



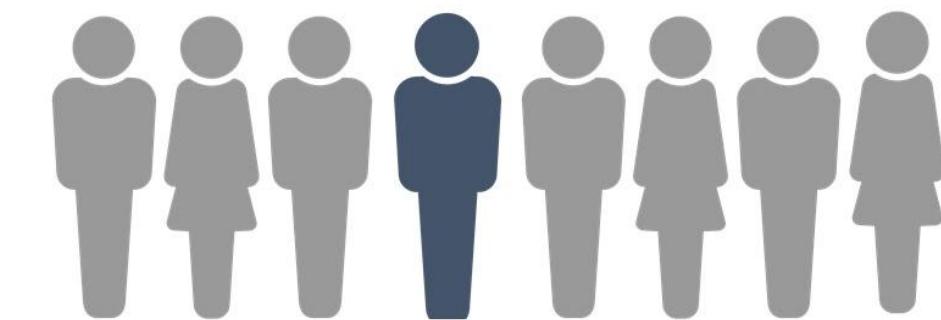
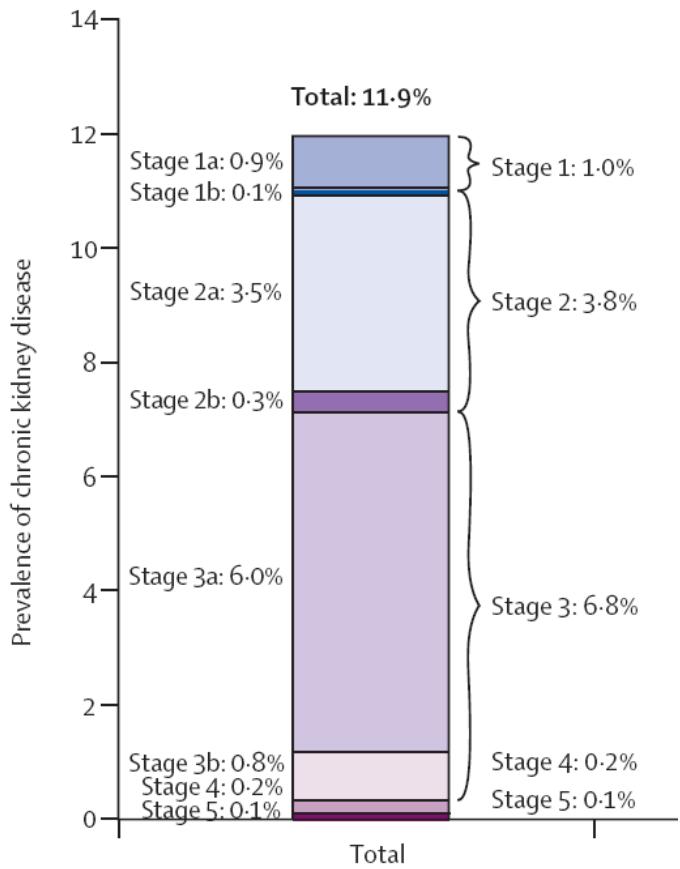
Per- and Polyfluoroalkyl substances (PFAS) and kidney function: From environmental exposure to biological mechanisms

Emily, Yiting Lin, MD, PhD

Associate professor in Kaohsiung Medical University

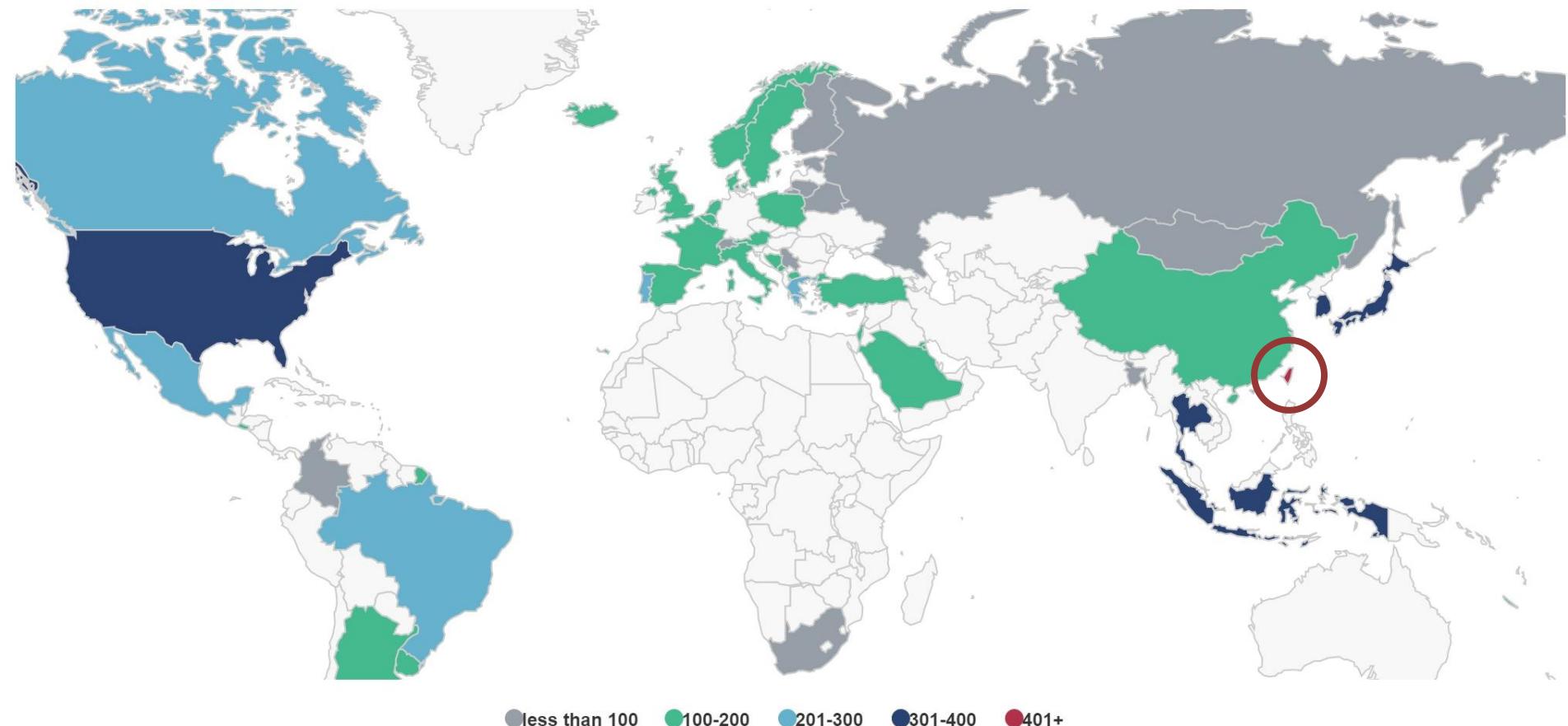
Welcome to
The Splendor Kaohsiung

CKD prevalence in Taiwan



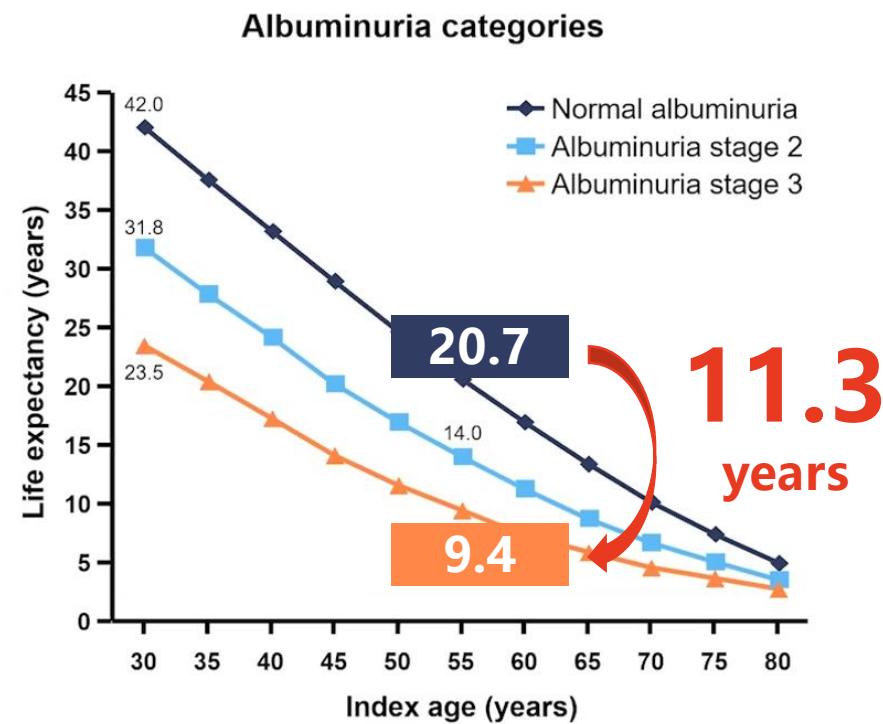
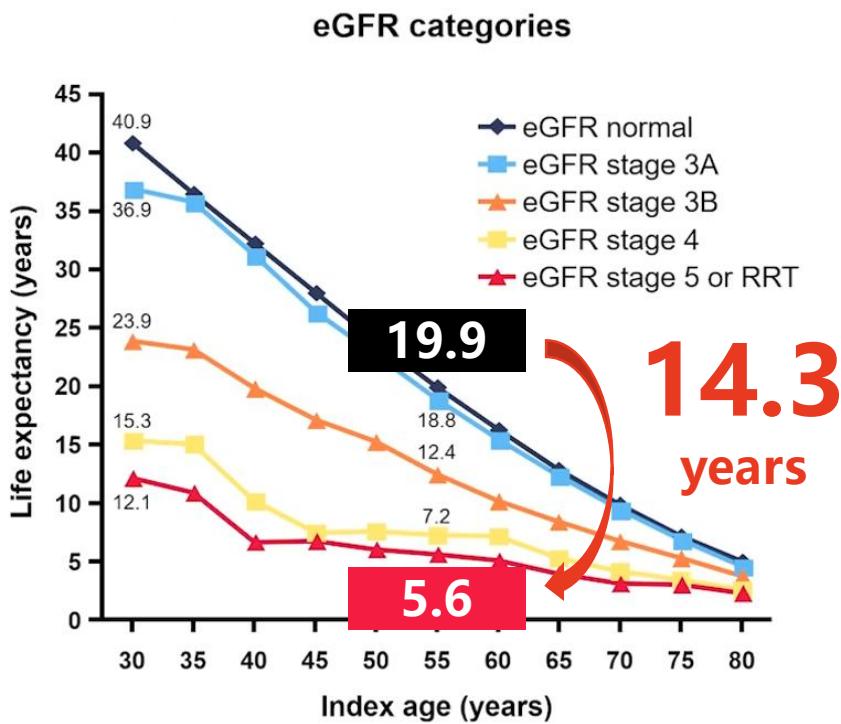
**One in every 8 people —
12% of Taiwan's population, or 3 million people —
Truth No. 1: High Prevalence Rate.**

