates for residential water PFOA exposure were based on Shin et al. (2011a, b). Yearly serum estimates from the occupational exposure model were used for the years when people worked at the plant if these were higher than residential estimates; if they were lower, the residential (community) estimates were used. Based on modelled PFOA serum concentrations (ng/mL-years) x years. Cumulative PFOA concentration.	Workers in Parkersburg, WV. Both occupational and residential history were included. Worked at least one day between 1948 and 2002 PFOA only	PFOA.	Occupational and drinking-water exposure.	Cumulative serum PFOA concentration based on residential and occupational history. Modelled both as continuous and quartiles. F	Blood measurements used for the exposure characterization differed for occupational and residential exposure. Occupational measured used 3 different measurement techniques over time (whole blood and then two different serum methods; Woskie et al., 2012) and residential measurements were based on state-of-the-art methods at the time (Shin et al., 2011a, b). Estimates based on ng/mL-year	Smoking and alcohol were considered.	Non-Differential exposure misclassification is unlikely. Differential exposure may occur through loss to follow-up for ~40% of workers if loss to follow-up was related to exposure.
Steenland & Woskie (2012) Mortality (mesothelioma significant, other cancers not)	cohort study 5791 workers	Cumulative PFOA serum concentrations estimated based on JEMs. Estimated historical PFOA serum levels via a job-exposure matrix based on over 2000 serum measurements. Estimates for occupational exposures was based on Woskie et al. (2012). Based on modelled PFOA serum concentrations (ng/mL-years) x years. Cumulative PFOA concentration.	Occupational cohort, workers from 1948 to 2002, at least one day in Dupont Parkersburg plant. Modelled PFOA using JEM for 8 job category/ job group of exposure with time varying concentrations. PFOA	PFOA blood levels were estimated via JEM	Occupational exposure	Cumulative serum levels, ppm-years, serum levels were estimated annually (ppm = µg/mL)	JEM (Woskie et al., 2012)	Yes, possible in the low exposed group – non-polymer production. Exposures were not described in detail.	Unlikely because all jobs were classified in the same way
Highly exposed communities									
Barry et al. (2013) All cancers	Cohort study	Cumulative PFOA serum concentrations were estimated from 1952 (or birth) to 2011 using model by Shin et al. for community participants. Cumulative PFOA serum concentrations for workers were based on Woskie et al. (2012) Residential and occupational exposure estimates were combined.	Residents exposed to drinking-water from the chemical plant and workers at the chemical plant. PFOA only	Cumulative PFOA concentration.	Drinking-water and occupational exposure	Cumulative serum PFOA concentration based on residential and occupational history. Modelled both as continuous and quartiles. 10-year lagged models presented.	Modelled exposures based on Shin et al 2011a, b	No analysis of co-exposures except for smoking.	Differential and non-differential exposure misclassification is unlikely.
Li et al. (2022b) Incidence many cancer types	Cohort study Ronneby Sweden Register Cohort Residence in Ronneby 1985–2013 60 507 residents 5702 cancers	Exposure categories assigned by residential location (water source) considering highest exposure during 2014–2016. Serum levels collected in 2014–2015 for residents and neighbouring municipality used to validate categories	Cohort entry if registered as residing in Ronneby Jan 1, 1985-Dec 31, 2013. Follow up till Dec 31, 2016 Presumed that blood levels increased 1985-2013 and then declined after 2013 when contaminated drinking water eliminated from water supply	Serum samples in 2014-2015 for 3084 residents in Ronneby and 226 persons in reference municipality in 2016. Measured for: Perfluorooctane sulfonic acid (PFOS), Perfluorohexane sulfonic acid (PFHxS), and Perfluorooctanoic acid (PFOA). Measurements only used for validation of categorical assignments Other PFAS measured in serum (Xu et al., 2021) PFHpA, PFNA, PFDA Other PFAS found in Ronneby drinking water but not measured in serum (Li et al., 2018): Perfluoropentanoic acid Perfluorohexanoic acid Perfluoroheptanoic acid Perfluorononanoic acid Perfluorodecanoic acid Perfluoroundecanoic acid	Environmental contamination of water supply by firefighting foam	Each person assigned to categories of drinking water exposure based on residential location: Never High = reside in Ronneby but not supplied by contaminated waterworks or had own well 1985-2013 Ever high = reside in Ronneby and received water supply form contaminated waterworks any time from 1985-2013 Early high = Reside in Ronneby and received water from contaminated waterworks 1985-2004 but not later Late high = reside in Ronneby and received contaminated water 2005-2013 (individual could be both early high and late high if continued living in area)	Li et al. (2018): Plasma samples analysed by liquid chromatography-tandem mass spectrometry (LC/MS/MS) with labeled internal standards. Limits of detection were 0.5 ng/mL for PFHxS and PFOS, and 0.4 ng/mL for PFOA. Xu et al. (2021) Detection frequency in exposed residents: PFOA, PFOS, PFHxS, PFNA 100% PFDA 89%, PFHpA 56%	No info on Alcoholic beverages (IARC Grp 1) or Tobacco Smoking (IARC Grp 1) No info on occupation	Non-differential exposure misclassification possible since no information on water consumption including use of bottled water or water filtration. Not specific for individual PFAS, based on residential history. PFOS and PFHxS higher than PFOA

