



Human health effects of PFAS exposure: *Focus on PFOS*

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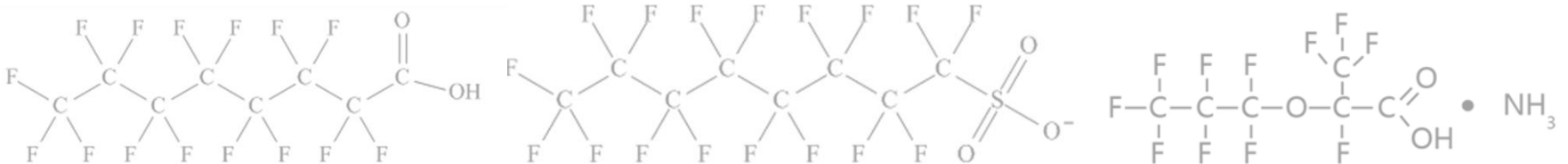
Department of Pharmacology & Toxicology

Brody School of Medicine

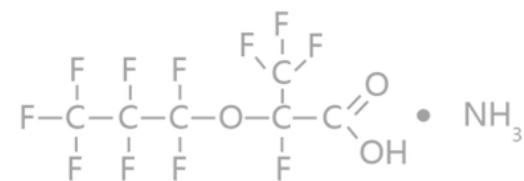
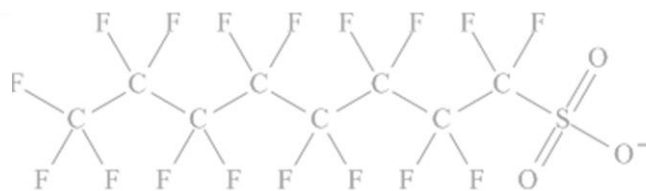
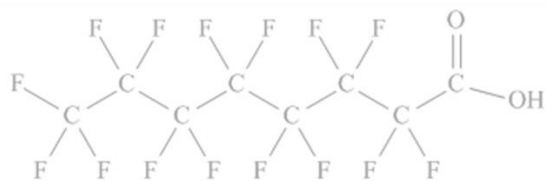
East Carolina University

Greenville, North Carolina, United States

Presented to: Flemish parliamentary committee of inquiry PFAS-PFOS, 2 July 2021



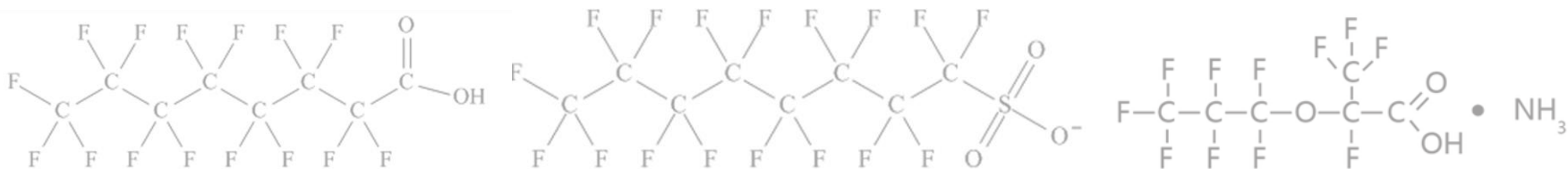
Brief introduction



Potential conflicts of interest

I currently am funded to study immune system effects of PFAS (sources of funding: North Carolina Policy Collaboratory & NC General Assembly, US EPA/Oregon State University (83948101), NIEHS/NC State University (1 P42 ES031009-01), NC State University Center for Human Health and the Environment, Brody Brothers Endowment)

I have spoken publicly about my understanding of PFAS toxicity, serve/have served as a plaintiff's expert witness, advocate for the need to protect the public from their exposures to PFAS, and am a proponent of the essential use concept and the class approach for PFAS management.