Hemodialysis prevalence in Taiwan



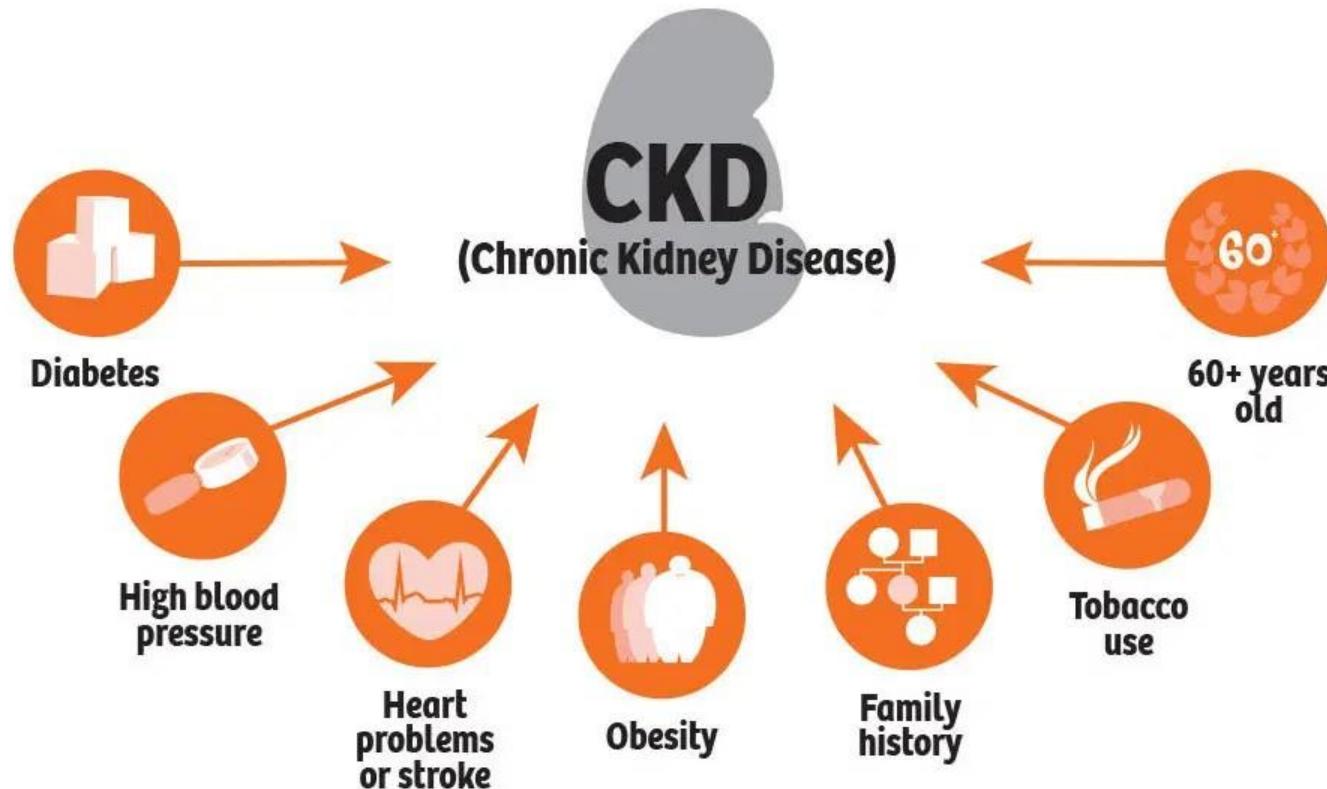
Data Source: 2022 United States Renal Data System Annual Data Report

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 \geq 300 mg/g)

Increased risk of chronic kidney disease



Environmental Pollution & Kidney Diseases

Kidney News

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 stress, 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

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.



Water contaminants

Pesticides (herbicides, insecticides)

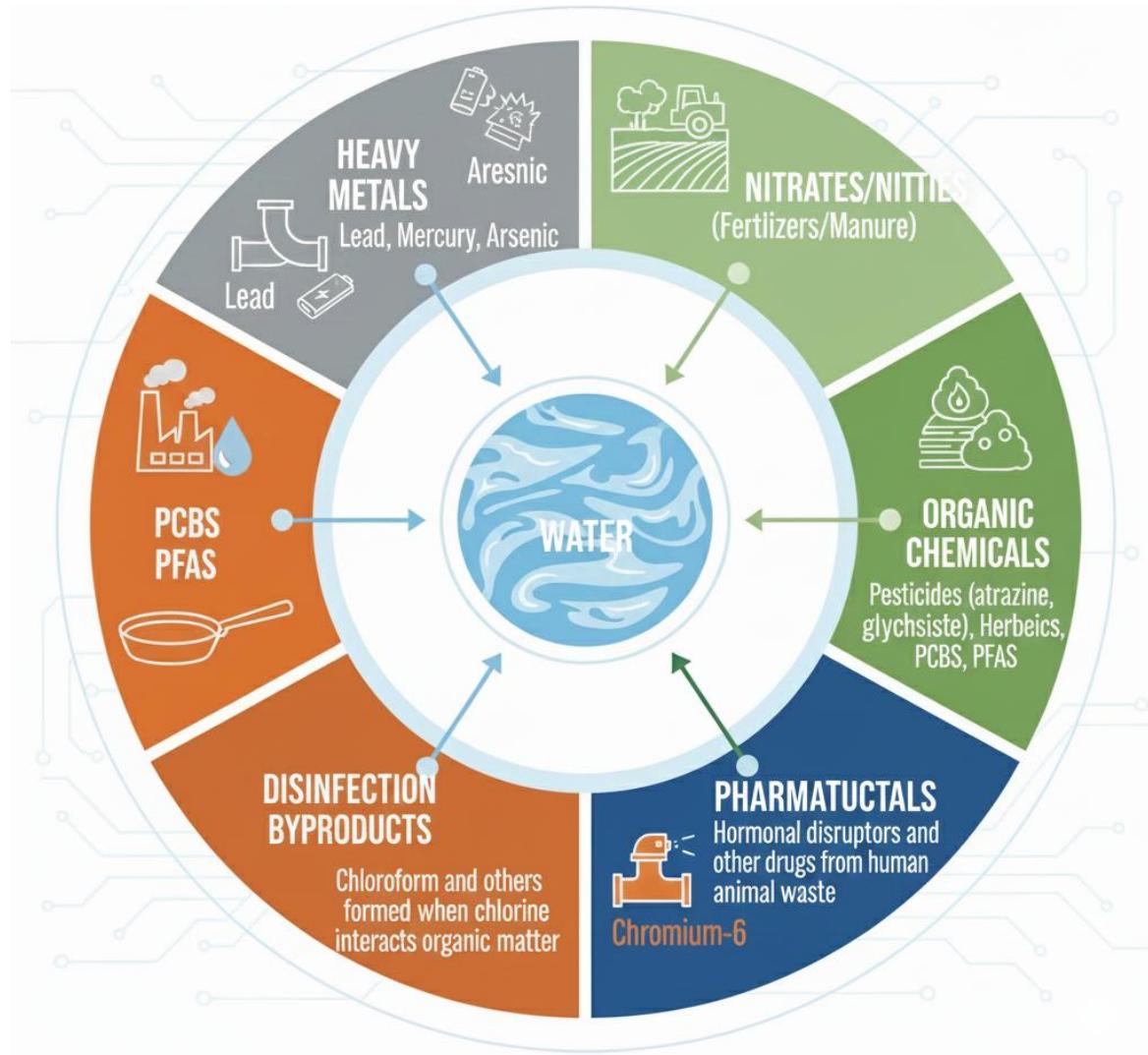
- Mechanism of injury:**
 - Toxic compounds cause oxidative damage and mitochondrial dysfunction in renal tubules, leading to tubular atrophy and interstitial fibrosis.
- Associated kidney diseases:** Chronic kidney disease
 - Increased risk of kidney failure in individuals exposed to pesticides
 - Spouses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



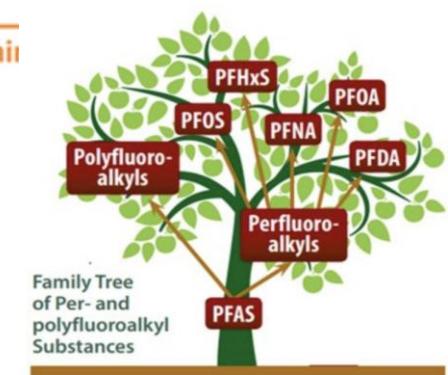
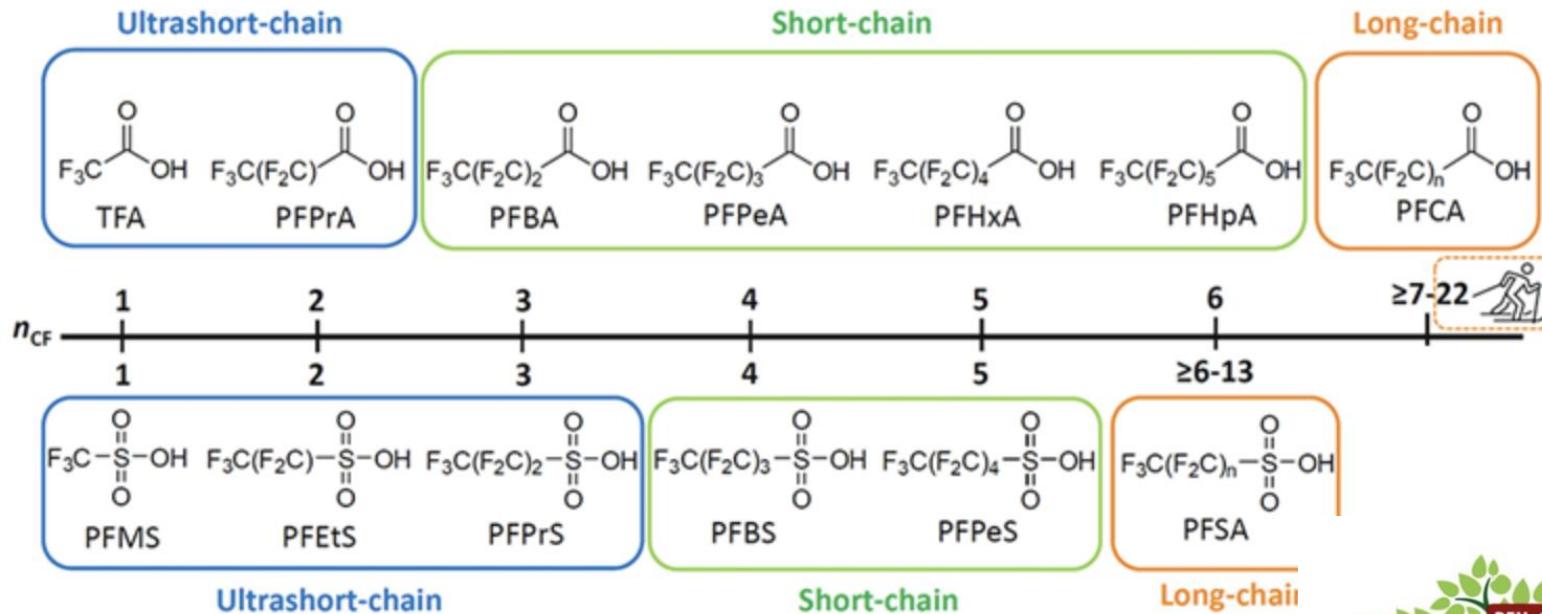
Toxins and occupational hazards

VA: Dr. Alejandro Garcia-Rivera  @alexgr23

Common Environmental toxins in the water



What are PFAS?



