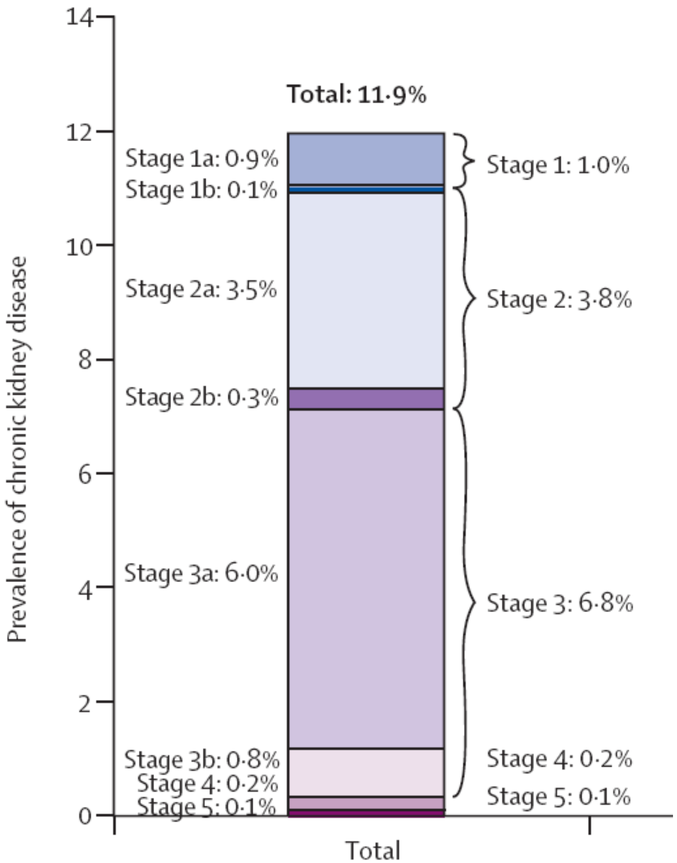
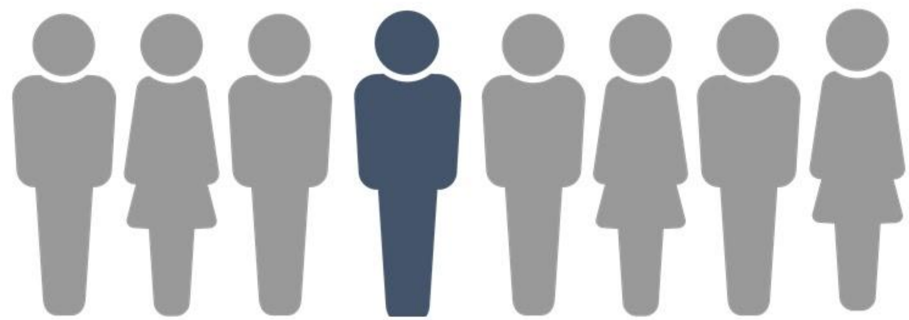
Per- and Polyfluoroalkyl substances (PFAS) and kidney function: From environmental exposure to biological mechanisms

Emily, Yiting Lin, MD, PhD

Associate professor in Kaohsiung Medical University

CKD prevalence in Taiwan

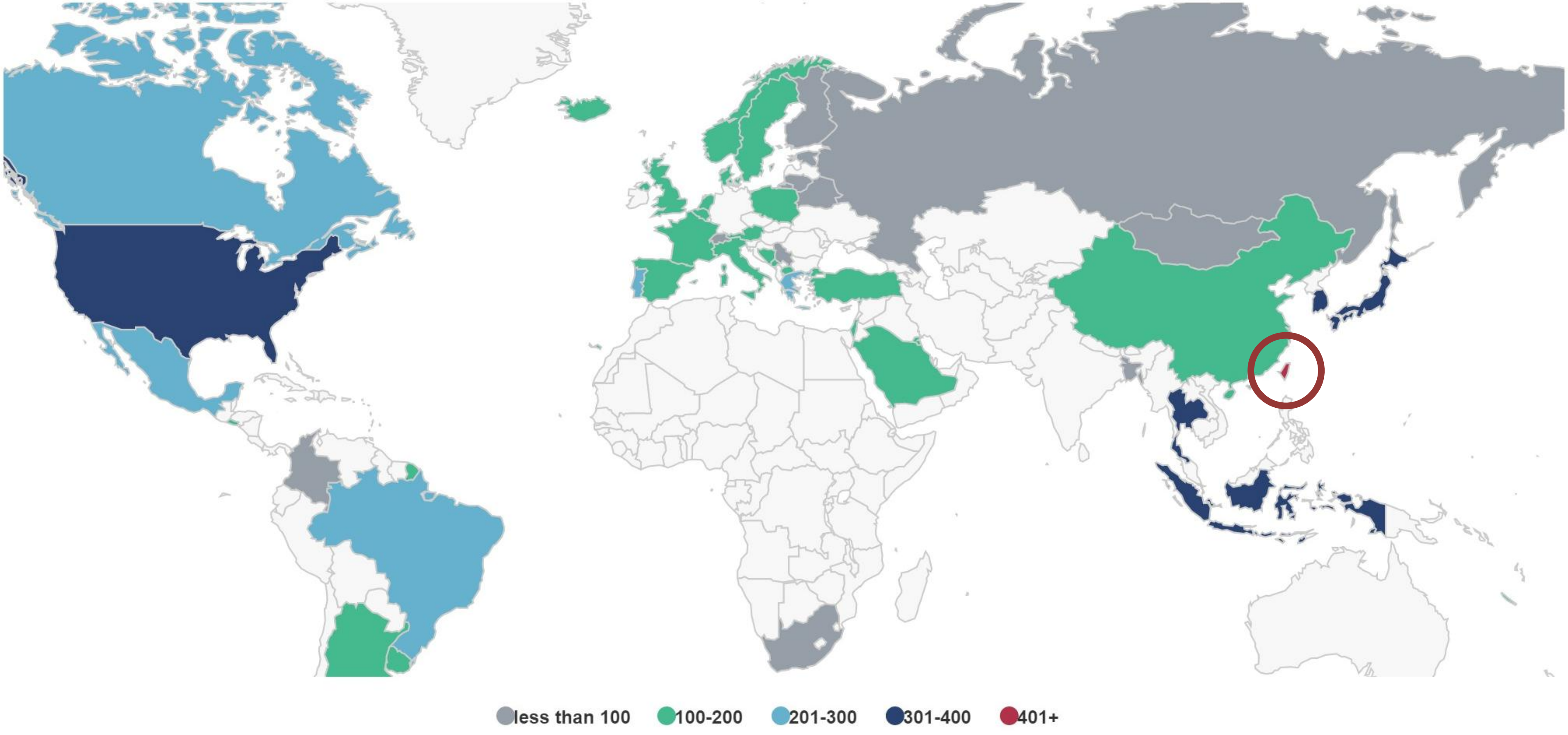




One in every 8 people —
12% of Taiwan's population, or 3 million people —
Truth No. 1: High Prevalence Rate.

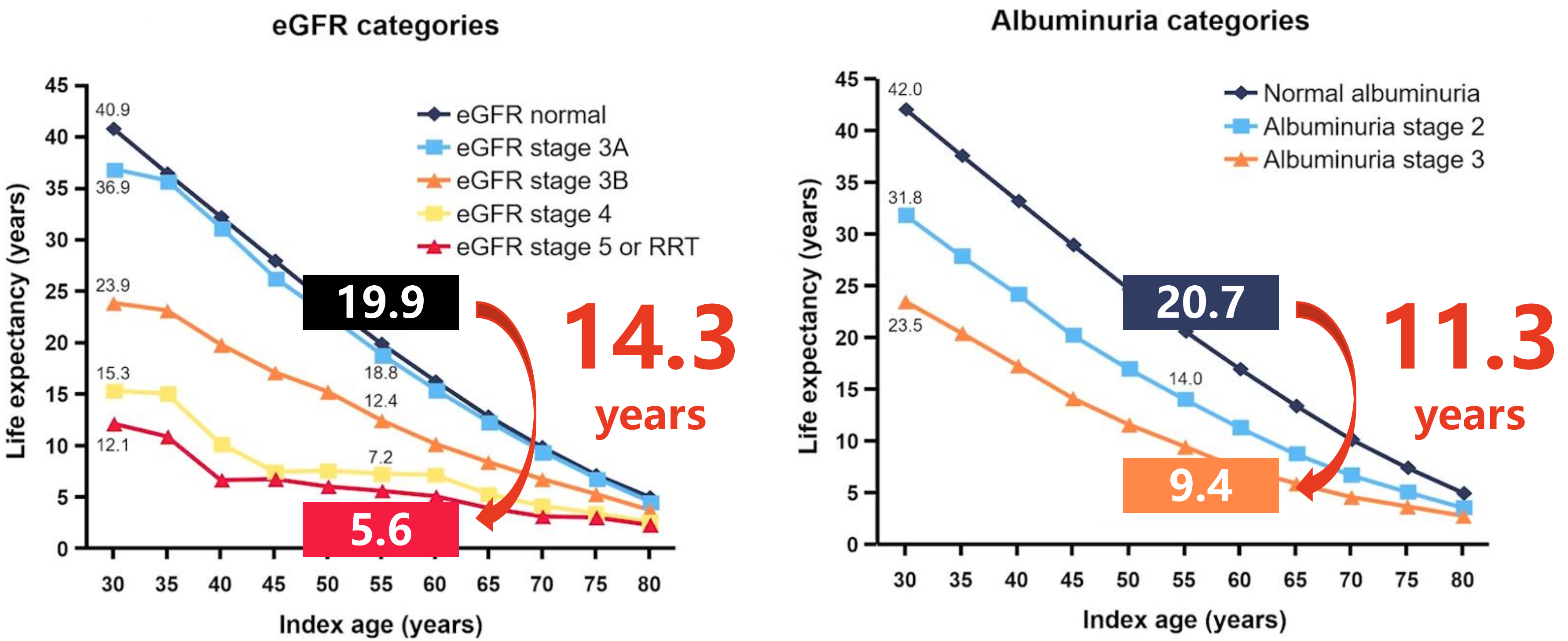
Lancet. 2008 Jun 28;371(9631):2173-82

Hemodialysis prevalence in Taiwan



Data Source: 2022 United States Renal Data System Annual Data Report

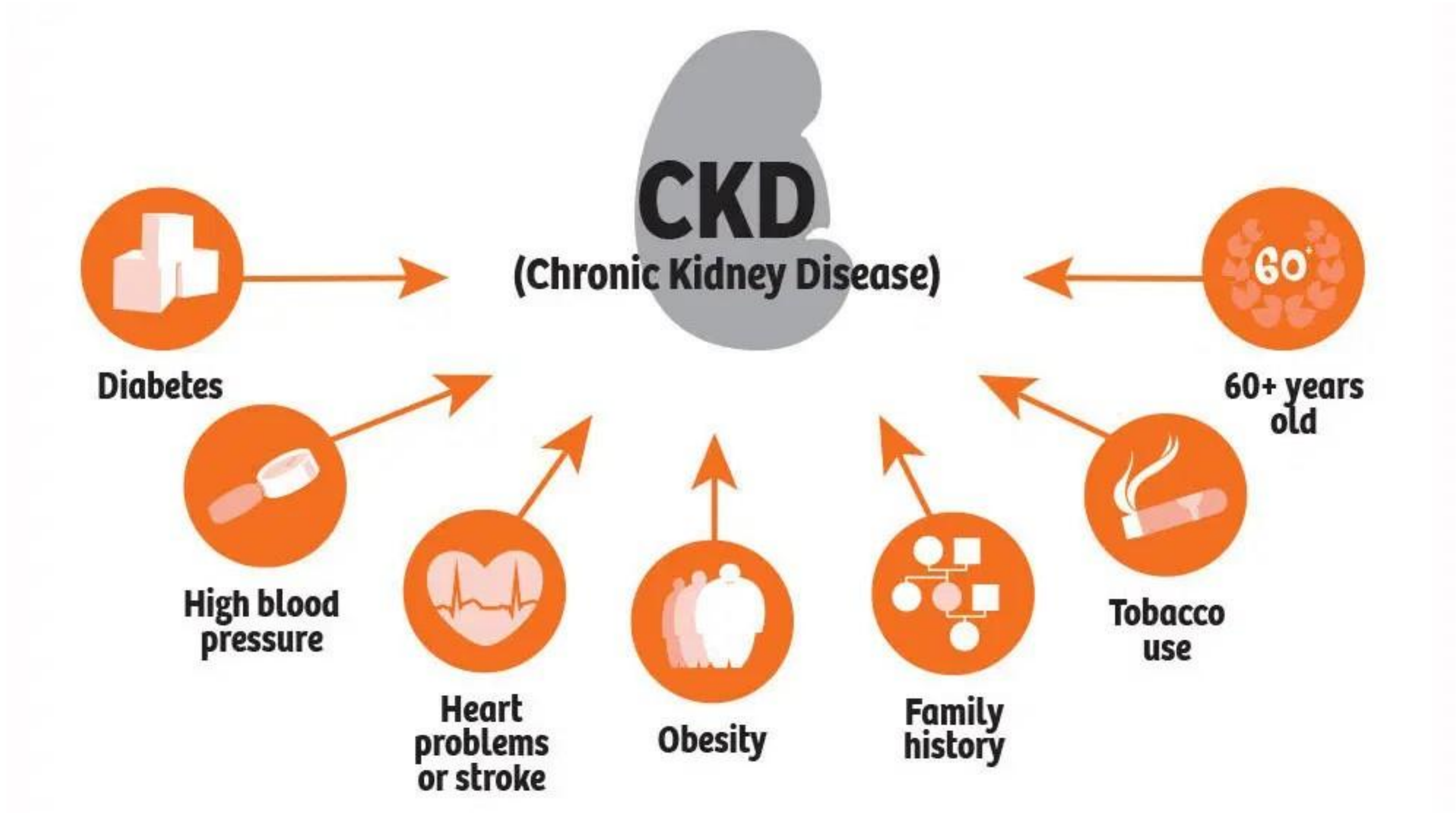
Life expectancy and CKD



Albuminuria stage 1, normal or mildly increased (ACR <30 mg/g); albuminuria stage 2, moderately increased (ACR 30-299 mg/g); albuminuria stage 3, severely increased (ACR ≥300 mg/g)

Lancet. 2013 Jul 27;382(9889):339-52.