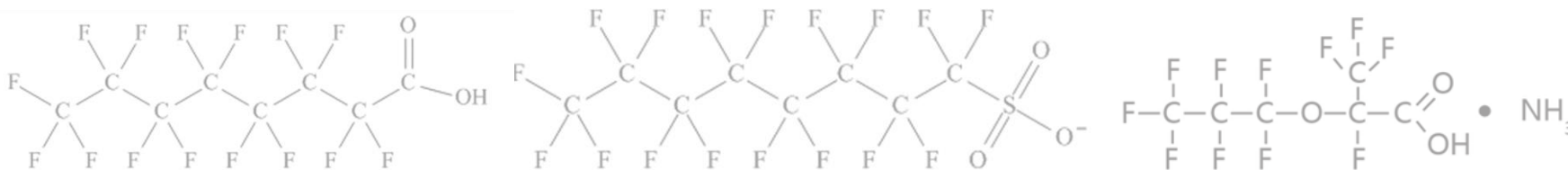
Brief biography

Training:

- Began studying PFAS immunotoxicity in 2005 during postdoctoral training at the United States Environmental Protection Agency

Publications:

- 16 primary research articles concerning PFAS immunotoxicity/developmental immunotoxicity, developmental neurotoxicity, developmental cardiotoxicity, dosimetry, and epidemiological associations
- 14 reviews/commentaries on PFAS toxicity, use, and management
- Two book chapters on PFAS immunotoxicity
- One edited book on PFAS toxicity



Why scientists are concerned about PFAS

E P B M T

Emissions

Persistence

Bioaccumulation

Mobility

Toxicity

Multiple lines of evidence within these five categories support that ***PFAS are human and environmental health concerns.***

Persistence in the environment AND in living organisms



PFOS: 3 to 6 weeks



PFOS: 5 to 6 years

Environmental persistence = continuation of exposure unless PFAS are removed from sources of exposure.

