

Plenary: PFASs: Clinical Impacts, Diagnosis and Intervention

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Fluorocarbons “Forever Chemicals”

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Conflicts of Interest

- Dr Pizzorno is a scientific consultant for Bioclinic Naturals and Mosaic Diagnostics



Overview

- Description
- Sources
- Prevalence
- Excretion/Detoxification
- Mechanism of Damage
- Diseases Caused
- Assessment of Body Load
- Elimination
- Conclusion



Challenges

- Animal research of limited value (rodents detoxify PFAS 10-1000 times faster than humans)
- Mechanisms of damage poorly understood
- Non-linearity of effects
- Transitioning from banned PFOA and PFOS to other perfluorinateds
- Ultra-short length not usually measured, but 100 times higher levels in water
- Many disease associations—but weak and marginal statistical strength



Chemical Toxins

- **Non-Persistent**

- Bisphenols (BPx)
- Glyphosate
- Polycyclic aromatic hydrocarbons (PAHs)
- Phthalates
- Solvents

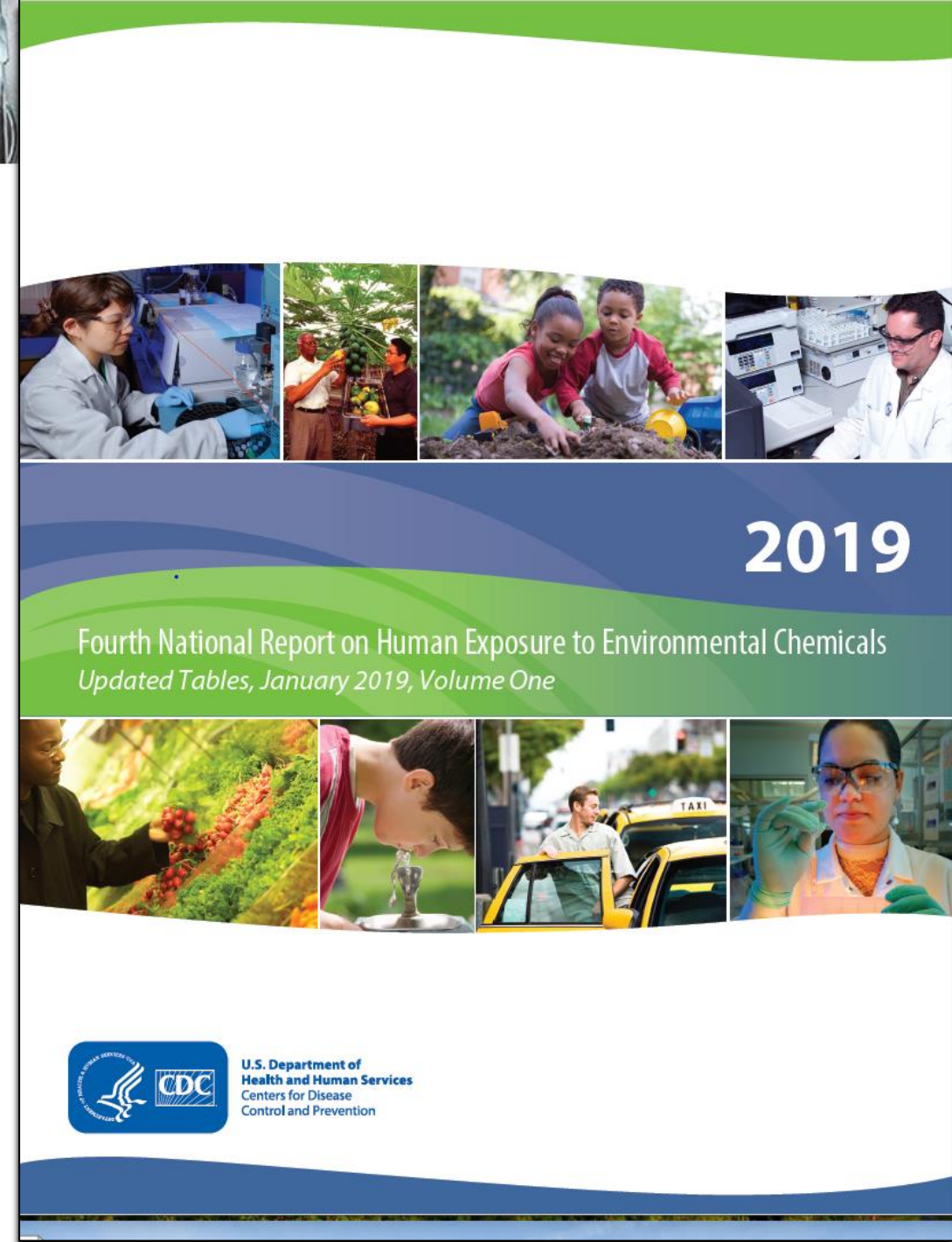
- **Persistent**

- (Typically halogenated)
- Organochlorine pesticides
- Organophosphate pesticides
- **Fluorocarbons**
- Polybrominated diphenyl ethers (PBDEs)
- Polychlorinated biphenyls (PCBs)
- Pyrethroid pesticides

- **MANY more!**

Source of US Population Toxicant Load

- Regularly updated
- 2,000 pages
- Decades of trends



PFAS Resource

- 1,000 pages
- Clearly differentiates animal, human and epidemiological data



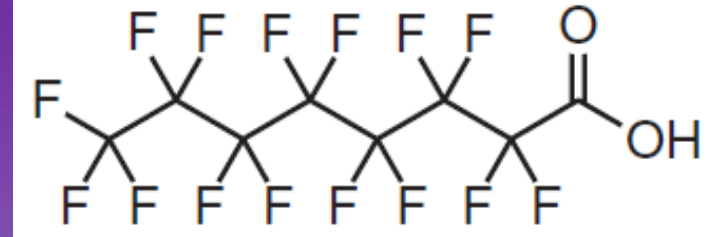
Toxicological Profile for Perfluoroalkyls

Released May 2021

Last Updated March 2020



U.S. Department of Health and Human Services
Agency for Toxic Substances and Disease Registry



Description



Nomenclature

- Many terms are used somewhat interchangeably
- Perfluorocarbons: organofluorine compounds with the formula C_xF_y
- This PPT uses PFAS as the generic term for all per/poly-fluorinated compounds



PFAS

- Highly fluorinated molecules that are widely used in diverse products and processes
 - Water-repelling textiles
 - Grease-resistant paper
 - Non-stick packaging and cooking appliances
 - Medical and laboratory tubing
 - Aqueous film-forming foams
 - Industrial detergents
- Persistent toxins
 - $\frac{1}{2}$ lives 2-7 years
- Environment hugely contaminated

Family Tree of Per- Poly-fluoroalkyls

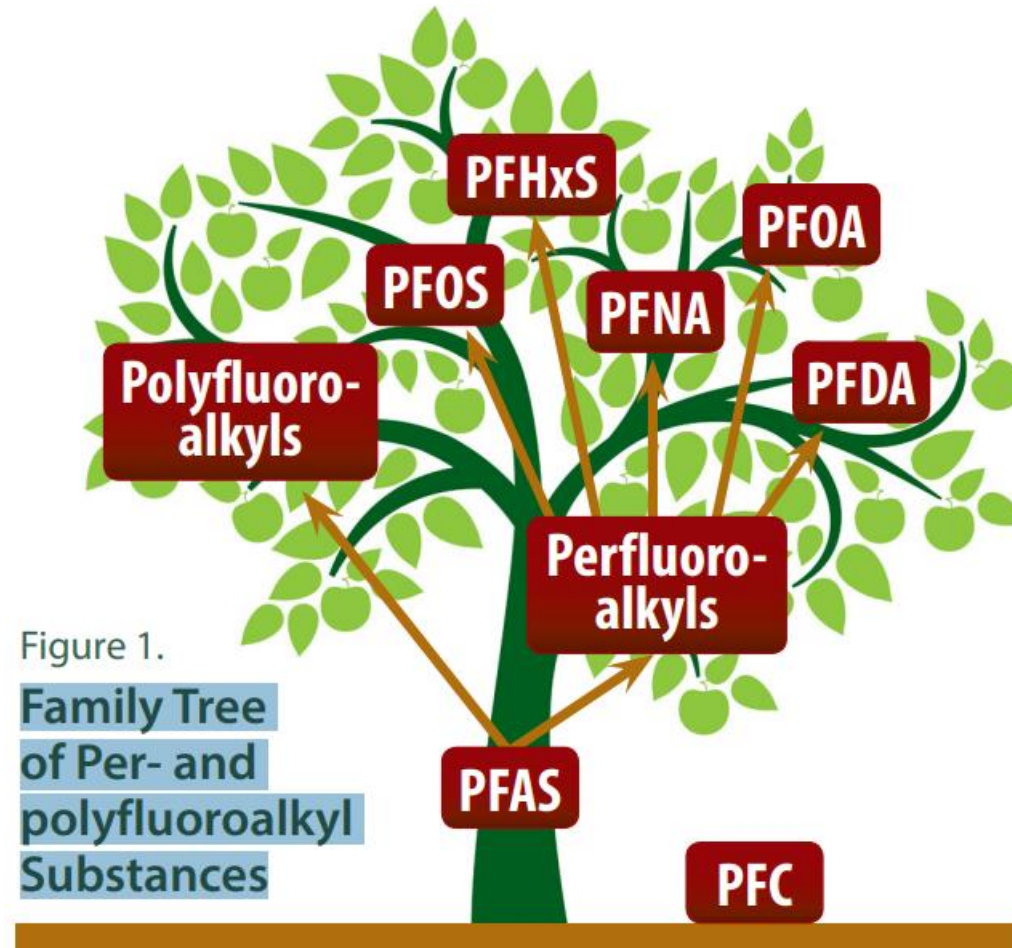


Figure 1.
Family Tree
of Per- and
polyfluoroalkyl
Substances



Terms

- PFAS: general term for perfluorinated chemicals
- PFC: Traditional term

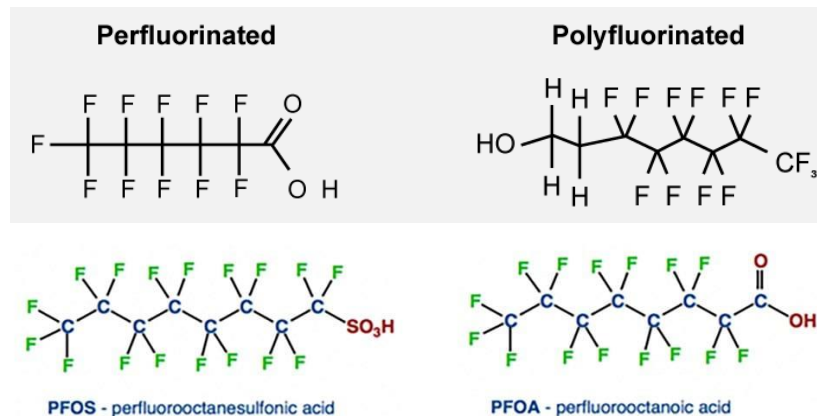
Abbreviation	Chemical name
PFOS	Perfluorooctane sulfonic acid
PFOA (aka C8)	Perfluorooctanoic acid
PFNA	Perfluorononanoic acid
PFDA	Perfluorodecanoic acid
PFOSA (aka FOSA)	Perfluorooctane sulfonamide
MeFOSAA (aka Me-PFOSA-AcOH)	2-(N-Methyl-perfluorooctane sulfonamido) acetic acid
Et-FOSAA (aka Et-PFOSA-AcOH)	2-(N-Ethyl-perfluorooctane sulfonamido) acetic acid
PFHxS	Perfluorohexane sulfonic acid



PFAS Classification

- Class of over 12,000 compounds with: a carbon chain of varying length that is either fully or partially saturated with fluorine atoms and a polar end group.
- Key identification criteria for PFASs

- Per- Poly-



- End molecule
 - Hydroxyl
 - Sulfate

- Length (3rd letter usually indicates carbon chain length)

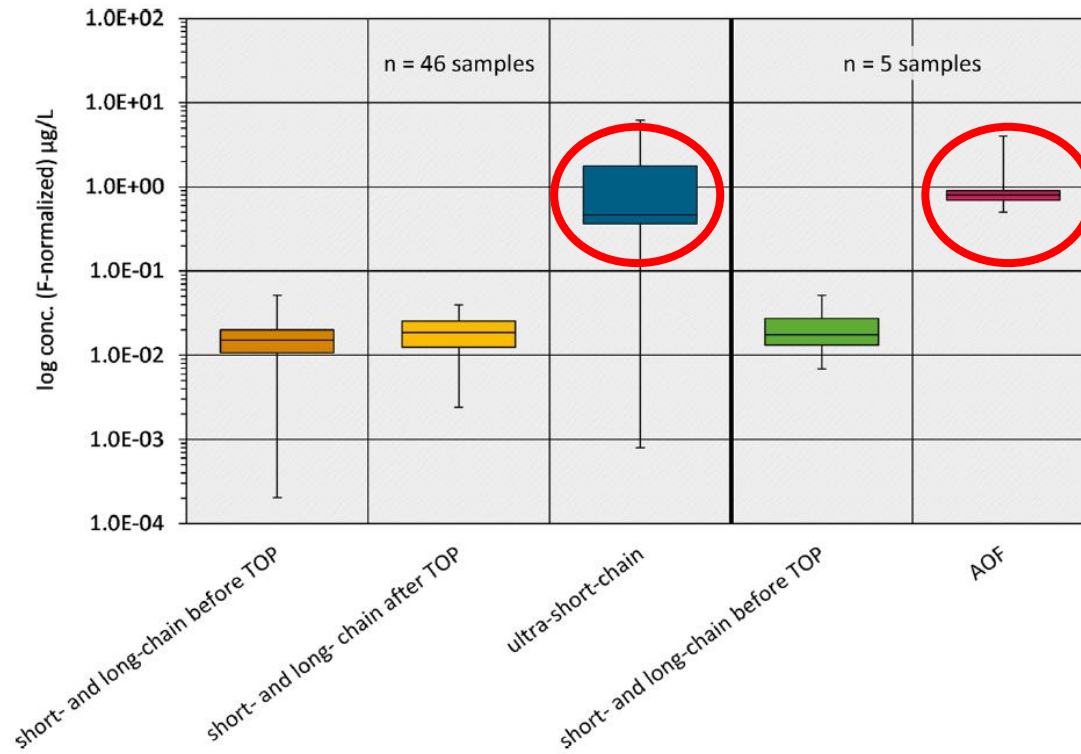
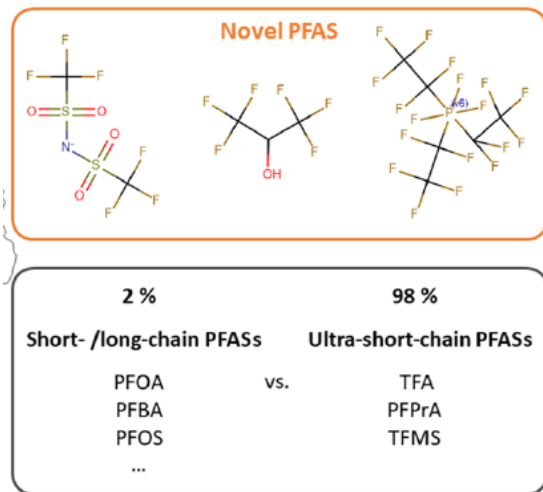
Chain Length

- Long-chain: 7+ perfluorocarbons for perfluorocarboxylates (PFCAs) and 6 or more for perfluorosulfonates (PFSAs)
- Short-chain: 3-7 perfluorocarbons for PFCAs and 4-5 for PFSAs
- Ultra-short chain: ≤ 2 perfluorocarbon atoms for PFCAs, ≤ 3 for PFSAs & other PFASs
 - Are degradation products of longer chain PFASs
 - Labs do not measure most ultra-short PFCs
 - Drinking water commonly contaminated
 - Major body load
 - Not included in past environmental regulations
 - **Water soluble!**

Neuwald IJ, Hübner D, Wiegand HL, et al. (2022). Ultra-Short-Chain PFASs in the Sources of German Drinking Water: Prevalent, Overlooked, Difficult to Remove, and Unregulated. *Environmental science & technology*, 56(10), 6380–6390.

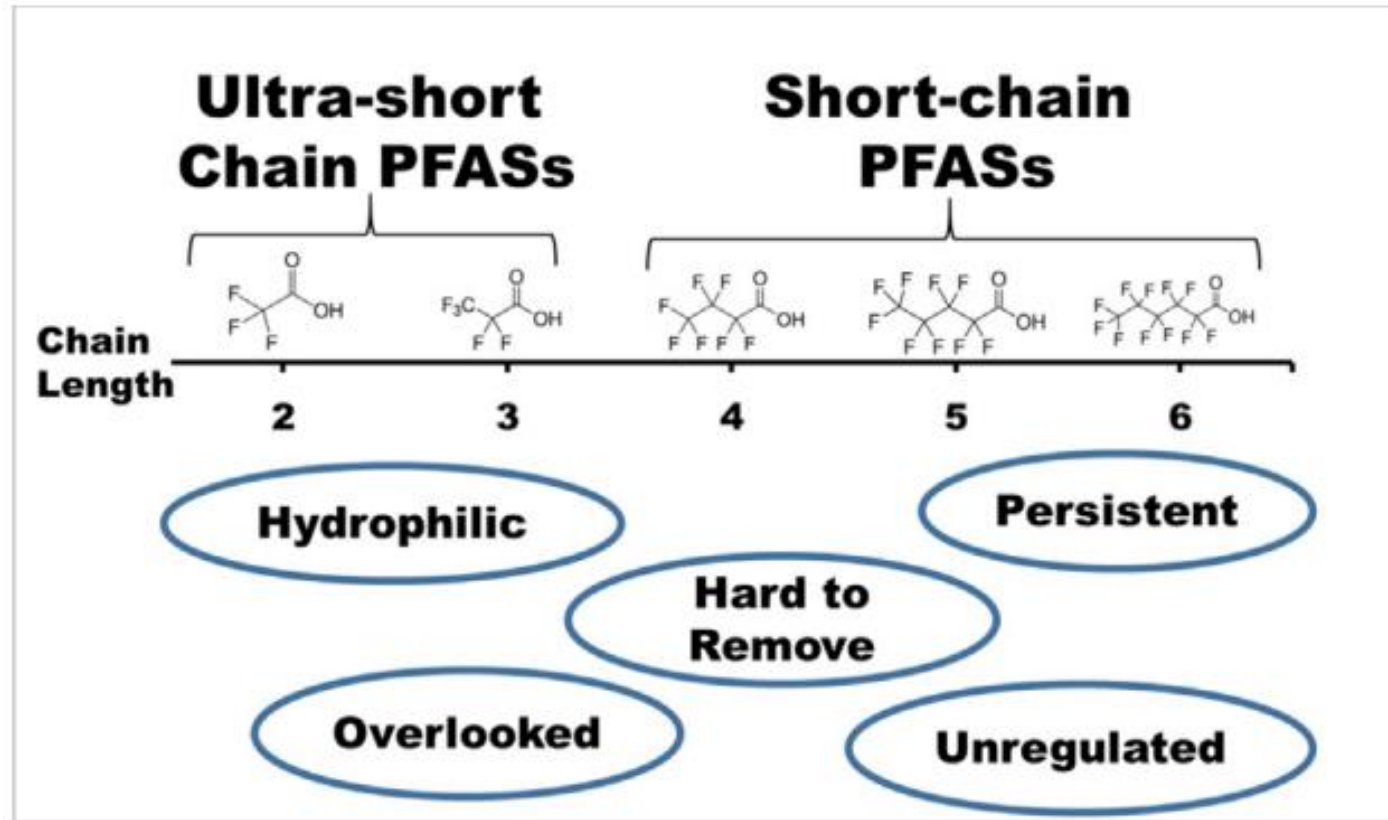
The Problem of Under-Recognized Ultrashort Chain Perfluorocarbons

- German drinking water samples (log scale)
- Ultra-short chain perfluorinateds dominate



Neuwald IJ, Hübner D, Wiegand HL, et al. (2022). Ultra-Short-Chain PFASs in the Sources of German Drinking Water: Prevalent, Overlooked, Difficult to Remove, and Unregulated. *Environmental science & technology*, 56(10), 6380–6390.