Increased risk of chronic kidney disease



Environmental Pollution & Kidney Diseases

KidneyNews

Air pollution

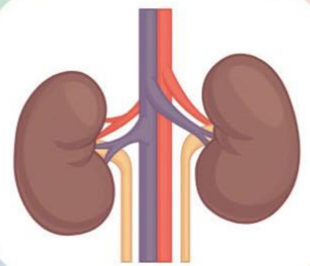
Fine particulate matter ($PM_{2.5}$), nitrogen dioxide, ozone

- **Mechanism of injury:**
  - Airborne pollutants enter the bloodstream through the lungs, inducing systemic inflammation and oxidative stres, leading to endothelial dysfunction.
  - Chronic exposure promotes microvascular damage.
- **Associated kidney diseases:** Chronic kidney disease and glomerular disease
  - Increased risk of albuminuria, progressive decline of GFR
  - Higher incidence of glomerular disease, particularly membranous nephropathy
  - Greater susceptibility in individuals with hypertension and diabetes

Climate change and heat stress

Extreme heat, dehydration, vector-borne diseases

- **Mechanism of injury:**
  - Heat exposure and inadequate hydration causing recurrent dehydration lead to repeated episodes of subclinical rhabdomyolysis.
  - Multifactorial in vector-borne diseases (e.g., dengue fever and malaria)
- **Associated kidney diseases:** Chronic kidney disease of unknown etiology (CKDu)
  - Nontraditional CKD seen in agricultural workers in hot climates
  - Chronic tubulointerstitial nephritis with progressive loss of GFR



Water contaminants

Heavy metals (lead, cadmium, mercury)

- **Mechanism of injury:**
  - Accumulation in proximal renal tubules, causing direct cellular toxicity
  - Autoimmune dysfunction with activation of T cell-dependent polyclonal B cells
- **Associated kidney diseases:** Acute kidney injury and glomerular disease
  - **Lead**: Exposure is associated with tubulointerstitial inflammation and fibrosis.
  - **Cadmium**: Chronic exposure leads to proximal tubular dysfunction & proteinuria.
  - **Mercury**: Acute exposure causes acute tubular necrosis, and chronic exposure can cause membranous nephropathy and minimal change disease.

Toxins and occupational hazards

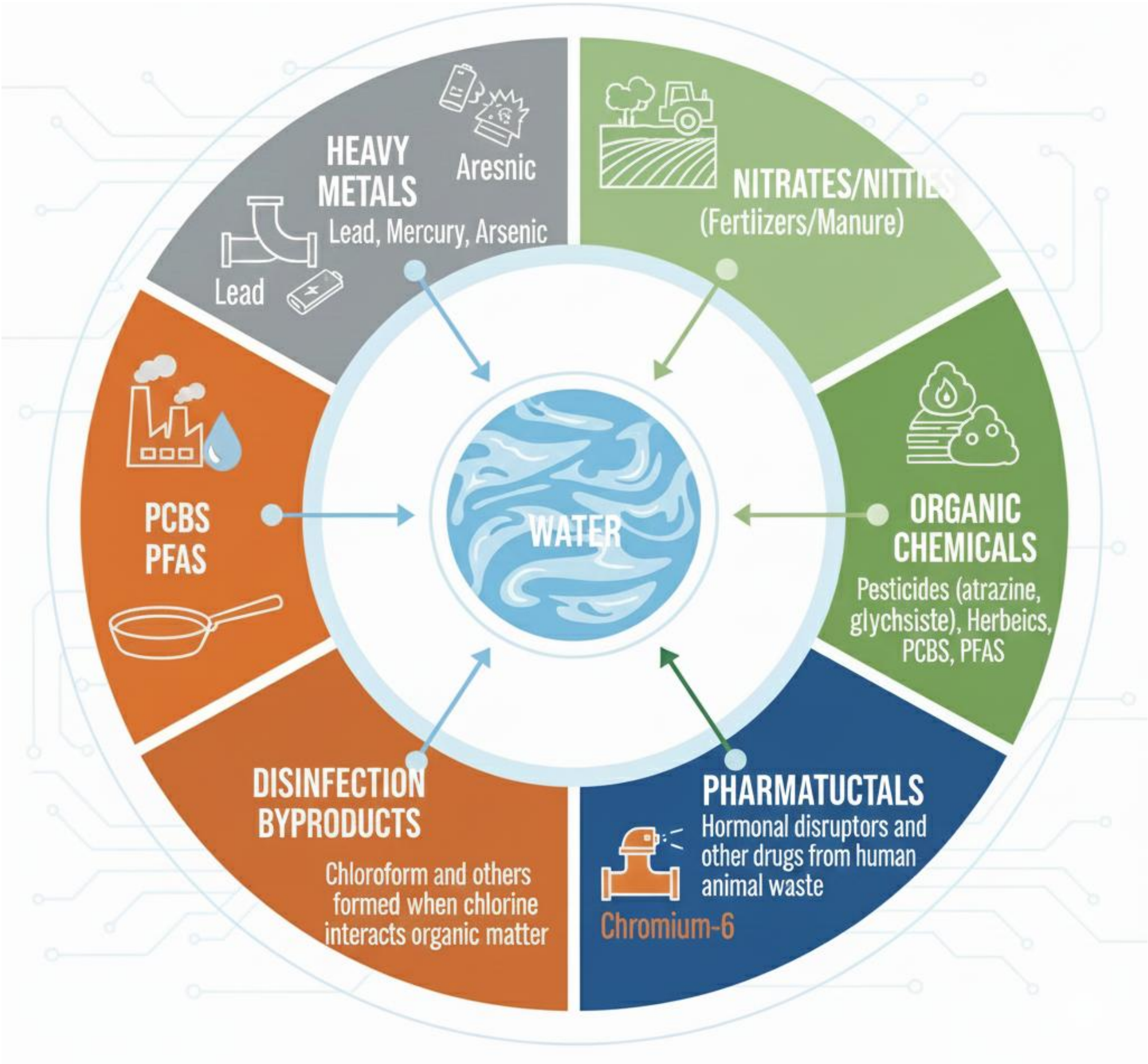
Pesticides (herbicides, insecticides)

- **Mechanism of injury:**
  - Toxic compounds cause oxidative damage and mitochondrial dysfunction in renal tubules, leading to tubular atrophy and interstitial fibrosis.
- **Associated kidney diseases:** Chronic kidney disease
  - Increased risk of kidney failure in individuals exposed to pesticides
  - Spouses of individuals exposed to pesticides may also be affected (without having had direct contact with pesticides).

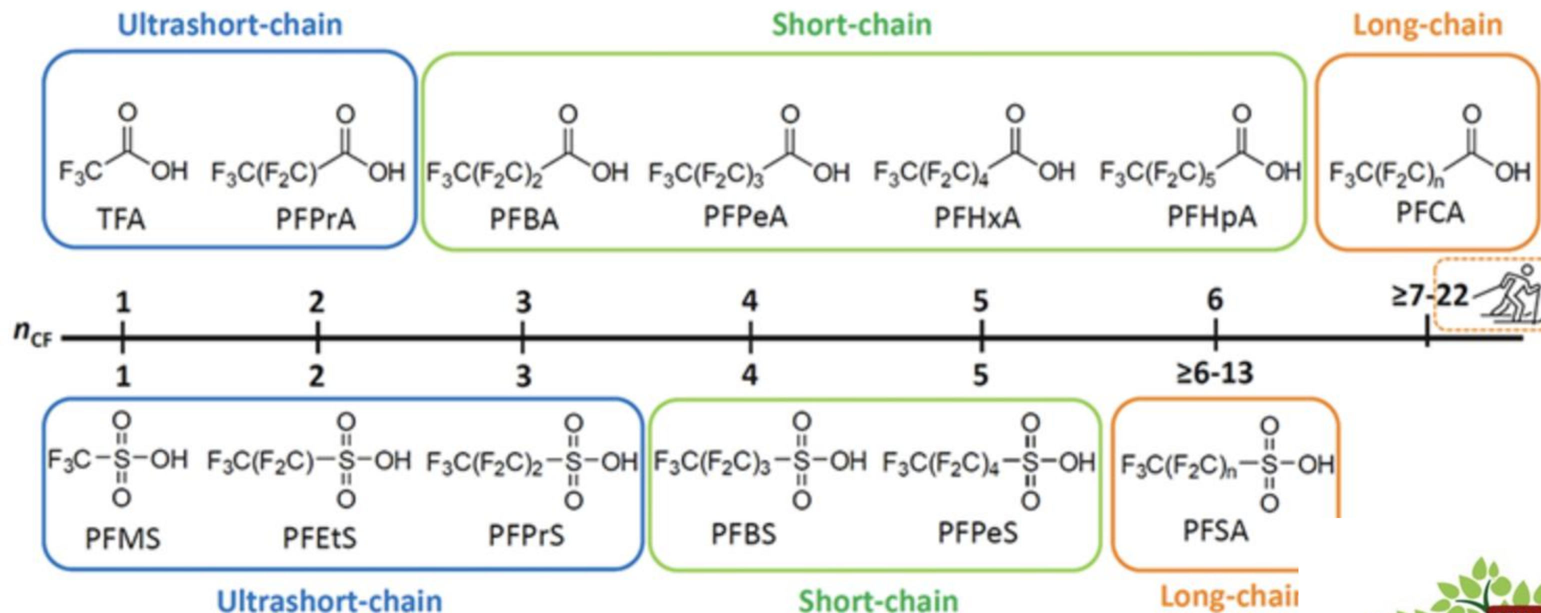
VA: Dr. Alejandro Garcia-Rivera @alexgr23

Kidney news; Volume 17: Issue 5

Common Environmental toxins in the water



What are PFAS?