PFAS around the world

A SAMPLING OF GLOBAL PFC CONTAMINATION



AUSTRALIA

Highest average levels of PFOS in human blood



CANADA

PFCs in three arctic lakes



CHINA

Highest level of PFOS ever detected in human blood



DENMARK

PFOS and PFOA levels in children's blood tied to immune suppression



FRANCE

PFOS detected in 27 percent of samples from French public water systems



GERMANY

PFCs detected in drinking water consumed by more than 5 million people



GREENLAND

Rising PFC levels in polar bears



INDIA

15 different PFCs detected in the Ganges River



ITALY

Two chemical plants near the Po River are a major source of PFOA



JAPAN

PFOA contamination near former DuPont plant



NORWAY

12 different PFCs detected in samples of food and beverages



SOUTH AFRICA

PFOA and PFOS were detected in 100 percent of samples from 3 major rivers



SPAIN

PFCs detected in tap water, river water, and bottled water in Tarragona Province



SWEDEN

Elevated levels of PFOA and PFOS near military bases



UNITED KINGDOM

Elevated levels of airborne PFOA in Manchester

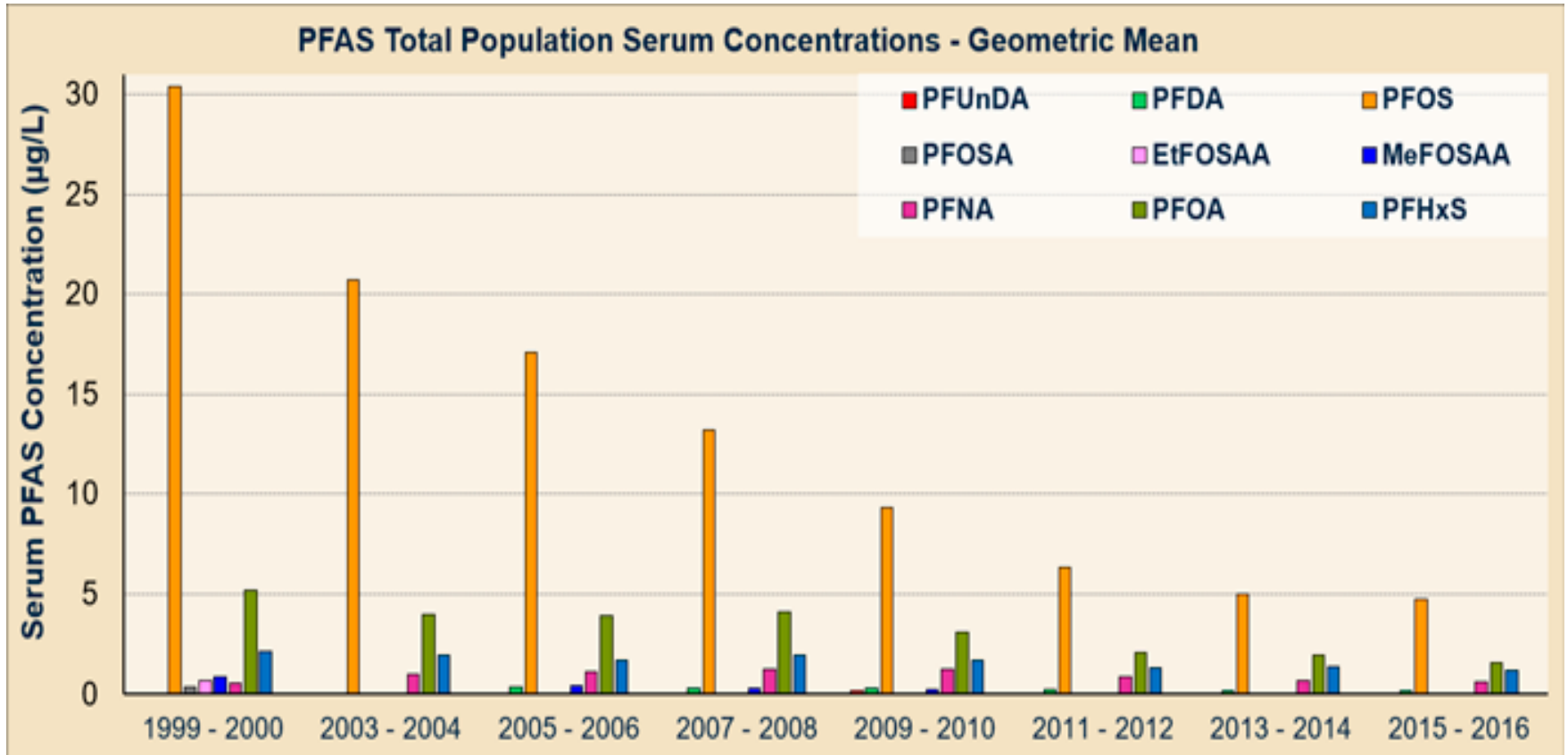


VIETNAM

Study found PFCs in 98–100 percent of Vietnamese women giving birth

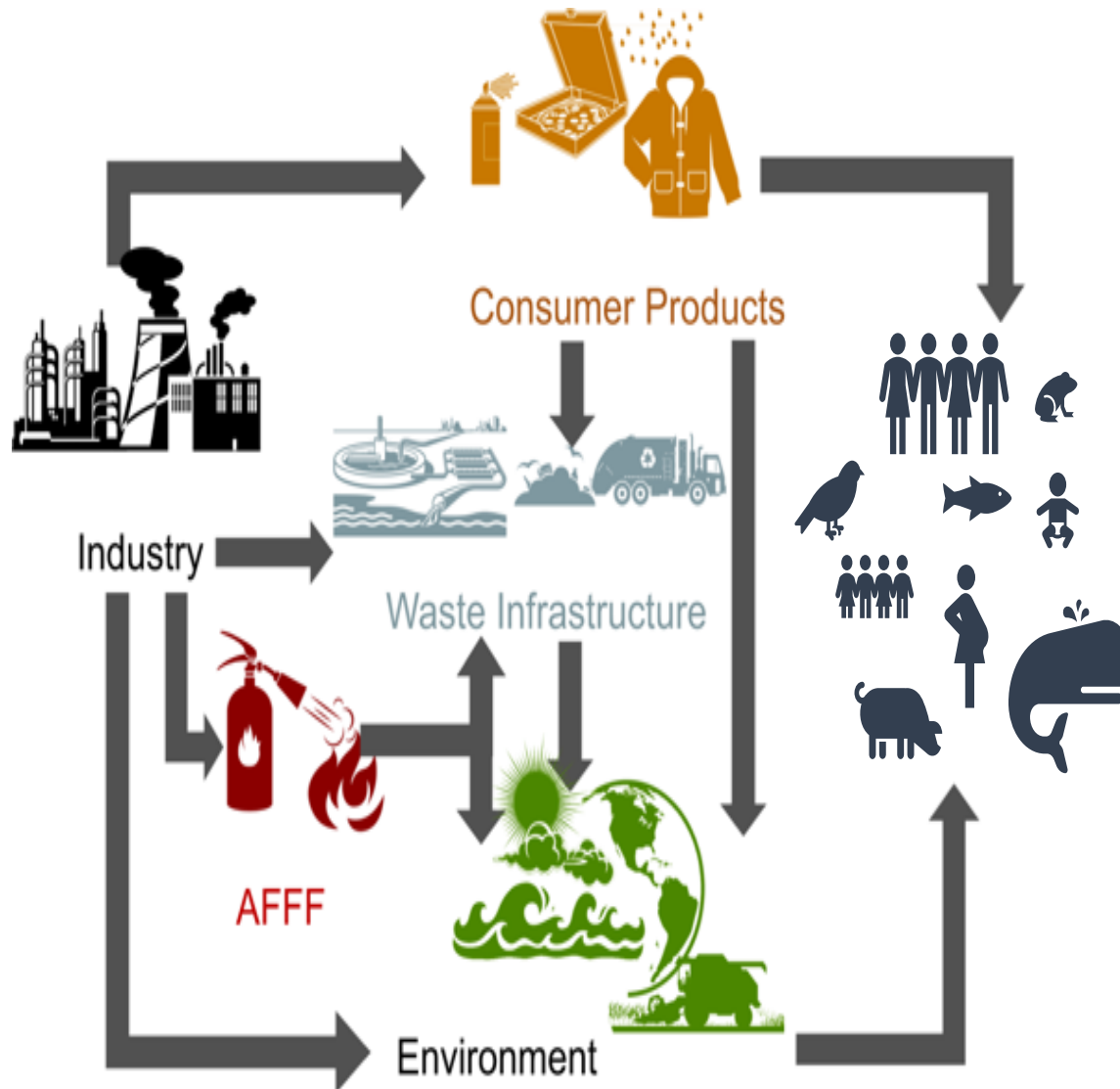
PFOS is a global contaminant (so are PFAS).