The Ultra-Short Chain PFAS Problem



Sources



Sources

- Industrial
- Some professions
- Air
- Water
- Dust
- Food
- Straws
- Clothing
- Carpet (esp. when new and after stain guard)



Exposure Routes

- PFOA: oral exposure from food packaging, general food and water ingestion, inhalation from impregnated clothes, and dust ingestion
- PFOS: food and water ingestion, dust ingestion, and hand-to-mouth transfer from mill-treated carpets
- Adults: 30 & 47 ng/kg/day for PFOS & PFOA
- Children <12: 101–219 & 65.2–128 ng/kg/day
 - 2-4x adults!
- PFOA and PFOS are no longer produced or used in the United States

Industrial PFAS Release into Environment

[Multi-Industry Per- and Polyfluoroalkyl Substances \(PFAS\) Study – 2021 Preliminary Report \(epa.gov\)](#) (Accessed 9/2023)

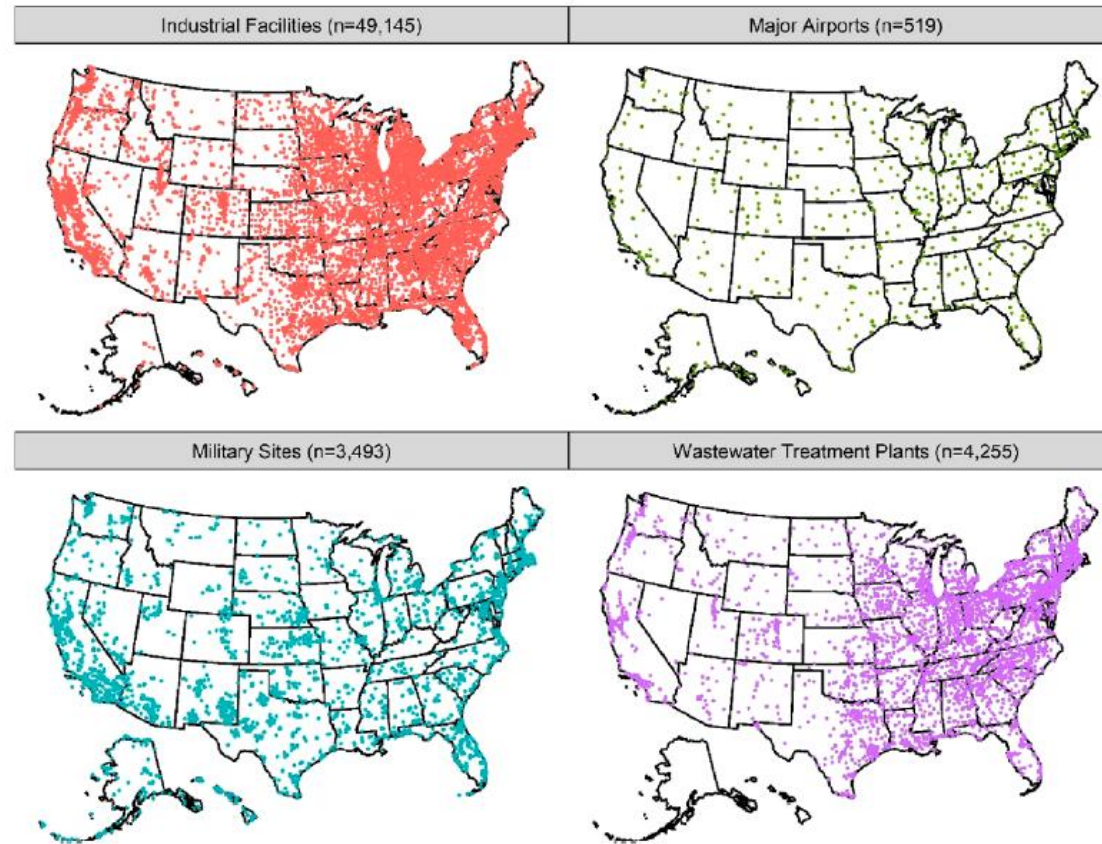
Table 1. Point Source Categories Included in Multi-Industry PFAS Study

Point Source Category	Description	Uses or Sources of PFAS ^a
Organic Chemicals, Plastics, and Synthetic Fibers (OCPSF)	Industrial facilities that manufacture organic chemicals, plastics, synthetic fibers or resin products, including those that manufacture PFAS or process PFAS in production of such products. Subject to ELGs in 40 CFR Part 414 .	<ul style="list-style-type: none"> - Manufacture PFAS through electrochemical fluorination, telomerization, or other processes. - Polymerization processing aids. - Production of plastic, rubber, and resin. - Present in manufacture of commercial chemical products (e.g., carpet cleaning sprays, cleaning agents, protective coatings).
Metal Finishing	Industrial facilities that change the surface of an object to improve its appearance or durability. Includes six primary operations: electroplating, electroless plating, anodizing, coating, printed circuit board manufacturing, and chemical etching and milling. Subject to ELGs in 40 CFR Part 433 .	<ul style="list-style-type: none"> - PFAS-containing chemicals used as wetting agents, mist and fume suppressants to prevent air emissions of toxic metal fumes, agents to reduce mechanical wear, and surface coatings to impart certain characteristics (e.g., reduced corrosion, enhanced appearance).
Pulp, Paper, and Paperboard	Mills that convert wood into pulp, paper, paperboard, and other cellulose-based products. Subject to ELGs in 40 CFR Part 430 .	<ul style="list-style-type: none"> - PFAS-containing chemicals used to impart products with water and grease repellency (e.g., food packaging, coated papers). - Recycling of paper and paperboard products treated with PFAS.
Textile Mills	Mills that receive and prepare fibers; transform materials into yarn, thread, or webbing; convert yarn and webbing into fabric or related products; or finish these materials to produce consumer products (e.g., thread, yarn, bolt fabric, hosiery, towels, sheets, carpet). Subject to ELGs in 40 CFR Part 410 .	<ul style="list-style-type: none"> - PFAS-containing chemicals used to impart outdoor gear, clothing, household, and other textile products with water, oil, soil, and heat resistance.
Commercial Airports	Commercial facilities associated with commercial air transport or aircraft flight operations. Excludes facilities operated by the United States Department of Defense (DOD). Subject to ELGs in 40 CFR Part 449 .	<ul style="list-style-type: none"> - PFAS are a component of aqueous film-forming foam (AFFF), used for exterminating hydrocarbon fuel fires and firefighting training.

^a – In general, PFAS may be used as coatings or surfactants for mechanical components (e.g., semiconductors, wiring, tubing, piping, seals, gaskets, etc.) used at many types of industrial facilities.

Widespread Industrial Contamination

Presumptive Contamination Sites (n=57,412)





Water Regulatory Standards

- Federal
 - PFOA: 70 ng/L
 - PFOS: 70 ng/L
- State
 - PFOA: 8-35 ng/L
 - PFOS: 10-40 ng/L
- European
 - PFAS: 100 ng/L

PFAS Contaminate Many Water Supplies

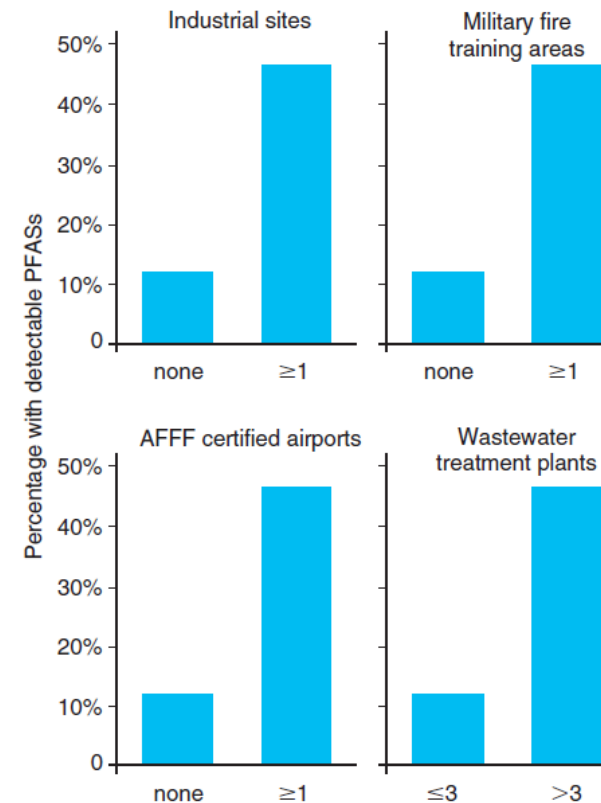
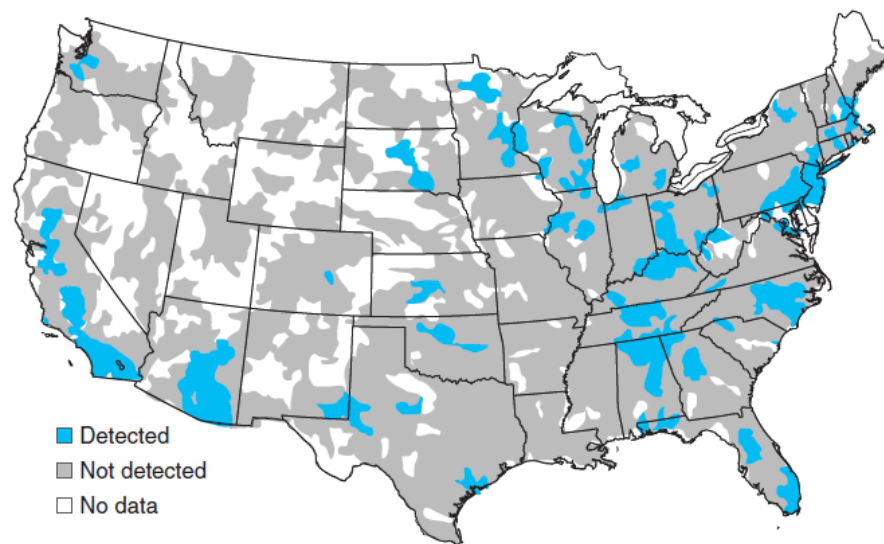
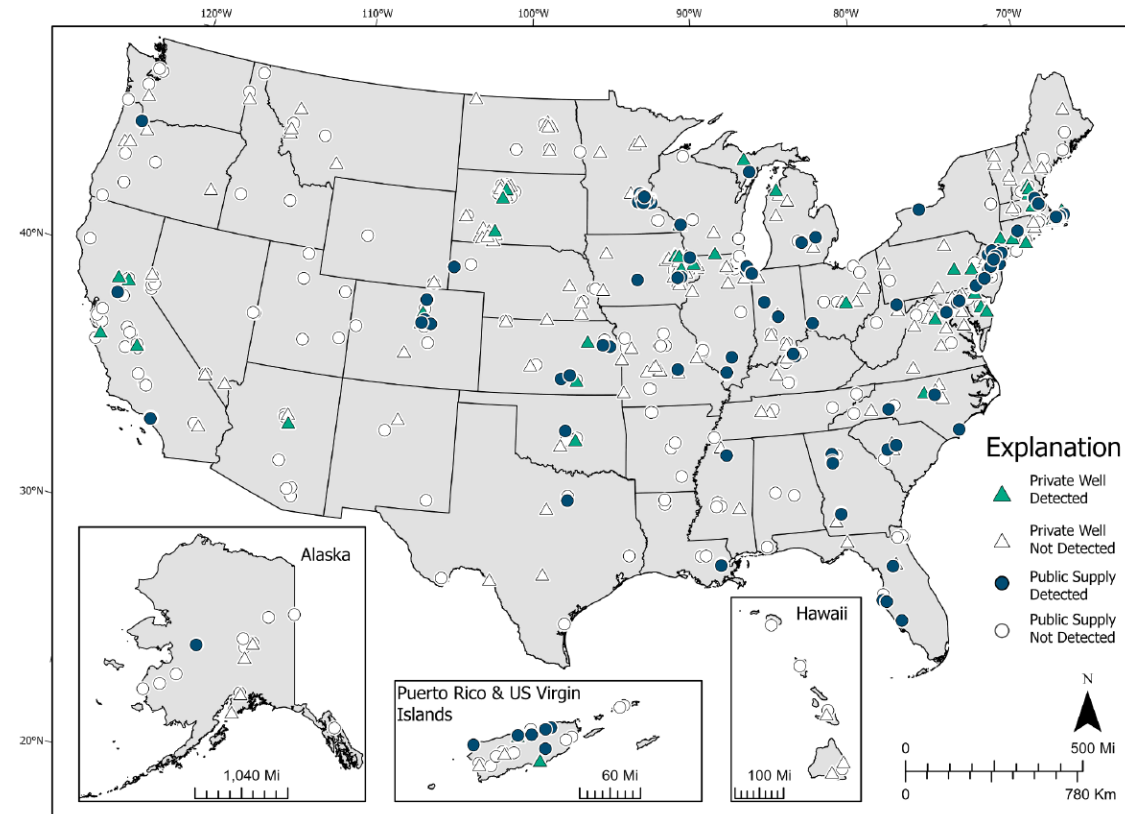


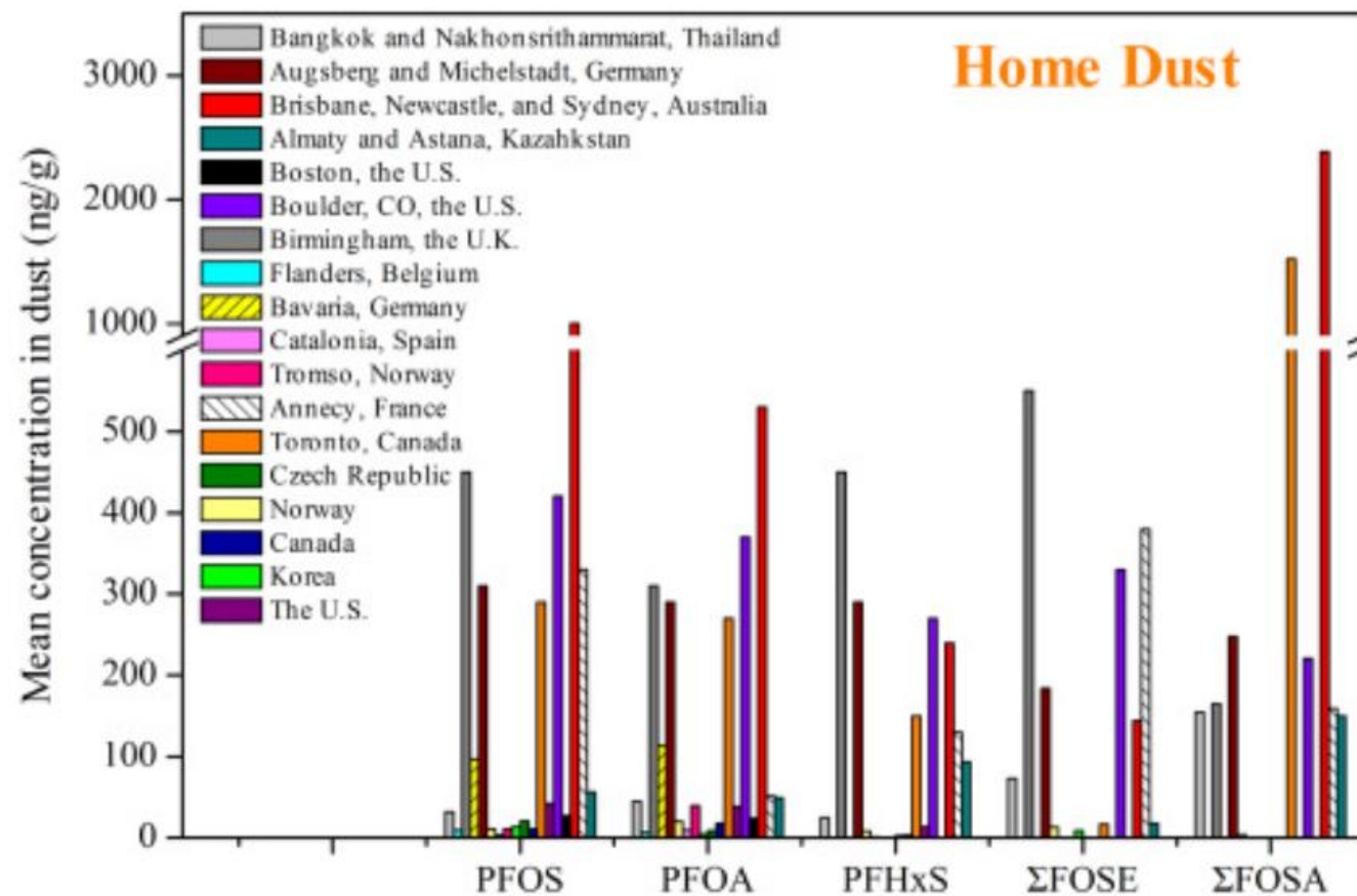
FIG. 29.2 U.S. groundwater sites with elevated perfluorinated compounds. (From Hu, X. C., Andrews, D. Q., Lindstrom, A. B., Burton, T. A., Schaider, L. A., Grandjean, P., Lohmann, R., Carignan, C. C., Blum, A., Balan, S. A., Higgins, C. P., Sunderland, E. M. [2016]. Detection of poly and perfluoroalkyl substances (PFASs) in U.S. drinking water linked to industrial sites, military fire training areas, and wastewater treatment plants. *Environmental Science & Technology Letters*, 3(10), 344–350.)

Half of Measured Public and Private Tap Water are Contaminated



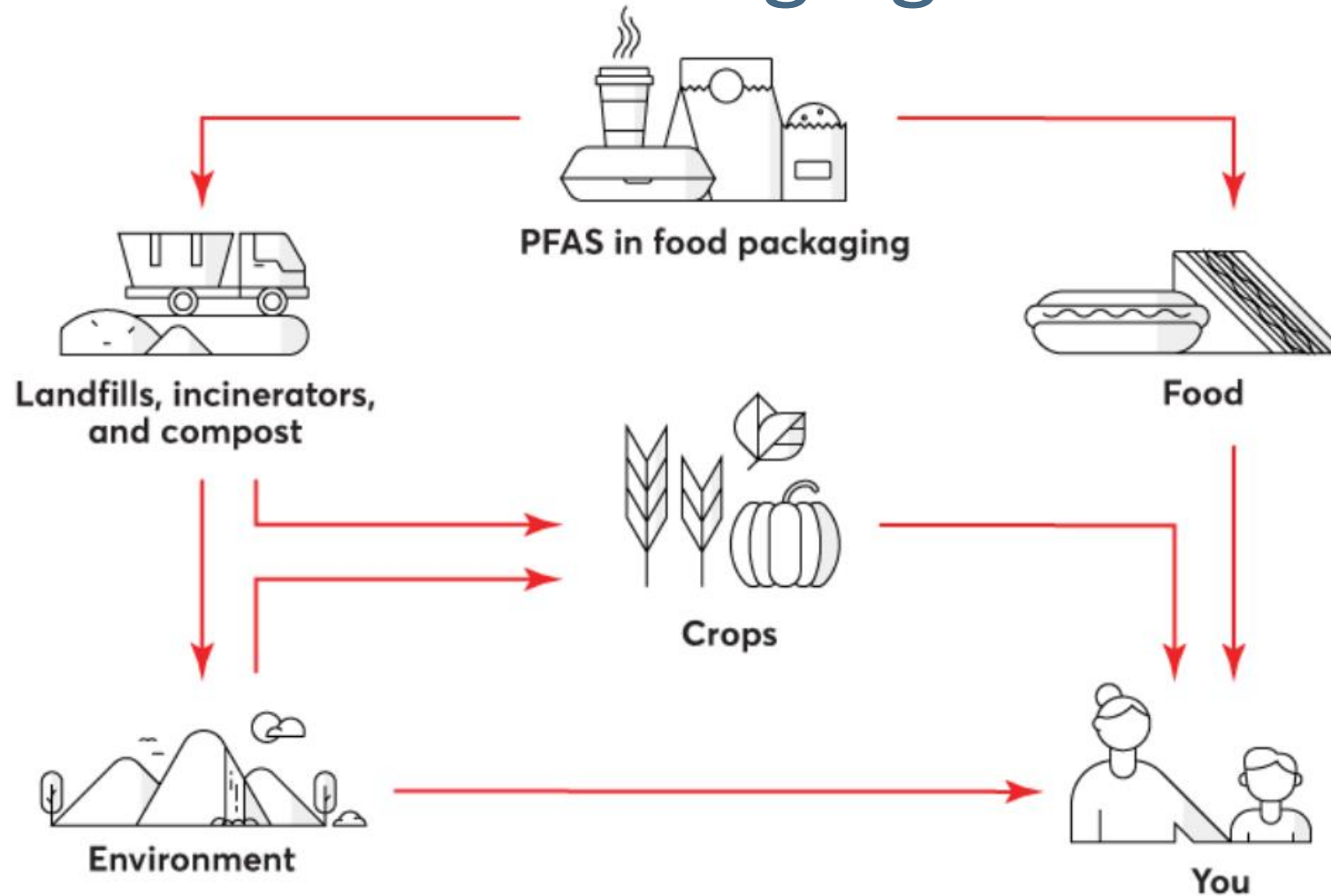
Smalling KL, Romanok KM, Bradley PM, et al. (2023). Per- and polyfluoroalkyl substances (PFAS) in United States tapwater: Comparison of underserved private-well and public-supply exposures and associated health implications. *Environment international*, 178, 108033.