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
				Perfluorododecanoic acid Perfluorobutane sulfonic acid Perfluorohexane sulfonic acid Perfluoroheptane sulfonic acid Correlations in serum (Xu et al., 2021) PFOA and PFOS 0.95 PFOA and PFHxS 0.93 PFOS and PFHxS 0.98 PFHpA, PFNA, PFDA with with PFOA, PFOS, PFHxS correlation < 0.4 PFNA and PFDA correlation 0.7		Short high = those in Ronneby receiving contaminated water for 1-10 years. Long High = those in Ronneby receiving contaminated water for 11 or more years. Reference = subjects in neighbouring municipality who never lived in Ronneby 1985-2013 (no contaminated water).			
General population studies, including nested case–control									
Bonefeld-Jørgensen et al. (2014) Breast cancer	Nested case–control study from Prospective Birth Cohort 1996–2002 Danish population 250 breast cancer cases and 233 controls matched on age and parity	Maternal serum collected at 6–14 weeks gestation Measured for 15 PFAS	Blood and questionnaires collected at enrolment. Serum PFAS measurements at time of id of case or control	Bonefeld-Jørgensen et al. (2014): 10 perflurocarboxylated acids: perfluoro-n-pentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorooctanate acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnA), perfluorododecanoic acid (PFDoA), perfluorotridecanoic acid (PFTrA), perfluorotetradecanoic acid (PFTeA) 5 perfluoroalkylsulphonates: perfluorobutane sulfonate (PFBS), perfluorohexane sulfonate (PFHxS), perfluoroheptane sulfonate (PFHpS), Perfluorooctanesulfonate (PFOS) perfluorodecane sulfonate (PFDS) 1 perfluroalkyl sulfonamide: perfluorooctane-sulfonamide, (PFOSA). Units: ng/mL Significant correlations found between PFOS vs PFOA (0.69), vs PFOSA (0.58), vs PFNA (0.42), and PFHxS (0.15). Also significant correlations: PFOSA vs PFOA (0.36), PFNA vs PFOA (0.46) vs PFHxS (0.29), and PFHxS vs PFOA (0.17). Authors say knowing that PFOSA is a precursor for PFOS can partly explain their relatively high correlation coefficient, whereas the correlation coefficient of 0.36 for PFOSA versus PFOA might suggest common sources of exposure.	General population	Single measurement of maternal PFAS during gestation for cases and controls. The PFAS concentrations were grouped into: SumPFSA (sum of PFBS, PFHxS, PFHpS, PFOS, PFDS, and PFOSA) and SumPFCA (sum of PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnA, PFDoA, PFTrA, and PFTeA) and SumPFSA (all PFAS). In addition, analyses were performed for the 5 single PFAS compounds detected in all samples; PFOS, PFHxS, PFOA, PFNA, and PFOSA. PFOSA was also analysed alone because it is chemically different from the other PFSA (amide precursor to PFOS and not an acid), If below the detection limit, assigned detection limit divided by two.	Bonefeld-Jørgensen et al. (2014): Solid phase extraction using labelled internal standard and analysis with liquid chromatography–tandem mass spectrometry (LC–MS–MS) with electrospray ionization (ESI) in negative mode. 10 perflurocarboxylated acids**:** PFPeA, (2% >MDL 0.1 ng/mL) PFHxA, (2% > MDL 0.17 ng/mL) PFHpA (86% > MDL 0.02 ng/mL) PFOA (100% > MDL 0.07 ng/mL) PFNA, (100% > MDL 0.09 ng/mL) PFDA (89% > MDL 0.07 ng/mL) PFUnA (50% > MDL 0.25 ng/mL) PFDoA (60% > MDL 0.14 ng/mL) PFTrA (53%> MDL unspecified) PFTeA (01% > MDL unspecified) 5 perfluoroalkyl-sulphonates: PFBS (4% > MDL 0.02 ng/mL) PFHxS (100% > MDL 0.04 ng/mL) PFHpS (99.8% > MDL 0.05 ng/mL) PFOS (100% > MDL 0.41 ng/mL) PFDS (18% > MDL 0.12 ng/mL) 1 perfluroalkyl sulfonamide**:** PFOSA (100% > MDL 0.4 ng/mL)	By questionnaire: oral contraceptives (Estrogen-progestogen combined) IARC Grp 1, Alcoholic beverages IARC Grp 1, Tobacco Smoking Grp 1 No information on occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development.
Cohn et al. (2020) Breast cancer	Nested case control study 102 cases 310 control	Measured PFAS exposure in blood samples	Maternal blood samples collected 1–3 days postpartum. Breast cancer in daughters (prenatal exposure). Previous work identified good correlation between these early postpartum samples and prenatal PFAS levels.	Serum measurements of seven PFAS (EtFOSAA, MeFOSAA, PFDoA, PFHpA, PFHxS, PFOA and PFOS)	General population exposure. Samples from 1959–1967	Serum levels of PFOA and PFOS (ng/mL). For PFOS, considered both EtFOSAA and PFOS in same models. PFOA median = 0.4 PFOS median = 32.1	Limits of detection were 0.11 ng/mL for PFOS, 0.05 ng/mL for PFOA, 0.028 ng/mL for PFHxS, and 0.032 ng/mL for EtFOSAA, PFOS were each detected in 100% of samples, PFOA in 98% of samples and PFHxS in 99% of samples.	Investigators included DDT isomers and metabolites. The authors also consider EtFOSAA levels as a pre-cursor for PFOS.	Differential and non-differential exposure misclassification is Unlikely because all blood samples were handled in the same way. The authors indicate that they matched on trimester of blood draw; yet for 78% of subjects, they used postpartum samples. This is anticipated to be non-differential. All models were controlled for DDT exposure.
Eriksen et al. (2009) Prostate, bladder, pancreatic, liver cancer	Nested Case–control study from Prospective cohort of non-cancer subjects age 50–65 enrolled Dec 1, 1993–May 31, 1997 Danish Population 713 prostate Ca 332 bladder Ca 128 pancreatic Ca 67 liver Ca Comparison group 772	Plasma collected for all subjects at enrolment	Plasma and questionnaires collected at enrolment, plasma PFAS measurements at time of id as case or control Cases identified Dec 1, 1993–July 1, 2006 680 men and 92 women randomly selected as controls.	Perfluorooctanate (PFOA) and perflurooctanesulfonate (PFOS) No information on correlation of measurements Units; ng/mL	General populations	Single measurement of PFAS for cases and controls. Analysed as quartiles of PFOA and PFOS separately.	Ehresman et al. (2007): extractions were performed using solid phase extraction analysis with High pressure liquid chromatography coupled to tandem mass spectrometry use of labelled internal standards Whole blood used for standard curve matrix Three PFOA values that were below the lower limit of quantification (LOQ) of 1 ng/mL were assigned the value *Lod* / √ 2	By questionnaire: Tobacco Smoking IARC Grp 1 Rubber Industry IARC Grp 1 Textile Mfg IARC Grp 2B Painter IARC Grp 1 Glass Industry IARC Grp 3 Diesel Exhaust IARC Grp 1 No info on alcohol IARC Group 1,	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
Feng et al. (2022) Breast cancer	Nested case–control study Subjects are retired Dongfeng Motor Company (DMC) employees from a cohort recruited 2008-2010 and 2013 Dongfeng-Tongji (DFTJ) cohort, Shiyan, China 226 Breast cancer cases including 13 cases among the subcohort of 990 controls.	Measured serum concentration at “baseline’ which presumably means sample collected at the time of cohort enrolment	Subjects are retired Dongfeng Motor Company employees from a cohort recruited 2008-2010 and 2013 Follow up 18387 females without cancer for case ascertainment for 9.6 years till end 2018 Random sub cohort of 990 women matched by age as controls.	Four perfluorinated carboxylic acids (PFCAs): perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), and perfluoroheptanoic acid (PFHpA)] Two perfluorinated sulfonic acids (PFSAs): [perfluorooctane sulfonic acid (PFOS) perfluorohexane sulfonic acid (PFHxS)] Correlation of 6 PFAS: 0.21 (PFDA with PFHpA & PFHxS) 0.26 (PFHxS & PFNA) 0.32 (PFOA & PFOS) 0.52 (PFOS & PFNA)	General Population	Used individual PFAS and Sum of four perfluorinated carboxylic acids (PFCAs), Sum of two perfluorinated sulfonic acids (PFSAs), and sum of all PFAS as metrics. Units ng/mL In addition, the subjects were classified into low- and high-PFAS exposure subgroups by the median level of each individual PFAS and the summed PFAS, PFSAs, PFCAs,	Ultra-high-performance liquid chromatography system coupled with electrospray tandem mass spectrometry using internal standards LODs ranged from 0.001 to 0.01 ng/mL. The detection rate of PFHpA was 94.6% and of the other five PFASs were 100%. Concentrations below the LOD were replaced with LOD/2.	By questionnaire: oral contraceptives (Estrogen-progestogen combined) (IARC Grp 1), Tobacco Smoking (IARC Grp 1), Alcoholic beverages (IARC Grp 1). Occupation types were grouped into three categories: manufacturing or manual labour, service or sale, and office work	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to cancer development impacting serum levels of PFAS since serum sample prior to diagnosis although no info on average time between blood collection and diagnosis.
Frenoy et al. (2022) Breast cancer	Nested case–control E3N prospective cohort study of French women in National Education System 1990	Blood samples collected 1994-1998 from ~ 25% of cohort (volunteer) and serum analysed for PFOA and PFOS	Breast cancer cases collected from 1994-2003 but excluded if diagnosis before blood sampling or dietary questionnaire (1993). Controls matched on age, year of blood collection, menopausal status, and BMI at blood collection.	Measured in blood from 1994-1999 18 PFAS: perfluorobutane sulfonicacid (PBFS), perfluorodecane sulfonic acid (PFDS), perfluorobutanoic acid (PFBA), perfluoroalkyl phosphonic acid (PFPA), perfluorohexane sulfonic acid (PFHxA), perfluorododecanoic acid (PFDoA), perfluorohexane sulfonic acid (PFHxS), perfluoroheptane sulfonic acid (PFHpS), perfluorooctane sulfonic acid (PFOS), perfluorooctane sulfonamide (PFOSA), N-Methyl perfluorooctane sulfonamidoacetic acid (N_MeFOSAA), N-Ethyl perfluorooctane sulfonamidoacetic acid (N_EtFOSAA), perfluoroheptanoicacid (PFHpA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA) and perfluoroundecanoic acid (PFUnA). Correlations 0.5 or greater: PFOA & PFNA, PFHpA; PFOS & PFNA, PFDA, PFUnA; PFNA & PFDA, PFUnA; PFDA & PFUnA; Correlation 0.2-0.4 : PFOS & PFOSA, N_EtFOSAA, PFHpA; PFOSA & N-MeFOSAA, N_EtFOSAA, PFHpA, PFOA, PFNA, PFDA, PFUnA; N-EtFOSAA & N-MeFOSAA, PFHpA, PFOA; PFHpA & PFNA, PFDA, PFUnA PFOA & PFDA, PFUnA;	General Population	Single serum level of PFAS and BFR Units ng/mL Principal Components analysis on log transformed biomarker concentrations. For each of 4 principal components, components are used in continuous and quintiles in logistic regression models. Bayesian Kernel Machine Regression (BKMR) where biomarker concentrations were treated as continuous, log-transformed, and centered variables (subtraction of the mean) and produce Posterior Inclusion Probabilities (PIPs) for each of the two groups PFAS and BFR. BKMR also used to estimate univariate exposure-response function for each individual PFAS and BFR. Lastly, a “cumulative effect” of the overall exposure to the substances (more like a summed effect) is estimated.	Alkaline digestion followed by a two-stage solid phase extraction then liquid chromatography coupled to tandem mass spectrometry (LC–MS/MS) with labelled internal standards. No info on LOD 100% < LOD PBFS, PFDS, PFBA, PFPA, PFHxA, PFDoA (all eliminated from analysis) 0-1% < LOD PFHxS, PFHpS, PFOS, PFOA, PFNA, PFOSA, PFDA, PFUnA 4-9% < LOD N-Me4FOSAA, N-EtFOSAA, PFHpA, If < LOD imputation to ½ LOD	By questionnaire: Oral contraceptives (Estrogen-progestogen combined) (IARC Grp 1), Tobacco Smoking (IARC Grp 1), Alcoholic beverages (IARC Grp 1) collected but not utilized in analysis 6 polybrominated diphenyl ethers (PBDE): 2,2’,4,4’,6-pentabromodiphenyl ether (PBDE-100), 2,2’,4,4’,5,5’-hexabromodiphenyl ether (PBDE-153), 2,2’,4,4’,5,6’-hexabromodiphenyl ether (PBDE-154), 2,4,4’-tribromodiphenyl ether (PBDE-28), 2,2’,4,4’-tetrabromodiphenyl ether (PBDE-47), 2,2’,4,4’,5-pentabromodiphenyl ether (PBDE-99), 1 polybrominated biphenyl (PBB): 2,2’,4,4’,5,5’-hexabromobiphenyl (PBB-153), all PBDE were positively and strongly correlated, while no or weak correlations were observed between PBDE and PBB-15 or between PFAS and PBDE or between PFAS and PBB-153.	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to cancer development impacting serum levels of PFAS since serum sample prior to diagnosis although no info on time between blood collection and diagnosis.