PFOS in people in the United States

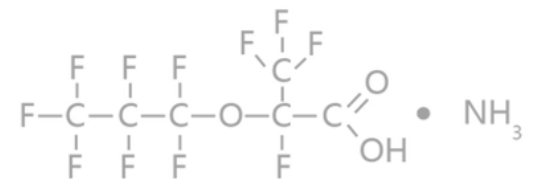
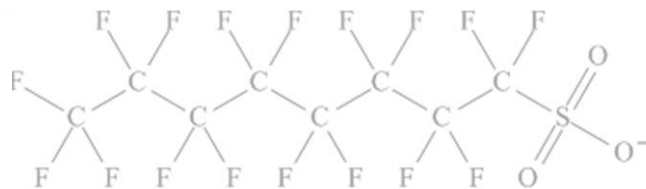
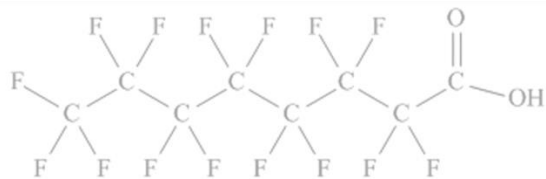


Even with production halted, PFOS is still the PFAS with the highest measured serum concentrations in people (of those PFAS measured).

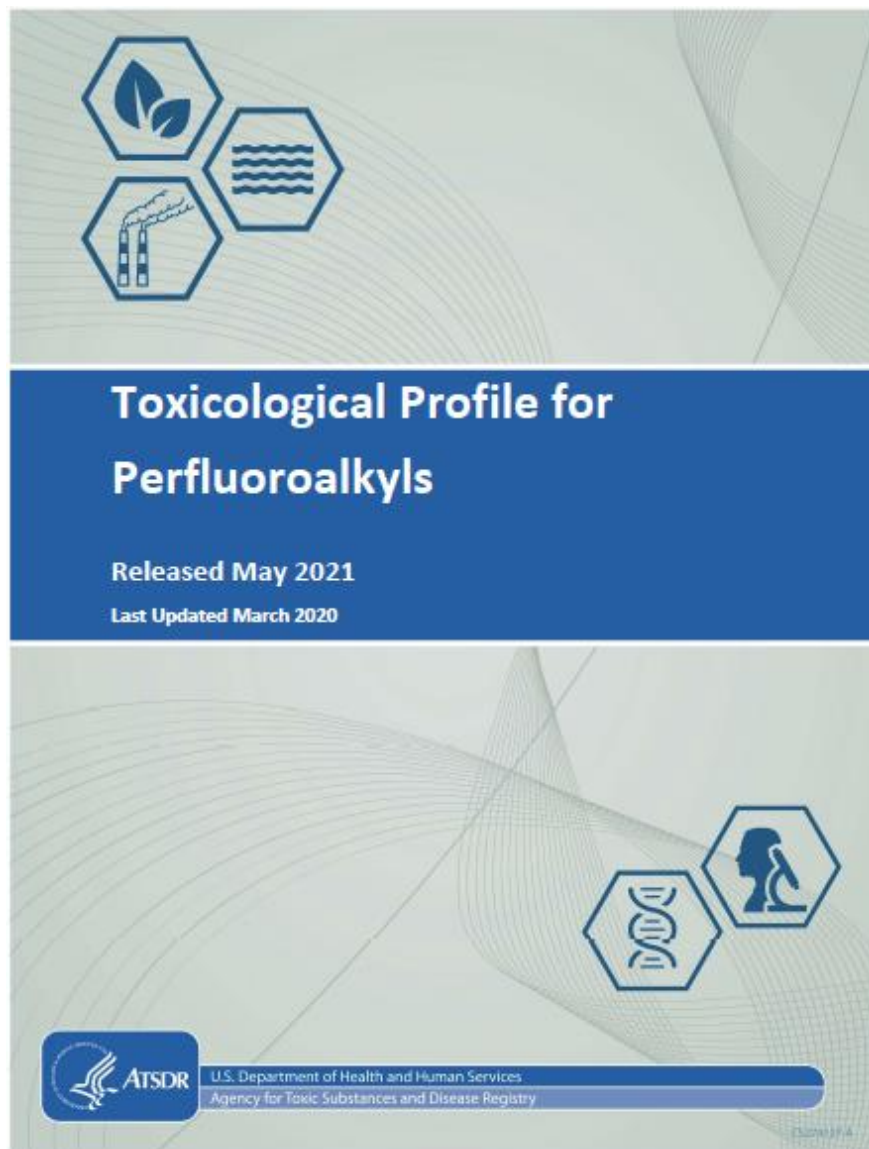
Exposure is via multiple sources and pathways