Dust

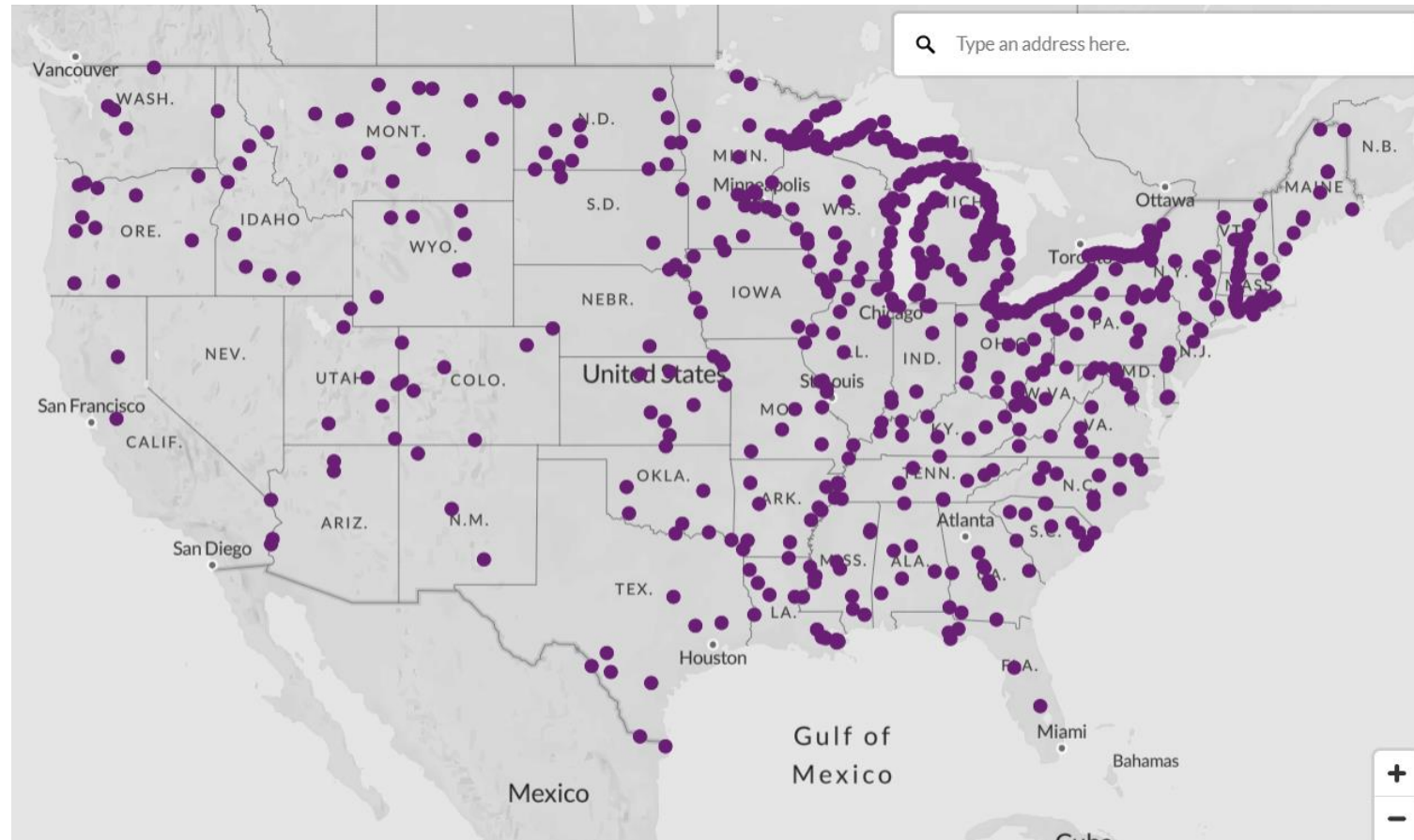


Jian, J. M., Guo, Y., Zeng, L., Liang-Ying, L., Lu, X., Wang, F., & Zeng, E. Y. (2017). Global distribution of perfluorochemicals (PFCs) in potential human exposure source-A review. *Environment international*, 108, 51–62. <https://doi.org/10.1016/j.envint.2017.07.024>

Food and Food Packaging



EWG Resource for PFOA/S Contamination in Fish





PFASs in Packaging Migrates into Food

- **Increased by:**

- Packaging concentration
- Food:
 - Fat content
 - Lower pH
 - Salt
 - Alcohol
- Time & Heat
- Surface area
- Shorter chain PFCs

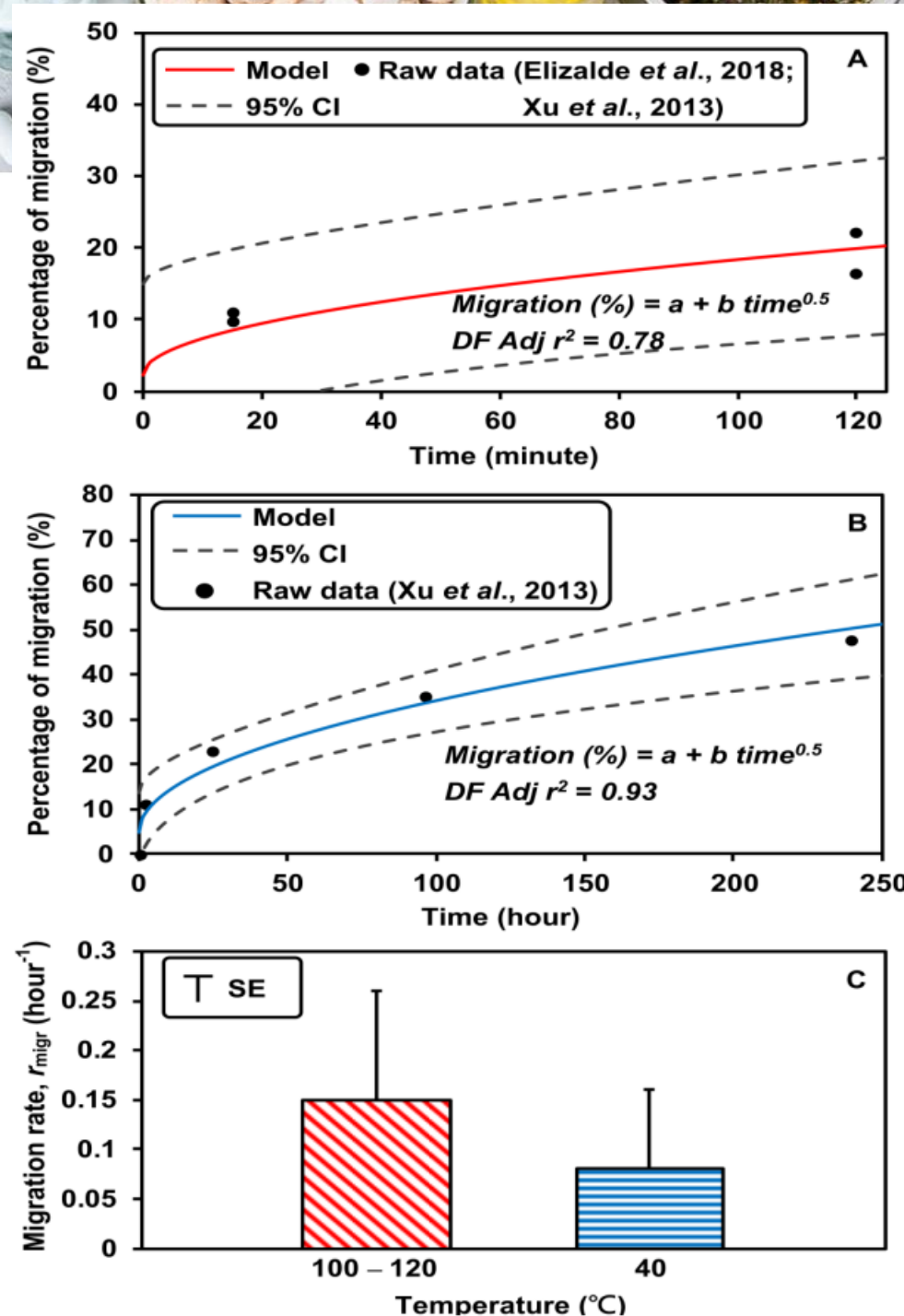
- **Decreased by:**

- Food:
 - Moisture content

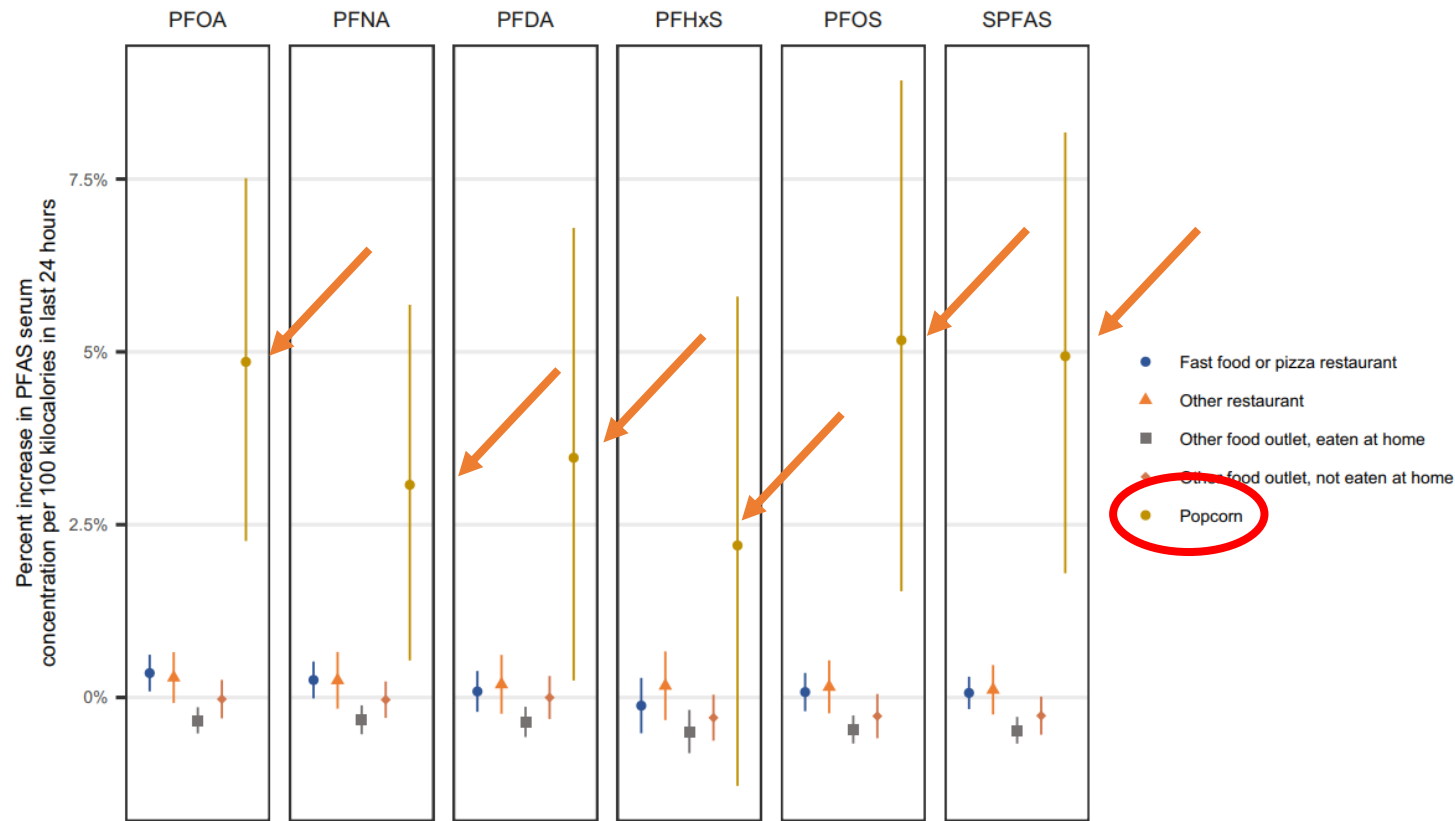
Ramírez Carnero, A., Lestido-Cardama, A., Vazquez Loureiro, P., Barbosa-Pereira, L., Rodríguez Bernaldo de Quirós, A., & Sendón, R. (2021). Presence of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS) in Food Contact Materials (FCM) and Its Migration to Food. *Foods* (Basel, Switzerland), 10(7), 1443.

Time & Temperature

You, S. H., & Yu, C. C. (2023). Health Risk Exposure Assessment of Migration of Perfluorooctane Sulfonate and Perfluorooctanoic Acid from Paper and Cardboard in Contact with Food under Temperature Variations. *Foods* (Basel, Switzerland), 12(9), 1764.



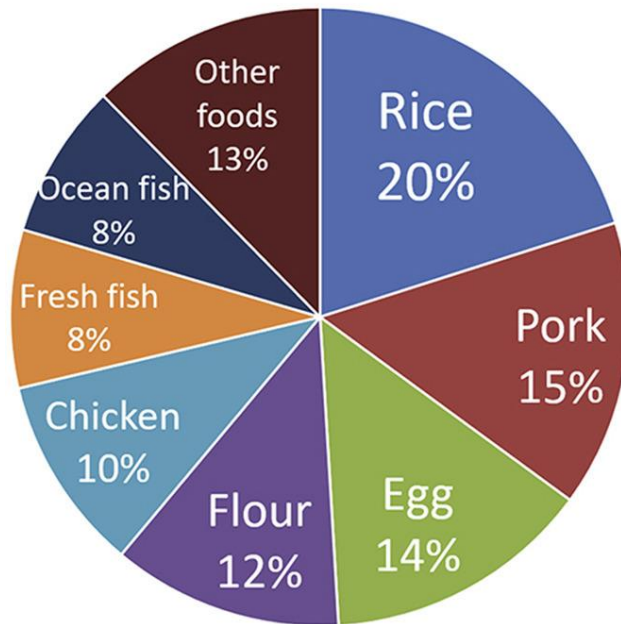
Eating Out And Popcorn Increase PFCs



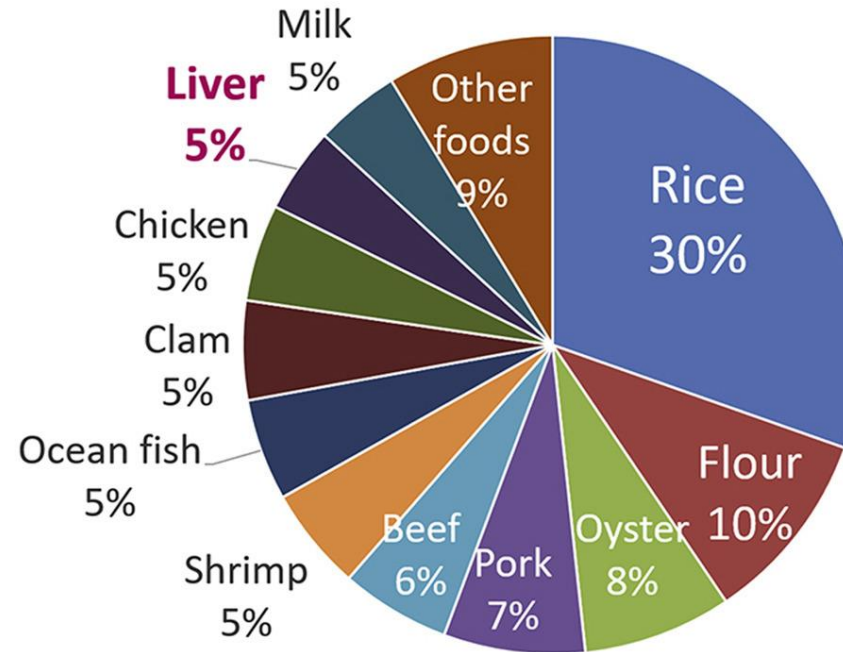
Susmann, H. P., Schaider, L. A., Rodgers, K. M., & Rudel, R. A. (2019). Dietary Habits Related to Food Packaging and Population Exposure to PFASs. *Environmental health perspectives*, 127(10), 107003. <https://doi.org/10.1289/EHP4092>

Food Sources of PFAS (Taiwan)

Daily PFAS intake among the general population in Taiwan:
11.7 $\mu\text{g}/\text{person}/\text{day}$

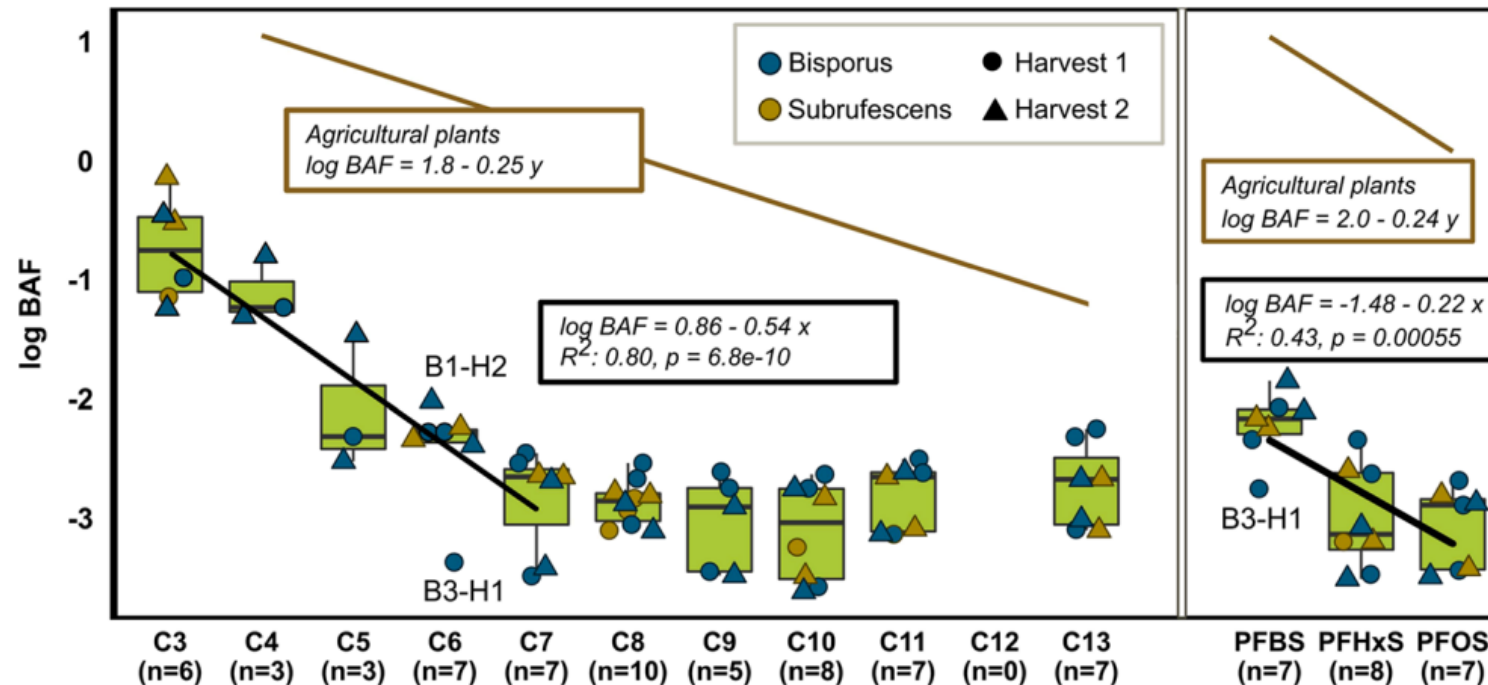


Upper limits of 95% probability that pregnant women are exposed to PFASs:
16.6 $\mu\text{g}/\text{person}/\text{day}$



Chen, W. L., Bai, F. Y., Chang, Y. C., Chen, P. C., & Chen, C. Y. (2018). Concentrations of perfluoroalkyl substances in foods and the dietary exposure among Taiwan general population and pregnant women. *Journal of food and drug analysis*, 26(3), 994–1004.