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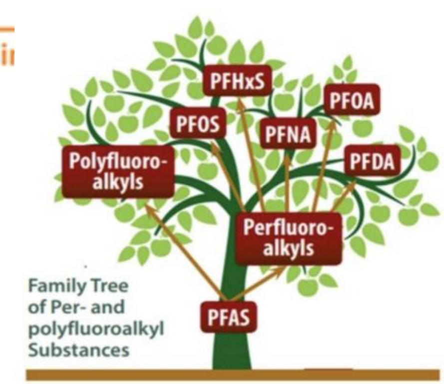


Image provided courtesy of Phenomenex and SCIEX

WHY WE CREATED PFAS: THE GOOD SIDE

1. Pushes Away Water & Oil

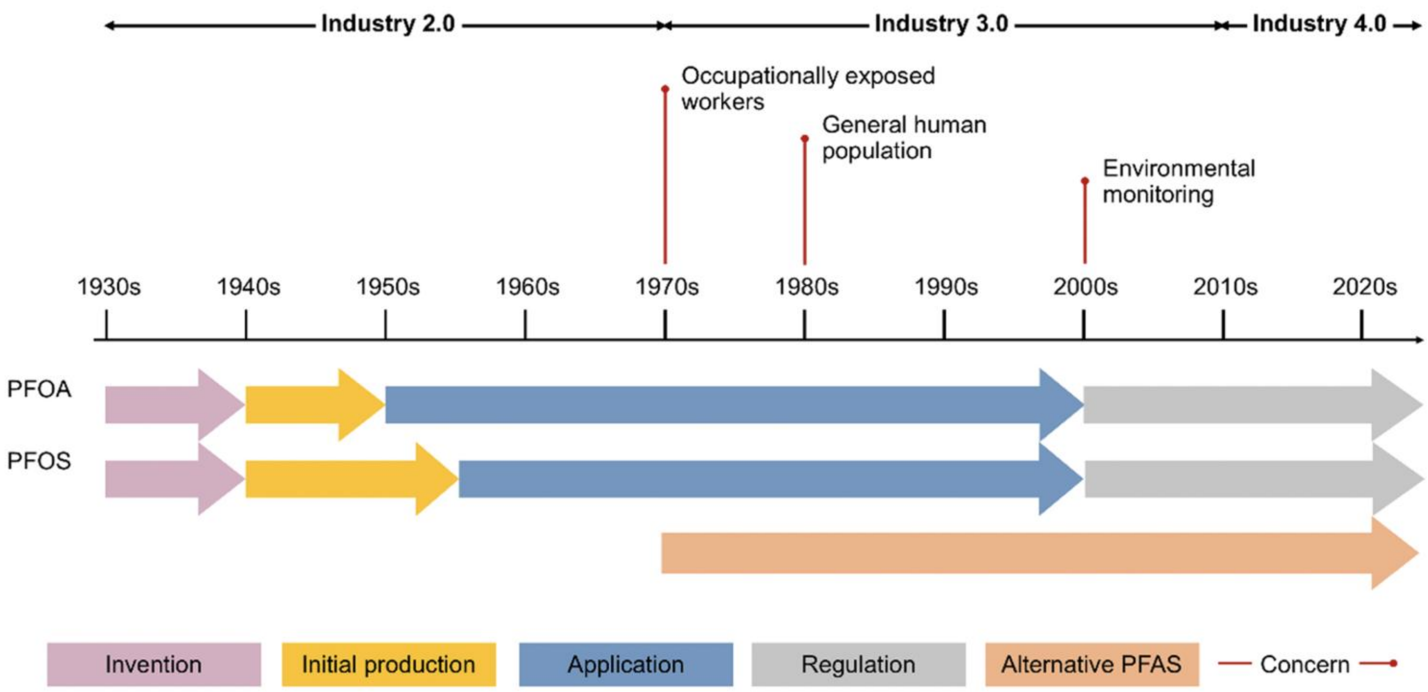
2. Puts Out Fires FAST

3. Super Strong & Lasts Long

Common sources of PFAS

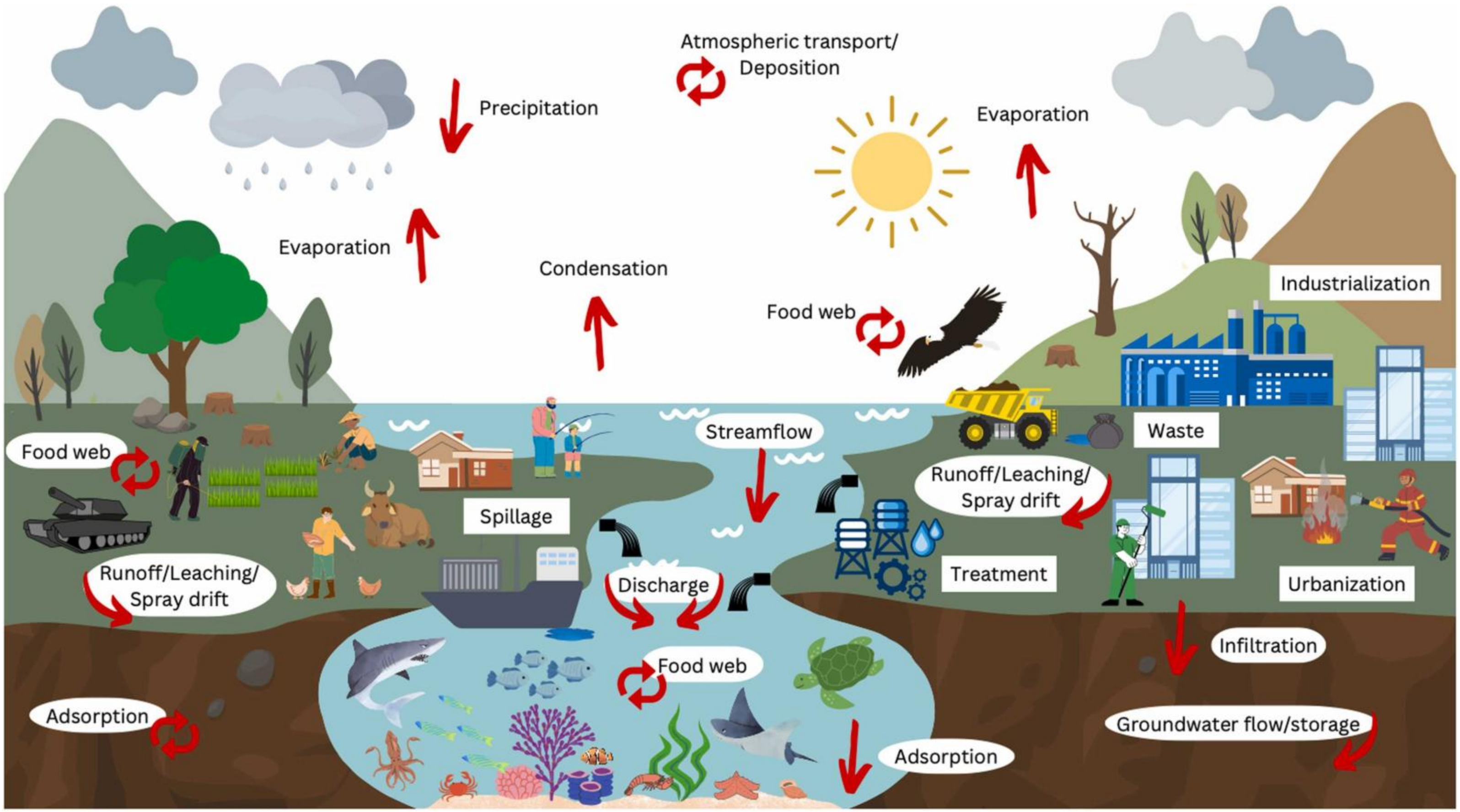
www.avondaleaz.gov

PFAS history and global use



Ecotoxicology and Environmental Safety Volume 267, 15 November 2023, 115663

Environmental Sources and Transport Pathways



Ecotoxicology and Environmental Safety Volume 267, 15 November 2023, 115663
https://www.kalispell.com/850/Consumer-Drinking-Water-Notice---Emergin

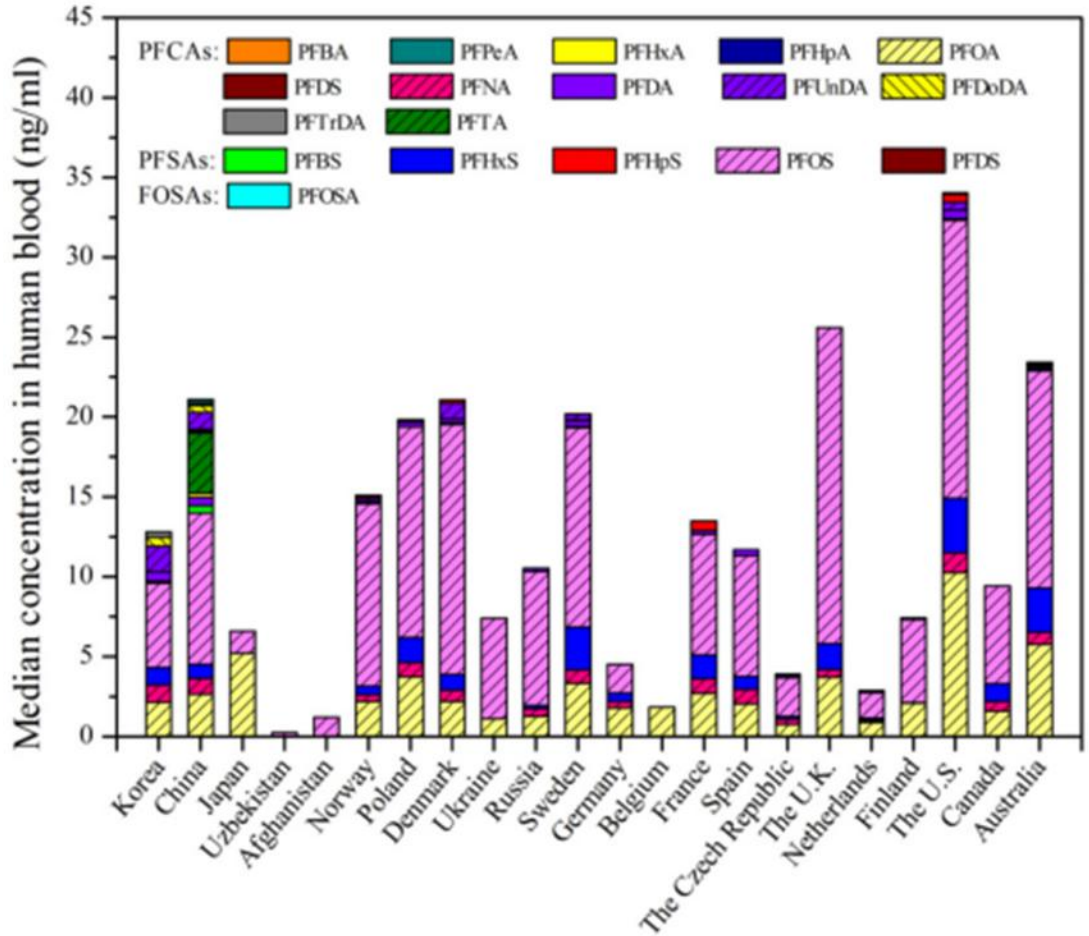
Global PFAS Contamination and Exposure

•Fire-training areas = major hotspots (e.g., Sweden, US, Germany, Australia)

Ecotoxicology and Environmental Safety Volume 267, 15 November 2023, 115663

Blood PFAS Profiles Across Countries

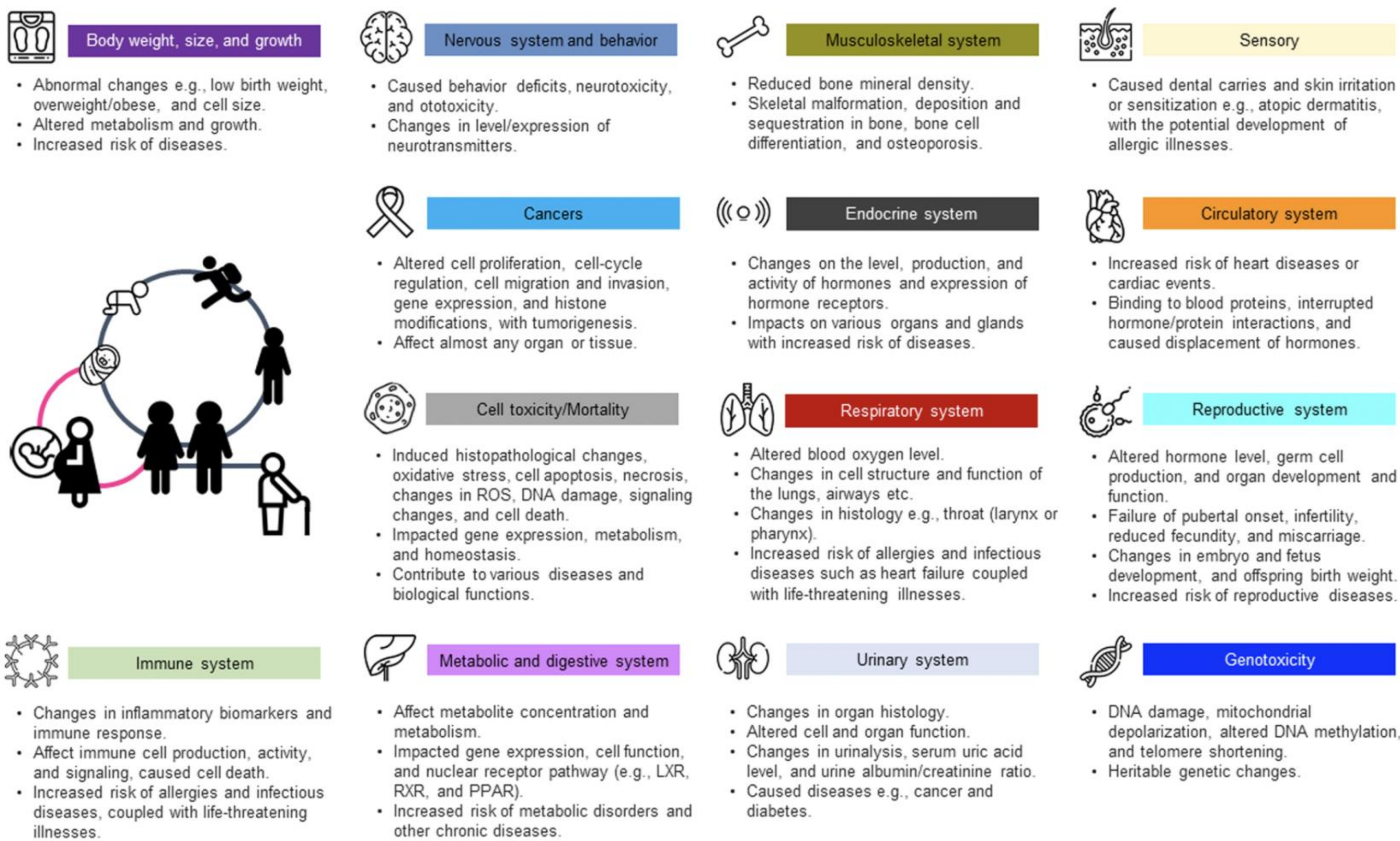
- PFOS is the dominant PFAS detected in blood globally.
- Profiles differ by region, gender, and sample type (serum, plasma, whole blood).