WHY WE CREATED PFAS: THE GOOD SIDE



1. Pushes Away
Water & Oil

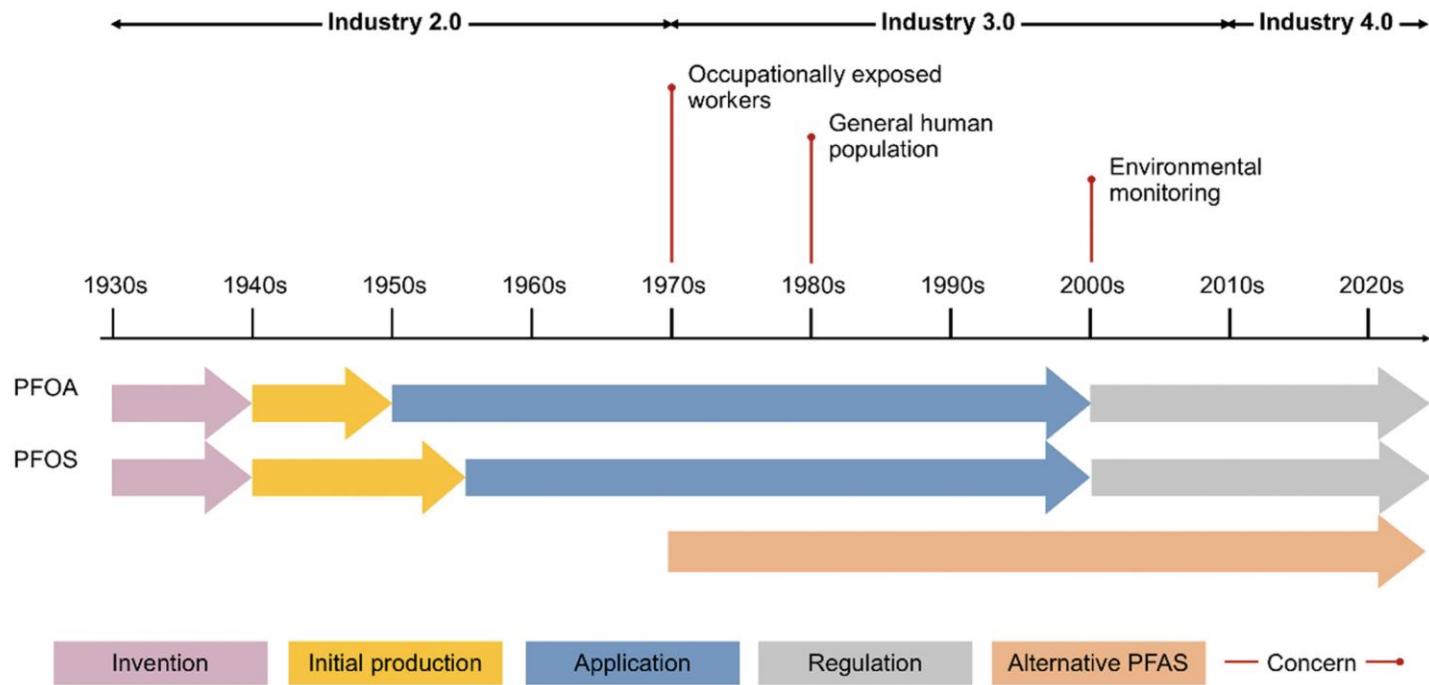
2. Puts Out Fires
FAST

3. Super Strong
& Lasts Long

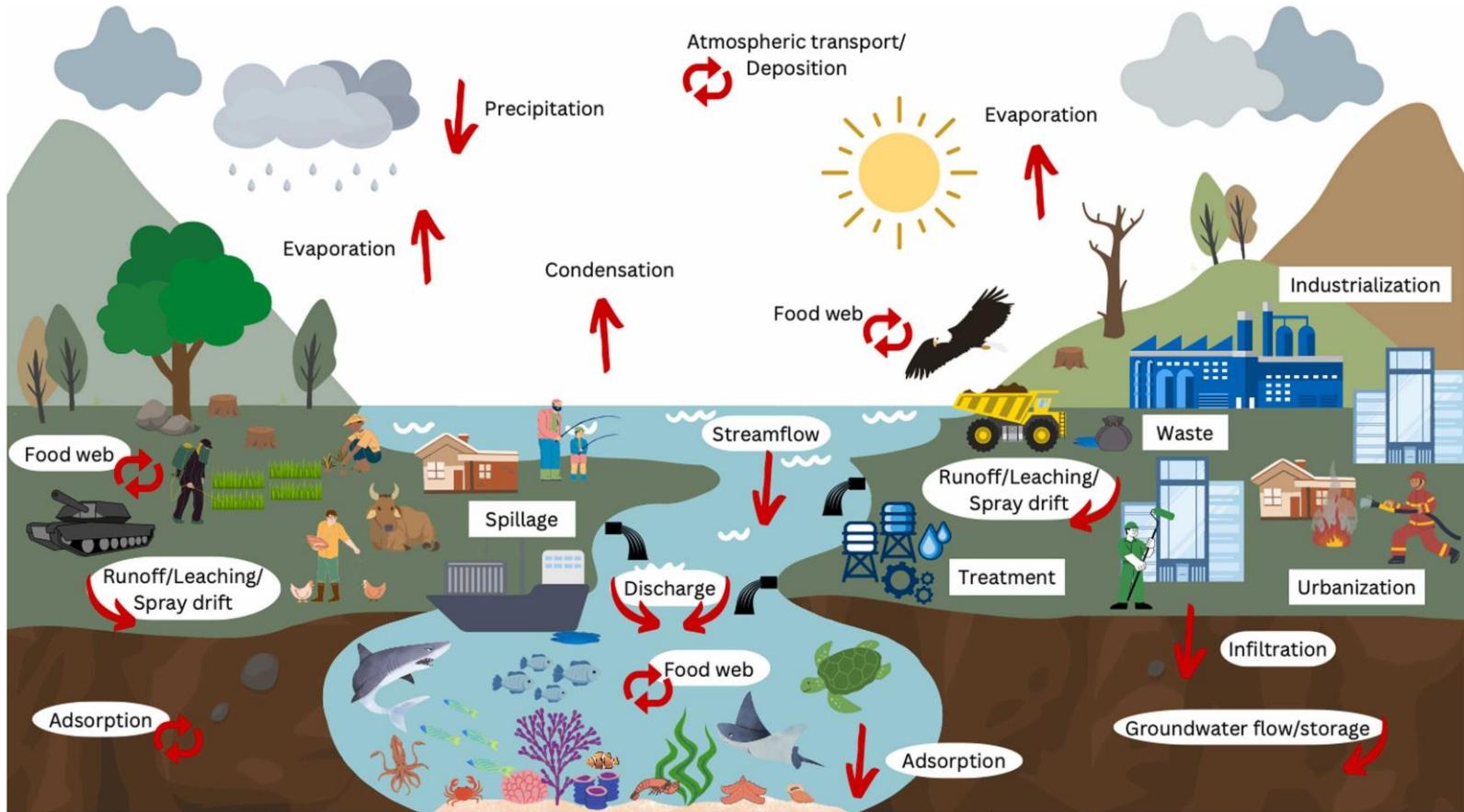
Common sources of PFAS



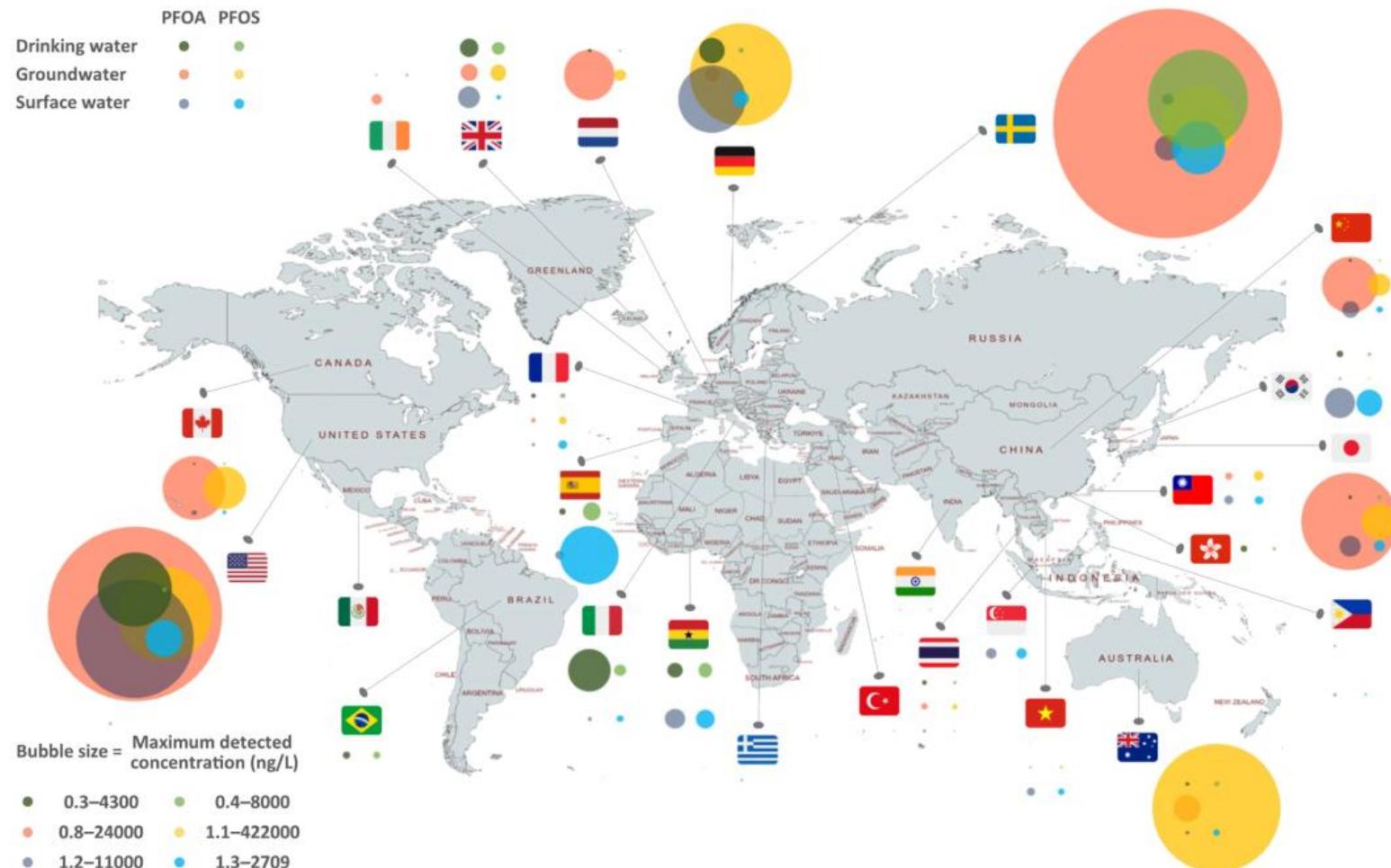
PFAS history and global use



Environmental Sources and Transport Pathways



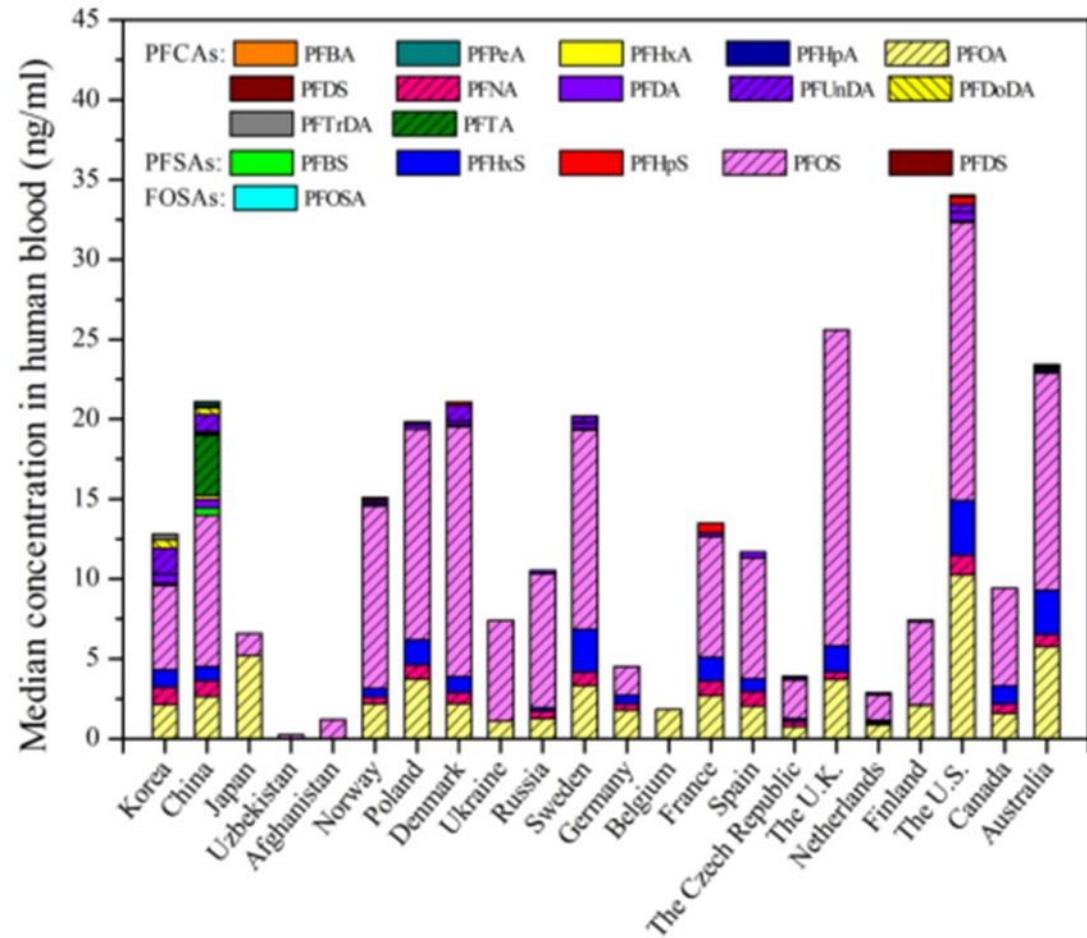
Global PFAS Contamination and Exposure



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

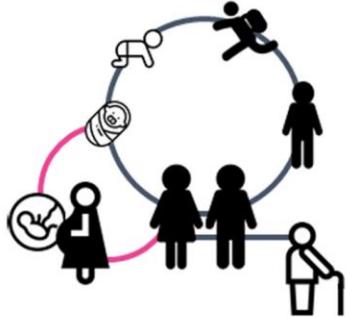
Blood PFAS Profiles Across Countries

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

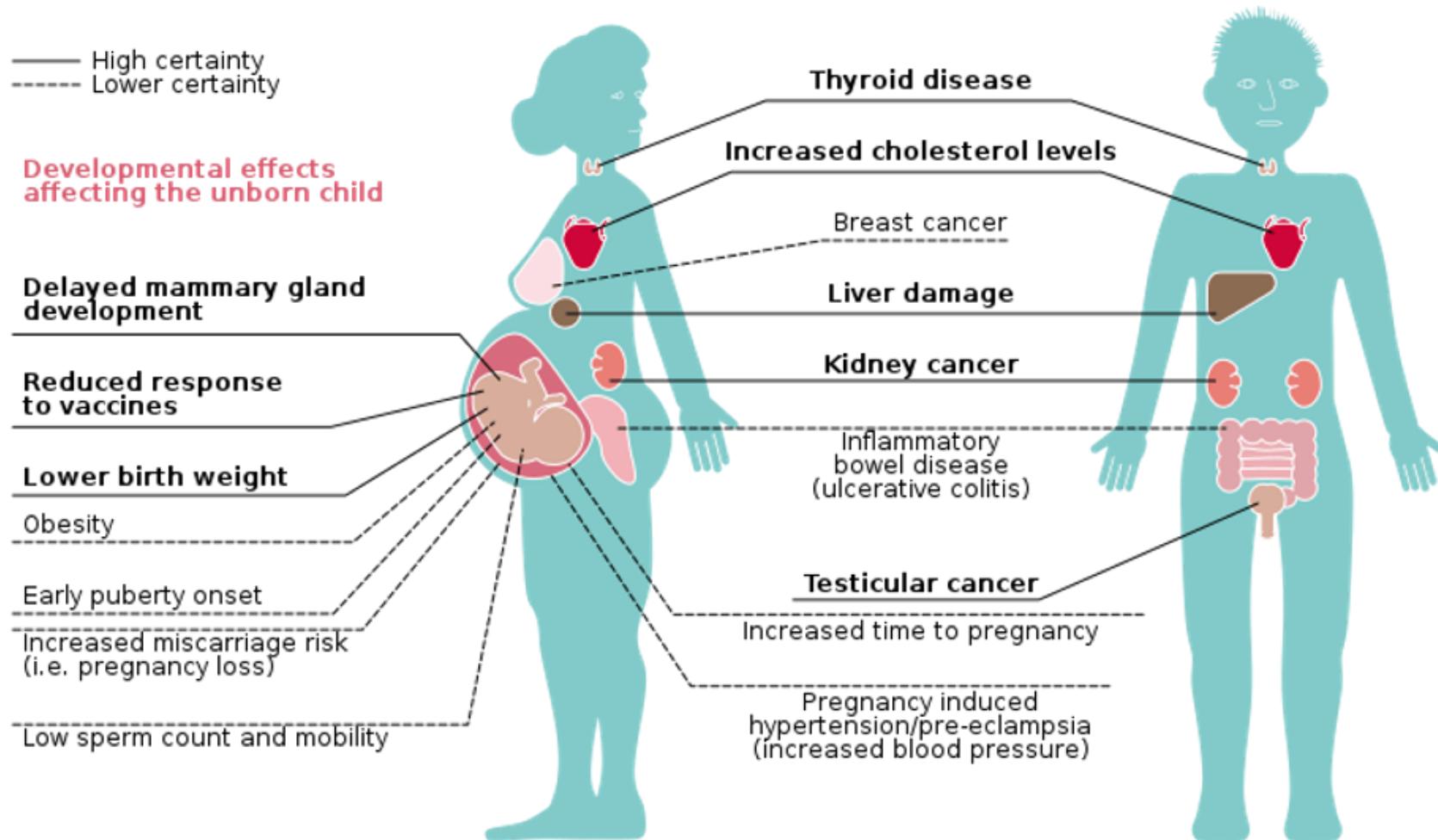


Toxicological Mechanisms and Health Effects

- PFAS induce oxidative stress, inflammation, mitochondrial dysfunction

 Body weight, size, and growth	 Nervous system and behavior	 Musculoskeletal system	 Sensory
<ul style="list-style-type: none">Abnormal changes e.g., low birth weight, overweight/obese, and cell size.Altered metabolism and growth.Increased risk of diseases.	<ul style="list-style-type: none">Caused behavior deficits, neurotoxicity, and ototoxicity.Changes in level/expression of neurotransmitters.	<ul style="list-style-type: none">Reduced bone mineral density.Skeletal malformation, deposition and sequestration in bone, bone cell differentiation, and osteoporosis.	<ul style="list-style-type: none">Caused dental carries and skin irritation or sensitization e.g., atopic dermatitis, with the potential development of allergic illnesses.
 Cancers	 Endocrine system	 Respiratory system	 Circulatory system
<ul style="list-style-type: none">Altered cell proliferation, cell-cycle regulation, cell migration and invasion, gene expression, and histone modifications, with tumorigenesis.Affect almost any organ or tissue.	<ul style="list-style-type: none">Changes on the level, production, and activity of hormones and expression of hormone receptors.Impacts on various organs and glands with increased risk of diseases.	<ul style="list-style-type: none">Altered blood oxygen level.Changes in cell structure and function of the lungs, airways etc.Changes in histology e.g., throat (larynx or pharynx).Increased risk of allergies and infectious diseases such as heart failure coupled with life-threatening illnesses.	<ul style="list-style-type: none">Increased risk of heart diseases or cardiac events.Binding to blood proteins, interrupted hormone/protein interactions, and caused displacement of hormones.