Ghisari et al. (2017) Breast Cancer	Nested Case–control study from Prospective Birth Cohort 1996-2002 Danish Population 178 breast cancer cases and 233 controls (nulliparous and frequency matched on age)	Maternal serum collected at 6-14 weeks gestation Measured for 15 PFAS .	Blood and questionnaires collected at enrolment. Serum PFAS measurements at time of id of case or control	Bonefeld-Jørgensen et al. (2014): 10 perflurocarboxylated acids: perfluoro-n-pentanoic acid (PFPeA), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorooctanate acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnA), perfluorododecanoic acid (PFDoA), perfluorotridecanoic acid (PFTrA),	General population	Single measurement of maternal PFAS during gestation for cases and controls. Analysis focused on only 4 separate log transformed PFAS concentrations where all samples above detection limit: PFOS, PFHxS, PFOSA and PFOA Reported that each of these exposure variables was dichotomized into two categories, “low” or “high”, based on the median levels found in the controls but results not reported.	Bonefeld-Jørgensen et al. (2014): Solid phase extraction using labled internal standard and analysis with liquid chromatography–tandem mass spectrometry (LC–MS–MS) with electrospray ionization (ESI) in negative mode. 10 perflurocarboxylated acids**:** PFPeA, (2% > MDL 0.1 ng/mL) PFHxA, (2% > MDL 0.17 ng/mL) PFHpA (86% > MDL 0.02 ng/mL) PFOA (100% > MDL 0.07 ng/mL) PFNA, (100% > MDL 0.09 ng/mL) PFDA (89% > MDL 0.07 ng/mL)	By questionnaire: oral contraceptives (estrogen-progestogen combined) IARC Grp 1 Alcoholic beverages Grp 1 Tobacco Smoking Grp 1 No information on occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
				perfluorotetradecanoic acid (PFTeA) 5 perfluoroalkylsulphonates: perfluorobutane sulfonate (PFBS), perfluorohexane sulfonate (PFHxS), perfluoroheptane sulfonate (PFHpS), Perflurooctanesulfonate (PFOS) perfluorodecane sulfonate (PFDS) 1 perfluroalkyl sulfonamide: perflurooctane-sulfonamide, (PFOSA). Units ng/mL Significant correlations found between PFOS vs PFOA (0.69), vs PFOSA (0.58), vs PFNA (0.42), and PFHxS (0.15). Also significant correlations: PFOSA vs PFOA (0.36), PFNA vs PFOA (0.46) vs PFHxS (0.29), and PFHxS vs PFOA (0.17). Authors say knowing that PFOSA is a precursor for PFOS can partly explain the relatively high correlation coefficient, whereas the correlation coefficient of 0.36 for PFOSA versus PFOA might suggest common sources of exposure.			PFUnA (50% > MDL 0.25 ng/mL) PFDoA (60% > MDL 0.14 ng/mL) PFTrA (53% > MDL unspecified) PFTeA (01% > MDL unspecified) 5 perfluoroalkyl-sulphonates: PFBS (4% > MDL 0.02 ng/mL) PFHxS (100% > MDL 0.04 ng/mL) PFHpS (99.8% > MDL 0.05 ng/mL) PFOS (100% > MDL 0.41 ng/mL) PFDS (18% > MDL 0.12 ng/mL) 1 perfluroalkyl sulfonamide**:** PFOSA (100% > MDL 0.4 ng/mL)		
Goodrich et al. (2022) Hepatocellular Cancer (HCC)	Nested case–control Multi-ethnic cohort Prospective study California and Hawaii 50 cases HCC 50 controls	Pre-diagnostic (at recruitment) plasma samples analysed for 6 PFAS. Years between blood collection and diagnosis, Median (range) 7.2 (0.9, 16.4) Metabolomics analysis also conducted.	Cohort recruited in early 2000's Cases diagnosed during 20 year follow up using SEER Controls matched on age, sex race/ethnicity and study area.	Measured 6 PFAS in serum: two perfluorinated sulfonic acids (PFSAs): [perfluorooctane sulfonic acid (PFOS) perfluorohexane sulfonic acid (PFHxS)] four perfluorinated carboxylic acids (PFCAs): perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), and perfluoroundecanoic acid (PFUnDA). PFNA & PFDA correlation 0.9 PFUnDA & PFDA, PFNA correlation 0.7 PFOS & PFOA correlation 0.7 PFHxS & PFOA, PFOS correlation 0.6 PFOA & PFNA, PFDA correlation 0.5 PFOS & PFNA, PFDA correlation 0.3 PFNA & PFHxS correlation 0.3 The remainder PFDA & PFHxS and PFUnDA & PFOA, PFOS correlation ≤ 0.2 PFHxS & PFUndA correlation –0.03	General Population	Analysed as individual PFAS in conditional logistic regression, modeling PFAS exposure as a continuous variable scaled to a mean of zero and a standard deviation of one. Units µg/L (= ng/mL) PFAS also categorized as high vs. low based on the 90th percentile of exposure in NHANES 1999-2000, the earliest date that PFAS monitoring was performed in NHANES. This corresponded to the 85th percentile for PFOS in this study, and so to maintain consistency, the 85th percentile was used to define high vs. low exposure for all other PFAS. A metabolome wide association study examined the metabolic pathways associated with exposure to high levels of PFOS or HCC	Liquid chromatography with high-resolution mass spectrometry (LC-HRMS) with labelled internal standards. The limit of detection for plasma PFAS 0.43 µg/L for PFOS, 0.01 µg/L for PFOA, PFHxS, PFNA, PFDA 0.05 µg/L for PFUnDA PFOS, PFHxS, PFOS, PFDA, PFNA were detected in all participants. PFUnDA was detected in 29% of all participants. No info on how < LOD values of PFUnDA handled	By questionnaire: Tobacco Smoking (IARC Grp 1), Alcoholic beverages (IARC Grp 1). No information on occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method with minimal differences in LOQ over NHANES rounds, however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to HCC development impacting plasma levels of PFAS since plasma sample prior to HCC diagnosis, although no info on average time between blood collection and HCC diagnosis
Hurley et al. (2018) Breast cancer	Nested case–control study from Prospective California Teachers Study Cohort (1995-1996) 902 breast cancer cases and 858 controls	Serum measurements Blood draws Oct 2011 toAug 2015 average 35 month after case diagnosis (range, 9 mo-8.5 years)	Cases diagnosed with invasive breast cancer Jan 1, 2006-Aug 1, 2014. Controls age matched on age, race/ethnicity. residence	12 PFAS: PFOA (Perfluorooctanoic acid), PFNA (Perfluorononanoic acid), PFUnDA (Perfluoroun-decanoic acid), PFHxS (Perfluorohexane sulfonic acid), PFOS (Perfluorooctane sulfonic acid), MeFOSAA (2-(*N*-Methyl-perfluorooctane sulfonamido) acetic acid) PFOSA (Perfluorooctane sulfonamide), PFBS (Perfluorobutane sulfonic acid), EtFOSSA (2-(N-Ethyl-perfluorooctane sulfonamido) acetic acid), PFDA (Perfluorodecanoic acid), PFDoDA (Perfluorododeconic acid), PFHpA (Perfluoroheptanoic acid) Statistically significant positive correlations were observed between all the PFASs ranging from 0.21 (for PFHxS and PFUnDA) to 0.63 (for PFOS and PFOA). Correlations between the PFASs were generally similar among cases and controls	General Population	Risk analyses were restricted to the single point measurement of six PFAS with detection frequency ≥ 95%: PFOA, PFNA, PFUnDA, PFHxS, PFOS, MeFOSAA, PFNA Used either log of concentration or low, medium, high categories based on tertiles of the PFAS concentrations in the controls. Six PFASs with detection frequencies (DF) below 95% were excluded from analysis ng/mL units	Sample solid phase extraction analysed by HPLC-MS/MS with labelled internal standards Detection Frequency > 95% for: PFOA (LOD 0.8 ng/mL) PFNA (LOD 0.03 ng/mL) PFUnDA (LOD 0.02 ng/mL) PFHxS (LOD 0.02 ng/mL) PFOS (LOD 0.08 ng/mL) MeFOSAA (LOD 0.02 ng/mL) Detection Frequency 8-89%) for: PFOSA (LOD 0.02 ng/mL) PFBS (LOD 0.05 ng/mL) EtFOSSA (LOD 0.02 ng/mL) PFDA {LOD 0.06 ng/mL) PFDoDA (LOD 0.1 ng/mL) PFHpA (LOD 0.03 ng/mL) Samples with PFAS concentrations below the LOD were imputed as LOD/ √ 2	By questionnaire: oral contraceptives (Estrogen-progestogen combined) IARC Grp 1, Alcoholic beverages Grp 1, Tobacco Smoking Grp 1. No information on occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development. Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS
Madrigal et al. (2024) Thyroid cancer	Nested case–control study from a population-based national maternity cohort in Finland	400 primary papillary thyroid cancer cases (diagnosed at least 3 years after their delivery) and who had no prior cancer.	Blood collection in 1987 to 2010 Cases diagnosed at least 3 years after their delivery	PFAS measured: PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeDA, PFHxS, PFHpS, PFOS, PFDS, MeFOSAA, EtFOSAA, FOSA, MeFOSA, EtFOSA, 6:2 diPAP, Spearman's rank correlations:	General population	Single measurement of PFAS for cases and controls. Individual congeners Units: ng/mL	PFASs: LC-MS/MS LOQs (ng/mL): PFOA: 0.15 PFOS: 0.2	Measured: HCB, β-HCH, TRANSNONACHLOR, *p,p*-DDT, *p,p*-DDE, PCB 74, PCB 99, PCB 118, PCB 138, PCB 153, PCB 156, PCB 170, PCB 180, PCB 183, PCB 187 Medical Birth Registry: smoking	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
		400 individually matched controls based on strata of calendar year of delivery and age at first birth Serum measurements of all subjects		PFOA:PFDA:0.02 PFOA:EtFOSAA: 0.39 PFOA:MeFOSAA: 0.20 PFOA:PFHxS: 0.20 PFOA:PFNA:0.27 PFOA:PFOS: 0.61 PFOS:PFDA:-0.21 PFOS:EtFOSAA: 0.70 PFOS:MeFOSAA: 0.18 PFOS:PFHxS: 0.24 PFOS:PFNA:-0.07			PFHxS: 0.2 PFNA: 0.15 EtFOSAA: 0.15 MeFOSAA: 0.15 PFDA: 0.15 PFUnDA: 0.2 PFHpS: 0.2 PFHpA: 0.15 PFTeDA: 0.2 PFDS: 0.2 PFHxA: 0.15 MeFOSA: 0.5 6:2 di-PAP: 0.2 PFTrDA: 0.2 FOSA: 0.2 EtFOSA: 0.5 PFDoDA: 0.2 Detection frequencies: PFOA: 100% PFOS: 100% PFNA: 84% PFHxS: 83% EtFOSAA: 77% MeFOSAA: 77% PFDA:57% PFUnDA: 29% PFHpS: 9.7% PFHpA: 7.0% PFTeDA: 3.0% 6:2 diPAP: 2.7% PFHxA, MeFOSA, PFDoDA, PFTrDA, PFDS, FOSA and EtFOSA: < 2.5%	No information: Alcohol consumption, occupation Spearman rank correlations: PFOA: HCB: 0.20 PFOA: β-HCH: 0.26 PFOA: TRANSNONACHLOR: 0.18 PFOA: *p,p*-DDT: 0.23 PFOA: *p,p*-DDE: 0.18 PFOA: PCB 74: 0.26 PFOA: PCB 99: 0.20 PFOA: PCB 118: 0.23 PFOA: PCB 138: 0.23 PFOA: PCB 153: 0.24 PFOA: PCB 156: 0.24 PFOA: PCB 170: 0.25 PFOA: PCB 180: 0.25 PFOA: PCB 183: 0.22 PFOA: PCB 187: 0.25 PFOS: HCB: 0.56 PFOS: β-HCH: 0.57 PFOS: TRANSNONACHLOR: 0.46 PFOS: *p,p*-DDT: 0.54 PFOS: *p,p*-DDE: 0.49 PFOS: PCB 74: 0.55 PFOS: PCB 99: 0.52 PFOS: PCB 118: 0.54 PFOS: PCB 138: 0.54 PFOS: PCB 153: 0.53 PFOS: PCB 156: 0.53 PFOS: PCB 170: 0.54 PFOS: PCB 180: 0.53 PFOS: PCB 183: 0.54 PFOS: PCB 187: 0.52	reflect relevant exposure during cancer development. Cases and matched controls were analysed in the same batch
Mancini et al. (2020) Breast cancer	Nested case–control E3N prospective cohort study of French women in National Education System 1990 194 breast cancer cases and 194 controls	Blood samples collected 1994–1998 from ~ 25% of cohort (volunteer) and serum analysed for PFOA and PFOS	Breast Cancer cases collected from 1994-2003 but excluded if diagnosis before blood sampling or dietary questionnaire (1993). Controls matched on age, year of blood collection, menopausal status, and BMI at blood collection.	Measured PFOA and PFOS 1994-1998 No information on correlation of PFOA and PFOS	General population	Single serum level of PFOA and PFOS. Each PFAS separately analysed as tertiles	Alkaline digestion followed by a two-stage solid phase extraction then liquid chromatography coupled to tandem mass spectrometry (LC–MS/MS) with labelled internal standards. PFOS and PFOA were detected in all samples.	By questionnaire: oral contraceptives (Estrogen-progestogen combined) (IARC Grp 1), Tobacco Smoking (IARC Grp 1). No info on Alcoholic beverages (IARC Grp 1)	Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to cancer development impacting serum levels of PFAS since serum sample prior to diagnosis although no info on time between blood collection and diagnosis.
Purdue et al. (2023) Testicular cancer	Nested case–control study in US Air Force Service men 530 cases 530 controls matched on birthdate, race and ethnicity, year entered service and year of sample collection. Cases collected between 1990 and 2018	Serum samples collected 1988–2018 187 subjects (cases and controls) had a second blood sample collected a median of 4 years after first sample 9 PFAS measured	All exposures measured prior to cancer diagnosis Median time between sample collection and diagnosis = 5 years (0, 19.8 years) 2nd sample population, median time = 10.3 years (5–19.8 years)	Nine PFAS measured in serum 2-(*N*-methyl-perfluorooctane sulfonamido)aceticacid (MeFOSAA), perfluorohexanesulfonic acid (PFHxS), perfluorononanoicacid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoicacid (PFUnDA), Total PFOS = sum of branched PFOS isomers (Sm-PFOS) and linear PFOS (n-PFOS), Total PFOA = sum of linear PFOA (n-PFOA), and branched perfluorooctanoicacids (Sb-PFOA)] PFOS & PFOA; PFDA & PFNA or PFUnDA Correlation 0.7 PFHxS & PFOS correlation 0.6 PFOA and PFHxS or MeFOSSA correlation 0.5	General population exposure Considered military occupation as a firefighter	Main analyses focus on one sample (530 cases/controls) Additional analysis focusing on second sample PFAS categorized using quartiles among controls as cut points or for subjects with 2 samples both samples used to categorize subject based on dichotomized categories (using the median among controls) Some analysis focused on a specific PFAS and others included all other PFAS as covariates (using same definitions for categories) Units ng/mL	LOD was 0.1 ng/mL for all analytes. Detection frequency was 100% for PFOS, PFOA, PFHxS; PFNA 99.8% PFDA 98.9% MeFOSAA 97.8%, PDUnDA 89.4% Values below LOD were assigned ½ LOD.	Consideration of other potential PFAS sources: working as a firefighter or living at a base with elevated PFAS in ground water, years of service. Other covariates in models were military grade and number of deployments	Unlikely, because all samples were collected before disease and analysed in the same fashion. If testicular cancer alters ADME of PFAS there could be possible differential exposure misclassification; given that samples were collected on average 5 years prior to diagnosis this is thought to be unlikely.