Sci Total Environ 2018 Sep 15:636

Toxicological Mechanisms and Health Effects

- PFAS induce oxidative stress, inflammation, mitochondrial dysfunction



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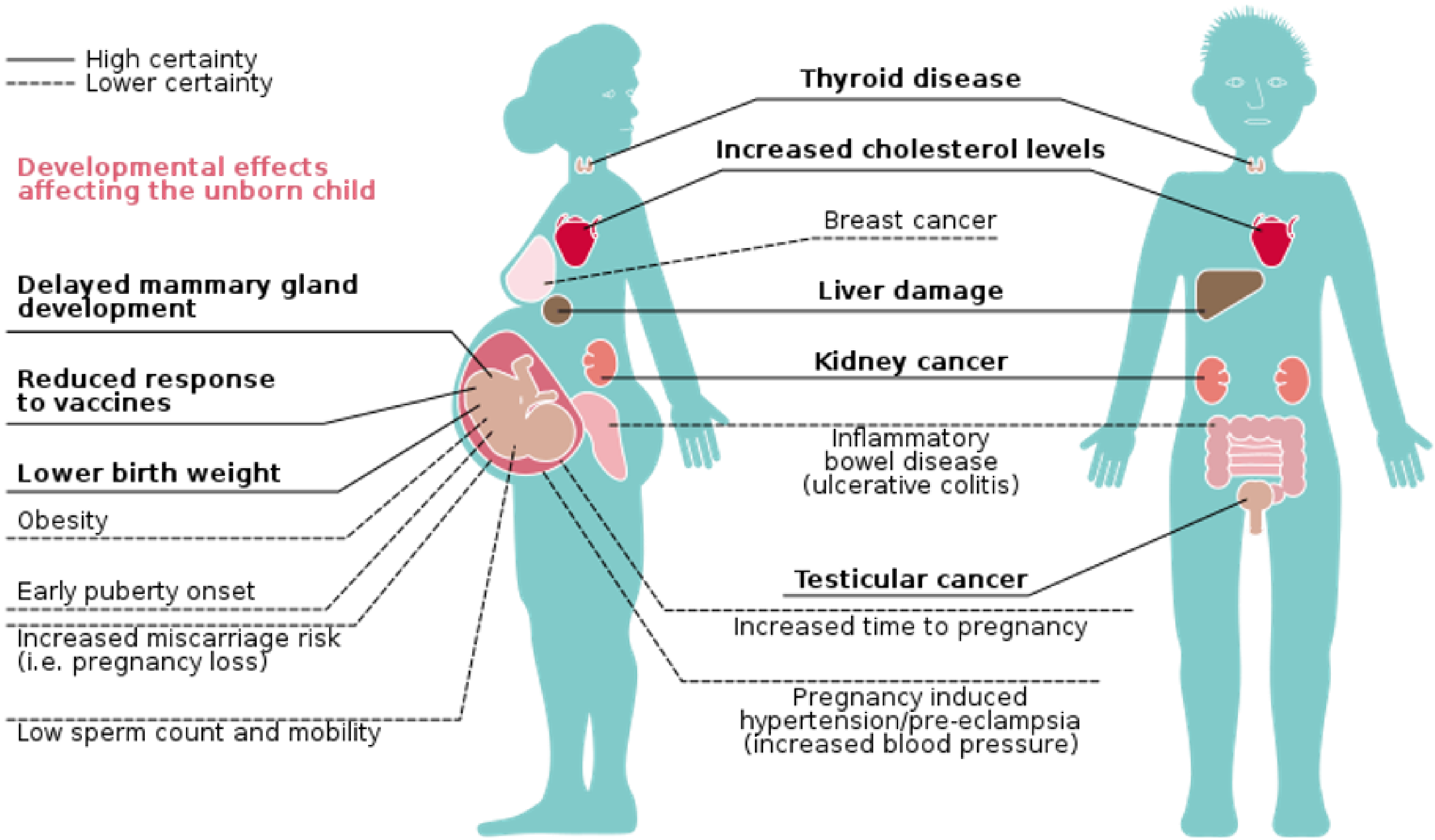
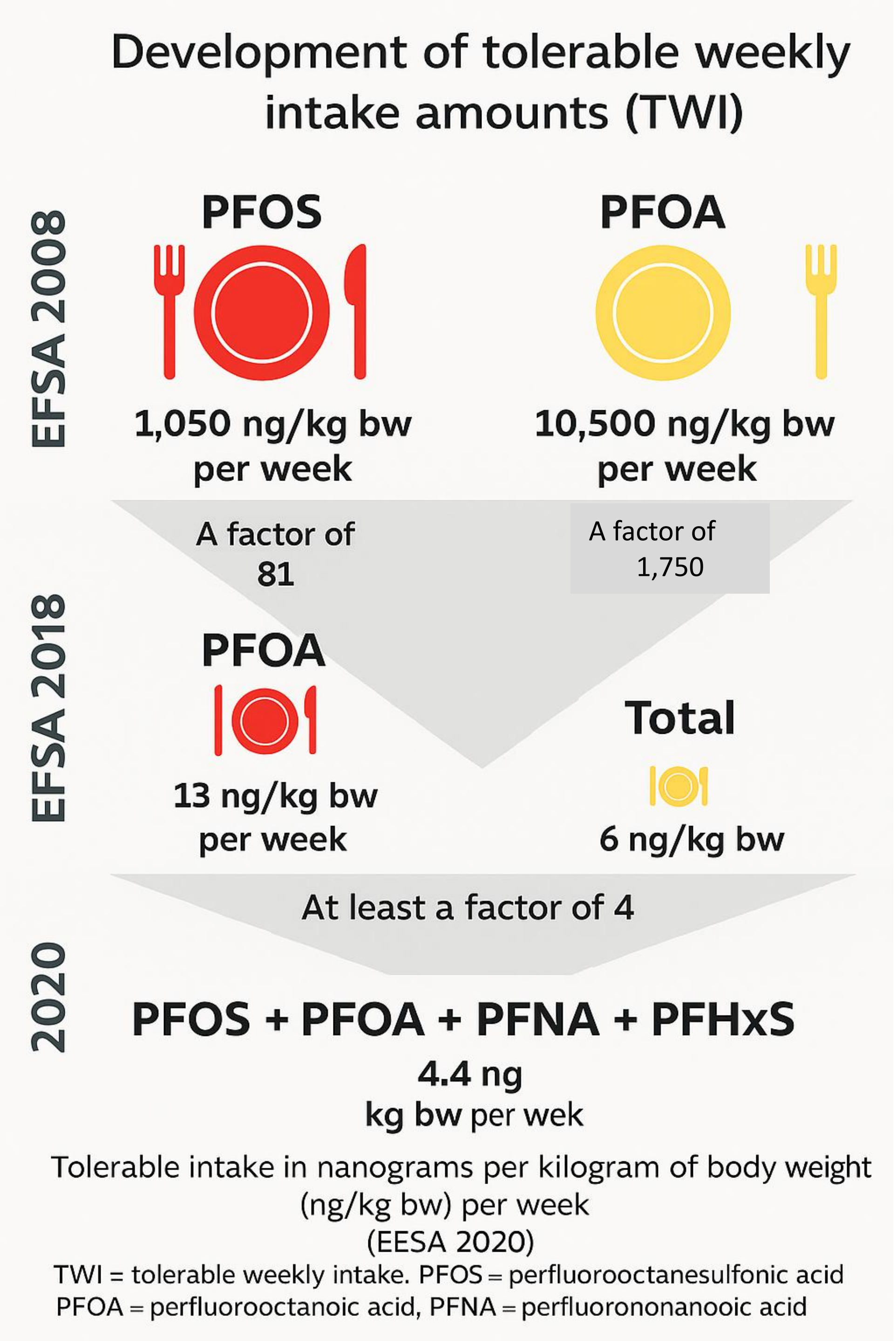
Toxicological Mechanisms and Health Effects



anh-usa.org

Development of tolerable weekly intake amounts (TWI)

- from 2008 to 2020 with increasing knowledge of the biological properties and the toxicity of PFAS the values for the tolerable weekly intake (TWI) were reduced in EFSA (European food safety authority).



Environ Sci Eur **35**, 20 (2023)

PFAS and Kidney Function

- Kidney is the primary organ for PFAS elimination
- PFAS exposure may accelerate CKD progression
  - through mechanisms involving tubular injury, mitochondrial dysfunction, and oxidative stress.

Environmental Research Volume 285, 15 November 2025

PFAS and Kidney Function

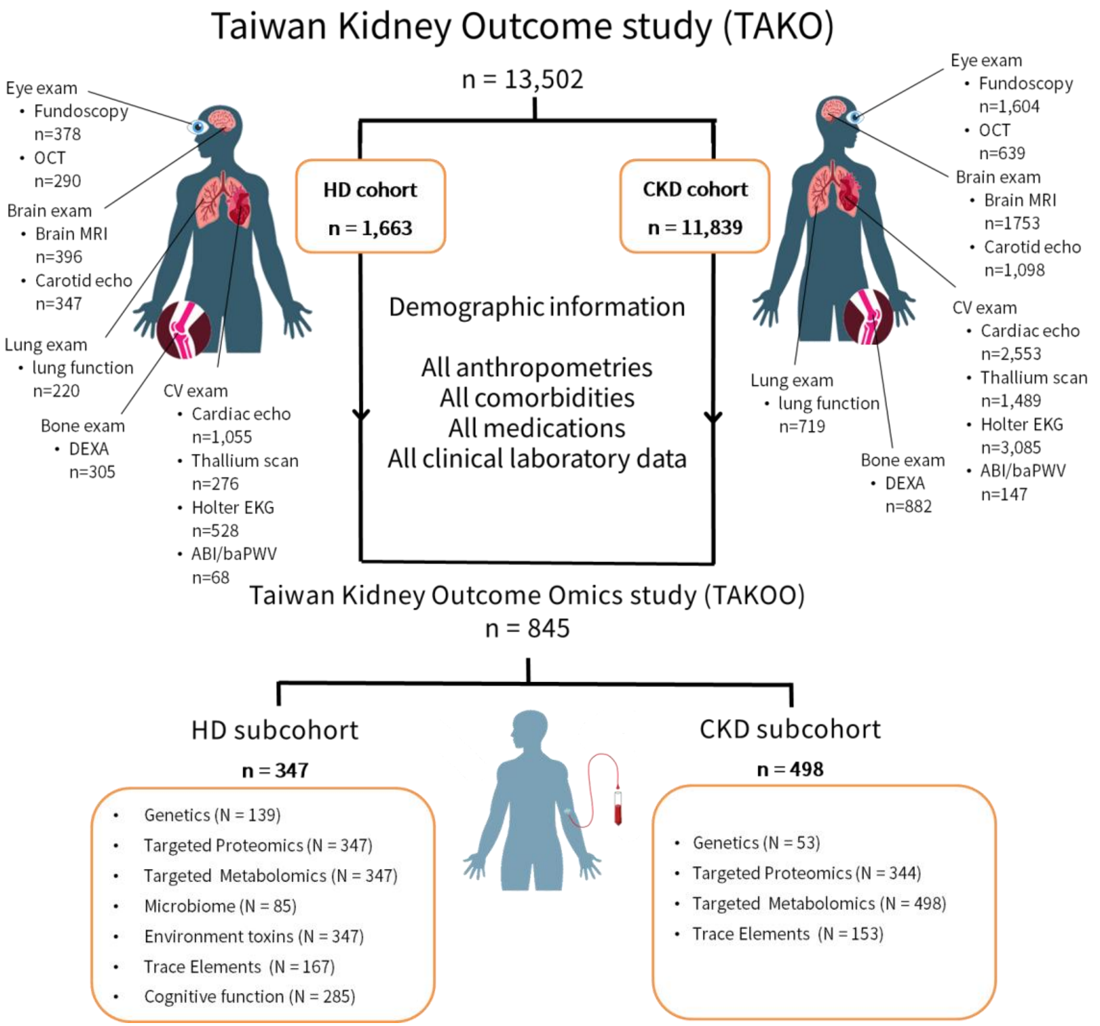
- Highly protein-bound (esp. serum albumin) → limited glomerular filtration
- Partly reabsorbed in proximal tubules (OAT transporters)

Arch Toxicol 2022 Nov 27

Knowledge Gaps

- **PFAS levels across CKD stages and hemodialysis**
  - How PFAS concentrations change with declining kidney function remains poorly defined.
- **Dialysis clearance of PFAS**
- **Impact of dialysis membrane characteristics**
  - Differences in PFAS removal between membranes are unknown.
- **Role of albumin binding**
  - High albumin affinity may limit dialytic clearance and prolong retention.
- **Nutritional and metabolic influences**
  - How albumin, uric acid, and nPCR relate to PFAS accumulation has not been systematically studied.