 Immune system	 Metabolic and digestive system	 Urinary system	 Genotoxicity
<ul style="list-style-type: none">Changes in inflammatory biomarkers and immune response.Affect immune cell production, activity, and signaling, caused cell death.Increased risk of allergies and infectious diseases, coupled with life-threatening illnesses.	<ul style="list-style-type: none">Affect metabolite concentration and metabolism.Impacted gene expression, cell function, and nuclear receptor pathway (e.g., LXR, RXR, and PPAR).Increased risk of metabolic disorders and other chronic diseases.	<ul style="list-style-type: none">Changes in organ histology.Altered cell and organ function.Changes in urinalysis, serum uric acid level, and urine albumin/creatinine ratio.Caused diseases e.g., cancer and diabetes.	<ul style="list-style-type: none">DNA damage, mitochondrial depolarization, altered DNA methylation, and telomere shortening.Heritable genetic changes.

Toxicological Mechanisms and Health Effects



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).

Development of tolerable weekly intake amounts (TWI)

EFSA 2008



1,050 ng/kg bw
per week

A factor of
81

EFSA 2018



13 ng/kg bw
per week

2020

PFOS + PFOA + PFNA + PFHxS

4.4 ng
kg bw per week

Tolerable intake in nanograms per kilogram of body weight
(ng/kg bw) per week
(EESA 2020)

TWI = tolerable weekly intake. PFOS = perfluorooctanesulfonic acid
PFOA = perfluorooctanoic acid, PFNA = perfluorononanoic acid

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.

PFAS and Kidney Function

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

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

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Q AI Discovery Assistant



Volume 54, Issue 5
October 2025
(In Progress)

JOURNAL ARTICLE

Cohort Profile: Taiwan Kidney Outcome (TAKO) and Taiwan Kidney Outcome Omics (TAKOO) cohorts

Ping-Hsun Wu, Ming-Yen Lin, Teng-Hui Huang, Yun-Shiuan Chuang, Yi-Chun Tsai, Szu-Chia Chen, I-Ching Kuo, Wei-Chung Tsai, Hsiu-Fen Lin, Tien-Ching Lee ... Show more

International Journal of Epidemiology, Volume 54, Issue 5, October 2025, dyaf152, <https://doi.org/10.1093/ije/dyaf152>