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
				MeFOSAA & PFDA -0.4 The rest ≤ 0.3 or -0.3 Among controls, two distinct clusters of PFAS correlated with one another: a) PFOS, PFOA, PFHxS, and MeFOSAA b) PFNA, PFDA,and PFUnDA with PCA accounting for 75% variance					
Rhee et al. (2023) Aggressive Prostate Cancer	Nested case–control study PLCO 750 cases 750 controls	PFAS were measured in serum samples.	Median time between sample collection and diagnosis = 9 years (IQR: 5–13 years) All samples collected prior to diagnosis	EtFOSAA MeFOSAA FOSA PFHxS PFHpS PFNA n-PFOA sum branched PFOA (sb-PFOA) n-PFOS sum of perfluoromethylheptane sulfonate isomers (sm-PFOS) correlation between PFOA and PFOS = 0.7 ICC for PFOA at 3 points in time = 0.73 ICC for PFOS at 3 points in time = 0.85	General population exposures	PFAS measured in serum One measurement for most (ng/mL serum) 60 controls analysed at 0,1, and 5 years past enrolment to assess intra-individual variability.	Not specifically reported. 95% or more detection frequency.	Co-exposures to smoking, alcohol were collected. Smoking was included as a confounder in statistical models. No information on how these correlate with PFAS.	unlikely
Rhee et al. (2023) Renal Cell Carcinoma (RCC)	Nested case–control Multi-ethnic Cohort Prospective study California and Hawaii 428 RCC cases 428 individually matched controls	Some samples post-diagnosis (1994–2001) (21%) and the remainder of samples pre-diagnostic (79%) (2001–2006) Samples analysed for 11 PFAS.	Cohort recruited 1993-1996 Cases diagnosed during 20-year follow-up using SEER & state registries Controls matched on age, sex race/ethnicity and study area, age at serum collection (±1 year), date of serum collection (±1 year), time of serum collection (±3 h), and fasting status	Measured 11PFAS in serum: Three sulonamides: Perfluorooctane sulfonamide (FOSA), 2-N-methyl-perfluorooctane sulfonamido acetate (MeFOSAA), 2-N-ethyl-perfluorooctane sulfonamido acetate (EtFOSAA), three perfluorinated sulfonic acids (PFSAs): linear perfluorooctane sulfonic acid (n-PFOS) sum of perfluoromethylheptane sulfonic acid isomers (Sm-PFOS), [total PFOS = n-PFOS + sm-PFOS] perfluorohexane sulfonic acid (PFHxS)] five perfluorinated carboxylic acids (PFCAs): linear perfluorooctanoic acid (n-PFOA), sum of branched PFOA isomers (Sb-PFOA) Total PFOA = n-PFOA + Sb-PFOA] perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA). PFOS & PFOA correlation 0.61 PFNA & PFDA and PFUnDA & PFDA correlation 0.8 PFDA & PFNA, PFHxS & PFOS, PFOA & PFNA, PFNA & PFUnDA, MeFOSAA & EtFOSAA correlation 0.6 PFOA & PFHxS & PFDA, PFOS & MeFOSAA, EtFOSAA, PFNA correlation 0.5 PFOS & PFDA correlation 0.4 The remainder of correlations < 0.4	General Population	Analysed as individual PFAS in conditional logistic regression, modelling PFAS exposure as a continuous variable (log2 transformed) and as quartiles Also analysed for individual PFAS adjusted for log2 transformed) serum concentrations of PFOA, PFOS, PFHxS, and FOSA (non-detectable, detectable, missing) Units µg/L (= ng/mL)	high-performance liquid chromatography–isotope dilution-tandem mass spectrometry The limit of detection for serum PFAS 0.1 µg/L PFHxS, PFOS, PFOA, and PFNA were detected in ≥ 97% of participants samples. MeFOSAA, EtFOSAA, PFDA, and PFUnDA were detectable in 70-85% of samples, 24% of results were detectable for FOSA below the LOD were assigned a value of the LOD/√2 (0.071 µg/L).	By questionnaire: Tobacco Smoking (IARC Grp 1), Alcoholic beverages (IARC Grp 1). No information on occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to RCC development impacting serum levels of PFAS since sample collected prior to RCC diagnosis, although no info on average time between blood collection and RCC diagnosis
Shearer et al. (2021) Renal Cell Carcinoma	Nested case–control study 324 cases 324 controls	Serum measurements of 8 PFAS (including PFOA and PFOS) using standard methods	Blood samples collected at study enrolment in 1993–2001; cancer diagnosed on average 8.8 years after blood draw (range 2–18 years)	Measured 10 different PFAS. Total PFOA (sum of linear and branched PFOA). Total PFOS (sum of PFOS isomers)	General population exposure	Serum levels of PFOA and PFOS (divided into quartiles and continuous µg/L = ng/mL)) PFOA range (< 4–27.2 ng/mL) PFOS range (< 26.3–154.2 ng/mL)	The limit of detection (LOD) was 0.1 µg/L for all analytes; concentrations below the LOD were assigned a value of one-half the LOD	Controlled for smoking, BMI and eGFR Spearman correlation coefficients of 0.62 for PFOA vs PFOS, 0.42 for PFOA vs PFHxS, and 0.45 for PFOS vs PFHxS	Differential and non-differential exposure misclassification are unlikely, all blood samples were handled in the same way. Controls were matched on study year of blood draw.
Wen et al. (2022) Mortality (all, cancer, heart disease)	Cohort Study NHANES population 1999–2014 11 747 subjects 372 heart disease deaths, 248 cancer deaths	Measured serum PFOA & PFAS	Subjects from US nationally conducted survey	Measured 12 serum PFAS but used 7 in analysis: PFDE, perfluorodecanoic acid, PFHS, perfluorohexane sulfonate acid, PFNA, perfluorononanoic acid, PFOA, perfluorooctanoic acid, PFOS, perfluorooctane sulfonic acid, PFUA, perfluoroundecanoic acid MPAH, 2-(N-methyl-perfluorooctane sulfonamido) acetic acid;	General Population	Used tertiles of PFOA, PFOS concentrations Units ng/mL Also used categories of low, medium high for Total PFAS, Total PFAS excluding PFOA and Total PFAS excluding PFOS Exposure categories (L/M/H) determined by the k-means algorithm which is a non–model-based method that can be used to categorize mixture data.by	PFAS were quantified in serum by solid-phase extraction–high-performance liquid chromatography–turbo-ion spray ionization–tandem mass spectrometry (SPE-HPLC-TCI-MS/MS). The Limit of quantification (LOQ) was 0.1 ng/mL for all PFAS 2013-2014 as well as for PFOS, PFOA, PFHS, PFNA in 1999–2000. It was 0.3 ng/mL for PFDE, MPAH, PFUA in 1999–2000 Detection rate for 1999–2014 PFOS 99%	By questionnaire: Tobacco Smoking (IARC Grp 1), Alcoholic beverages (IARC Grp 1). No information on occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method with minimal differences in LOQ over NHANES rounds, however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to cancer or heart disease development impacting serum levels of PFAS