TAKO & TAKOO cohorts



Prospective cohort in CKD/HD patients

Systemic complications: CV, Lung, Brain, Bone, Eye

Omics data: Genetics, Epigenetics, Proteomics, Metabolomics, Gut microbiomics

International Journal of Epidemiology, Volume 54, Issue 5, October 2025

Decreased levels of perfluoroalkyl substances in hemodialysis

Science of the Total Environment 896 (2023) 165184

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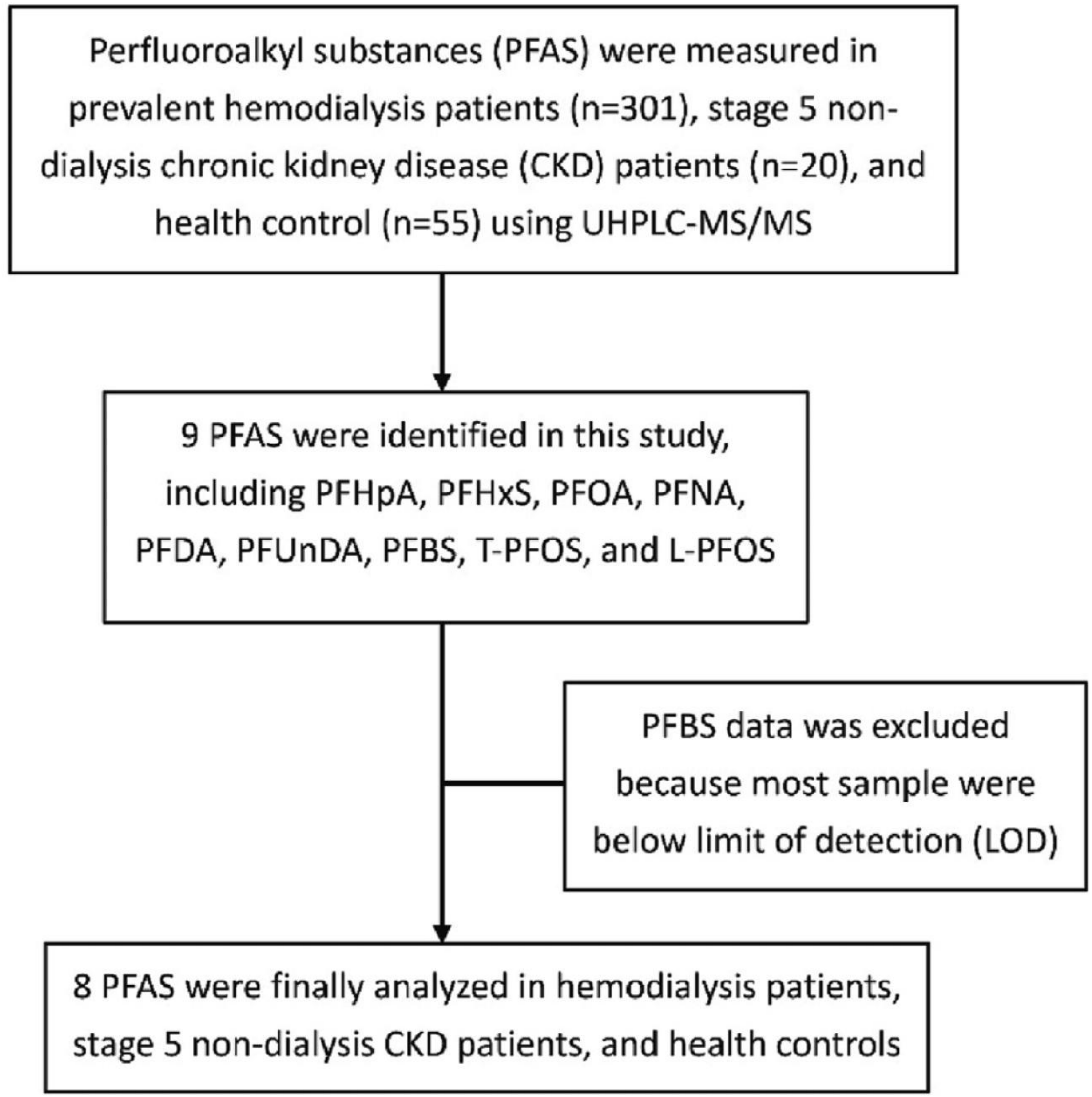
Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

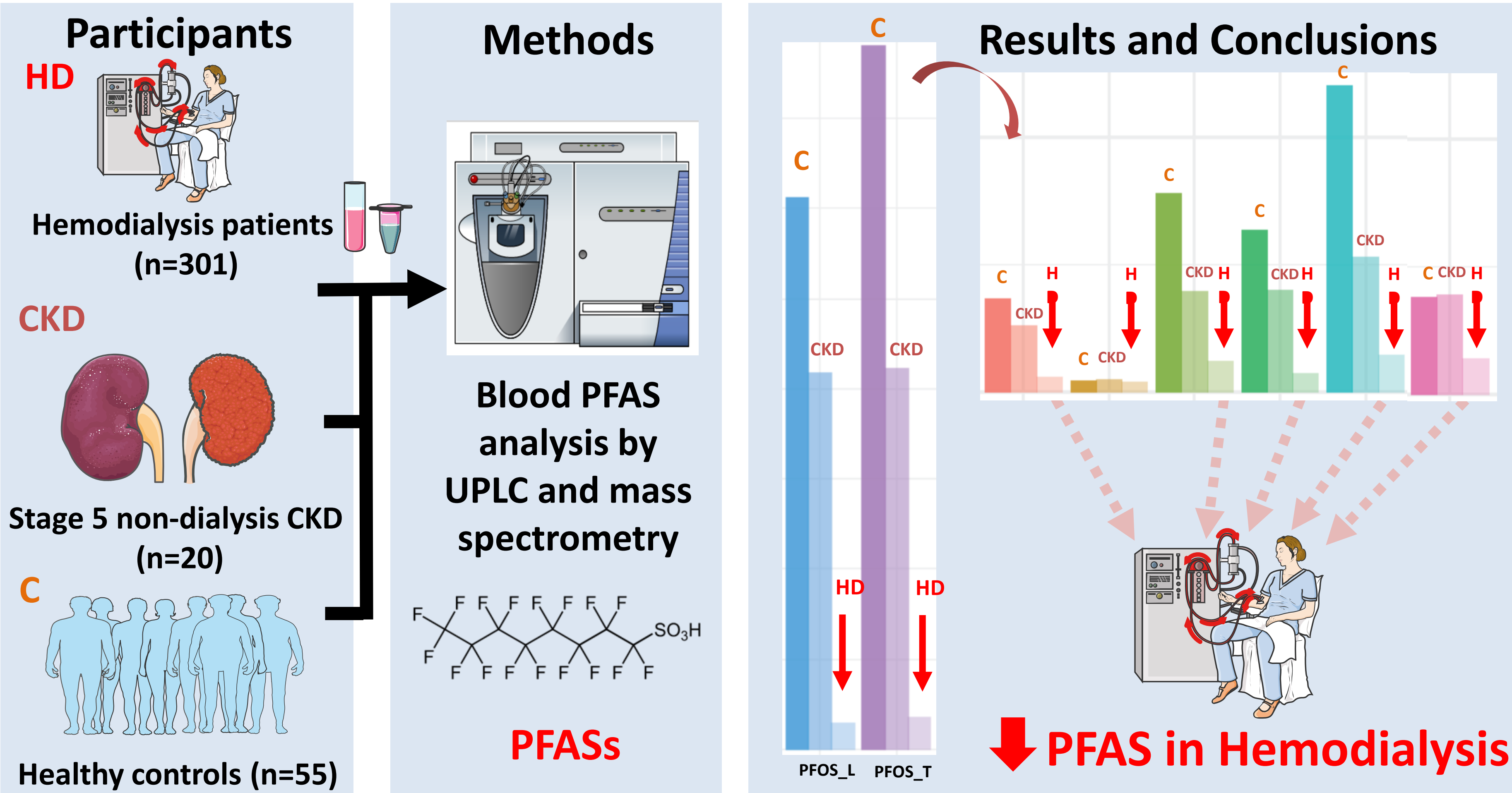
Decreased levels of perfluoroalkyl substances in patients receiving hemodialysis treatment

Check for updates



Sci Total Environ 2023 Oct 20:896:165184

Decreased levels of PFAS in patients with HD



Sci Total Environ 2023 Oct 20:896:165184

The perfluoroalkyl substance level associated with filter type in patients with hemodialysis

Ecotoxicology and Environmental Safety, 2025

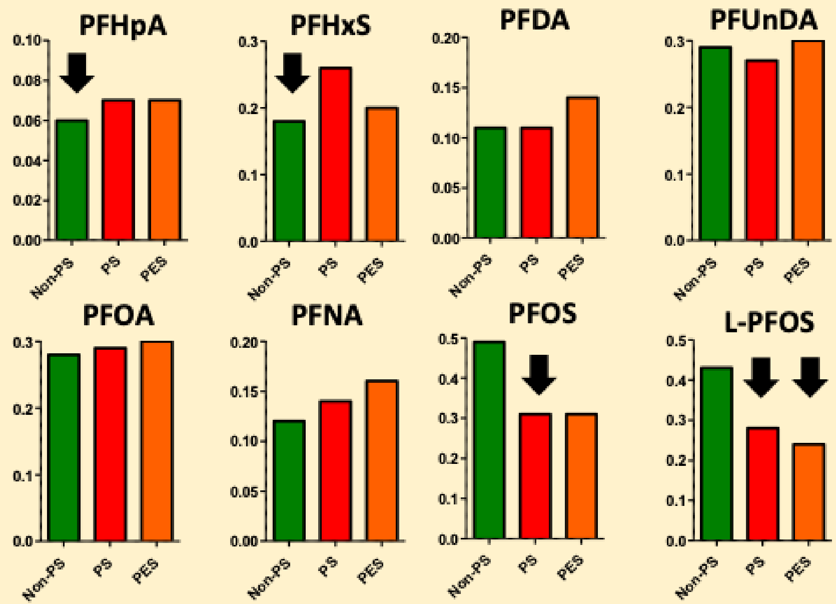
The perfluoroalkyl substance level associated with filter type and nutrition status in patients with hemodialysis

30 – 85 years Taiwan hemodialysis patients (n = 301)