Published: 04 September 2025 Article history ▾



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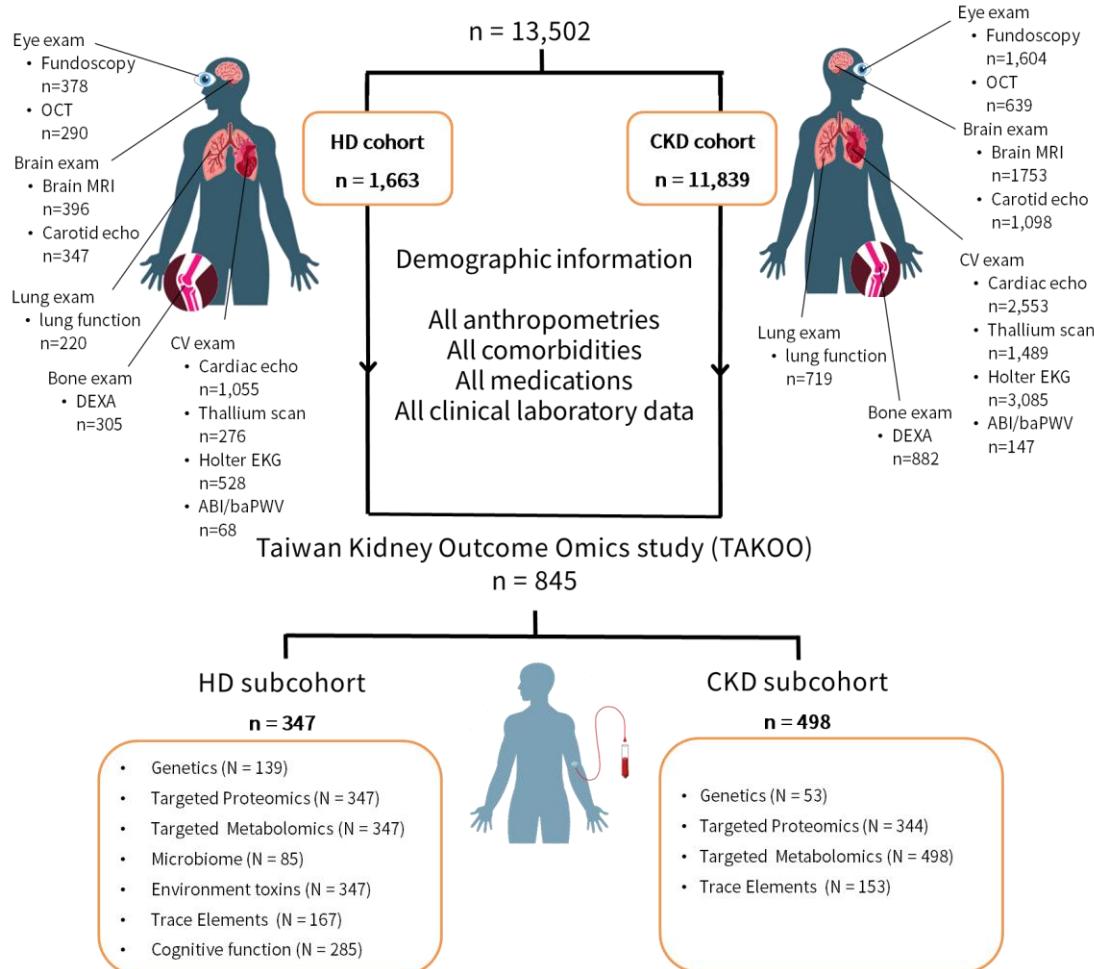
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Help



Taiwan Kidney Outcome study (TAKO)



Prospective cohort in CKD/HD patients

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

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

Decreased levels of perfluoroalkyl substances in hemodialysis

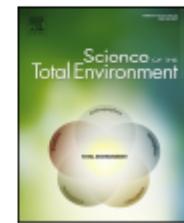
Science of the Total Environment 896 (2023) 165184



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Decreased levels of perfluoroalkyl substances in patients receiving hemodialysis treatment



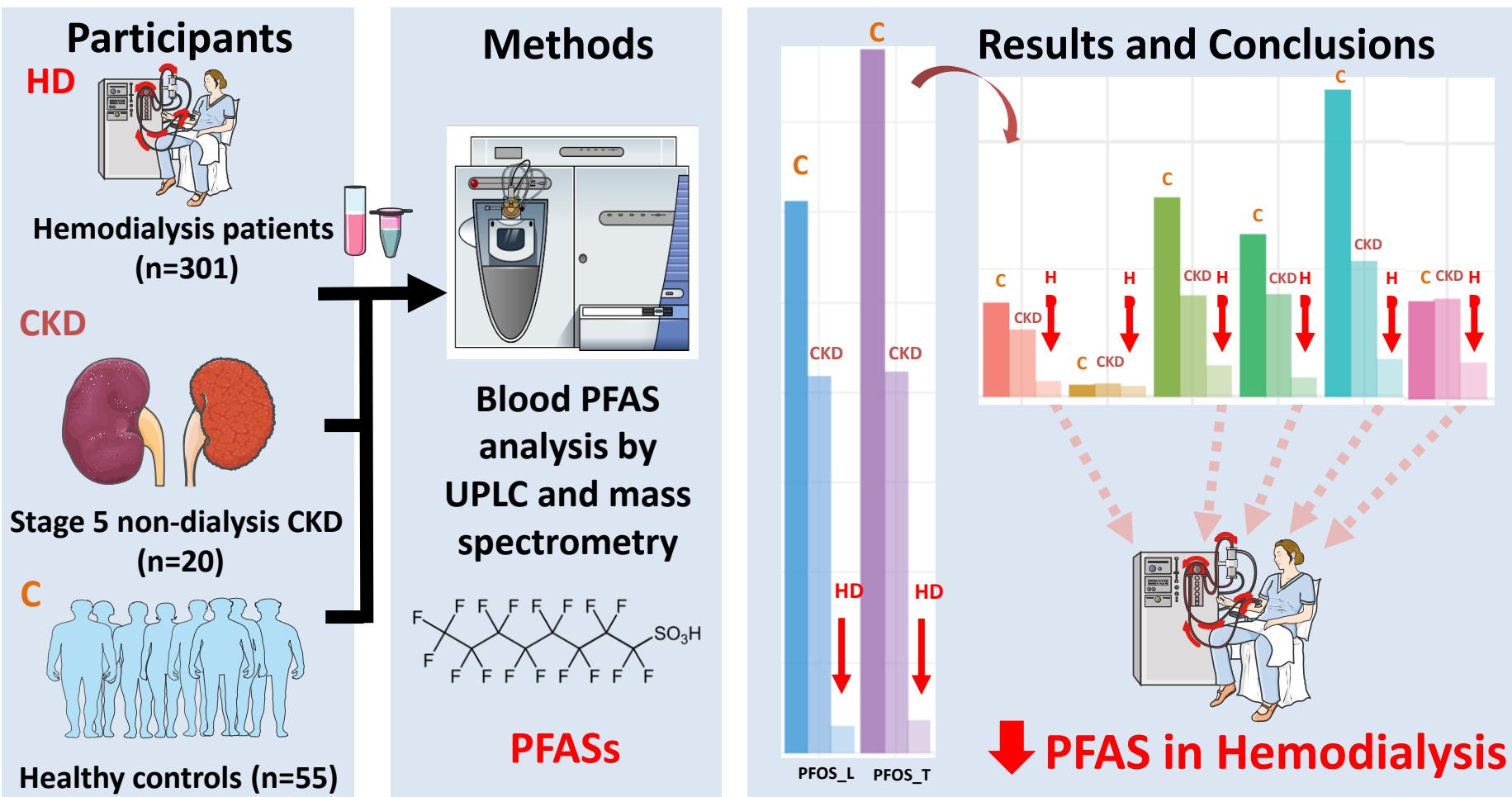
Perfluoroalkyl substances (PFAS) were measured in prevalent hemodialysis patients (n=301), stage 5 non-dialysis chronic kidney disease (CKD) patients (n=20), and health control (n=55) using UHPLC-MS/MS

9 PFAS were identified in this study, including PFHpA, PFHxS, PFOA, PFNA, PFDA, PFUnDA, PFBS, T-PFOS, and L-PFOS

PFBS data was excluded because most sample were below limit of detection (LOD)

8 PFAS were finally analyzed in hemodialysis patients, stage 5 non-dialysis CKD patients, and health controls

Decreased levels of PFAS in patients with HD



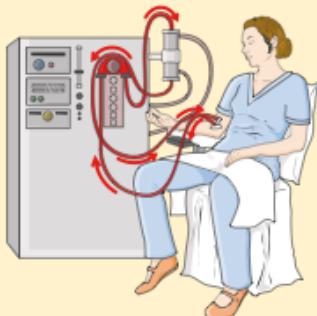
***The perfluoroalkyl substance level associated
with filter type in patients with hemodialysis***

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

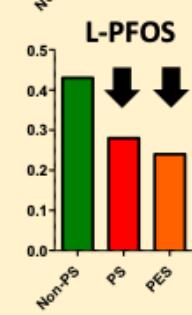
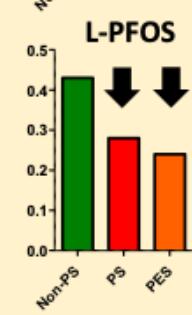
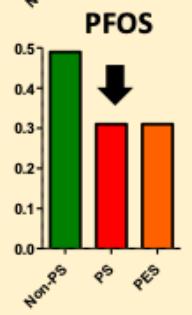
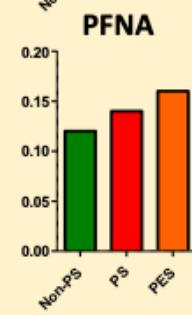
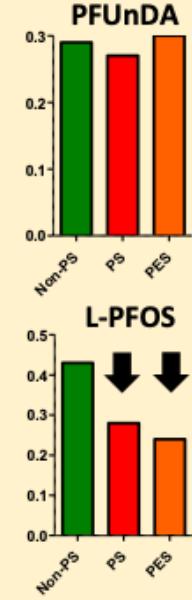
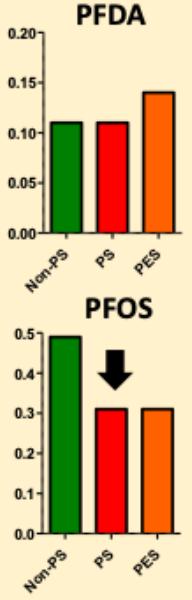
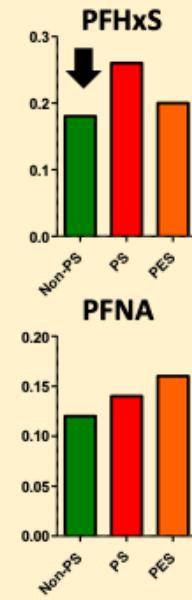
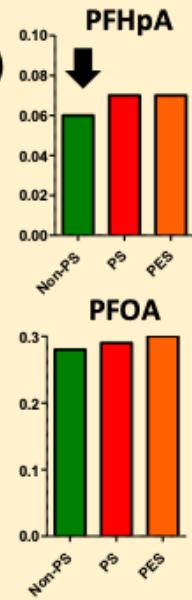
Nutritional markers
Albumin, Uric acid, nPCR