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
				Excluded three PFAS whose serum concentrations were not measured in one or more NHANES cycles from 1999 to 2014: [2-(N-ethyl-perfluorooctanesulfona- mido) acetic acid(EPAH), perfluorooctanesulfonamide (PFSA), and perfluorobutanesulfonicacid (PFBS)]' Also excluded two PFAS whose detection rates in the population were ~10% or less: [perfluorododecanoicacid (PFDO) and perfluoroheptanoicacid (PFHP)] The most significant correlation was observed between serum concentrations of PFUA and PFDE (correlation=0.83). Serum concentrations of other PFAS showed weak-to-moderate correlations (0.02<correlation≤0.50).		constructing clusters so that the squared Euclidean distance between the row vector for any object and the centroid vector of its respective cluster is at least as small as the distances to the centroids of the remaining clusters. Clusters are visualized by t-Distributed Stochastic Neighbor Embedding (t-SNE).	PFOA 99% PFHS 98% PFNA 98% PFDE 66% MPAH 50% PFUA 43% Samples with PFAS concentrations below the LOQ were substituted with the value of the LOQ/√2		since serum sample prior to death, tho no info on average time between blood collection and death
Winquist et al. (2023) Various cancers	Nested case–control American Cancer Society's Cancer Prevention Study II LifeLink cohort Originally 1 185 106 participants from 50 US states and the District of Columbia. 1998–2001 39 371 surviving CPS-II Nutrition Cohort participants residing in urban or suburban areas of 20 states were recruited for participation in the CPS-II LifeLink Cohort Cases: All participants with incident cancers for whom the first cancer diagnosis was kidney, bladder, breast (females only), prostate (males only), or pancreatic cancer, or lymphoma or leukaemia Controls: 500 men and 499 women	Serum collected 1998–2001	Serum collected 1998–2001 median follow-up time for members of the sub-cohort was 14.3 years (median 13.1 years for males and 14.7 years for females; minimum 1 month, maximum 17 years)	6 PFAS linear isomers (only) of PFOA, PFOS, PFNA,PFHxS, FOSA, perfluorobutane sulfonic acid (PFBS) and perfluoroheptanoic acid (PFHpA)	General population	Log 2 concentration and quartiles determined by cases used for each individual PFAS	LC-MS/MS specimens prepared by protein precipitation using acetonitrile and filtration through a phospholipid depletion phase and isotopically labelled internal standards added, Reporting Limit (ng/ml) PFOA 0.5; PFBS 0.05; PFHxS 0.05; PFOS 0.5; PFHpA 0.05; PFNA 0.05; and FOSA 0.1. If < LOD replace with LOD/sq rt 2	Information on smoking and alcohol by questionnaire. No information on occupation	Non-differential exposure misclassification unlikely from method as all measurements using same method however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to cancer development impacting serum levels of PFAS since sample collected prior to diagnosis,
Zhang et al. (2023) Incident Pancreatic Cancer	Nested case–control ATBC Cohort (Alpha-tocopherol, beta carotene cancer prevention study) (male Finnish smokers) 251 cases 251 controls PLCO Cohort (Prostate, Lung, Colon, and Ovarian Cancer Screening Trial) (US population, males and females) 360 cases 360 controls Controls matched to cases based on age at blood draw, date at blood draw and for PLCO, sex and race	Serum measured using non-targeted methods (Metabolon) ATBC samples were analysed in 2013/2014; PLCO samples were analysed in 2017/2018	General population samples ATBC is male Finnish smokers aged 50–69 years at enrolment (1985–1988); PLCO enrolled men and women at 10 sites in the US ages 55–74 years at enrolment (1992–2001) Time between sample collection and cancer diagnosis: ATBC median = 12 years (range = 0–24 years) PLCO median = 9 (0–18 years)	PFOA and PFOS Correlations not reported Other PFAS not reported	General population exposures (different countries – Finland and US)	PFAS levels were divided in quintiles, with separate analyses for each cohort.	Non-targeted methods PFOA and PFOS were detected in all samples	Smoking, BMI, No other IARC carcinogens	Non-differential exposure misclassification unlikely from method as all measurements using same method however a single measurement may not reliably reflect relevant dose during cancer development. Unlikely differential exposure misclassification due to cancer development impacting serum levels of PFAS since sample collected prior to diagnosis,
Liu et al. (2022) Thyroid cancer	Case–control One hospital in Shandong, China	Cases (n = 134) were diagnosed with thyroid cancer and treated in hospital Controls (n = 185) were undergoing routine medical visits in the hospital Serum measurements of all subjects	Blood collection in 2016–2017, between treatment periods (cases) or enrolment (controls)	PFAS measured; PFOS, PFOA, PFBA, PFPeA, PFHxA, PFHpA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeDA, PFBS, PFPeS, PFHxS, PFHpS, PFNS, PFDS, 6:2 Cl-PFESA, 8:2 Cl-PFESA, 10:2 Cl-PFESA Correlations between PFAS not reported	General population	Single measurement of PFAS for cases and controls. Individual congeners Units: ng/mL	LC-MS/MS LODs (ng/mL) were: 0.009 for PFOA, 0.008 for PFNA, 0.007 for PFDA, 0.011 for PFUnDA, 0.009 for PFHxS, 0.003 for PFOS, 0.01 for 8:2 Cl-PFESA Detection frequencies: PFOA: 100% of cases, 100% of controls PFNA: 100% of cases, 100% of controls PFDA: 100% of cases, 99% of controls PFUnDA: 99% of cases, 100% of controls PFHxS: 99% of cases, 98% of controls PFOS: 100% of cases, 100% of controls 8:2 Cl-PFESA: 100% of cases, 100% of controls	No information on any potential co-exposures to other carcinogens	Possible differential exposure misclassification if cancer diagnosis impacts serum levels of PFAS. Non-differential exposure misclassification unlikely from method as all measurements using same method in same time frame, however a single measurement may not reliably reflect relevant exposure during cancer development.
Vieira et al. (2013) All cancers	Case–control study of all cancer cases within C8 study region and neighbouring counties (13 counties total). Case–control comparisons of specific cases versus all other cases	Address at diagnosis was used to assign PFOA exposure. Individuals from OH (~1/3 of sample) were geocoded while individuals from WV were assigned exposure based on geographic unit. Water district PFOA levels was available for all individuals; for OH individuals PFOA serum values could be estimated based on exposure models (Shin et al., 2011a, b)	Water district at time of cancer diagnosis. Exposure estimation assumed a 10-year residency. Based on 1995 water exposure levels and serum concentrations. PFOA only	PFOA was estimated using quantitativemethods for OH residents	Contaminated drinking-water	For overall analysis, exposed versus unexposed. Exposed defined as PFOA contaminated water district. For OH residents, Analyses was based on five PFOA serum groups (ug/L-years): very high, high, medium, low, and background		Information on smoking status.	There is potential for exposure misclassification because address at time of diagnosis was used to assign exposure. This is likely to non-differential since all participants were individuals with cancer. The authors report that median residency time for individuals over 50 years was 17 years.