Nutritional markers
Albumin, Uric acid, nPCR

PFOS
PFHpA
PFNA
PFDA
PFUnDA

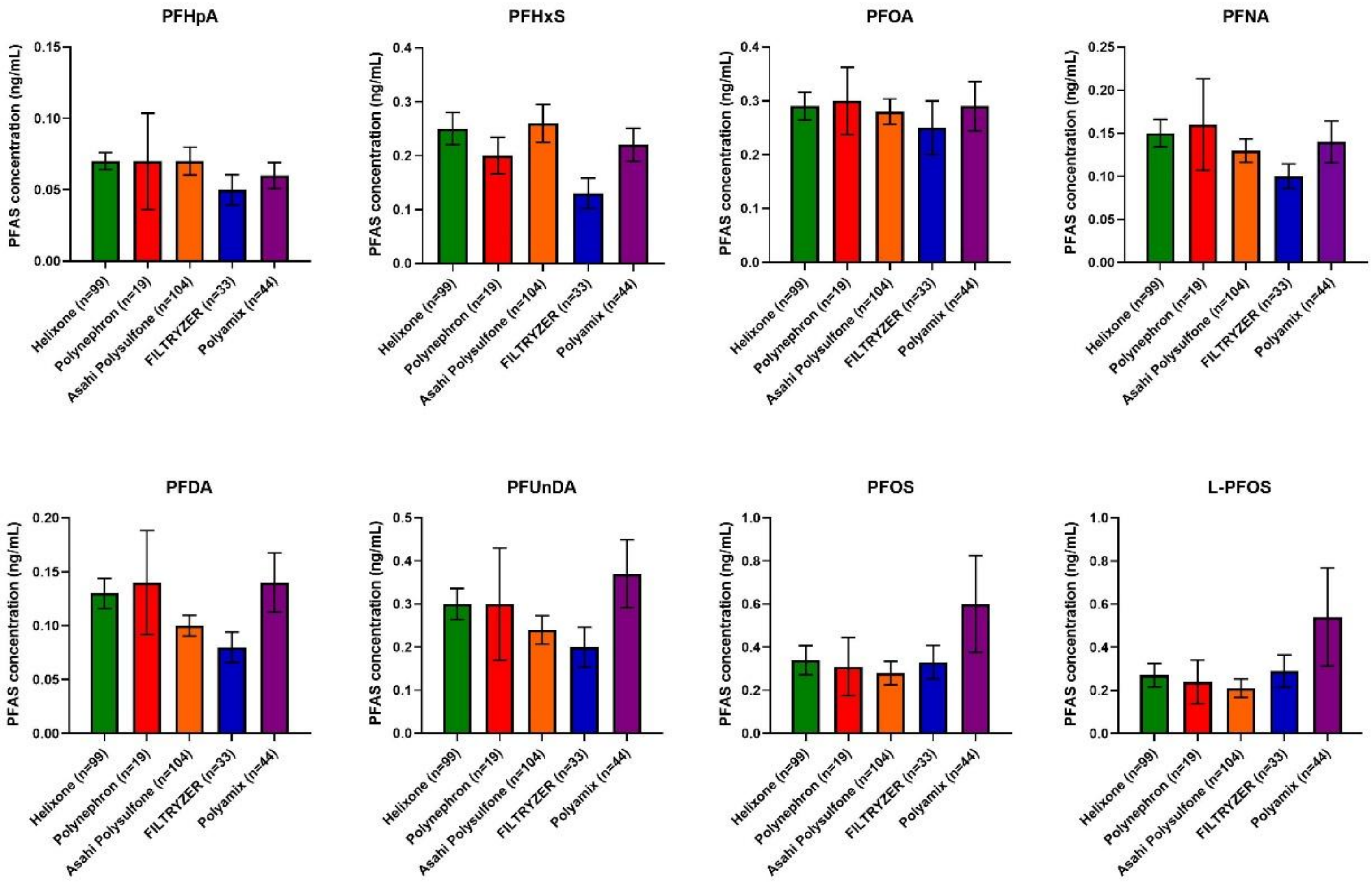
Dialysis membrane types:
polysulfone (PS)
polyethersulfone (PES)
non-polysulfone (non-PS)



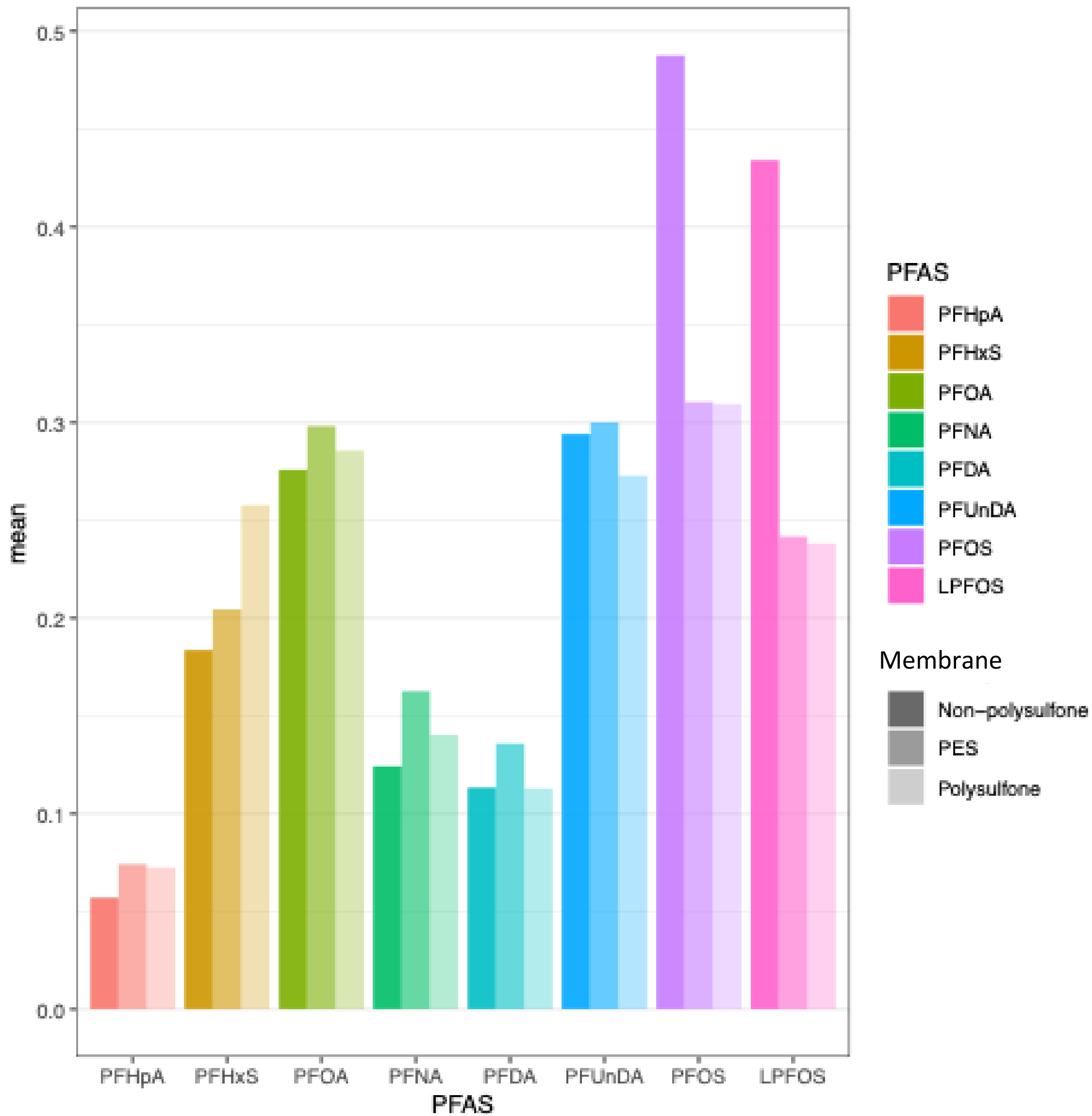
CONCLUSION

The levels of PFASs in hemodialysis patients were influenced by the dialysis membranes properties and were exhibited a positively associations with nutritional markers.