PFOS
PFHpA
PFNA
PFDA
PFUnDA

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



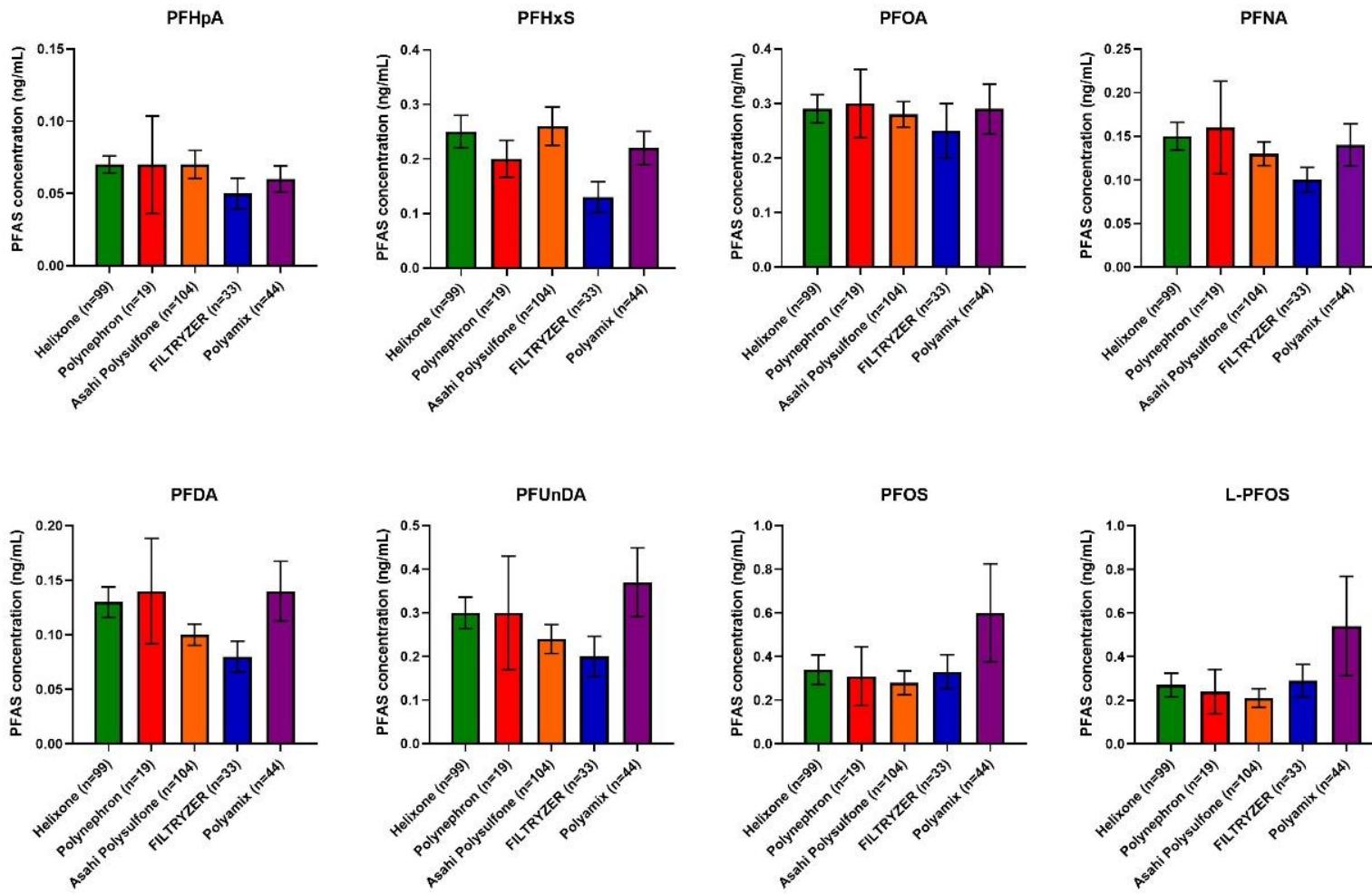
Dialysis membrane types:
polysulfone (PS)
polyethersulfone (PES)
non-polysulfone (non-PS)

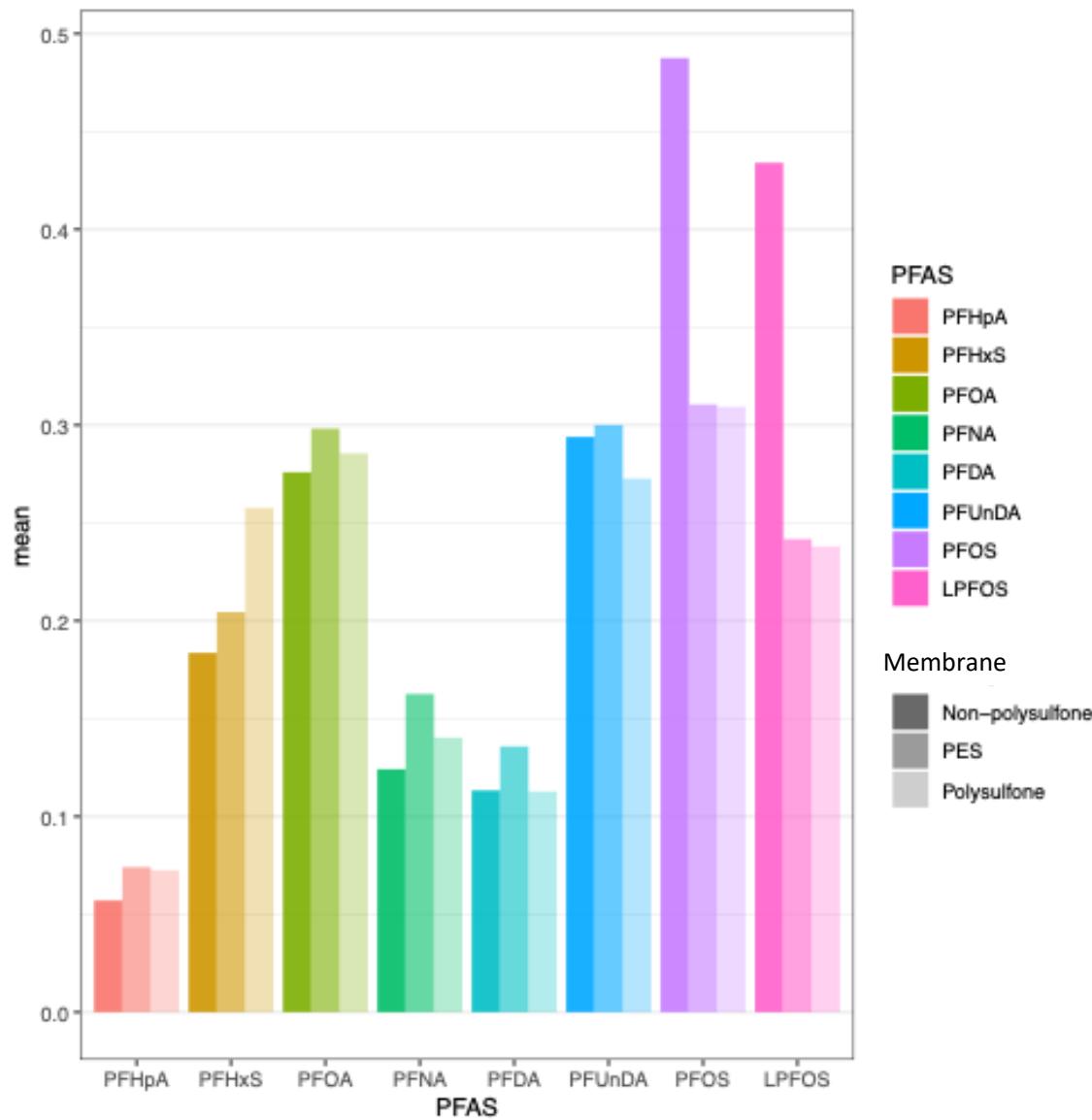


CONCLUSION

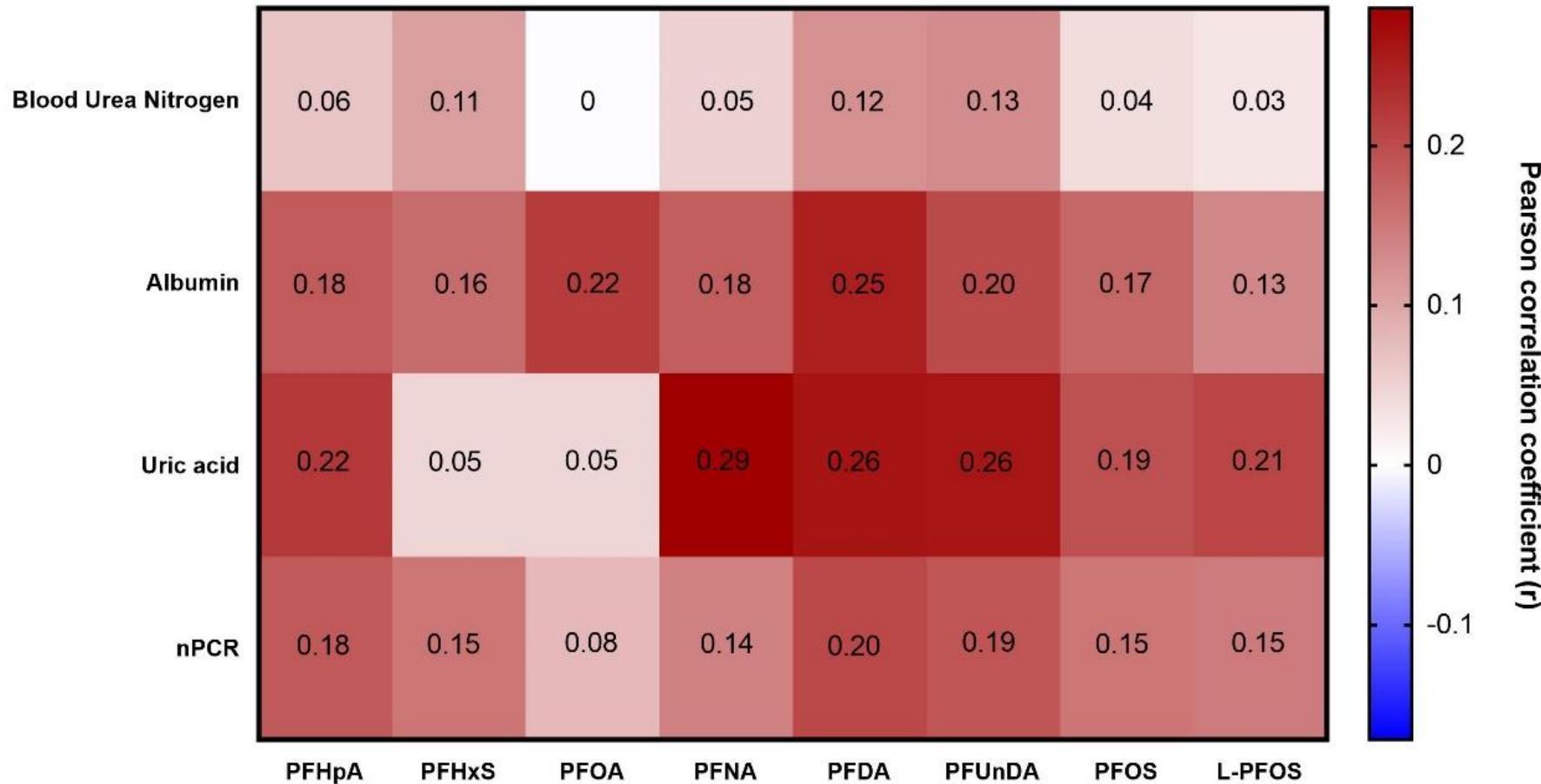
The levels of PFASs in hemodialysis patients were influenced by the dialysis membranes properties and were exhibited a positively associations with nutritional markers.