Table S1.22 Exposure assessment review and critique for epidemiological studies on cancer in humans exposed to PFOA and PFOS

Reference and outcome **(Cancer types)**	**What was the study design?** **(Prospect/case–control/Retro)** **Cohort name** **No. of cases and controls, matching criteria**	**What methods were used for the exposure assessment? (incl. data source, measured or modelled concentrations in environmental and biological media.)** **Specify if Serum or Environmental measurements** **If Env: air or water measurement?**	**What was the exposure context?** **Specify time period over which exposure data gathered, and how historical exposures were accounted for (if relevant)** **What was timing of exposure relative to outcome? Measurement at time of case ascertain or historical**	**What PFAS were measured?** **Which PFAS exposure was likely but unmeasured.** **Correlation of PFAS if available**	**Which exposure sources were assessed?** **Specific Occup exposure vs Gen pop sources** **Identified Env contam source (water etc)**	**What exposure metrics were derived for use in analyses (e.g. single point measurement, average exposure over time, exposure duration, cumulative exposure etc.)?** **(specify units)**	**Analytical method and LOD for each PFAS and% subjects < LOD if avail**	**Was there potential for co-exposures to other carcinogens?** **Which ones were measured?** **Use IARC List** **Any info on correlation of other exposures with PFAS levels**	**Was there potential for differential exposure misclassification?** **Was there potential for non-differential exposure misclassification?** **(Likely/unlikely)**
		Semiquantitative for full sample because in WV, residential history was not available. [exposed vs not exposed]							
Chang et al. (2023) Post-menopausal breast cancer	Nested case control study 621 cases; 621 controls Using incidence density sampling, controls were selected from among women who were postmenopausal at baseline, alive and cancer-free (excluding nonmelanoma skin cancer) at the time of case diagnosis, and were individually matched to cases by age at baseline (±2 years), date of blood draw (±3 months), and MHT use at baseline.	PFOA and PFOS were measured in pre-diagnostic serum using non-targeted methods	Blood samples collected at study enrolment in 1993–2001; cancer diagnosed 5.6 years after blood draw (range 2–18 years)	Non-targeted analysis for PFOA and PFOS. Used quartiles of exposure level within the sample. No other PFAS analysed.	General population exposure	Serum levels of PFOA and PFOS divided into quartiles Controlled for co-exposure by including a linear term for the other PFAS in the model.	Non-targeted analysis for PFOA and PFOS in serum	PFOA and PFOS in serum were correlated at 0.6 Smoking status was assessed	Non-differential and differential exposure misclassification is unlikely as all samples analysed in the same way. Models adjusted for smoking and BMI. MHT was included as a matching factor