PFAS in different HD filters

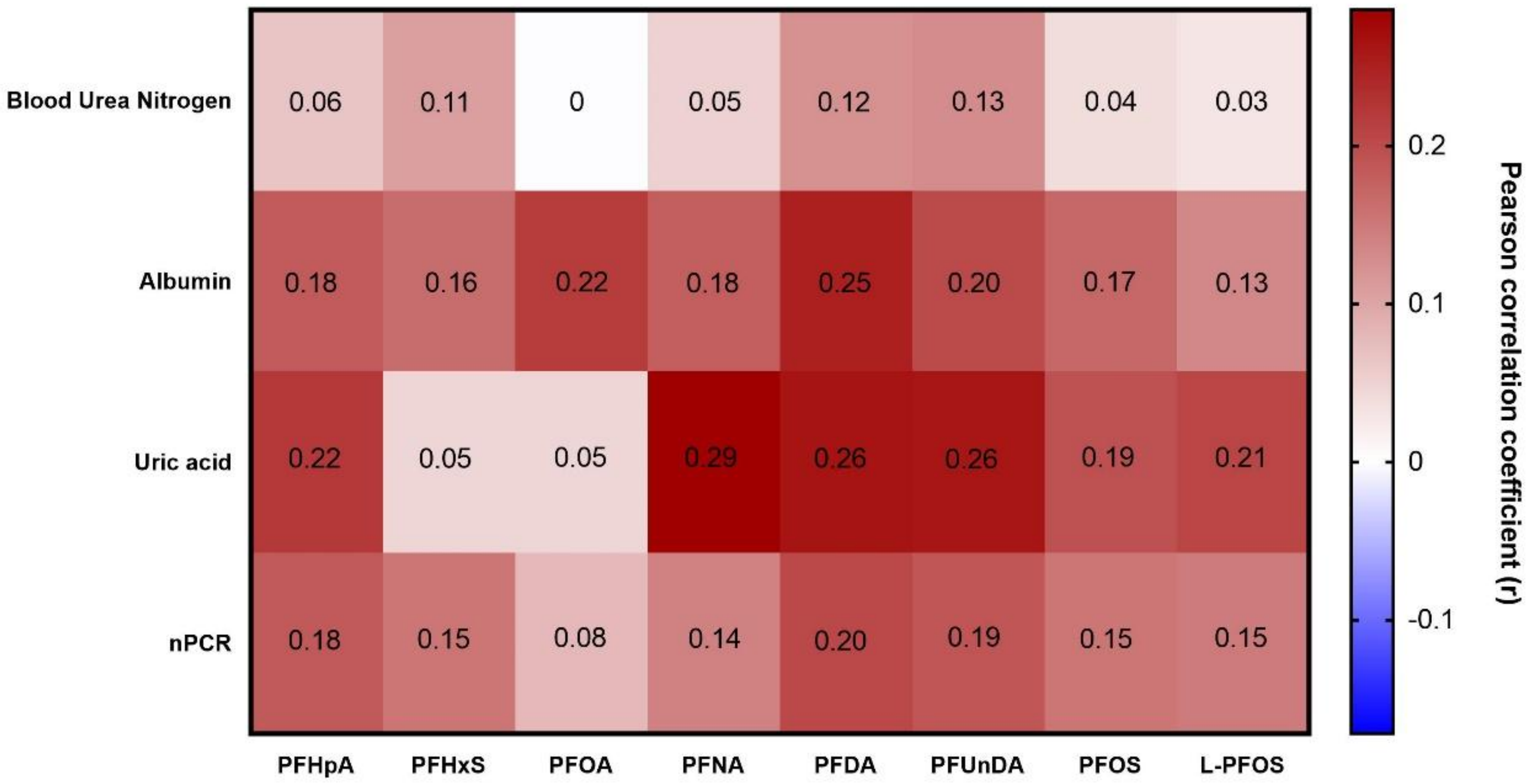


Ecotoxicology and Environmental Safety, 2025



Ecotoxicology and Environmental Safety, 2025

Nutritional marker and PFAS



Ecotoxicology and Environmental Safety, 2025

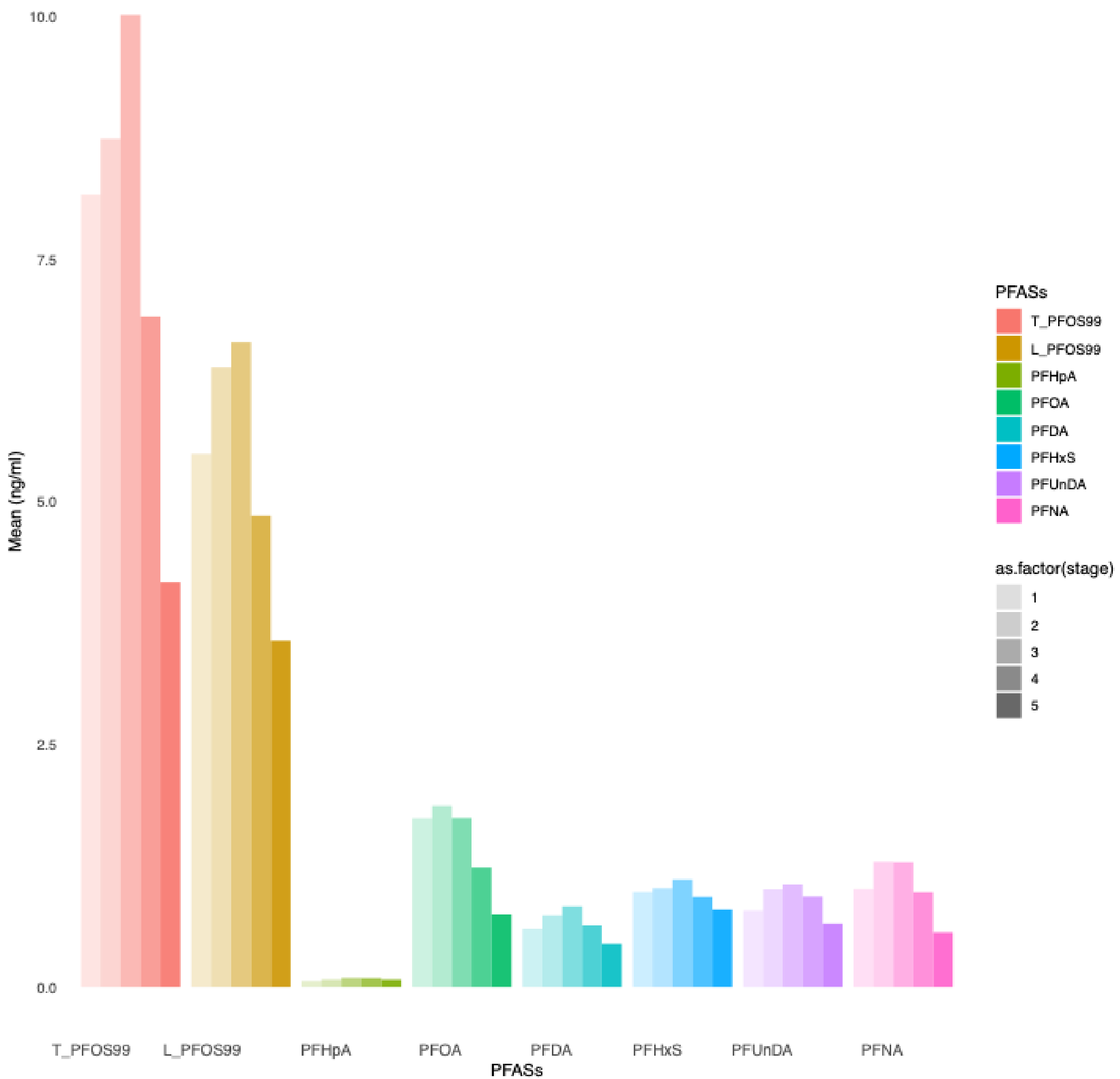
The distribution of PFAS in five CKD stages

Baseline Characteristics of Study Participants Across Five CKD Stages

	1	2	3	4	5
	N=9	N=33	N=219	N=116	N=97
AGE	52.2 (11.7)	60.4 (11.9)	65.8 (12.6)	67.5 (12.1)	66.4 (11.6)
GENDER	7 (77.8%)	22 (66.7%)	158 (72.1%)	65 (56.0%)	55 (56.7%)
BMI	25.4 (1.97)	27.1 (3.56)	25.8 (4.08)	25.3 (3.96)	24.7 (4.06)
DM	4 (44.4%)	13 (39.4%)	100 (45.7%)	63 (54.3%)	43 (44.3%)
HTN	8 (88.9%)	30 (90.9%)	172 (78.5%)	99 (85.3%)	84 (86.6%)
CAD	3 (33.3%)	5 (15.2%)	55 (25.1%)	22 (19.0%)	17 (17.5%)
eGFR	100 (9.53)	71.1 (10.2)	42.5 (8.28)	23.2 (4.58)	10.0 (3.04)
UACR	284 (473)	310 (540)	435 (766)	819 (1074)	1434 (1517)
PFHpA	0.06 (0.05)	0.09 (0.07)	0.66 (4.77)	1.81 (12.5)	0.45 (3.65)
PFHxS	0.98 (0.58)	1.23 (0.96)	47.9 (632)	22.2 (162)	2.95 (21.2)
PFOA	1.74 (0.75)	2.13 (1.63)	11.6 (82.3)	40.0 (300)	12.5 (116)
PFNA	1.01 (0.41)	1.56 (1.20)	40.2 (429)	124 (958)	2.10 (15.2)
L_PFOS	5.49 (1.92)	7.66 (6.55)	17.9 (154)	6.13 (7.60)	3.56 (2.88)
PFOS	8.16 (2.87)	10.5 (9.15)	25.9 (216)	8.62 (10.9)	4.17 (3.56)
PFDA	0.60 (0.32)	0.90 (0.69)	12.3 (103)	36.4 (298)	2.64 (21.6)
PFUnDA	0.79 (0.39)	1.25 (1.08)	13.9 (109)	46.5 (319)	5.17 (44.5)

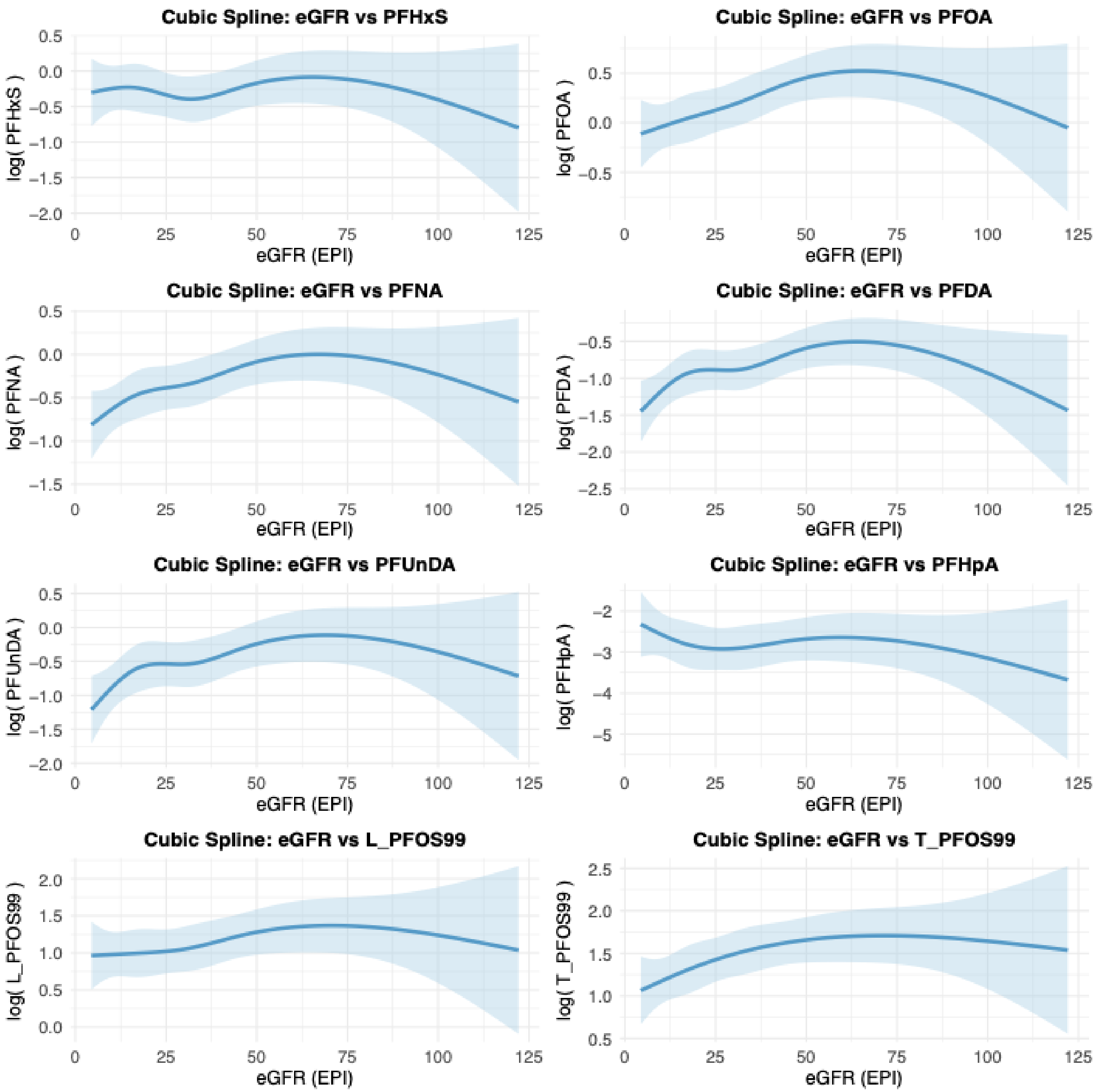
Unpublished data

Levels of PFAS in Patients Across CKD stages



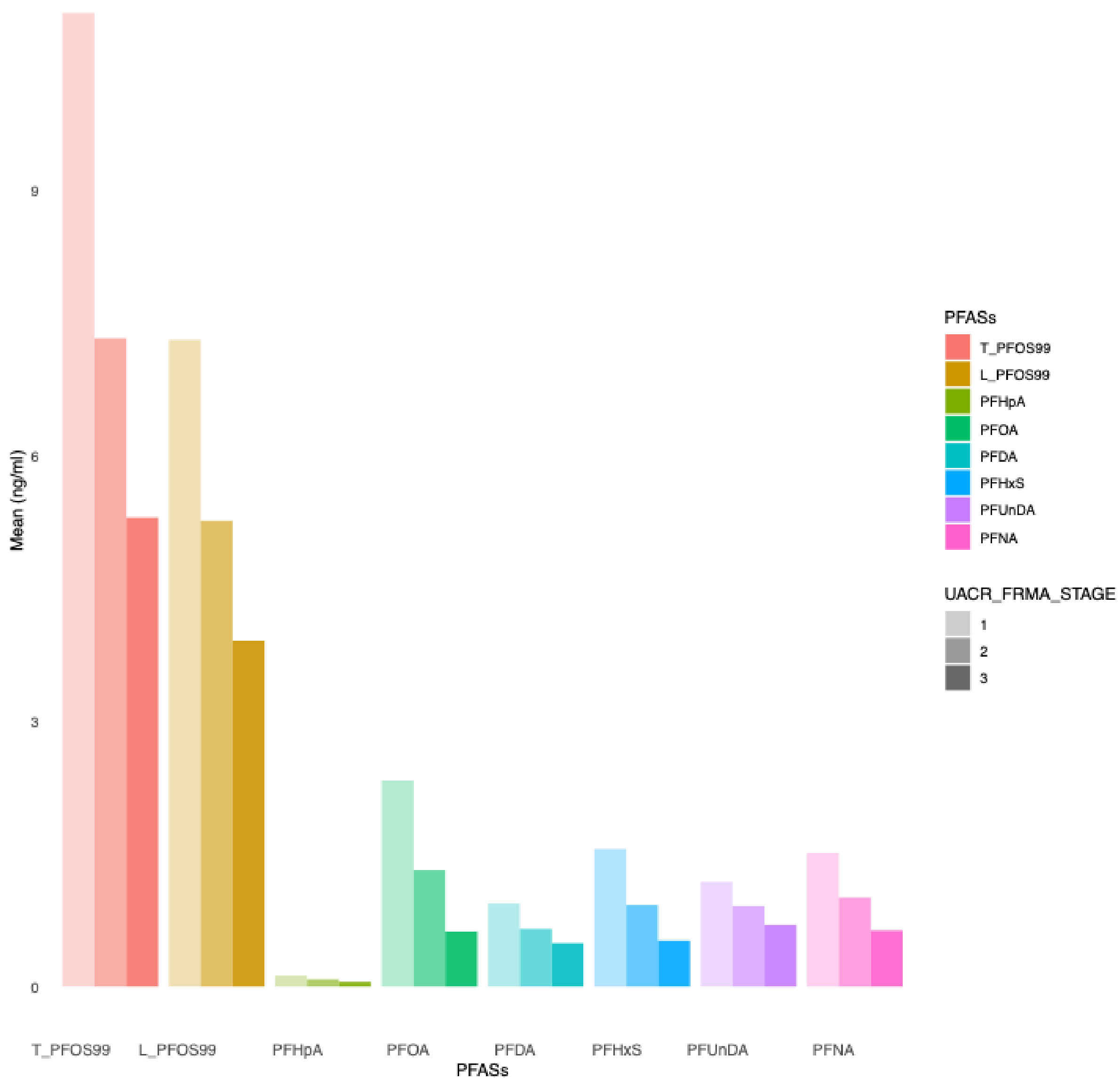
Unpublished data

Cubic spline plots showing the adjusted association between eGFR and log-transformed serum PFAS concentrations.