PFAS in different HD filters





Nutritional marker and PFAS

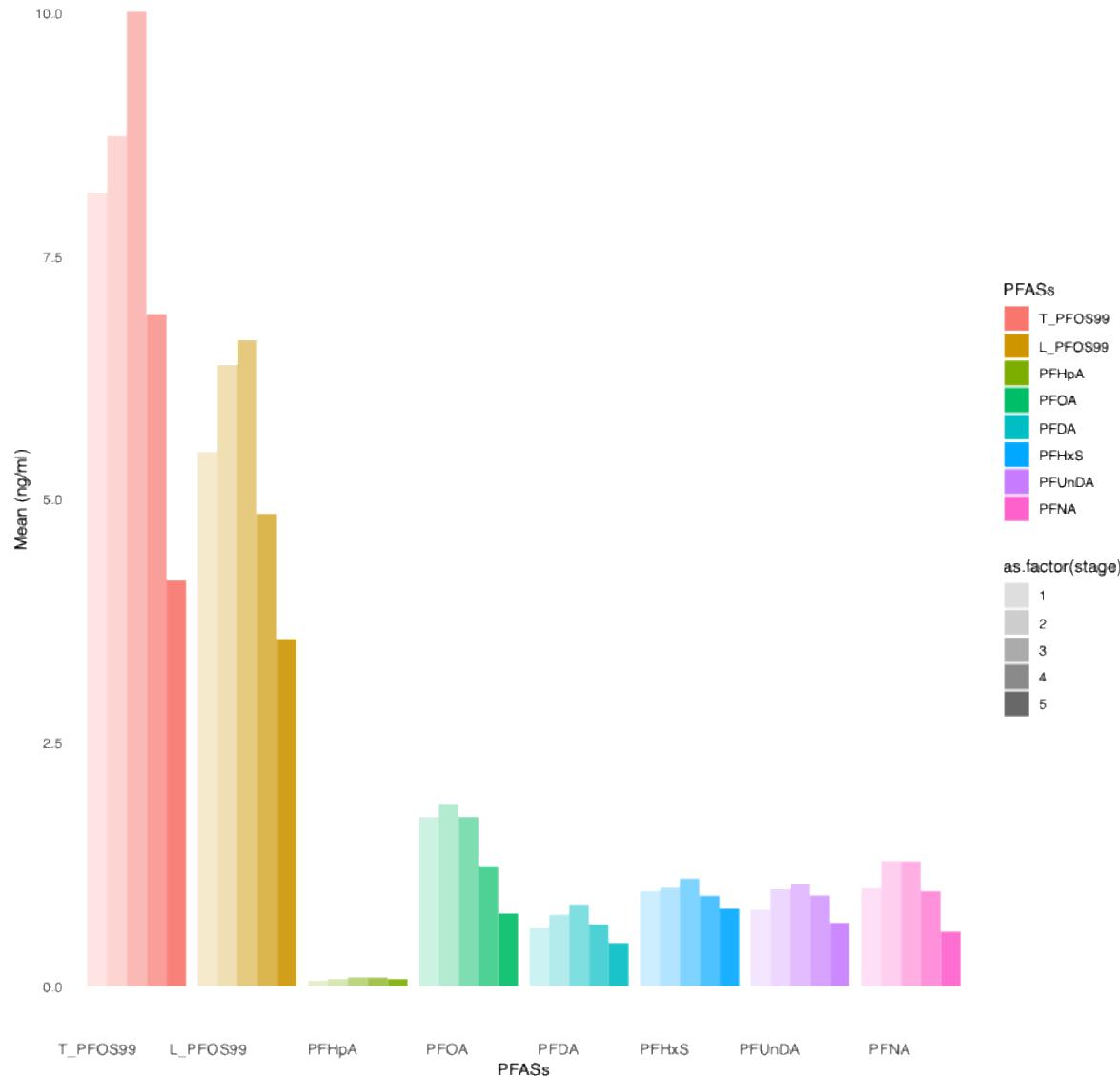


The distribution of PFAS in five CKD stages

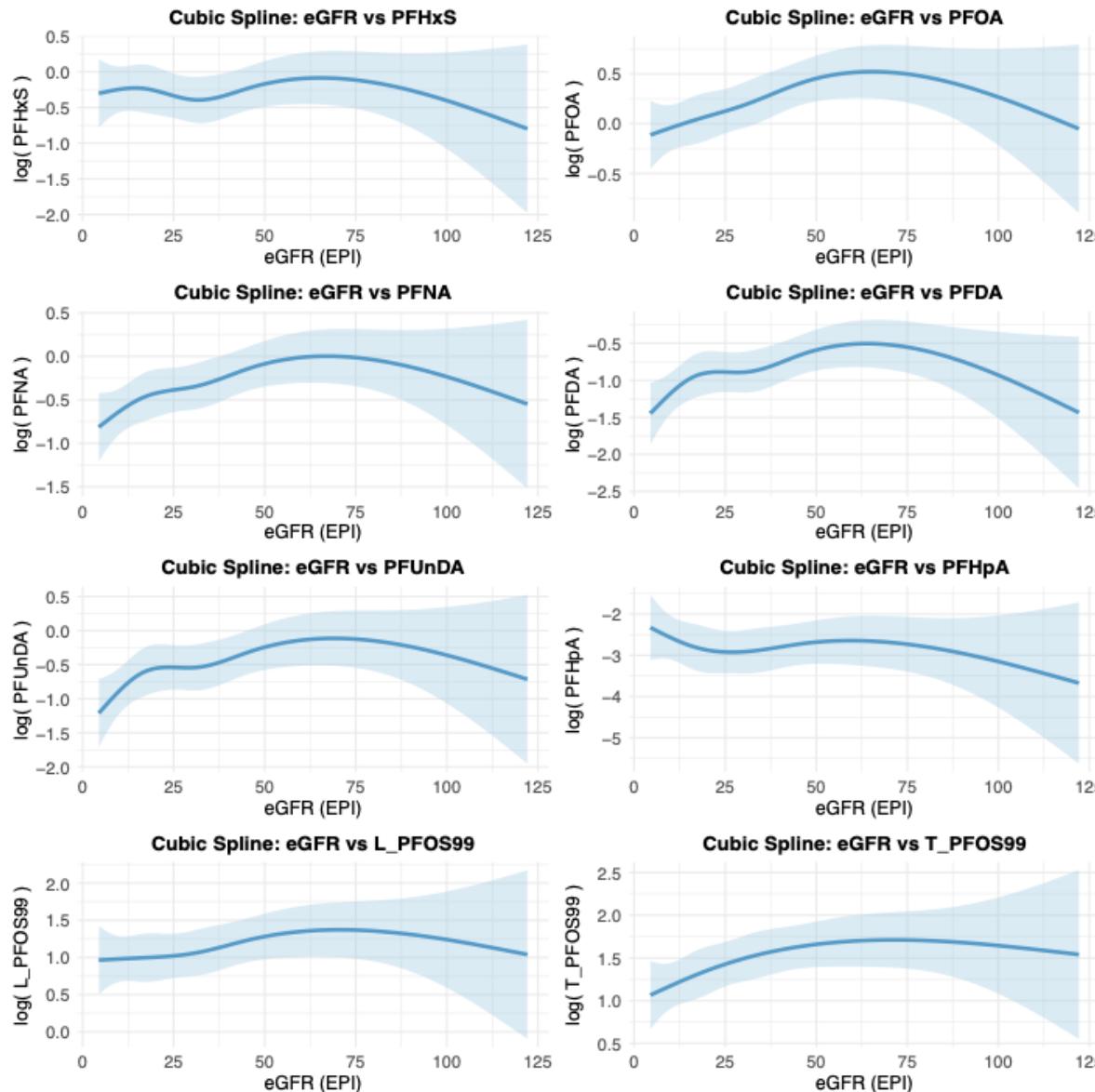
Baseline Characteristics of Study Participants Across Five CKD Stages

	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)

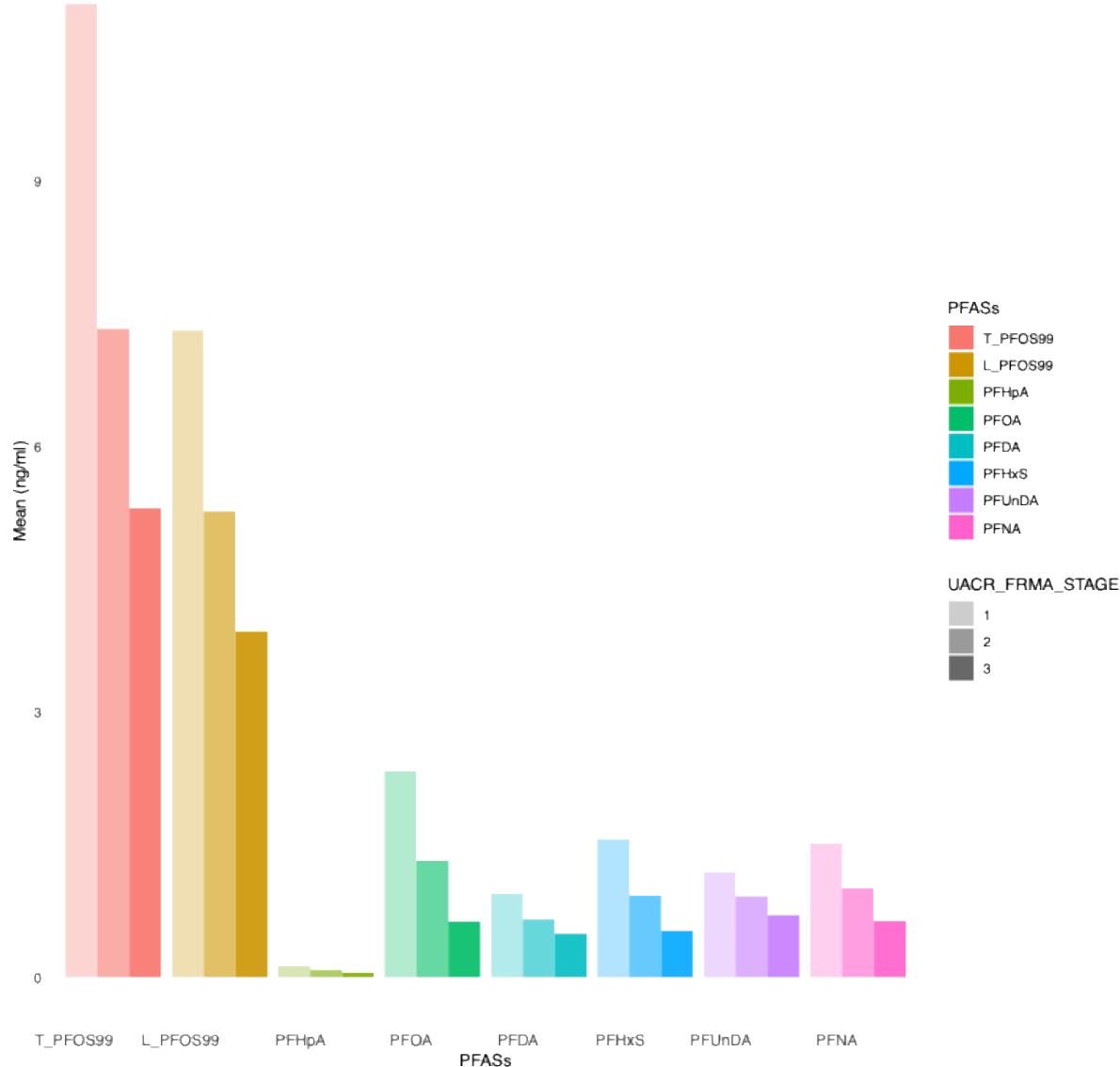
Levels of PFAS in Patients Across CKD stages