ADME, absorption, distribution, metabolism, and excretion; AFFF, aqueous film-forming foam; AL, Alabama; APFO, ammonium perfluorooctanoate; ATBC, Alpha-Tocopherol, Beta-Carotene cancer prevention study; BDE, polybrominated diphenyl ethers; BMI, body mass index; BTF, benzotrifluorides; Cd, cotinine; 9CL-PF3ONS, perfluoro(2-((6-chlorohexyl)oxy)ethanesulfonic acid); 11CL-PF3OUdS, 11-chloroperfluoro-3-oxaundecanesulfonic acid; CNBCSP, Chinese National Breast Cancer Screening Program; DFTJ, Dongfeng-Tongji; E3N, Etude épidémiologique auprès de femmes de la Mutuelle générale de l'Education nationale; ECD, electron capture dissociation; EM, exposure matrix; ESI, electrospray ionization; EtFOSAA, *N*-ethylperfluorooctane sulfonamidoacetic acid; FA, fluoroaromatics; FTS, fluorotelomer sulfonic acid; GC, gas chromatography; GCT, germ cell tumour; HCC, hepatocellular cancer; β-HCH, beta-hexachlorocyclohexane; HRMS, high-resolution mass spectrometry; IQR, interquartile range; JEM, job-exposure matrix; LC, liquid chromatography; LOD, limit of detection; LOQ, limit of quantification; M556, perfluorooctanesulfonamidoacetate; M570, *N*-methyl perfluorooctanesulfonamidoacetate; MDL, method detection limit; *N*-MeFOSAA, *N*-ethylperfluoro-octanesulfonamido-acetic acid; MHT, menopausal hormone therapy; mo, month(s); MS, mass spectrometry; MS/MS, tandem mass spectrometry; MQL, method quantification limit; *n*-, linear isomer; NHANES, National Health and Nutrition Examination Survey; NR, not reported; OCP, organochlorine pesticide; PCB, polychlorinated biphenyl, PFCA, total perfluoroalkyl carboxylic acids; PFBS, perfluorobutanesulfonic acid; PFBuS, perfluorobutane sulfonic acid; PFCA, perfluoroalkyl carboxylic acid; PFDA, perfluorodecanoic acid; PFDoA, perfluorododecanoic acid; PFDoDA, perfluorododecanoic acid; PFDS, perfluorodecanesulfonic acid; PFESA polyfluorinated ether sulfonate; PFHpA, perfluoroheptanoic acid; PFHpS, perfluoroheptane sulfonic acid; PFHxA, perfluorohexanoic acid; PFHxS, perfluorohexanesulfonic acid; PFNA, perfluorononanoic acid ; PFOA, perfluorooctanoic acid; PFOPA, perfluorooctylphosphonic acid; PFOS, perfluorooctane sulfonic acid; PFOSA, perfluorooctanesulfonylamid; PFOSAA, *N*-ethyl perfluorooctanesulfonamidoacetat; PFPeA perfluoro-*n*-pentanoic acid; PFSA, perfluoroalkyl sulfonic acid; PFTeDA, perfluorotetradecanoic acid; PFTrDA, perfluorotridecanoic acid; PFUnDA, perfluoroundecanoic acid; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer; POP, persistent organic pollutant; ppm, parts per million; RCC, renal cell carcinoma; *sb*-, sum of branched isomers; TFE, tetrafluoroethylene; TWA, time-weighted average; USA, United States of America; vs, versus; WV, West Virginia; yr, year(s).

References

Alexander BH, Olsen GW (2007). Bladder cancer in perfluorooctanesulfonyl fluoride manufacturing workers. Ann Epidemiol. 17(6):471–8. https://doi.org/10.1016/j.annepidem.2007.01.036 PMID:17448680

Alexander BH, Olsen GW, Burris JM, Mandel JH, Mandel JS (2003). Mortality of employees of a perfluorooctanesulphonyl fluoride manufacturing facility. Occup Environ Med. 60(10):722–9. https://doi.org/10.1136/oem.60.10.722 PMID:14504359

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):1313–8. https://doi.org/10.1289/ehp.1306615 PMID:24007715

Bonefeld-Jørgensen EC, Long M, Bossi R, Ayotte P, Asmund G, Krüger T, et al. (2011). Perfluorinated compounds are related to breast cancer risk in Greenlandic Inuit: a case control study. Environ Health. 10(1):88. https://doi.org/10.1186/1476-069X-10-88 PMID:21978366

Bonefeld-Jørgensen EC, Long M, Fredslund SO, Bossi R, Olsen J (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):1439–48. https://doi.org/10.1007/s10552-014-0446-7 PMID:25148915

Cao L, Guo Y, Chen Y, Hong J, Wu J, Hangbiao J (2022). Per-/polyfluoroalkyl substance concentrations in human serum and their associations with liver cancer. Chemosphere. 296:134083. https://doi.org/10.1016/j.chemosphere.2022.134083 PMID:35216980

Chang VC, Rhee J, Berndt SI, Moore SC, Freedman ND, Jones RR, et al. (2023). Serum perfluorooctane sulfonate and perfluorooctanoate and risk of postmenopausal breast cancer according to hormone receptor status: An analysis in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. Int J Cancer. 153(4):775-782. https://doi.org/10.1002/ijc.34487 PMID:36843273

Chen Y, Paul KC, Walker DI, Jones DP, Wang X, Ritz BR, et al. (2023). Neonatal per- and polyfluoroalkyl substance exposure in relation to retinoblastoma. Environ Res. 240(Part 2):117435. https://doi.org/10.1016/j.envres.2023.117435 PMID:37866539

Cohn BA, La Merrill MA, Krigbaum NY, Wang M, Park JS, Petreas M, et al. (2020). In utero exposure to poly- and perfluoroalkyl substances (PFASs) and subsequent breast cancer. Reprod Toxicol. 92:112–9. https://doi.org/10.1016/j.reprotox.2019.06.012 PMID:31323350

Consonni D, Straif K, Symons JM, Tomenson JA, van Amelsvoort LG, Sleeuwenhoek A, et al. (2013). Cancer risk among tetrafluoroethylene synthesis and polymerization workers. Am J Epidemiol. 178(3):350–8. https://doi.org/10.1093/aje/kws588 PMID:23828249

Ehresman DJ, Froehlich JW, Olsen GW, Chang SC, Butenhoff JL (2007). Comparison of human whole blood, plasma, and serum matrices for the determination of perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA), and other fluorochemicals. Environ Res. 103(2):176–84. https://doi.org/10.1016/j.envres.2006.06.008 PMID:16893538

Eriksen KT, Sørensen M, McLaughlin JK, Lipworth L, Tjønneland A, Overvad K, et al. (2009). Perfluorooctanoate and perfluorooctanesulfonate plasma levels and risk of cancer in the general Danish population. J Natl Cancer Inst. 101(8):605–9. https://doi.org/10.1093/jnci/djp041 PMID:19351918

Feng Y, Bai Y, Lu Y, Chen M, Fu M, Guan X, et al. (2022). Plasma perfluoroalkyl substance exposure and incidence risk of breast cancer: A case–cohort study in the Dongfeng-Tongji cohort. Environ Pollut. 306:119345. https://doi.org/10.1016/j.envpol.2022.119345 PMID:35472559

Frenoy P, Perduca V, Cano-Sancho G, Antignac JP, Severi G, Mancini FR (2022). Application of two statistical approaches (Bayesian Kernel Machine Regression and Principal Component Regression) to assess breast cancer risk in association to exposure to mixtures of brominated flame retardants and per- and polyfluorinated alkylated substances in the E3N cohort. Environ Health. 21(1):27. https://doi.org/10.1186/s12940-022-00840-4 PMID:35216589

Ghisari M, Long M, Røge DM, Olsen J, Bonefeld-Jørgensen EC (2017). Polymorphism in xenobiotic and estrogen metabolizing genes, exposure to perfluorinated compounds and subsequent breast cancer risk: A nested case–control study in the Danish National Birth Cohort. Environ Res. 154:325–33. https://doi.org/10.1016/j.envres.2017.01.020 PMID:28157646

Girardi P, Merler E (2019). A mortality study on male subjects exposed to polyfluoroalkyl acids with high internal dose of perfluorooctanoic acid. Environ Res. 179(Pt A):108743. https://doi.org/10.1016/j.envres.2019.108743 PMID:31542491

Goodrich JA, Walker D, Lin X, Wang H, Lim T, McConnell R, et al. (2022). Exposure to perfluoroalkyl substances and risk of hepatocellular carcinoma in a multiethnic cohort. JHEP Rep. 4(10):100550. https://doi.org/10.1016/j.jhepr.2022.100550 PMID:36111068

Hardell E, Kärrman A, van Bavel B, Bao J, Carlberg M, Hardell L (2014). Case–control study on perfluorinated alkyl acids (PFAAs) and the risk of prostate cancer. Environ Int. 63:35–9. https://doi.org/10.1016/j.envint.2013.10.005 PMID:24246240

Hurley S, Goldberg D, Wang M, Park JS, Petreas M, Bernstein L, et al. (2018). Breast cancer risk and serum levels of per- and poly-fluoroalkyl substances: a case–control study nested in the California Teachers Study. Environ Health. 17(1):83. https://doi.org/10.1186/s12940-018-0426-6 PMID:30482205

Itoh H, Harada KH, Kasuga Y, Yokoyama S, Onuma H, Nishimura H, et al. (2021). Serum perfluoroalkyl substances and breast cancer risk in Japanese women: A case–control study. Sci Total Environ. 800:149316. https://doi.org/10.1016/j.scitotenv.2021.149316 PMID:34392213

Li H, Hammarstrand S, Midberg B, Xu Y, Li Y, Olsson DS, et al. (2022b). Cancer incidence in a Swedish cohort with high exposure to perfluoroalkyl substances in drinking water. Environ Res. 204(Pt C):112217. https://doi.org/10.1016/j.envres.2021.112217 PMID:34662573

Li X, Song F, Liu X, Shan A, Huang Y, Yang Z, et al. (2022a). Perfluoroalkyl substances (PFASs) as risk factors for breast cancer: a case–control study in Chinese population. Environ Health. 21(1):83. https://doi.org/10.1186/s12940-022-00895-3 PMID:36085159