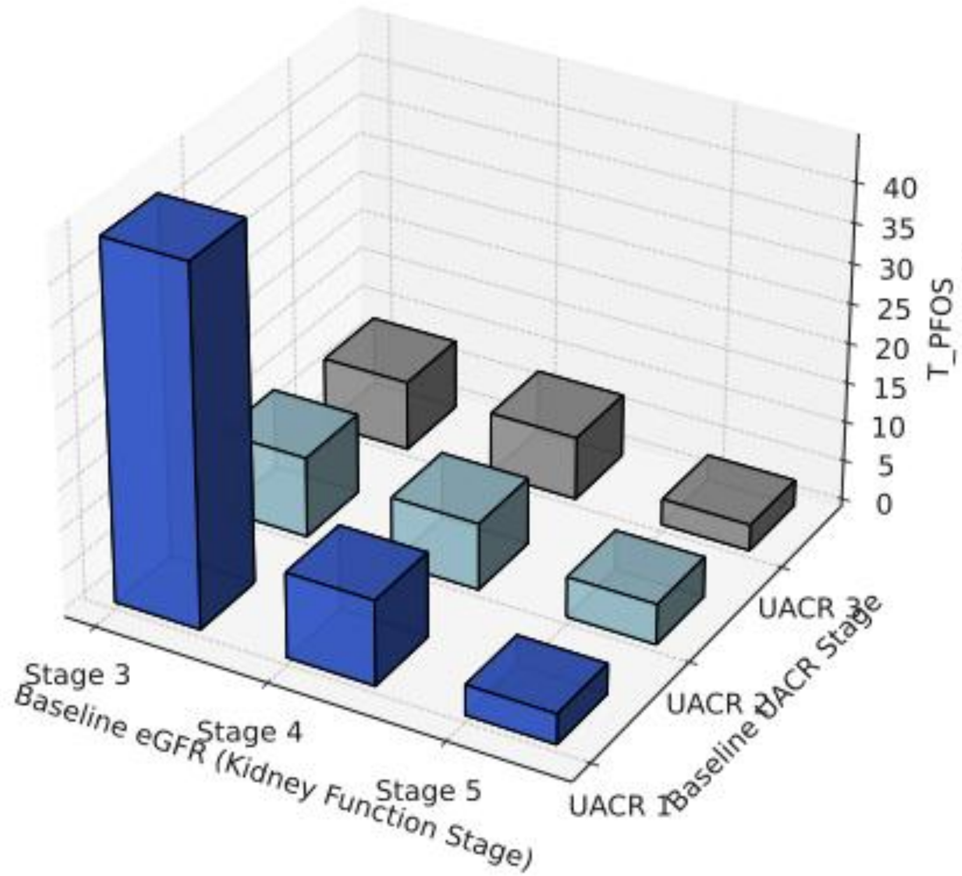
Unpublished data

Concentrations of PFAS in Normoalbuminuria, Microalbuminuria, and Macroalbuminuria



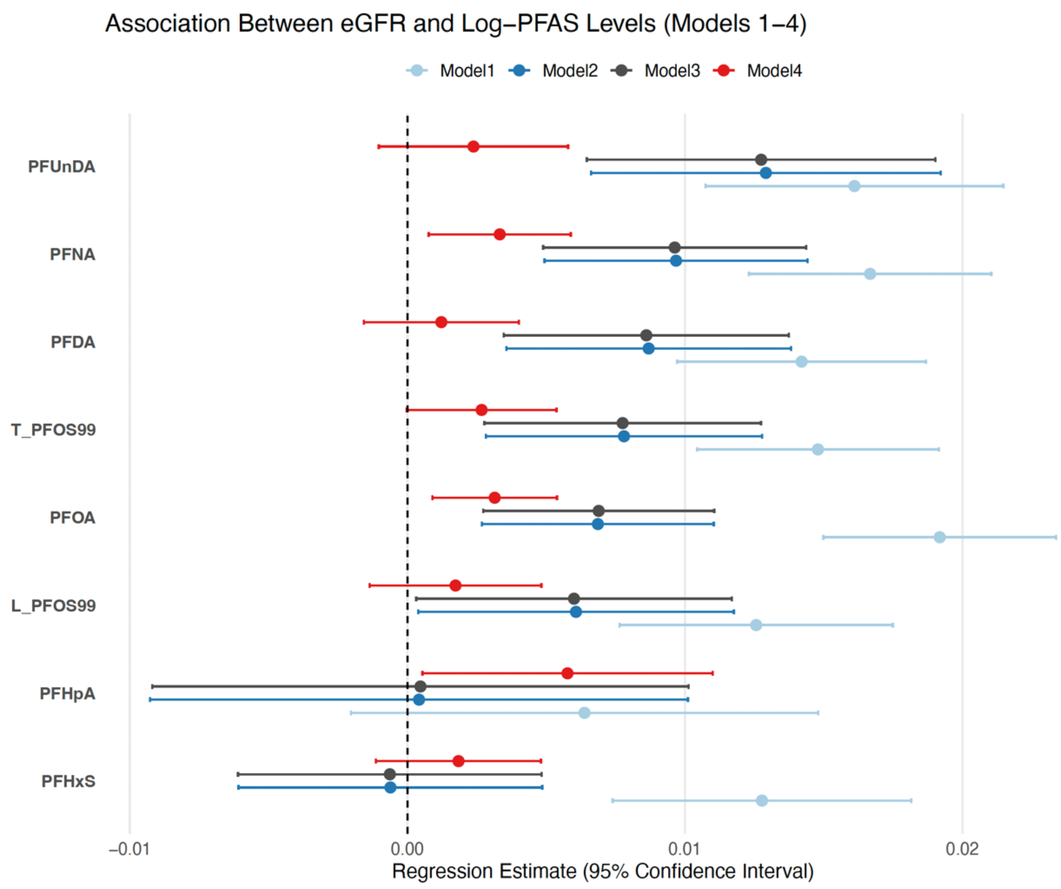
Unpublished data

Relationship Between total PFOS Concentrations and Kidney Function in Patients with Renal Impairment



Unpublished data

Association between eGFR and PFAS levels using linear regression.

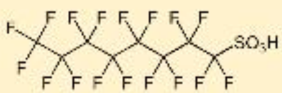


Unpublished data

FPAS and kidney function in patients with kidney disease

474 patients with chronic kidney disease

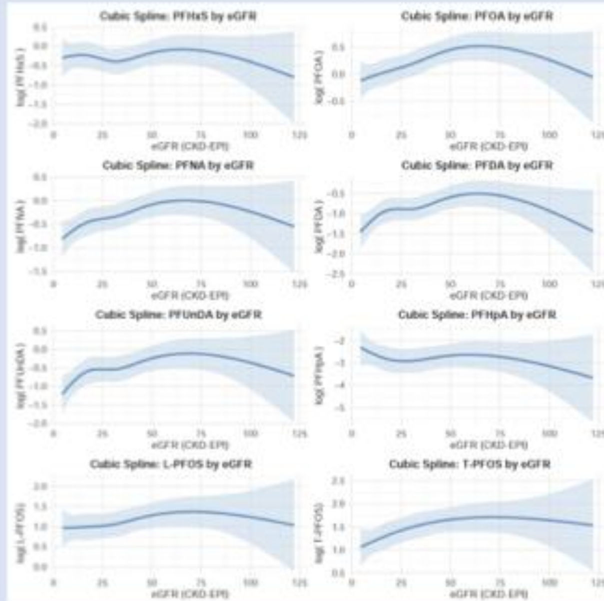
Kidney function by CKD-EPI eGFR and urine ACR

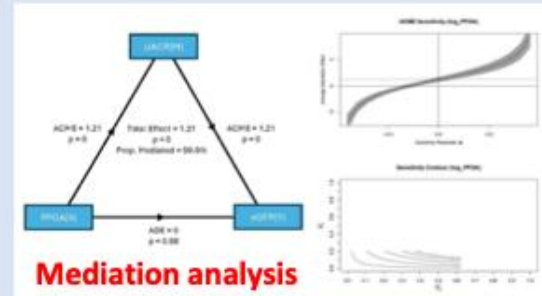


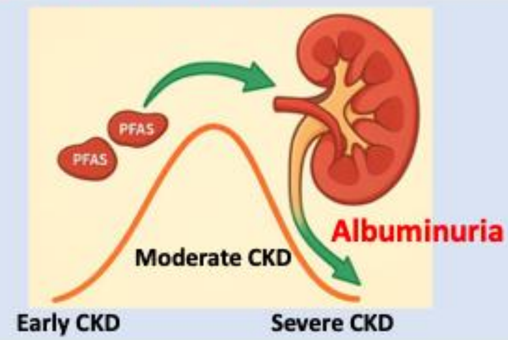
PFAS

Total PFOS, Linear PFOS, PFHxS, PFUnDA, PFDA, PFNA, PFOA, PFHpA

Main results







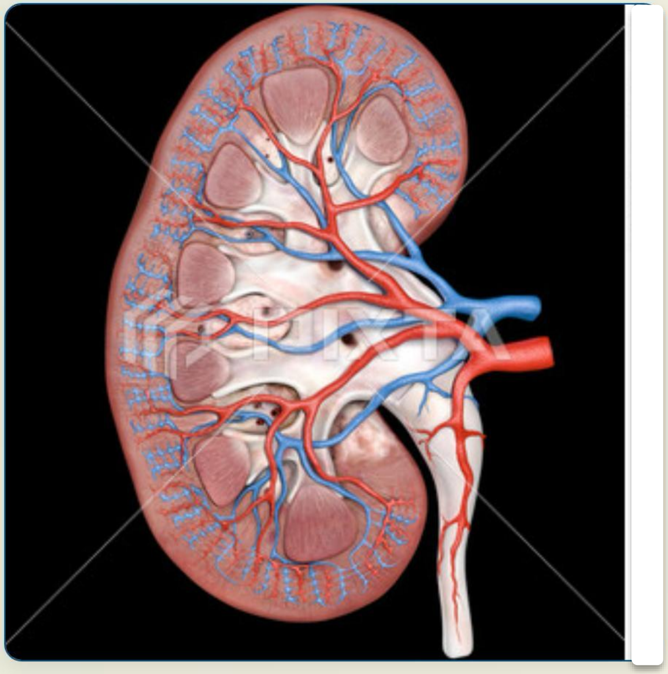
CONCLUSION

Albuminuria mediates the association between PFAS exposure and kidney function.

Unpublished data

Summary: PFAS and Kidney Function

- PFAS are persistent "forever chemicals" that accumulate via environmental exposure.
- Kidneys are the main elimination route; CKD impairs clearance, increasing body burden.
- Mechanisms of injury include oxidative stress, inflammation, and mitochondrial dysfunction.
- The relationship is bidirectional: low GFR causes accumulation, which accelerates CKD.
- Albumin binding and albuminuria significantly mediate PFAS retention and toxicity.
- Hemodialysis effectively lowers serum PFAS levels compared to non-dialysis CKD.



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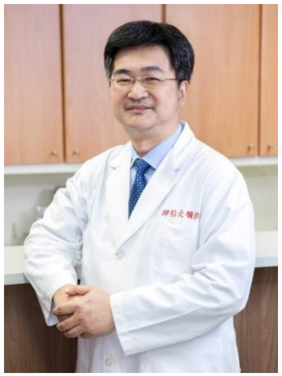

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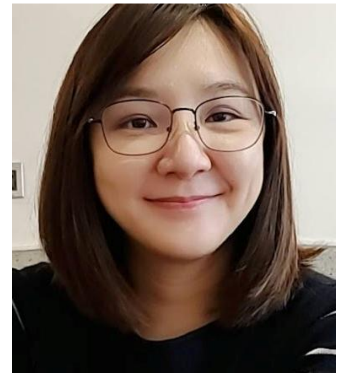

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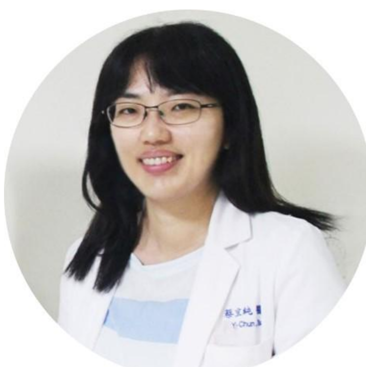

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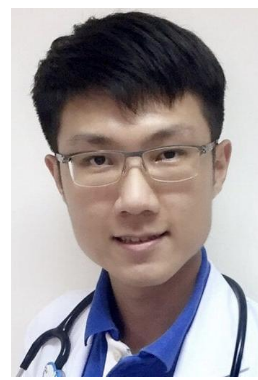

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