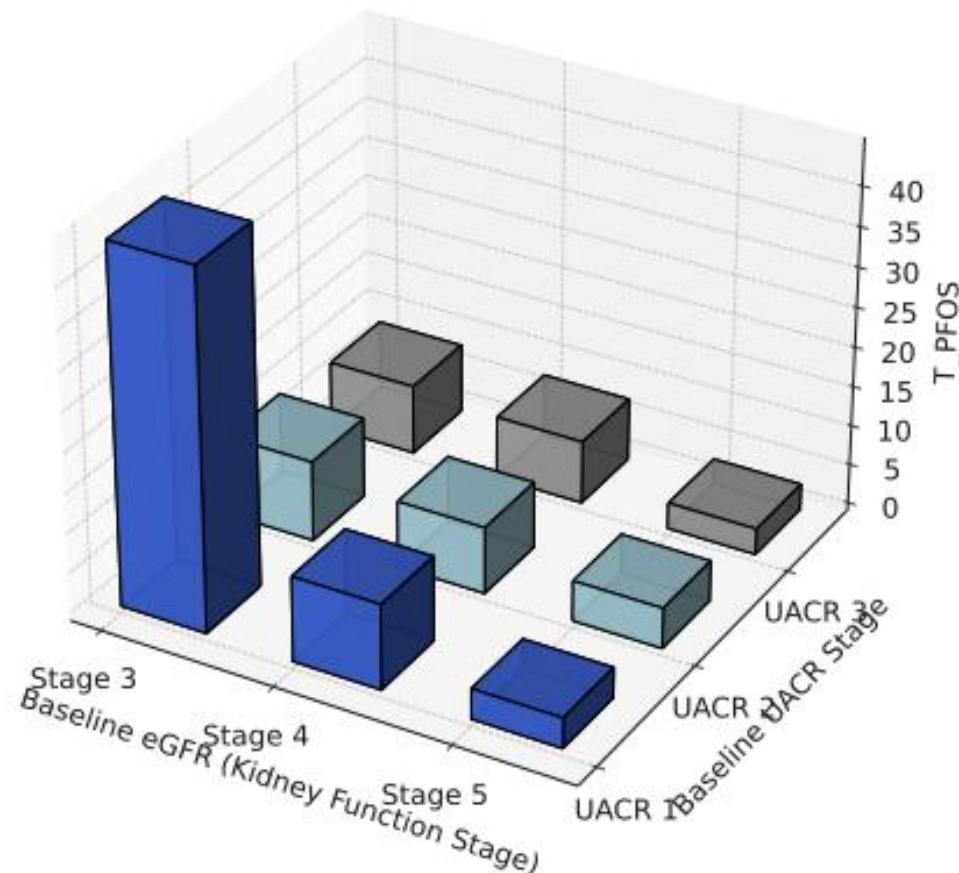
Cubic spline plots showing the adjusted association between eGFR and log-transformed serum PFAS concentrations.



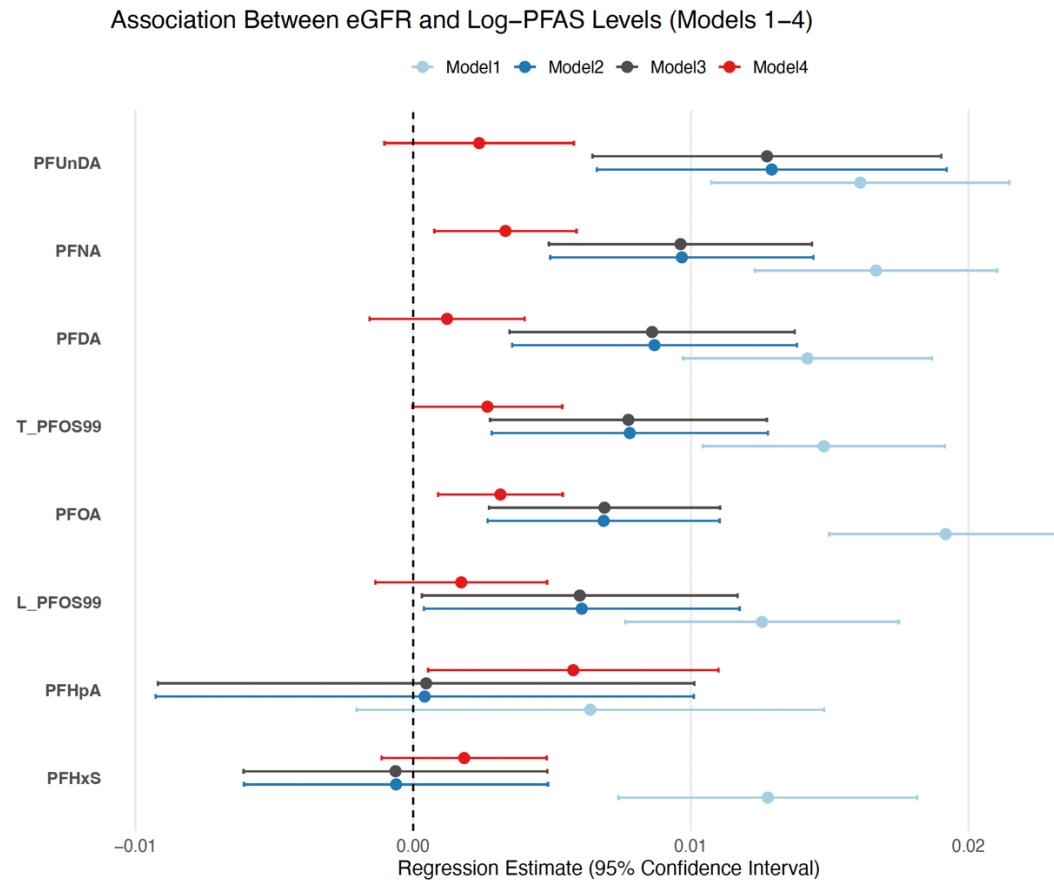
Concentrations of PFAS in Normoalbuminuria, Microalbuminuria, and Macroalbuminuria



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

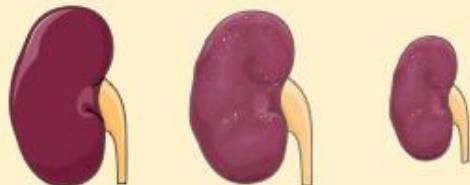


Association between eGFR and PFAS levels using linear regression.

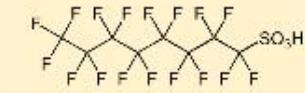


FPAS and kidney function in patients with kidney disease

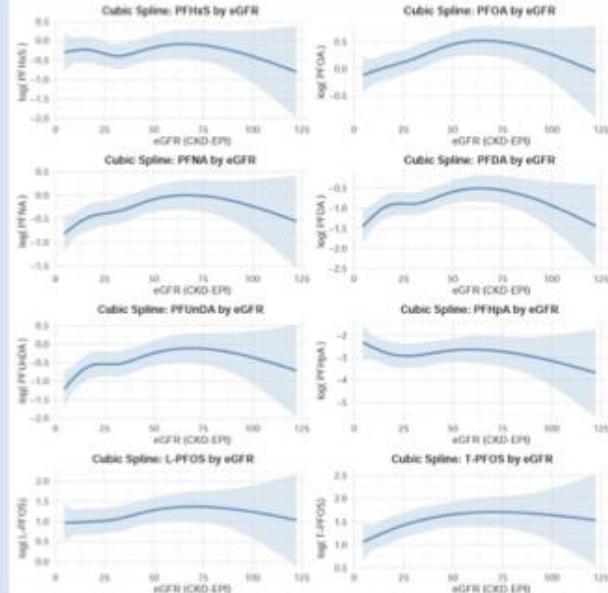
474 patients with chronic kidney disease



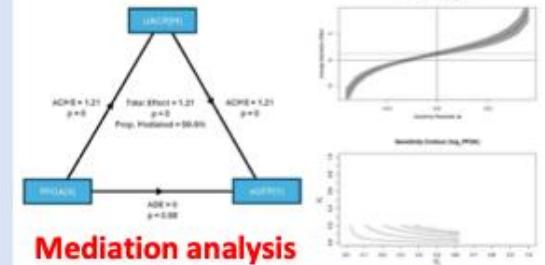
Kidney function by CKD-EPI eGFR and urine ACR



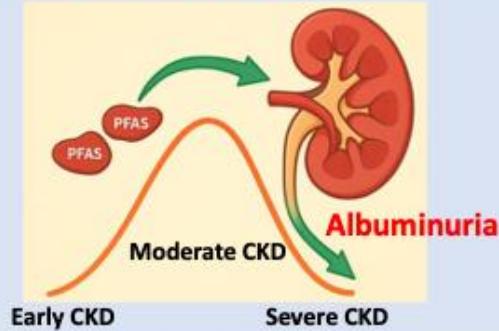
Total PFOS, Linear PFOS, PFHxS, PFUnDA, PFDA, PFNA, PFOA, PFHpA



Main results



Mediation analysis

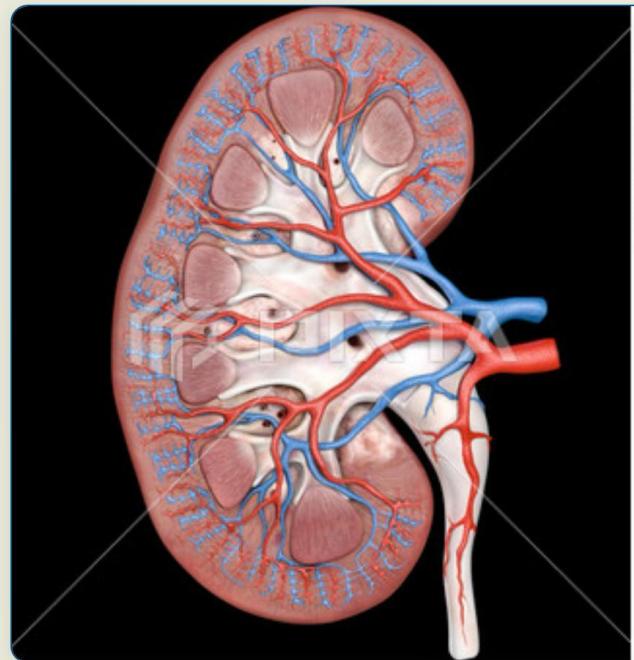


CONCLUSION

Albuminuria mediates the association between PFAS exposure and kidney function.

Summary: PFAS and Kidney Function

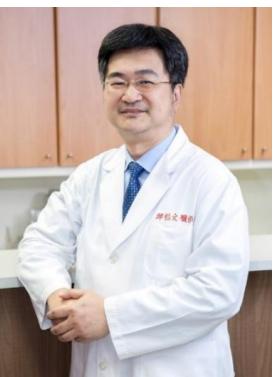
- ✓ PFAS are persistent "forever chemicals" that accumulate via environmental exposure.
- ✓ Kidneys are the main elimination route; CKD impairs clearance, increasing body burden.
- ✓ Mechanisms of injury include oxidative stress, inflammation, and mitochondrial dysfunction.
- ✓ The relationship is bidirectional: 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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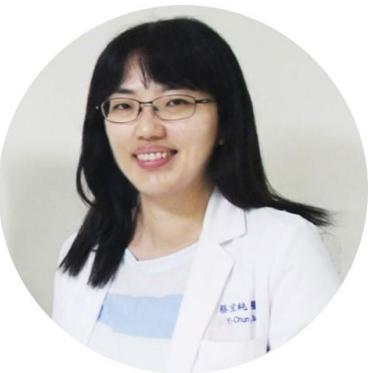
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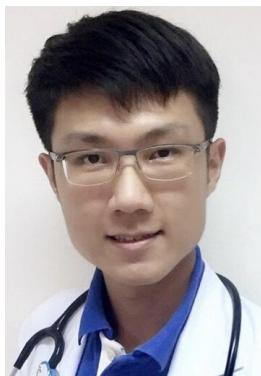
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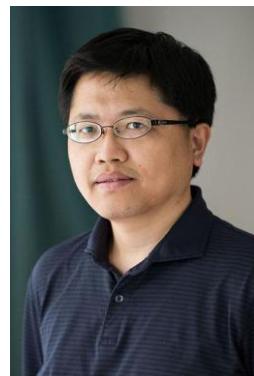
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Ping-Hsun Wu
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Thanks for your attention



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