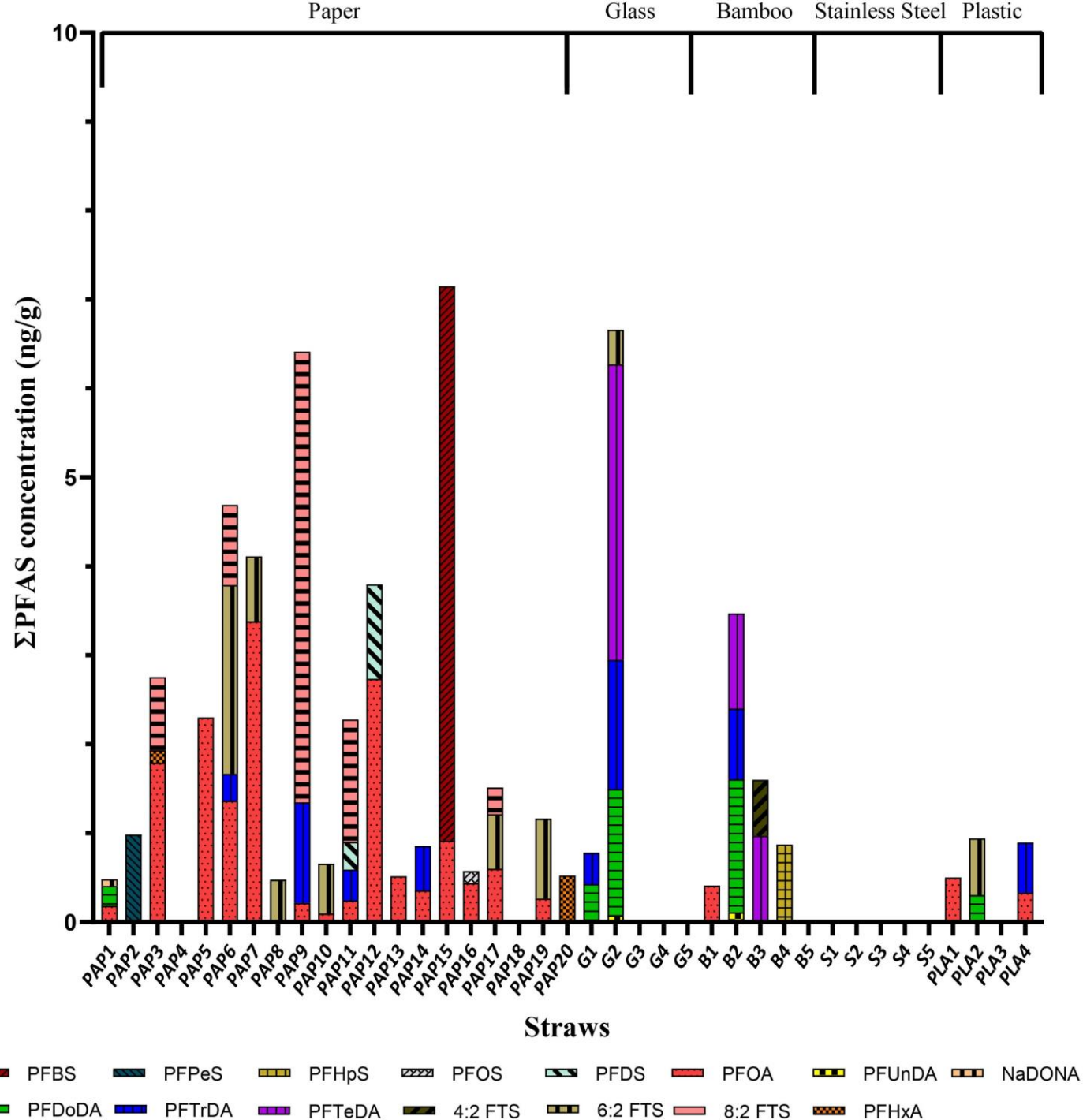
Increased Bioaccumulation of Ultra-Short Chain PFAS (Mushrooms)



Nesse, A. S., Jasinska, A., Ali, A. M., et al. (2023). Uptake of Ultrashort Chain, Emerging, and Legacy Per- and Polyfluoroalkyl Substances (PFAS) in Edible Mushrooms (*Agaricus* spp.) Grown in a Polluted Substrate. *Journal of agricultural and food chemistry*, 71(11), 4458–4465.

Even Straws!

Boisacq, P., De Keuster, M., Prinsen, E., et al. (2023). Assessment of poly- and perfluoroalkyl substances (PFAS) in commercially available drinking straws using targeted and suspect screening approaches. Food additives & contaminants. Part A, Chemistry, analysis, control, exposure & risk assessment, 40(9), 1230–1241.



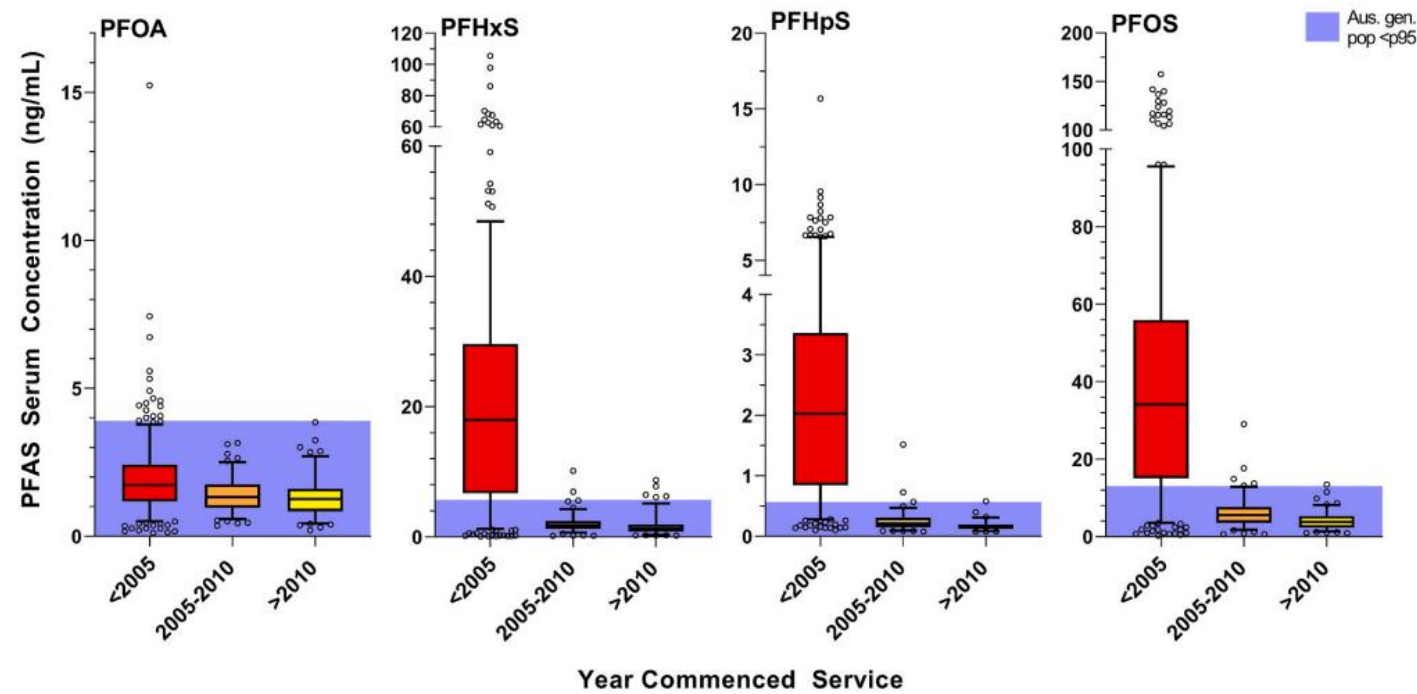


Professions

- **Firefighters**
- **Ski technicians (ski wax)**
 - Professional ski waxers have up to 25 times as much PFAS in their blood as the general population
- Building construction workers
- Furniture construction workers
- Anyone regularly using non-stick, stain guard, etc. products

Older Firefighters Have High PFAS Load

- Data from Australia
- High PFAS foams phased out 2010-2020



Nilsson S, Smurthwaite K, Aylward LL, et al. (2022). Serum concentration trends and apparent half-lives of per- and polyfluoroalkyl substances (PFAS) in Australian firefighters. *International journal of hygiene and environmental health*, 246, 114040.



Carpet

- Case report on Canadian family
- Disproportionately high serum:
 - High PFHxS (27.5-423 ng/mL)
 - Moderately high PFOS (15.2-108 ng/mL)
 - Moderately high PFOA (2.40-9.23 ng/mL)
 - All 3 highest in the youngest children
 - General population PFAS total: ~5 ng/ml
- Elevated PFHxS detected in household dust (2780 ng/g dust) and in family room carpet (2880 ng/g carpet)
- Over 15 years, the family's household carpets were treated 8 times with Scotchgard formulations.

Beesoon, S., Genuis, S. J., Benskin, J. P., & Martin, J. W. (2012). Exceptionally high serum concentrations of perfluorohexanesulfonate in a Canadian family are linked to home carpet treatment applications. *Environmental science & technology*, 46(23), 12960–12967.

HUGE Variation in Source Contamination Makes Exposure Route Difficult to Determine

Range of PFAS concentrations detected in key exposure sources.

Exposure source	Exposure Route	PFAS concentration range	Predominant PFAS	Reference
Water	Oral, dermal	9.0–3640 ng/L	PFOA	Exner and Färber (2006)
		0.22–24.0 ng/L		Ericson et al. (2008)
		0.051–501 ng/L		Boone et al. (2019)
		0.10–456 ng/L	PFOA	Saito et al. (2004)
Air	Inhalation	20–132 ng/L	PFOS	Nakayama et al. (2007)
		7–53 pg/m ³	PFOA, PFDA, PFNA	Ge et al. (2017)
		1.82–32.1 pg/m ³	6:2 FTOH, 8:2 FTOH	Bossi et al. (2016)
		18.0–109.9 pg/m ³	FTOH	Lai et al. (2016)
		3.4–34 pg/m ³	PFOA	Liu et al. (2020)
		2.8–68.8 pg/m ³	PFOA	Wang et al. (2015)
Soil	Incidental ingestion, dermal, inhalation	0.007–0.048 µg/kg		Rankin et al. (2016)
		0.527–34.1 µg/kg	PFOA	Strynar et al. (2012)
		11–2400 µg/kg	PFOS	Houtz et al. (2013)
		0.665–9700 µg/kg	PFOS	Anderson et al. (2016)
		10–48 µg/kg	PFOS	Zareitalabad et al. (2013)
Indoor dust	Incidental ingestion, dermal, inhalation	27–47739 pg/m ³		Fromme et al. (2015)
		5.93–70600 pg/m ³		Fraser et al. (2012)
		<1.0–3100 pg/m ³	MeFOSE	Goosey and Harrad (2012)
		890–47000 pg/m ³	MeFOSE	Shoeib et al. (2011)
		200–307000 pg/m ³	FTOH	Langer et al. (2010)
Biosolids	Transfer to fruit/vegetables/livestock	8–219 µg/kg	PFOS	Sepulvado et al. (2011)
		0.05–0.33 µg/kg	PFDA	Gottschall et al. (2017)
		9.7–6410 µg/kg	PFOA	Lindstrom et al. (2011)
		1.4–36 µg/kg	PFOS	Pepper et al. (2021)
		2.0–300 µg/kg	6:2 diPAP, 8:2 diPAP	Moodie et al. (2021)
Fruit/vegetables	Ingestion	0.014–50.7 µg/kg		Sznajder-Katarzyńska et al. (2018)
		0.27–33 µg/kg		Scher et al. (2018)
		58.8–8085 µg/kg		Liu et al. (2019)
		<10.0–87 µg/kg	PFBA	Bao et al. (2020)
		1.28–150 µg/kg	PFBA	Blaine et al. (2014)
Fish/meat	Ingestion	1.38–127 µg/kg	PFOS	Stahl et al. (2014)
		0.47–4000 µg/kg	PFOS	Delinsky et al. (2010)
		0.46–640 µg/kg	PFOS	Gewurtz et al. (2014)
		<0.5–406 µg/kg	PFOA	Becker et al. (2010)
		560–9349 µg/kg	PFOA	Lanza et al. (2017)
Fast food wrappers	Transfer to food - ingestion	6–290 µg/kg	PFOA	Begley et al. (2005)
		5.19–341.21 µg/kg	PFHxA	Zafeiraki et al. (2014)
		<0.40–8490 µg/kg	8:2 FTOH	Yuan et al. (2016)
		15.3–28.6 µg/kg	PFOA	Monge Brenes et al. (2019)
		8.6–948.7 µg/kg	PFOA	Elizalde et al. (2018)
Cosmetics	Dermal	0.01–142.8 µg/kg	PFOA	Keawmanee et al. (2015)
		0.03–1440 µg/kg	6:2 FTMAC	Whitehead et al. (2021)
		60–243000 µg/kg	6:2 triPAP, 6:2 diPAP, PFHxA	Eriksson et al. (2018)
		0.75–6500 µg/kg	PFHxA	Fujii et al. (2013)
		0.11–2160 µg/kg	PFOA	Brinch et al. (2018)

Typical Sources for Adults (World)

Table 9. Estimated adult daily intake of PFOS and PFOA for the general population. Mean intake based on mean or median concentrations; high intake based on upper percentile or maximum concentrations

	Concentration		Intake rate ^a	Intake (ng/day)		Daily intake pg/kg b.w. ^b	
	Mean	High		Mean	High	Mean	High
<i>PFOA</i>							
Indoor air	4.4 pg/m ³ ^c		12 m ³ /day	0.053	0.053	0.9	0.9
Outdoor air	58.4 pg/m ³ ^d	552 pg/m ³ ^d	1.3 m ³ /day	0.076	0.718	1.3	12.0
House dust	19.72 ng/g ^e	1234 ng/g ^e	50 mg/day	0.986	61.7	16.4	1028.3
Diet				169 ^h	689 ^h	2816.7	11483.3
Drinking water	1.0 ng/l ^f	4.0 ng/l ^f	1.3 l/day	1.3	5.2	21.7	86.7
Overall intake						2857.0	12611.2
<i>PFOS</i>							
Indoor air	23.7 pg/m ³ ^g		12 m ³ /day	0.284	0.284	4.7	4.7
Outdoor air	4.5 pg/m ³ ^d	46 pg/m ³ ^d	1.3 m ³ /day	0.006	0.060	0.1	1.0
House dust	37.8 ng/g ^e	5065 ng/g ^e	50 mg/day	1.9	253	31.7	4216.7
Diet				90 ^h	269 ^h	1500.0	4483.3
Drinking water	1.0 ^f	6.0 ^f	1.3 l/day	1.4	7.8	23.3	130.0
Overall intake						1559.8	8835.7

Fromme, H., Tittlemier, S. A., Völkel, W., Wilhelm, M., & Twardella, D. (2009). Perfluorinated compounds--exposure assessment for the general population in Western countries. *International journal of hygiene and environmental health*, 212(3), 239–270.

Prevalence

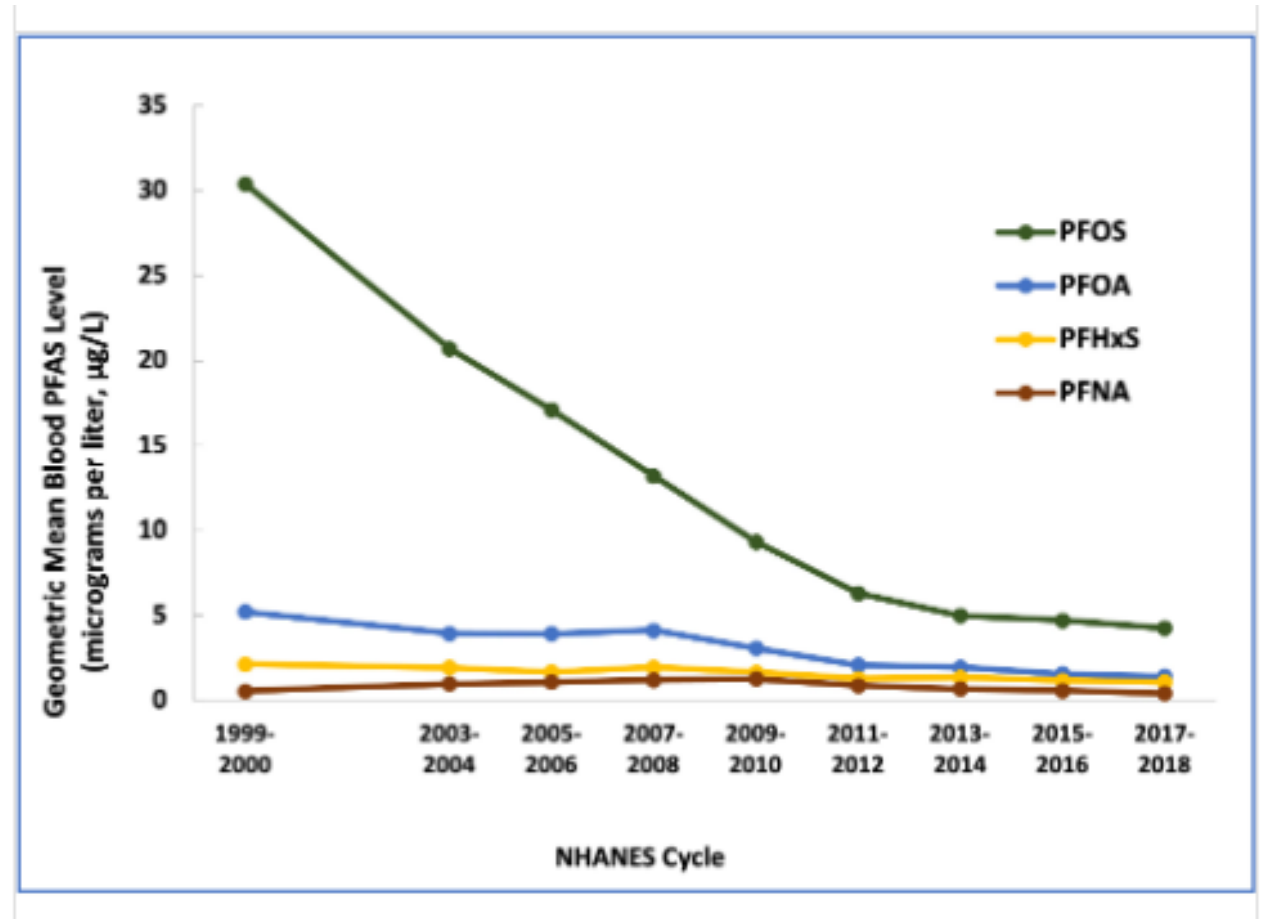


Serum Levels of PFAS

- Industrial: 1,000 ng/mL
- Highly-exposed residents (without occupational exposure): 423 ng/mL
- U.S. population: 4.9 ng/mL

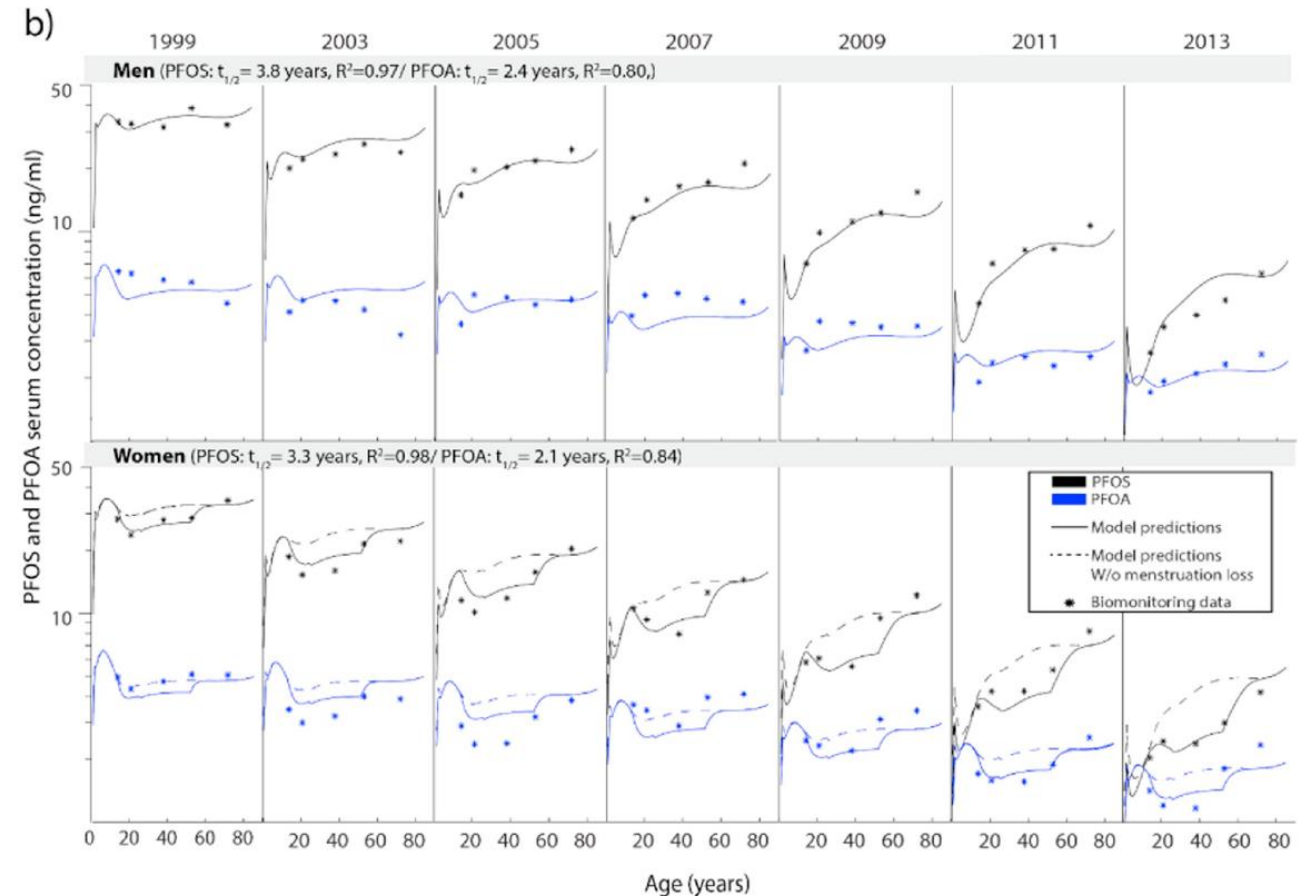
The Good News

- PFOA/PFOS banned by Geneva Convention 2019
- Inconsistent banning began in 1998
- But typically substituted with other PFAS



Mixed News

- Average levels (of **measured** PFOAs) have decreased
- However:
 - Levels go up with age
 - These have been replaced with unmeasured other perfluorinates
 - Does not include ultra-short
- Menstruation increases excretion (dotted line)



Gomis MI, Vestergren R, MacLeod M, et al. (2017). Historical human exposure to perfluoroalkyl acids in the United States and Australia reconstructed from biomonitoring data using population-based pharmacokinetic modelling. Environment international, 108, 92–102.