Li Y, Fletcher T, Mucs D, Scott K, Lindh CH, Tallving P, et al. (2018). Half-lives of PFOS, PFHxS and PFOA after end of exposure to contaminated drinking water. Occup Environ Med. 75(1):46–51. https://doi.org/10.1136/oemed-2017-104651 PMID:29133598

Lin HW, Feng HX, Chen L, Yuan XJ, Tan Z (2020). Maternal exposure to environmental endocrine disruptors during pregnancy is associated with pediatric germ cell tumors. Nagoya J Med Sci. 82(2):323–33. https://doi.org/10.18999%2Fnagjms.82.2.323 PMID:32581411

Liu M, Zhang G, Meng L, Han X, Li Y, Shi Y, et al. (2022). Associations between Novel and Legacy Per- and Polyfluoroalkyl Substances in Human Serum and Thyroid Cancer: A Case and Healthy Population in Shandong Province, East China. Environ Sci Technol. 56(10):6144–51. https://doi.org/10.1021/acs.est.1c02850 PMID:34618433

Lundin JI, Alexander BH, Olsen GW, Church TR (2009). Ammonium perfluorooctanoate production and occupational mortality. Epidemiology. 20(6):921–8. https://doi.org/10.1097/EDE.0b013e3181b5f395 PMID:19797969

Madrigal JM, Troisi R, Surcel HJ, Ohman H, Kivela J, Kiviranta H, et al. (2024). Prediagnostic serum concentrations of per- and polyfluoroalkyl substances and risk of papillary thyroid cancer in the Finnish Maternity Cohort. Int J Cancer. 154(6):979–991. https://doi.org/10.1002/ijc.34776 PMID:37902275

Mancini FR, Cano-Sancho G, Gambaretti J, Marchand P, Boutron-Ruault MC, Severi G, et al. (2020). Perfluorinated alkylated substances serum concentration and breast cancer risk: Evidence from a nested case–control study in the French E3N cohort. Int J Cancer. 146(4):917–28. https://doi.org/10.1002/ijc.32357 PMID:31008526

Olsen GW, Huang HY, Helzlsouer KJ, Hansen KJ, Butenhoff JL, Mandel JH (2005). Historical comparison of perfluorooctanesulfonate, perfluorooctanoate, and other fluorochemicals in human blood. Environ Health Perspect. 113(5):539–45. https://doi.org/10.1289/ehp.7544 PMID:15866760

Olsen GW, Logan PW, Hansen KJ, Simpson CA, Burris JM, Burlew MM, et al. (2003). An occupational exposure assessment of a perfluorooctanesulfonyl fluoride production site: biomonitoring. AIHA J (Fairfax, Va). 64(5):651–9. https://doi.org/10.1080/15428110308984859 PMID:14521435

Purdue MP, Rhee J, Denic-Roberts H, McGlynn KA, Byrne C, Sampson J, et al. (2023). A nested case–control study of serum per- and polyfluoroalkyl substances and testicular germ cell tumors among US Air Force Servicemen. Environ Health Perspect. 131(7):77007. https://doi.org/10.1289/EHP12603 PMID:37458713

Raleigh KK, Alexander BH, Olsen GW, Ramachandran G, Morey SZ, Church TR, et al. (2014). Mortality and cancer incidence in ammonium perfluorooctanoate production workers. Occup Environ Med. 71(7):500–6. https://doi.org/10.1136/oemed-2014-102109 PMID:24832944

Rhee J, Barry KH, Huang WY, Sampson JN, Hofmann JN, Silverman DT, et al. (2023). A prospective nested case–control study of serum concentrations of per- and polyfluoroalkyl substances and aggressive prostate cancer risk. Environ Res. 228:115718. https://doi.org/10.1016/j.envres.2023.115718 PMID:36958379

Shearer JJ, Callahan CL, Calafat AM, Huang WY, Jones RR, Sabbisetti VS, et al. (2021). Serum concentrations of per- and polyfluoroalkyl substances and risk of renal cell carcinoma. J Natl Cancer Inst. 113(5):580–7. https://doi.org/10.1093/jnci/djaa143 PMID:32944748

Shin HM, Vieira VM, Ryan PB, Detwiler R, Sanders B, Steenland K, et al. (2011a). Environmental fate and transport modeling for perfluorooctanoic acid emitted from the Washington Works Facility in West Virginia. Environ Sci Technol. 45(4):1435–42. https://doi.org/10.1021/es102769t PMID:21226527

Shin HM, Vieira VM, Ryan PB, Steenland K, Bartell SM (2011b). Retrospective exposure estimation and predicted versus observed serum perfluorooctanoic acid concentrations for participants in the C8 Health Project. Environ Health Perspect. 119(12):1760–5. https://doi.org/10.1289/ehp.1103729 PMID:21813367

Sleeuwenhoek A, Cherrie JW (2012). Exposure assessment of tetrafluoroethylene and ammonium perfluorooctanoate 1951-2002. J Environ Monit. 14(3):775–81. https://doi.org/10.1039/c2em10930a PMID:22322341

Steenland K, Woskie S (2012). Cohort mortality study of workers exposed to perfluorooctanoic acid. Am J Epidemiol. 176(10):909–17. https://doi.org/10.1093/aje/kws171 PMID:23079607

Steenland K, Zhao L, Winquist A (2015). A cohort incidence study of workers exposed to perfluorooctanoic acid (PFOA). Occup Environ Med. 72(5):373–80. https://doi.org/10.1136/oemed-2014-102364 PMID:25601914

Trowbridge J, Gerona RR, Lin T, Rudel RA, Bessonneau V, Buren H, et al. (2020). Exposure to perfluoroalkyl substances in a cohort of women firefighters and office workers in San Francisco. Environ Sci Technol. 54(6):3363–74. https://doi.org/10.1021/acs.est.9b05490 PMID:32100527

Tsai MS, Chang SH, Kuo WH, Kuo CH, Li SY, Wang MY, et al. (2020). A case–control study of perfluoroalkyl substances and the risk of breast cancer in Taiwanese women. Environ Int. 142:105850. https://doi.org/10.1016/j.envint.2020.105850 PMID:32580117

van Gerwen M, Colicino E, Guan H, Dolios G, Nadkarni GN, Vermeulen RCH, et al. (2023). Per- and polyfluoroalkyl substances (PFAS) exposure and thyroid cancer risk. EBioMedicine. 97:104831. https://doi.org/10.1016/j.ebiom.2023.104831 PMID:37884429

Velarde MC, Chan AFO, Sajo MEJV, Zakharevich I, Melamed J, Uy GLB, et al. (2022). Elevated levels of perfluoroalkyl substances in breast cancer patients within the Greater Manila Area. Chemosphere. 286(Pt 1):131545. https://doi.org/10.1016/j.chemosphere.2021.131545 PMID:34293563

Vieira VM, Hoffman K, Shin HM, Weinberg JM, Webster TF, Fletcher T (2013). Perfluorooctanoic acid exposure and cancer outcomes in a contaminated community: a geographic analysis. Environ Health Perspect. 121(3):318–23. https://doi.org/10.1289/ehp.1205829 PMID:23308854

Wen X, Wang M, Xu X, Li T (2022). Exposure to per- and polyfluoroalkyl substances and mortality in US adults: a population-based cohort study. Environ Health Perspect. 130(6):67007. https://doi.org/10.1289/EHP10393 PMID:35731224

Wielsøe M, Kern P, Bonefeld-Jørgensen 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. https://doi.org/10.1186/s12940-017-0269-6 PMID:28610584

Winquist A, Hodge JM, Diver WR, Rodriguez JL, Troeschel AN, Daniel J, et al. (2023). Case–cohort study of the association between PFAS and selected cancers among participants in the American Cancer Society's Cancer Prevention Study II LifeLink cohort. Environ Health Perspect. 131(12):127007. https://doi.org/10.1289/EHP13174 PMID:38088576

Woskie SR, Gore R, Steenland K (2012). Retrospective exposure assessment of perfluorooctanoic acid serum concentrations at a fluoropolymer manufacturing plant. Ann Occup Hyg. 56(9):1025–37. https://doi.org/10.1093/annhyg/mes023 PMID:22539556

Xu Y, Nielsen C, Li Y, Hammarstrand S, Andersson EM, Li H, et al. (2021). Serum perfluoroalkyl substances in residents following long-term drinking water contamination from firefighting foam in Ronneby, Sweden. Environ Int. 147:106333. https://doi.org/10.1016/j.envint.2020.106333 PMID:33360412

Zhang T, Fu S, Yu K, Albanes D, Moore SC, Purdue MP, et al. (2023). Nested case–control studies investigating serum perfluorooctanoate and perfluorooctane sulfonate levels and pancreatic ductal adenocarcinoma in two cohorts. Environ Health Perspect. 131(10):107702. https://doi.org/10.1289/EHP13208 PMID:37844029