Detoxification



Human Excretion/Detoxification of PFAS

- Excretion routes:
 - Urine
 - Menstrual blood
 - Breast milk
 - Stools
 - **NOT** sweat
- Detoxification
 - Liver



PFAS Detoxification

- PFAS appear to be primarily excreted by the liver and possibly the kidney
- Reabsorbed through enterohepatic recirculation
→Fiber!

PFAS Half-Lives

Table 4 Excretion rate and half-lives for serum PFAS concentrations in 106 participants in a panel study after end of exposure through contaminated drinking water

	All		Men aged 15–50		Women aged 15–50		
	Mean	95% CI	Mean	95% CI	Mean	95% CI	p*
Excretion rate constant (per year)†							
PFHxS	0.13	0.12 to 0.15	0.09	0.07 to 0.11	0.15	0.12 to 0.18	0.008
PFOS	0.20	0.19 to 0.22	0.15	0.11 to 0.18	0.22	0.19 to 0.26	0.004
PFOA	0.26	0.24 to 0.28	0.25	0.19 to 0.26	0.29	0.23 to 0.34	0.29
Half-life (years)‡							
PFHxS	5.3	4.6 to 6.0	7.4	6.0 to 9.7	4.7	3.9 to 5.9	0.008
PFOS	3.4	3.1 to 3.7	4.6	3.7 to 6.1	3.1	2.7 to 3.7	0.004
PFOA	2.7	2.5 to 2.9	2.8	2.4 to 3.4	2.4	2.0 to 3.0	0.29

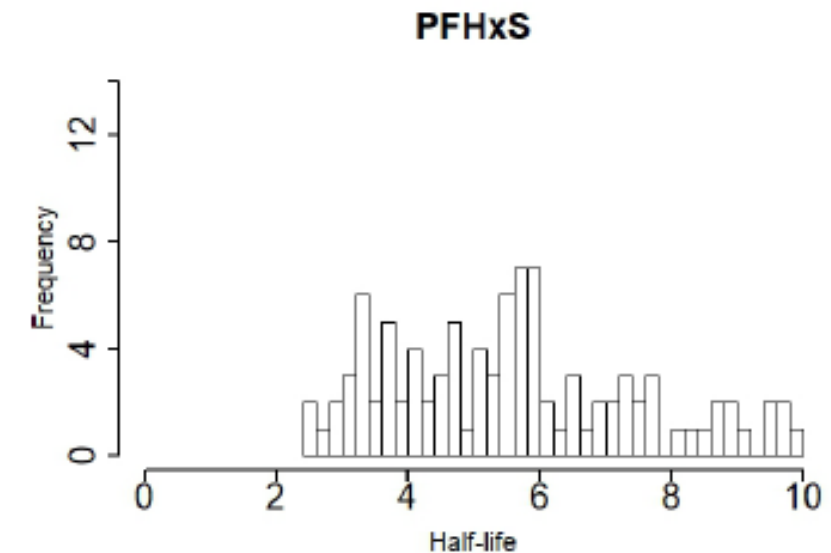
The subgroup aged 15–50 includes 20 men and 30 women.

*p Values for the difference between genders in the model for excretion rate.

†The estimates in the table are adjusted for age, gender and body mass index in a mixed-effects model.

‡Half-life values are all calculated from excretion rate constant.

PFAS, perfluorinated and polyfluorinated substance; PFHxS, perfluorohexane sulfonate; PFOA, perfluorooctanoate; PFOS, perfluorooctane sulfonate.



- In general, the longer the chain and the more F⁻ substitutions the longer the half-life

PFAS Half-Lives

Table 1-1. Summary of Estimated Elimination Half-lives for Select Perfluoroalkyls^a

	Humans	Nonhuman primates	Rats	Mice
PFOA	2.1–10.1 years	20.1–32.6 days	Males: 44–322 hours Females: 1.9–16.2 hours	
PFOS	3.3–27 years	110–170 days	179–1,968 hours	731–1,027 hours
PFHxS	4.7–35 years	87–141 days	Males: 382–688 hours Females: 1.03–41.28 hours	597–643 hours
PFNA	2.5–4.3 years		Males: 710–1,128 hours Females: 33.6–58.6 hours	619.2– 1,653 hours
PFBS	665 hours	8.0–95.2 hours	2.1–7.42 hours	
PFBA	72–81 hours	40.3–41.0 hours	1.03–9.22 hours	2.79–13.34 hours

- Note that rodents detoxify 10-1,000x faster
- In general, females better able to detoxify

Mechanism of Damage

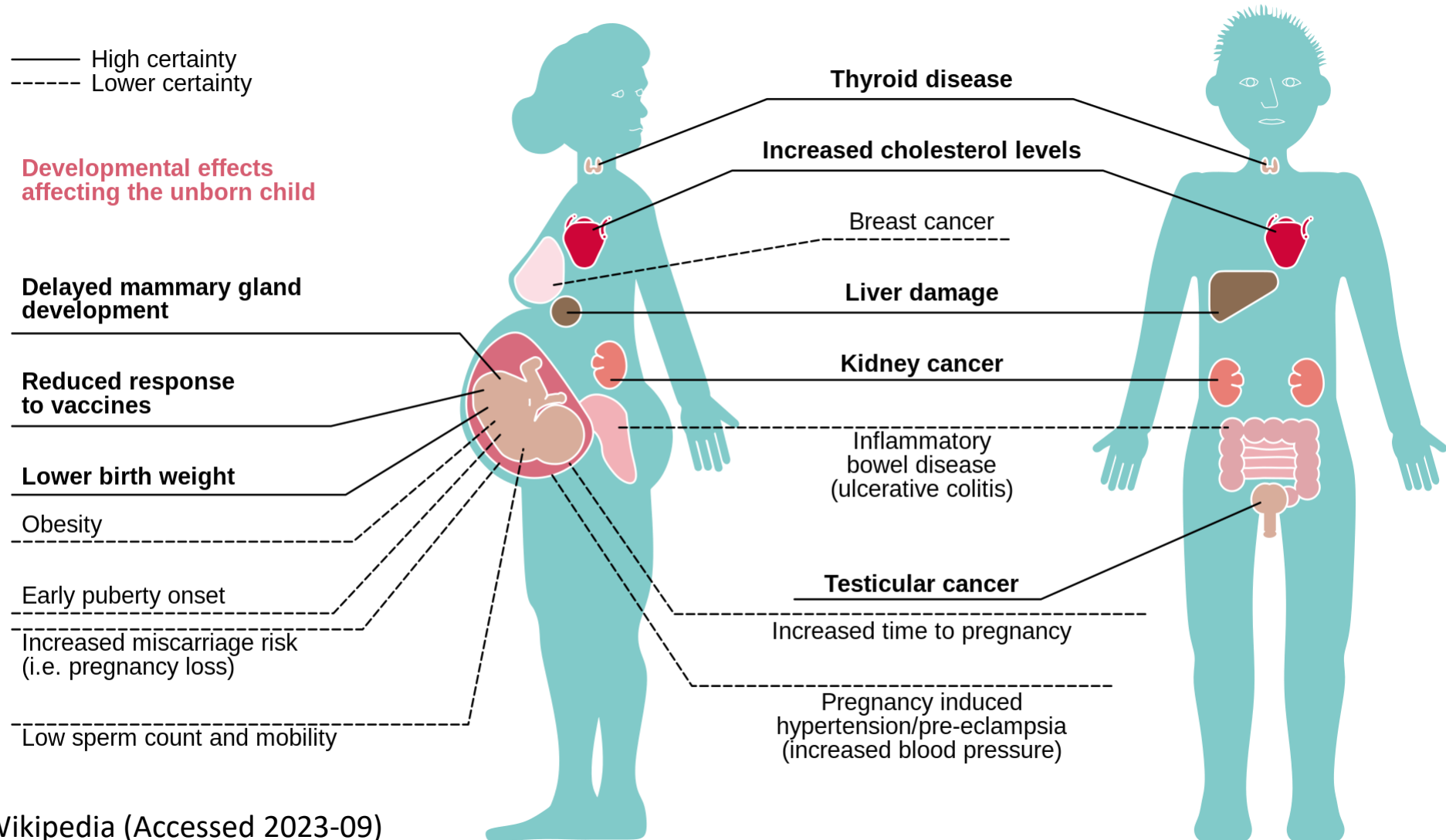


Mechanisms of Damage Still Being Elicited

- The lack of recognition and measurement of ultra-low chain PFCs greatly complicates the process
- Inappropriate PPAR α activation
- Liver, immune system and fetus most susceptible to PFOA damage

Disease Associations

Wide Range of Physiological Effects

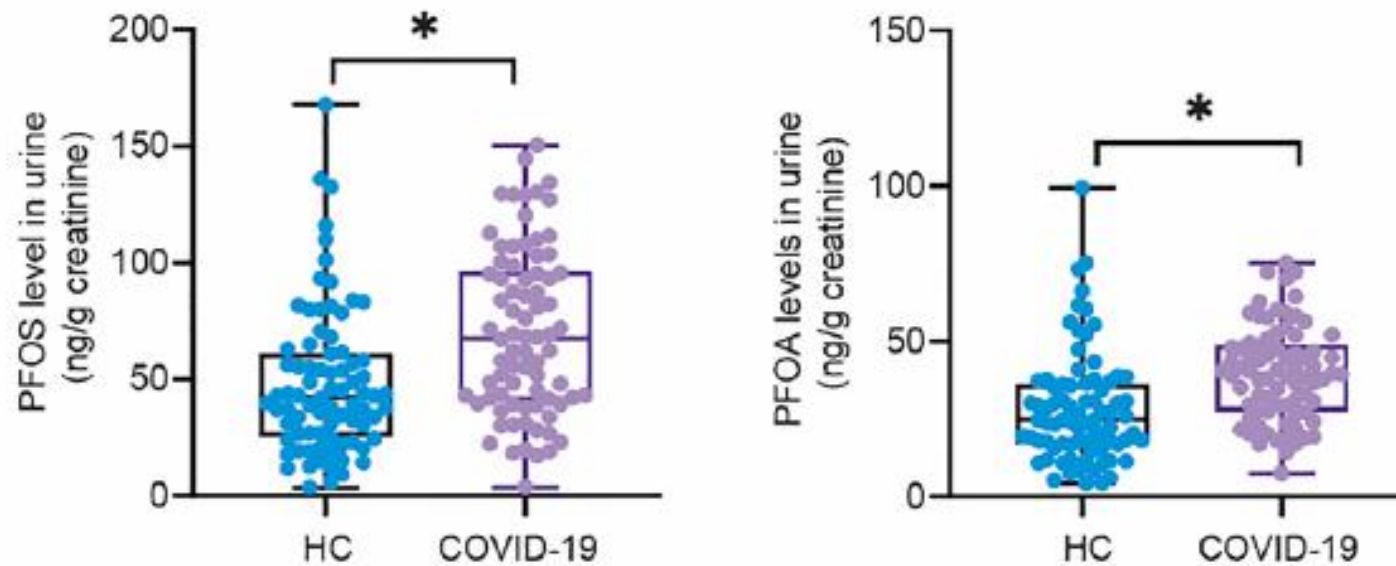




Diseases that Correlate w PFAS Level

- Cancer
- Cardiovascular
- Covid
- Diabetes
- Gout
- Infertility (male and female)
- Inflammatory bowel disease
- Impaired fetal development
- Kidney disease
- Lipid abnormalities
- Liver damage
- Mitochondrial dysfunction
- NAFLD
- Obesity
- Osteoporosis
- Thyroid dysfunction

PFOS/PFOA Increase COVID Risk

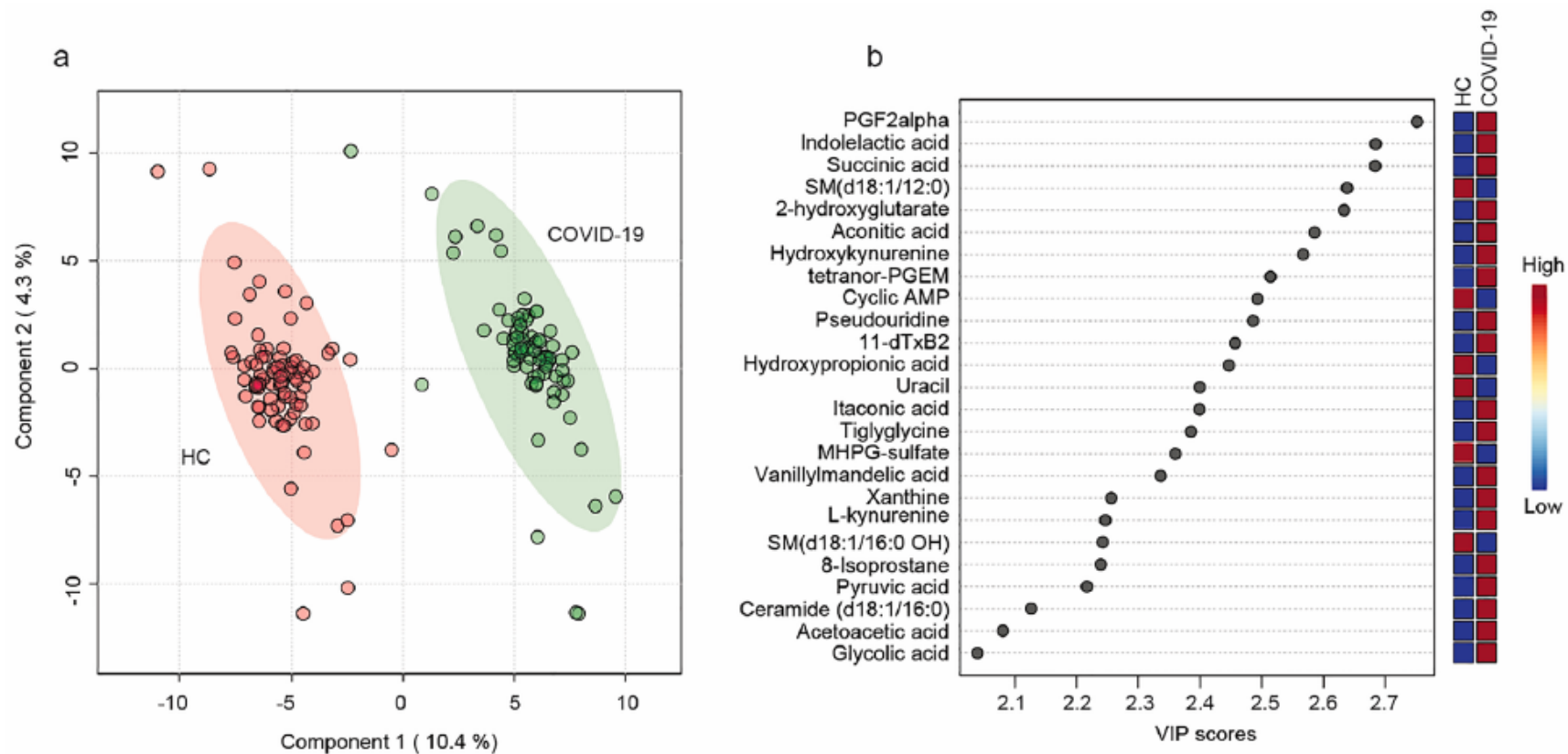


PFAS Increase COVID Risk

(Mediated by Mitochondrial Dysfunction)

- In unadjusted model:
 - Risk of COVID-19 infection positively associated with urinary levels of PFOS (OR: 2.3), PFOA (OR: 2.9) total PFASs (OR: 3.3)
- Controlling for age, sex, body mass index (BMI), comorbidities, and urine albumin-to-creatinine ratio the associations remained statistically significant
 - ORs 1.94, 2.73 and 2.82 respectively
 - 59% of PFASs-associated urinary endogenous metabolites in COVID-19 patients were identified to be produced or largely regulated by mitochondrial function

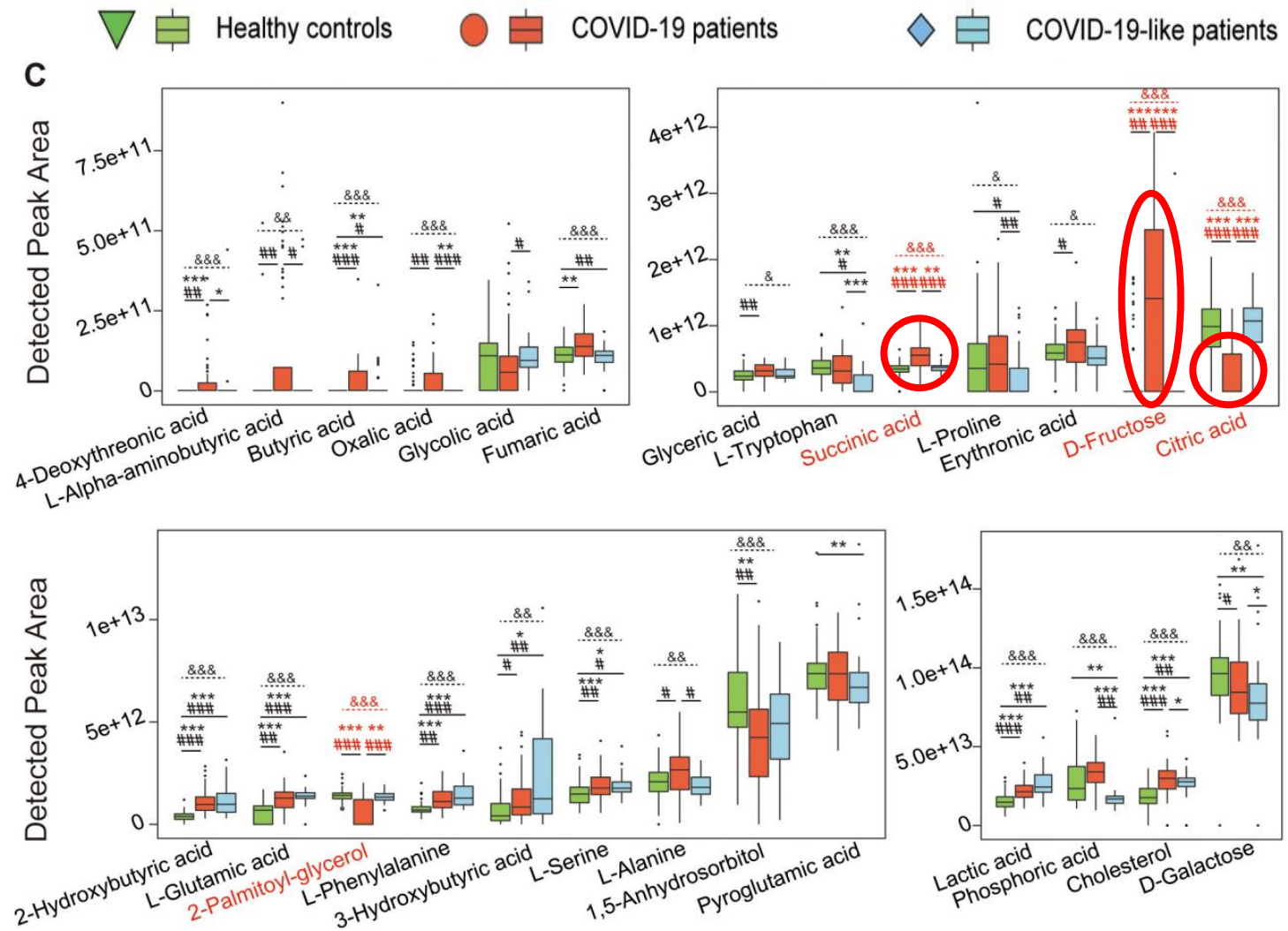
PFOA/PFOS Increase COVID-Induced Mitochondrial Abnormalities



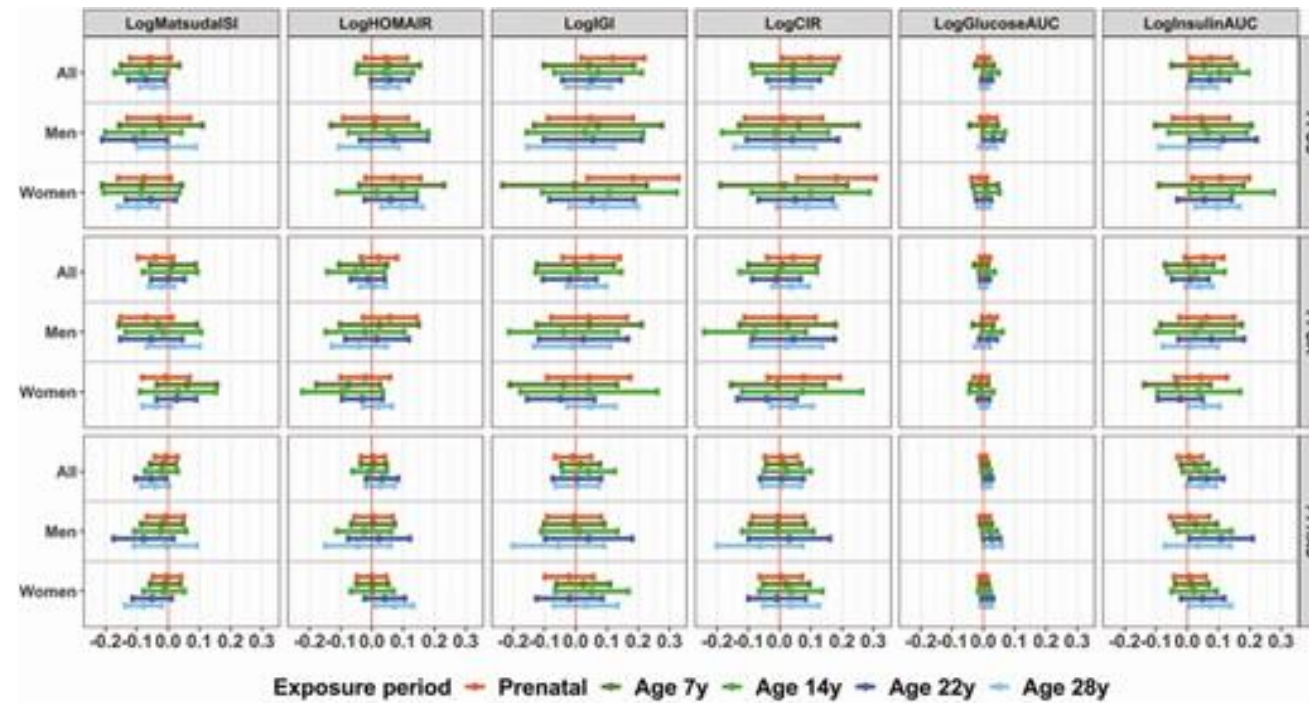


Mitochondrial Dysfunction in COVID

- Elevated:
 - D-fructose
 - Lactate
 - Succinic acid
- Decreased:
 - Citric acid



PFAS and Diabetes



- Log correlation of measures of loss of blood sugar control with each doubling of PFOAs
- PFOSs have strongest correlation

Valvi D, Højlund K, Coull BA, et al. Life-course Exposure to Perfluoroalkyl Substances in Relation to Markers of Glucose Homeostasis in Early Adulthood. J Clin Endocrinol Metab. 2021 Jul 13;106(8):2495-2504. doi PMID: 33890111

PFOA and PFOS Impair Fertility

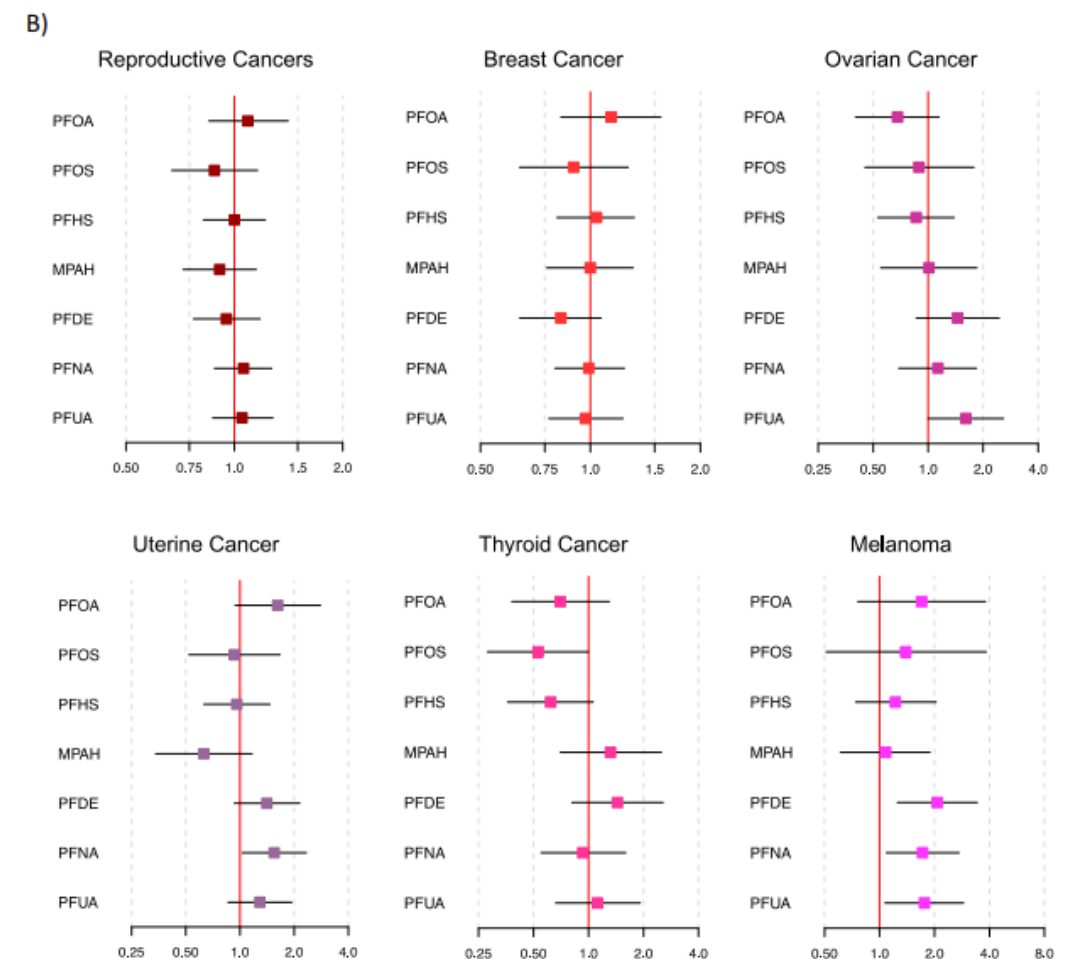
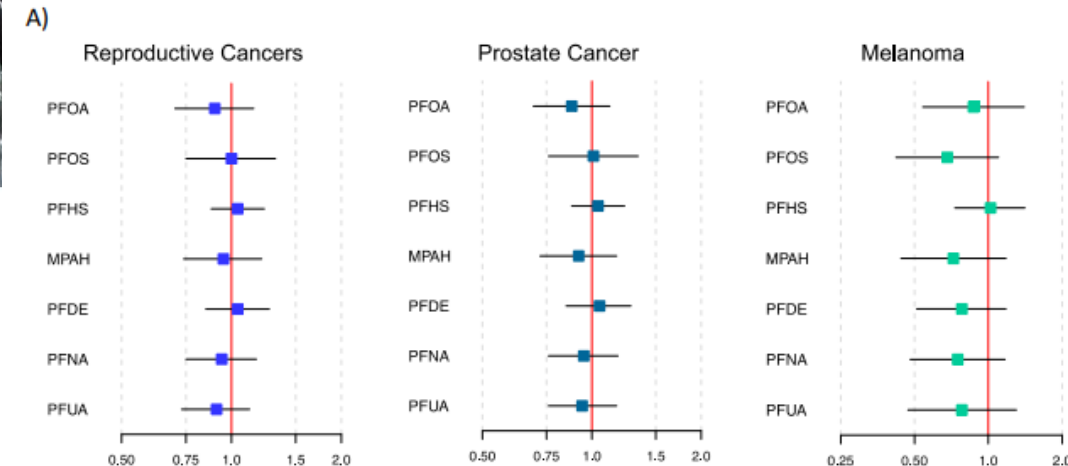
- Odds of female infertility comparing lowest to highest 3 quartiles of body load:
 - PFOSs: 70-134%
 - PFOAs: 60-154%

PFSA & Inflammatory Bowel Disease

Descriptive data for the study population.

	Ulcerative colitis (n = 114)	Crohn's disease (n = 60)	Controls (n = 75)
% male	57%	53%	39%
% white	80%	87%	3%
Mean age (std dev) at diagnosis	15 (11)	16 (9)	22 (12)
Mean year of diagnosis (range)	2006 (1999–2012)	2007 (1999–2012)	n.a.
Mean year of blood sample (year)	2008 (2004–2013)	2008 (2005–2012)	2011(2010–2013)
Mean/median PFOA (ng/mL)	3.76/2.93	3.63/1.78	2.46/1.33
Mean/median PFOS (ng/mL)	7.25/3.95	9.45/3.32	5.38/4.21
Mean/median PFNA (ng/mL)	0.99/0.43	1.81/0.54	1.24/0.91
Mean/median PHHxS (ng/mL)	2.12/0.93	3.66/1.46	2.04/1.55
Sum:	14.2	18.2	11.1

PFAS & Cancer



Cathey, A. L., Nguyen, V. K., Colacino, J. A., Woodruff, T. J., Reynolds, P., & Aung, M. T. (2023). Exploratory profiles of phenols, parabens, and per- and poly-fluoroalkyl substances among NHANES study participants in association with previous cancer diagnoses. *Journal of exposure science & environmental epidemiology*, 10.1038/s41370-023-00601-6.

Adjusted^a beta coefficient (95% CI) for serum uric acid and adjusted^a Odds Ratio (95% CI) for hyperuricemia and self-reported gout by single PFAA quartiles for adult participants (20 years of age and older) with chronic kidney disease^b (in NHANES 2009–2014).

	Serum Uric Acid β (95% CI)	Hyperuricemia OR (95% CI)	Gout OR (95% CI)
PFOA Q1	0 (Referent)	1 (Referent)	1 (Referent)
PFOA Q2	0.14 (–0.38, 0.65)	1.15 (0.69, 1.92)	1.83 (0.79, 4.19)
PFOA Q3	–0.05 (–0.63, 0.53)	0.95 (0.53, 1.69)	3.02 (1.28, 7.15)
PFOA Q4	0.60 (–0.04, 1.24)	1.82 (0.96, 3.47)	2.73 (1.28, 5.84)
p-trend	0.02	0.21	0.04
PFNA Q1	0 (Referent)	1 (Referent)	1 (Referent)
PFNA Q2	0.29 (–0.10, 0.68)	1.40 (0.82, 2.39)	0.65 (0.27, 1.54)
PFNA Q3	0.31 (0.01, 0.61)	1.41 (0.87, 2.30)	1.43 (0.74, 2.75)
PFNA Q4	0.47 (0.14, 0.80)	1.36 (0.78, 2.36)	0.86 (0.44, 1.69)
p-trend	0.04	0.47	0.21
PFDA Q1	0 (Referent)	1 (Referent)	1 (Referent)
PFDA Q2	0.34 (–0.03, 0.72)	1.32 (0.66, 2.65)	1.09 (0.52, 2.29)
PFDA Q3	0.19 (–0.13, 0.52)	0.98 (0.60, 1.61)	1.62 (0.79, 3.31)
PFDA Q4	0.26 (–0.09, 0.61)	1.26 (0.64, 2.46)	0.77 (0.35, 1.70)
p-trend	0.34	0.73	0.41
PFOS Q1	0 (Referent)	1 (Referent)	1 (Referent)
PFOS Q2	0.60 (0.15, 1.05)	1.93 (0.91, 4.06)	0.88 (0.26, 2.92)
PFOS Q3	0.31 (–0.02, 0.70)	0.85 (0.40, 1.77)	1.08 (0.38, 3.07)
PFOS Q4	0.38 (0.06, 0.83)	1.15 (0.53, 2.50)	1.08 (0.39, 2.94)
p-trend	0.08	0.12	0.97
PFHxS Q1	0 (Referent)	1 (Referent)	1 (Referent)
PFHxS Q2	0.40 (–0.03, 0.84)	0.91 (0.49, 1.70)	1.53 (0.57, 4.05)
PFHxS Q3	0.33 (–0.02, 0.67)	0.87 (0.49, 1.53)	1.85 (0.76, 4.52)
PFHxS Q4	0.42 (0.06, 0.78)	1.28 (0.52, 2.64)	2.31 (0.96, 5.57)
p-trend	0.12	0.49	0.31

Quartiles PFOA (ng/mL): Q1: ≤1.60; Q2: 1.61–2.47; Q3: 2.48–3.66; Q4: >3.66. Quartiles PFNA (ng/mL): Q1: ≤0.60; Q2: 0.61–0.90; Q3: 0.91–1.39; Q4: >1.39. . Quartiles PFDA (ng/mL): Q1: ≤0.12; Q2: 0.13–0.20; Q3: 0.21–0.35; Q4: >0.35, Quartiles PFHxS (ng/mL): Q1: ≤0.81; Q2: 0.82–1.49; Q3: 1.50–2.51; Q4: >2.51. Quartiles PFOS (ng/mL): Q1: ≤4.43; Q2: 4.44–7.33; Q3: 7.34–11.90; Q4: >11.90.

^a Adjusted for race/ethnicity, age, sex, education attainment, alcohol consumption, self-reported cigarette smoking, serum cotinine, BMI, diabetes, hypertension, and eGFR; when modeling self-reported gout as the outcome, serum uric acid was also entered as a covariate.

^b Chronic kidney diseases defined as eGFR ≥60 mL/min/1.73 m² and/or albuminuria (>30. mg/g).



Scinicariello, F., Buser, M. C., Balluz, L., Gehle, K., Murray, H. E., Abadin, H. G., & Attanasio, R. (2020).

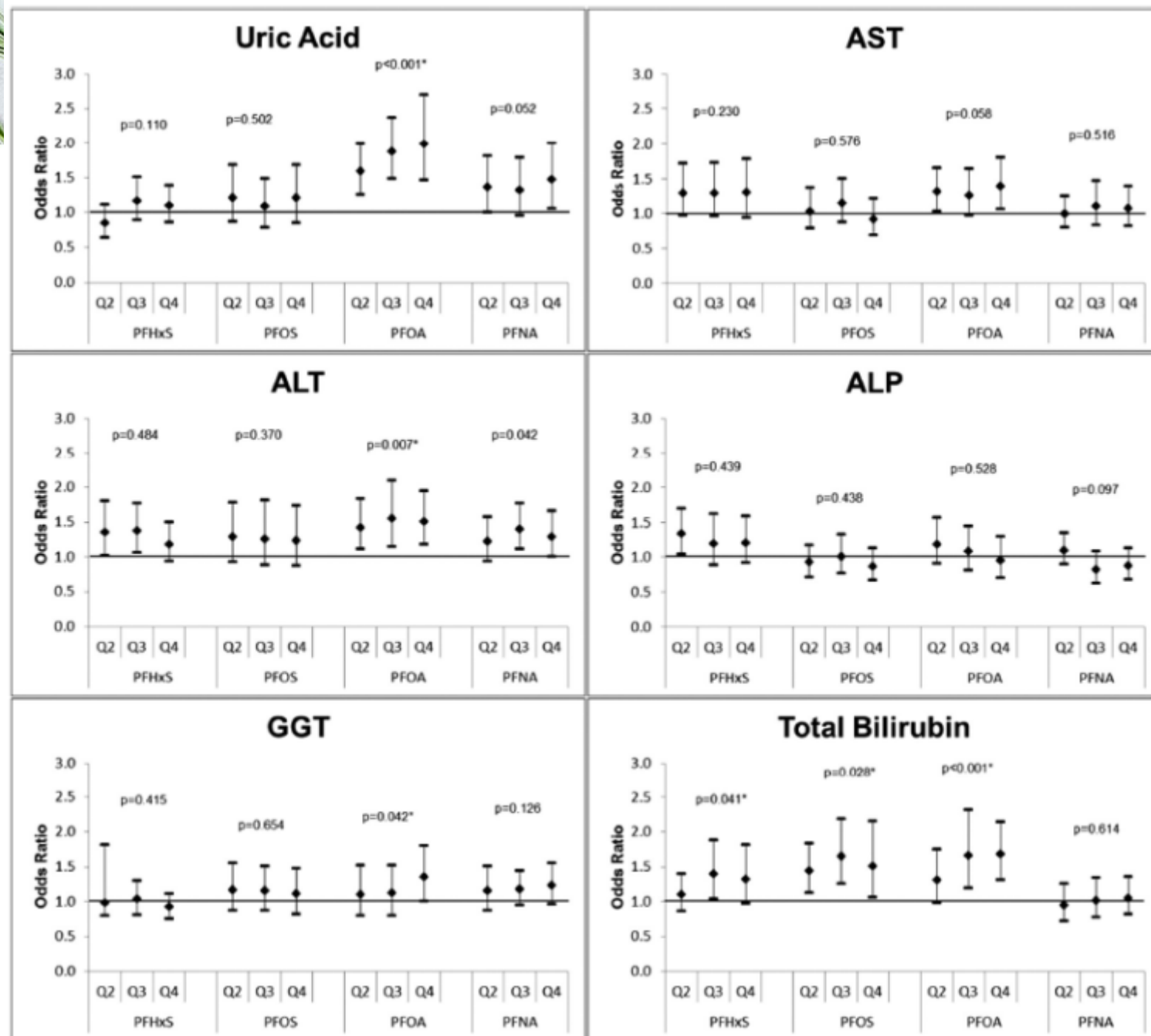
Perfluoroalkyl acids, hyperuricemia and gout in adults: Analyses of NHANES 2009-2014. Chemosphere, 259, 127446.

Assessment

Indirect Indicators

- Increase proportionately in normal range
 - ALT
 - Bilirubin
 - GGTP
 - Uric acid

PFAS and Common Blood Tests



AST, ASP, GGTP

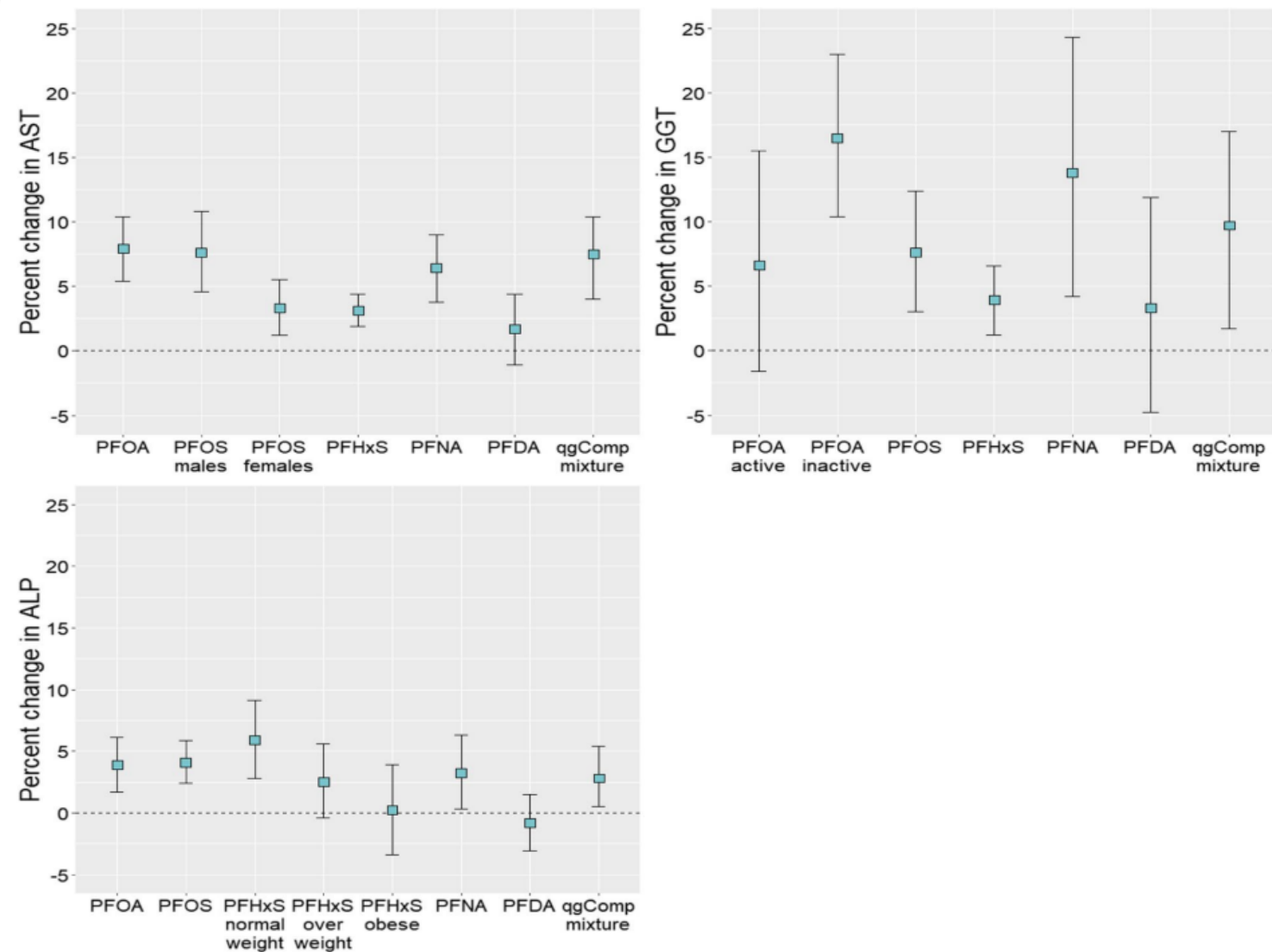
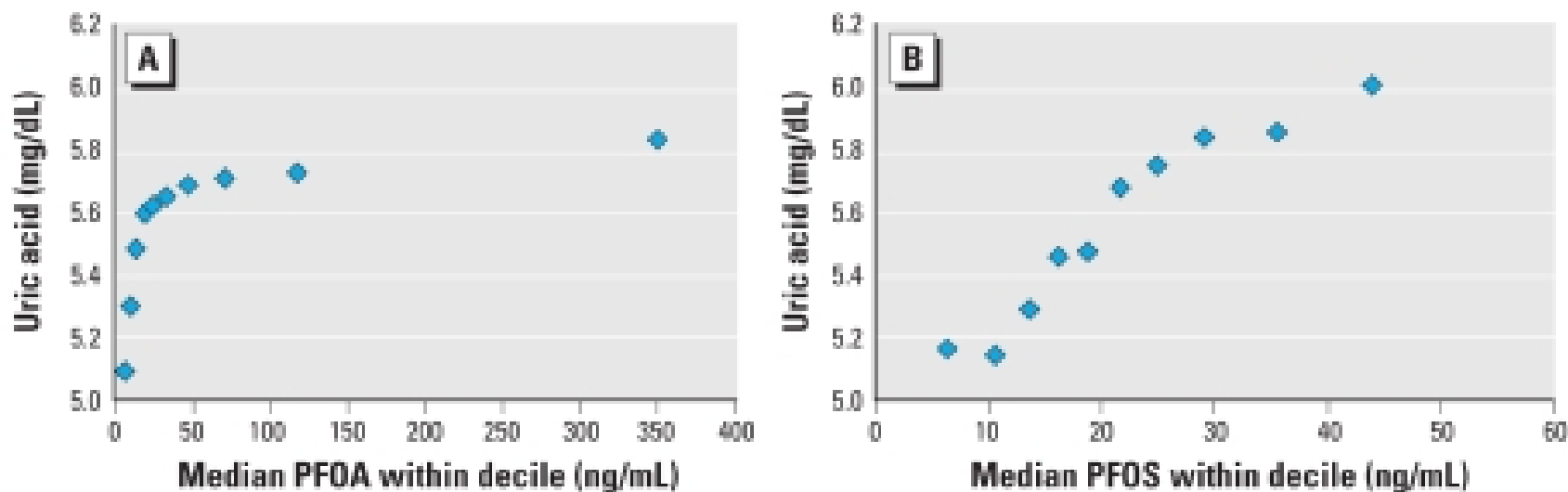


Fig. 1 Percent change (95%CI) in AST, GGT, and ALP for PFAS individually and as a mixture. Coefficients for individual PFAS represent the percent change for each two-fold increase in PFAS concentrations. Coefficients for qqComp mixture represents a simultaneous one-quartile increase in PFAS concentrations derived using quantile g-computation. Active and inactive refers to effects among individuals who either meet, or do not meet, Canada's physical activity guidelines, respectively

Borghese, M. M., Liang, C. L., Owen, J., & Fisher, M. (2022). Individual and mixture associations of perfluoroalkyl substances on liver function biomarkers in the Canadian Health Measures Survey. *Environmental health : a global access science source*, 21(1), 85.

Uric Acid Increases with Perfluorinates

- Perfluorinated hydrocarbons (PFOA and PFOS) associated with **increased serum uric acid**



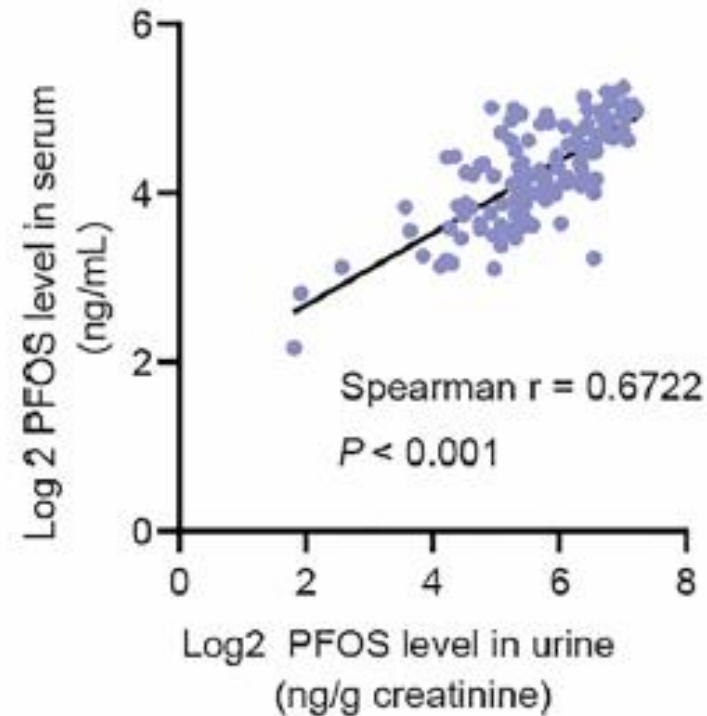
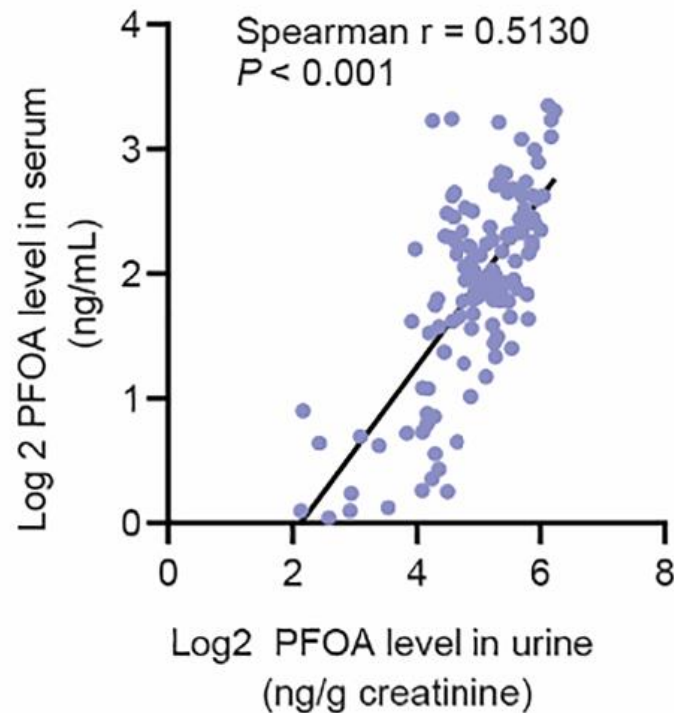
Steenland 2010: Open Access

Lin CY, et al. Association among serum perfluoroalkyl chemicals, glucose homeostasis, and metabolic syndrome in adolescents and adults. *Diabetes Care*. 2009 Apr;32(4):702-7.

Steenland K et al. Association of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) with uric acid among adults with elevated community exposure to PFOA. *Environ Health Perspect*. 2010 Feb;118:229-33.

Direct Measurement

Urine and Blood Levels Correlate



Note: these are log scales



Laboratories

- Environmental:
 - Babcock Laboratories ([PFAS Testing Laboratory — Babcock Laboratories, Inc. \(babcocklabs.com\)](https://babcocklabs.com))
 - tap score ([Independent Lab Water Testing For Home And Business – SimpleLab Tap Score \(mytapscore.com\)](https://mytapscore.com))
- Clinical:
 - Michigan State University Center for PFAS Research ([PFAS Testing - Center for PFAS Research \(msu.edu\)](https://msu.edu))
 - Mosaic Diagnostics ([Simplified, Scientific Laboratory Testing | MosaicDX](https://mosaicdx.com))
 - Vibrant Wellness ([PFAS Chemical Test by Vibrant Wellness - Learn More \(vibrant-wellness.com\)](https://vibrantwellness.com))

Intervention

Avoidance

Decrease Exposure - Food

- Don't eat out!
- NEVER eat microwave popcorn
- Safe food packaging:
 - Greaseproof vegetable parchment paper
 - Coatings with carboxymethylcellulose (CMC), polyvinyl alcohol (PVOH), starch, aqueous dispersions of styrene-butadiene copolymers, aqueous dispersions of waxes, or hydroxyethylcellulose soluble in water (HEC)
- Cookware: ceramic, stainless steel

Ramírez Carnero A, Lestido-Cardama A, Vazquez Loureiro P, et al. (2021). Presence of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS) in Food Contact Materials (FCM) and Its Migration to Food. Foods (Basel, Switzerland), 10(7), 1443. <https://doi.org/10.3390/foods10071443>

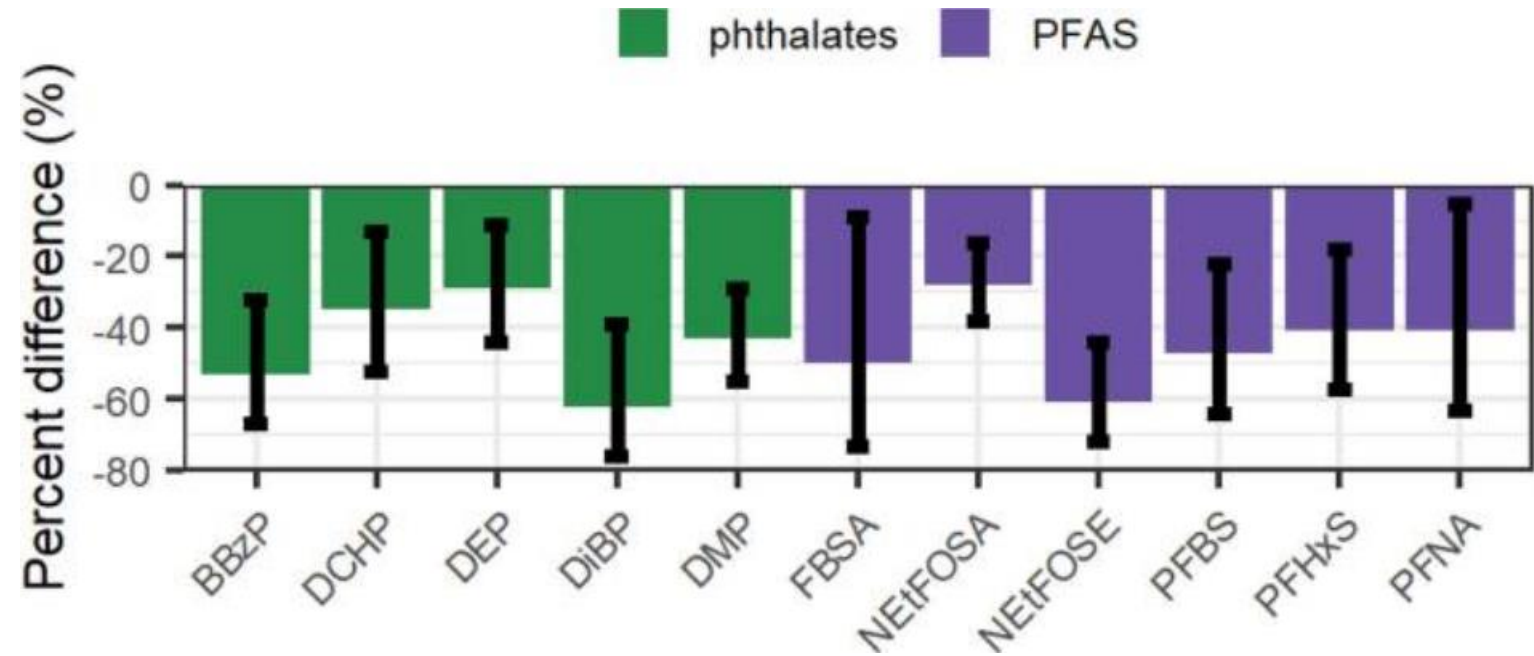
Decrease Exposure - Water

- Carbon block filters remove most PFCs
 - Whole house strongly recommended
 - Arbitrary example from Home Depot:



Decrease Exposure - Air

- Corsi–Rosenthal Box



Dodson, R. E., Manz, K. E., Burks, S. R., Gairola, R., Lee, N. F., Liu, Y., Pennell, K. D., Walker, E. D., & Braun, J. M. (2023). Does Using Corsi-Rosenthal Boxes to Mitigate COVID-19 Transmission Also Reduce Indoor Air Concentrations of PFAS and

Decrease Exposure - Apparel



SHOES AND SPORTS APPAREL BRANDS

COMPANY	SAMPLE APPAREL BRANDS	GRADE
KEEN FOOTWEAR	KEEN	A-
DECKERS BRANDS	UGG, TEVA	A-
NEW BALANCE	NEW BALANCE	C-
NIKE, INC.	NIKE	D+
UNDER ARMOUR	UNDER ARMOUR	F
SKECHERS	SKECHERS	F



APPAREL RETAILERS

COMPANY	GRADE
COSTCO WHOLESALE CORPORATION	D
TARGET CORPORATION	D
KOHL'S CORPORATION	F
NORDSTROM	F
JCPENNEY	F
MACY'S, INC.	F
WALMART INC.	F



OUTDOOR APPAREL BRANDS

COMPANY	SAMPLE APPAREL BRANDS	GRADE
PATAGONIA INC.	PATAGONIA	B
VF CORPORATION	THE NORTH FACE, TIMBERLAND	D
L.L. BEAN	L.L. BEAN	D
COLUMBIA SPORTSWEAR	COLUMBIA, PRANA	F
REI	REI CO-OP	F
WOLVERINE WORLDWIDE	WOLVERINE, MERRELL	F
ACADEMY SPORTS + OUTDOORS	ACADEMY SPORTS + OUTDOORS, MAGELLAN OUTDOORS	F

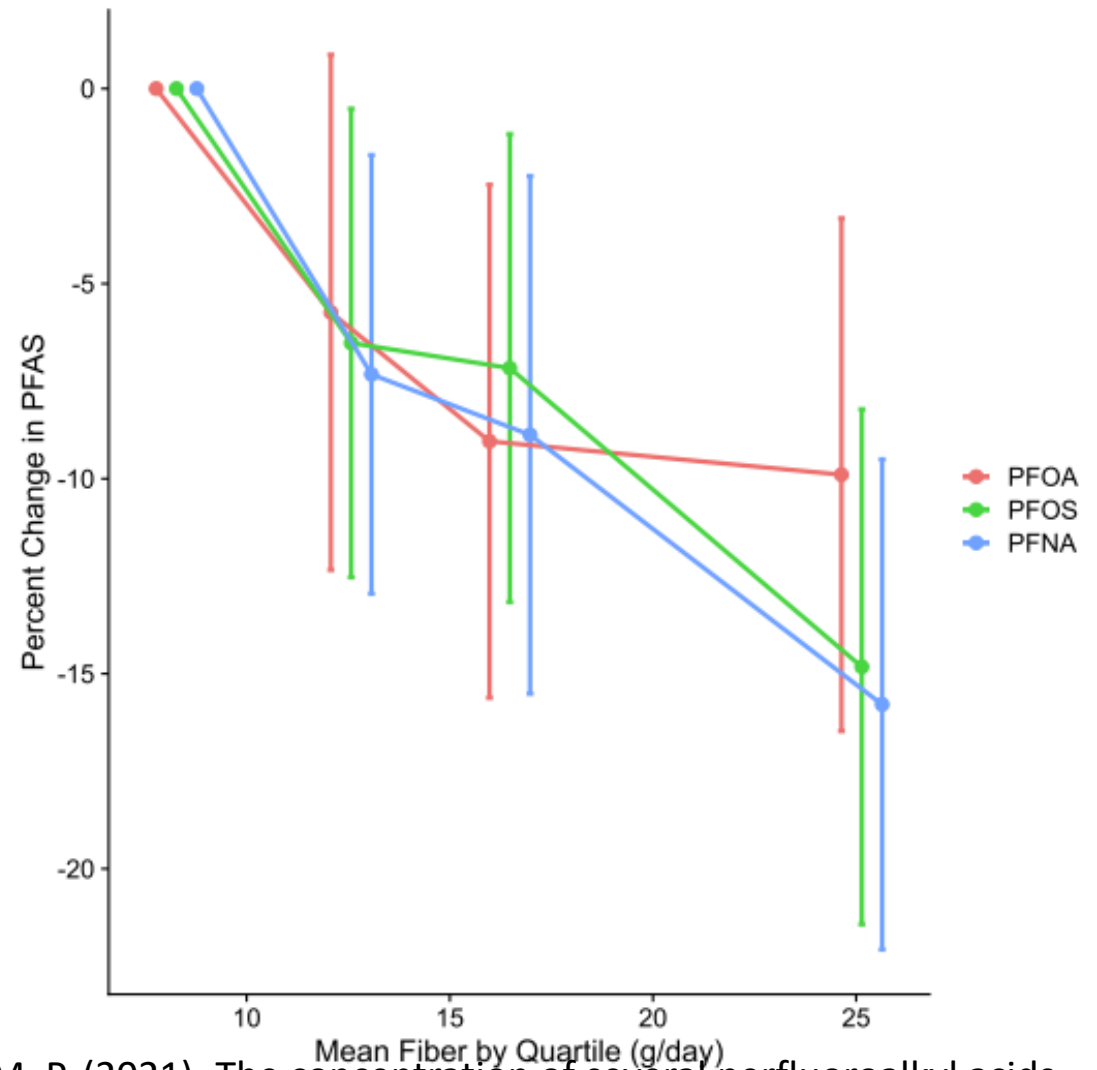


INDOOR APPAREL BRANDS

COMPANY	SAMPLE APPAREL BRANDS	GRADE
LEVI STRAUSS & CO.	LEVI'S, DOCKERS	A+
VICTORIA'S SECRET	VICTORIA'S SECRET, PINK	A-
RALPH LAUREN CORPORATION	RALPH LAUREN, POLO	B+
GAP INC.	GAP, OLD NAVY	B
AMERICAN EAGLE OUTFITTERS	AMERICAN EAGLE, AERIE	B-
PVH CORPORATION	CALVIN KLEIN, TOMMY HILFGER	B-
ABERCROMBIE & FITCH	ABERCROMBIE & FITCH, HOLLISTER	C+
CAPRI HOLDINGS	MICHAEL KORS, JIMMY CHOO	F
G-III APPAREL GROUP LTD.	DKNY, ANDREW MARC	F
TAPESTRY, INC.	COACH, KATE SPADE	F

Increase Excretion

Dietary Fiber



Dzierlenga, M. W., Keast, D. R., & Longnecker, M. P. (2021). The concentration of several perfluoroalkyl acids in serum appears to be reduced by dietary fiber. *Environment international*, 146, 106292.

Cholestyramine Increases Excretion

- Bile acid sequestrant cholestyramine (CSM) facilitates excretion of some PFCs
 - 4g tid for a week
- All members of family had elevated PFCs, but no other chemicals; child high
- Most of house carpeted; sprayed periodically with stain/soil repellence; AND in-floor heating Dramatic reduction in levels when carpet removed

Table 2 – Serum levels of perfluorinated compounds prior to and after treatment with cholestyramine (CSM).

Analyte	Serum (ng/g) June 2007 Prior to treatment	Serum (ng/g) March 2008 Prior to treatment	Serum (ng/g) June 2008 Immediately prior to treatment	Serum (ng/g) September 2008 After approx. 12 weeks of CSM treatment	Serum (ng/g) November 2008 After approx. 20 weeks of CSM treatment	Carpets removed from home in January 2009
PFHxS	60.0	59.1	58.0	50.4	46.8	–
PFOS	26.0	27.4	23.0	15.6	14.4	–
PFOA	6.8	5.5	5.9	4.4	4.1	–
PFNA	0.9	0.7	0.5	<0.5	<0.5	–

PFHxS, perfluorohexansulfonate; PFOS, perfluorooctanesulfonate; PFOA, perfluorooctanoic acid; PFNA, perfluorononanoic acid.

Cholestyramine, Saponins, Zeolite

Table 1 – Level of perfluorinated compounds in serum, urine, sweat and stool prior to and after treatment with cholestyramine (CSM) and after treatment with zeolite^a and saponins.^a

Analyte	Serum (ng/g) June 2007	Centile of serum level according to CDC reference range data ³⁹	Urine (ng/ml) June 2007	Sweat (ng/g) June 2007	Stool – no treatment (ng/g) June 2008	Stool – after treatment with CSM – Sample 1 (ng/g) June 2008	Stool – after treatment with CSM – Sample 2 (ng/g) June 2008	Stool – after treatment with saponins – Sample 1 (ng/g) Feb 2009	Stool – after treatment with saponins – Sample 2 (ng/g) Feb 2009	Stool – after treatment with zeolite (ng/g) Nov 2009
PFHxS	60.00	>>95 centile	<0.50	1.74	<0.50	5.73	5.62	<1.00	<1.00	<1.00
PFOS	26.00	50–75 centile	<0.50	<0.50	<0.50	9.06	7.94	<1.00	<1.00	1.40
PFDS	<0.50	–	<0.50	<0.50	<0.50	<0.50	<0.50	<1.00	<1.00	<1.00
PFOA	6.80	75–90 centile	3.72	<0.50	<0.50	0.96	0.96	1.03	1.19	<1.00
PFNA	0.93	25–50 centile	<0.50	<0.50	<0.50	0.55	0.54	<1.00	<1.00	<1.00
PFDA	<0.50	–	<0.50	<0.50	<0.50	<0.50	<0.50	<1.00	<1.00	<1.00
PFUA	<0.50	–	<0.50	<0.50	<0.50	<0.50	<0.50	<1.00	<1.00	<1.00
PFDoA	<0.50	–	<0.50	<0.50	<0.50	<0.50	<0.50	<1.00	<1.00	<1.00

PFHxS, perfluorohexansulfonate; PFOS, perfluorooctanesulfonate; PFOA, perfluorooctanoic acid; CDC, Centers for Disease Control and Prevention; PFDS, perfluorodecane sulfonate; PFNA, perfluorononanoic acid; PFDA, perfluorodecanoic acid; PFUA, perfluoro-*n*-undecanoic acid; PFDoA, perfluorododecanoic acid.

^a The Limit of detection (LOD) for the urine, sweat and stool samples (other than the post-treatment stool with saponins) is 0.50 ng/g. The LOD for the stool samples after treatment with saponins and zeolite is 1.00 ng/g. While the post-CSM stool sample was freeze-dried, the post-saponin and post-zeolite samples were extracted as wet samples and calculations were based on dry weight. As a result, a lower extraction weight determined that the LOD had to go up slightly. Both methods worked well with the matrix spikes.

- Cholestyramine increases stool excretion
- Saponins and Zeolite ineffective



Cholestyramine (CSM) and *Chlorella pyrenoidosa* (CP)

- 1 week
- CSM: 4g/d (effective)
- CP: 9g/tid (ineffective)

Genuis, S. J., Curtis, L., & Birkholz, D. (2013). Gastrointestinal Elimination of Perfluorinated Compounds Using Cholestyramine and *Chlorella pyrenoidosa*. *ISRN toxicology*, 2013, 657849.

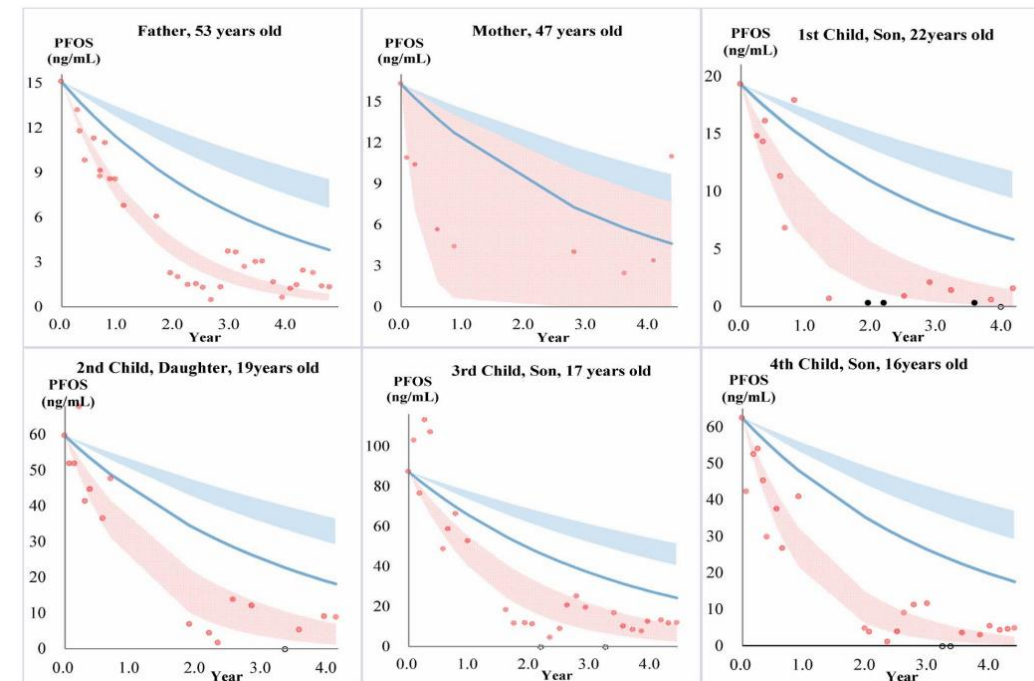
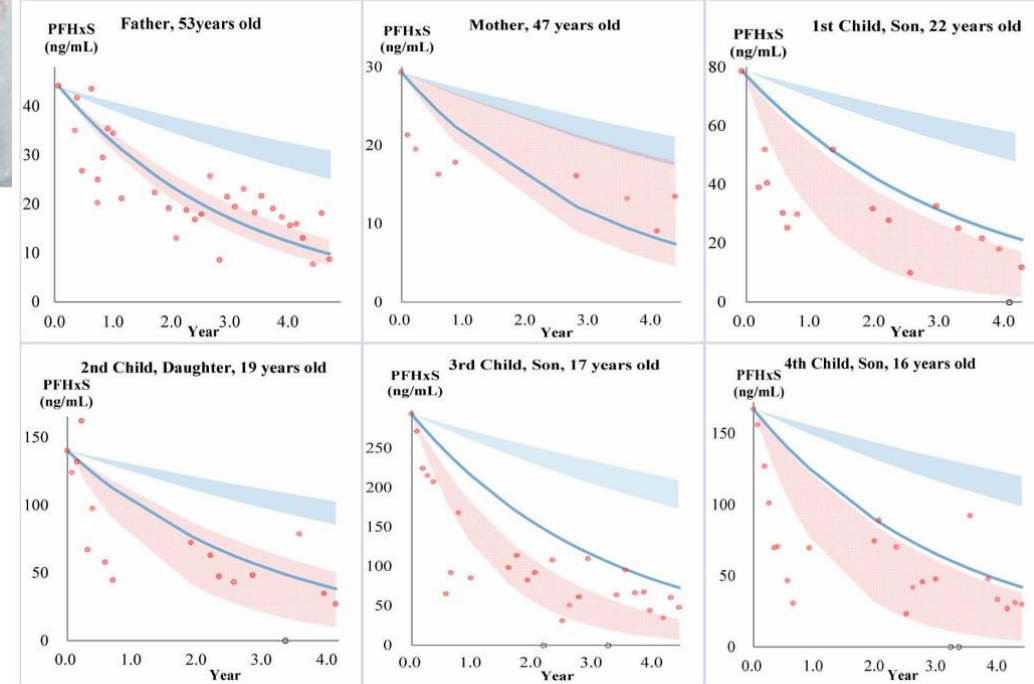
Subject	Type of test	PFHxS	PFOS	PFOA	PFNA
#1 female 48	Serum	16.3**	5.67	1.27	0
	Pretreatment stool	1.0	<1.0	<1.0	<1.0
	Post-CSM stool	3.4	1.0	1.1	<1.0
	Post-CP stool	<1.0	<1.0	<1.0	<1.0
#2 female 24	Serum	35.8**	26.5	2.17	0
	Pretreatment stool	<1.0	<1.0	<1.0	<1.0
	Post-CSM stool	460	2.1	2.1	<1.0
	Post-CP stool	<1.0	<1.0	<1.0	<1.0
#3 female 22	Serum	44.1**	27.3	2.33	0.74
	Pretreatment stool	<1.0	1.4	<1.0	<1.0
	Post-CSM stool	16	5.3	<1.0	<1.0
	Post-Chlorella stool	<1.0	1.1	<1.0	<1.0
#4 female 20	Serum	97.5**	44.7	5.04	0.62
	Pretreatment stool	1.7	1.5	<1.0	<1.0
	Post-CSM stool	26.6	36.9	2	<1.0
	Post-CP stool	1.1	<1.0	<1.0	<1.0

** Denotes PFC serum value above 95th percentile, NHANES study.

Phlebotomy

- Adult dose: ~1 pint/2 mo
- Blue:
 - Range: Distribution in general population with 95% limits
 - Line: Fastest detoxifiers in general population
- Red:
 - Treated with phlebotomy

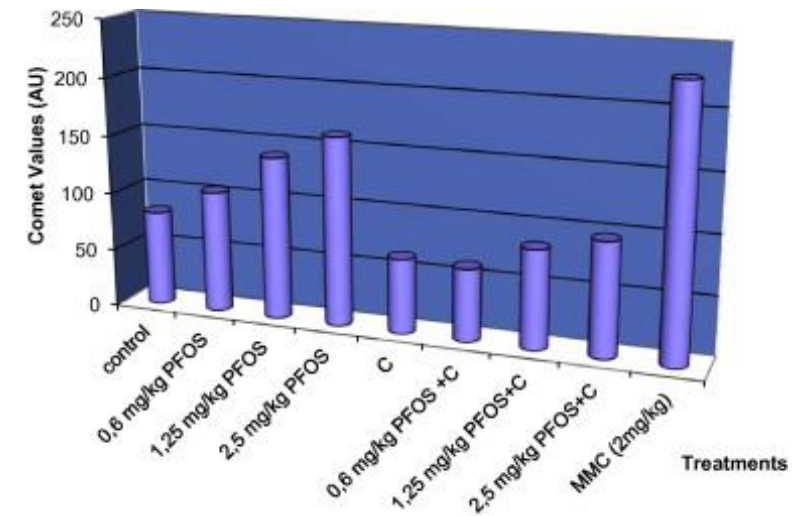
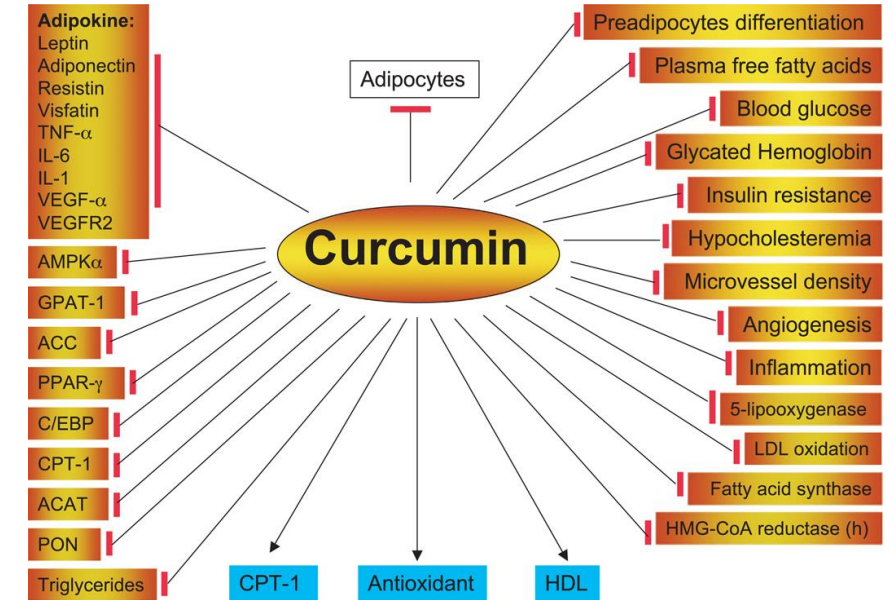
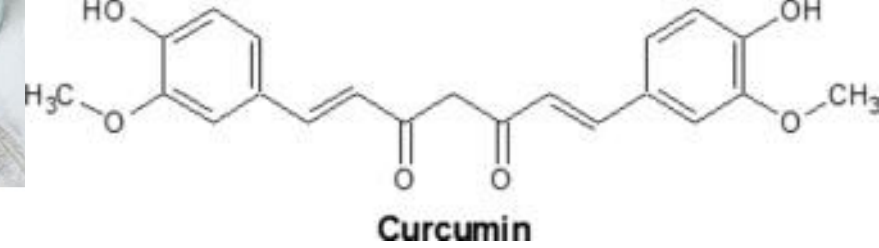
Genuis, S. J., Liu, Y., Genuis, Q. I., & Martin, J. W. (2014).
Phlebotomy treatment for elimination of perfluoroalkyl acids in a
highly exposed family: a retrospective case-series. PloS one, 9(12),
e114295.



Decrease Damage

Curcumin to the Rescue

- Many of the mechanisms of damage from toxins are mitigated by curcumin
- Emerging research showing direct protection from specific toxins
 - Protects DNA from perfluorooctane sulfonate



Çelik A, et al. The protective role of curcumin on perfluorooctane sulfonate-induced genotoxicity: single cell gel electrophoresis and micronucleus test. Food Chem Toxicol. 2013 Mar;53:249-55



Vitamin C

- Eliminates HOMA-IR induction by PFAS
- Dosage behind paywall

Kim, J. H., Park, H. Y., Jeon, J. D., Kho, Y., Kim, S. K., Park, M. S., & Hong, Y. C. (2016). The modifying effect of vitamin C on the association between perfluorinated compounds and insulin resistance in the Korean elderly: a double-blind, randomized, placebo-controlled crossover trial. *European journal of nutrition*, 55(3), 1011–1020.



Blueberries

- Animal study
- Neurotoxicity including locomotor impairment, regeneration lag, AChE activity inhibition, DNA damage, neurotransmitter contents decline, morphology defects and gene expression alterations.
- Blueberries attenuate these adverse effects.
- **Molecular mechanisms** underlying the effects of PFOA and blueberry on the planarian nervous system including the alterations in neurological enzymes, neurotransmitter levels and neuromorphogenesis are **unknown**.

Zhang, J., Shao, X., Zhao, B., Zhai, L., Liu, N., Gong, F., Ma, X., Pan, X., Zhao, B., Yuan, Z., & Zhang, X. (2020). Neurotoxicity of perfluorooctanoic acid and post-exposure recovery due to blueberry anthocyanins in the planarians *Dugesia japonica*. *Environmental pollution* (Barking, Essex: 1987), 263(Pt B), 114471. <https://doi.org/10.1016/j.envpol.2020.114471>



Environmental Working Group (EWG) Guidance

FILTER YOUR WATER

We tested water filter effectiveness. Here's what we found:

EWG found countertop filters that remove 100 percent of PFAS from water (or close to it).

GOOD GROOMING

With personal care products, don't believe in miracles

Choose personal care products without PTFE or fluoro ingredients. Use EWG's Skin Deep® and Healthy Living app to find safer choices instead. Or look for products with the EWG VERIFIED® mark, which are free from ingredients of concern.



COMING CLEAN

What's in your cleaners?

It's hard to know what's in your cleaners – they aren't required to disclose their ingredients. Consult our Guide to Healthy Cleaning, including EWG VERIFIED: Cleaners.

BEWARE FABRICS LABELED STAIN- AND WATER- REPELLENT

They're usually made with PFAS

Look for products that say they're PFAS-free, like furniture and carpets that haven't been pre-treated.

FISHY BUSINESS

Contamination of lakes and rivers

PFAS contaminate freshwater fish because of industrial discharges. Get the facts about what's in a body of water before eating fish that comes from it.

(NON)STICKY SITUATION

Avoid using nonstick cookware and utensils

Teflon, which makes your cookware nonstick, is the granddaddy of all forever chemicals. Don't use it. Choose stainless steel or cast iron instead.

TAKEOUT TIMEOUT

Cut back on fast food and greasy carry-out

Many containers are treated with PFAS, which then leach into our food. That includes microwave popcorn bags, often lined with PFAS.

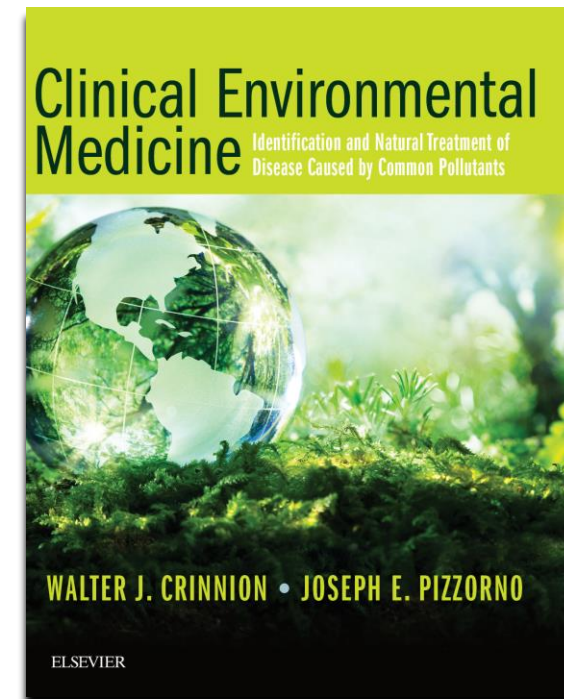
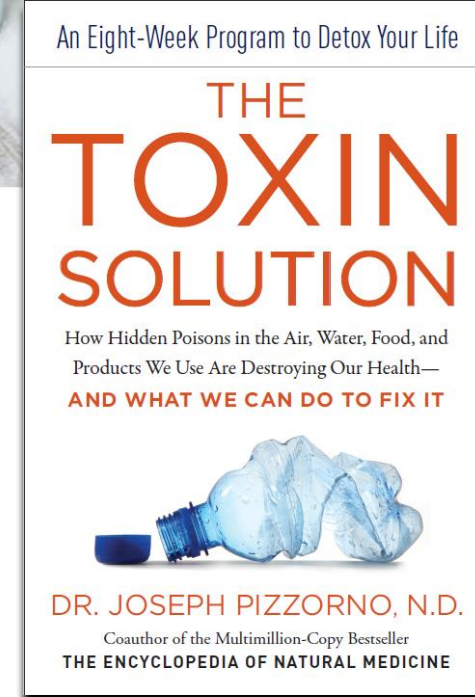
Conclusion

PFAS: Common Contaminants

- Exposure ubiquitous
 - Food primary source for most people
- Entire population has significant body load
- Disease associations real, but weak
- Long half-lives mean levels increase during entire lifespan
- Much of the research is problematic due to lack of measurement of ultra-short versions
- Clinically important—everyone needs to decrease body load

Resources

- Consumer:
 - Pizzorno J. *The Toxin Solution*. HarperOne, 2017
 - Minich D. *Whole Detox: A 21-Day Personalized Program to Break Through Barriers in Every Area of Your Life*. HarperOne, 2016
- Practitioners:
 - Crinnon W, Pizzorno J. *Clinical Environmental Medicine*, Elsevier, 2018





Friday 3:30pm – 5:00pm

**Plenary: PFASs: Clinical Impacts,
Diagnosis and Intervention**

Please scan this QR code on you mobile
or tablet device to access the session feedback survey



Plenary: PFASs: Clinical Impacts Diagn
osis and Intervention