Summary of PFOS epidemiological findings



Agency for Toxic Substances and Disease Registry (ATSDR)



Health effects linked to PFOS exposure

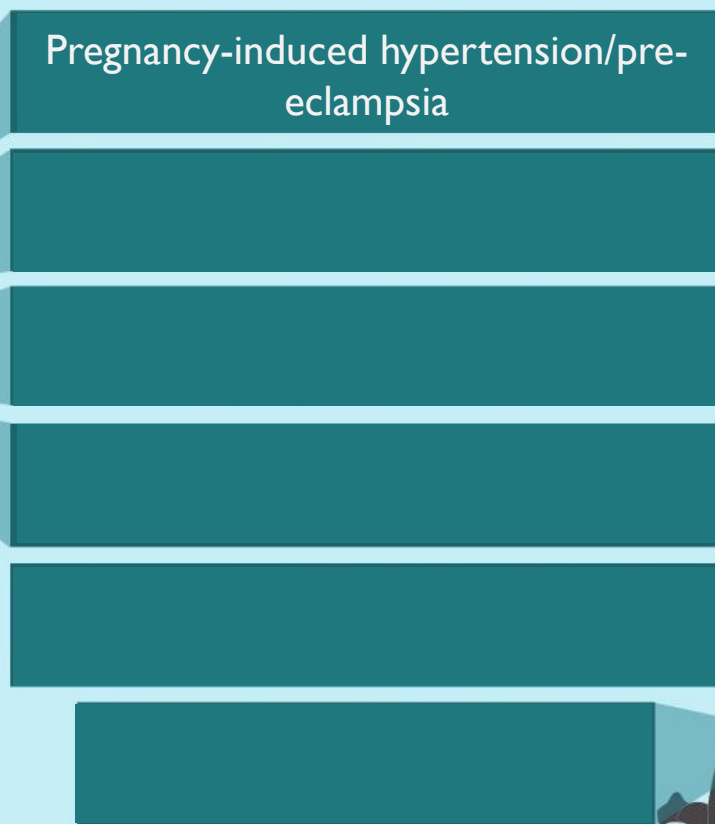
Human studies suggest
PFAS exposure may...



Pregnancy-induced hypertension/pre-eclampsia



in adults



in children

in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Preeclampsia is a disorder of pregnancy/placenta and is a leading cause of maternal morbidity and mortality, affecting ~2-10% of all pregnancies. Only cure is delivery.



in adults

in children

in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Increases in serum liver enzymes

in adults

in children

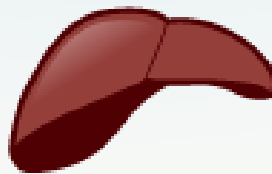
in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Increases in serum liver
enzymes can be an
indication of liver damage.



in adults

in children

in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Increases in serum lipids, including
cholesterol and LDL

in adults

in children

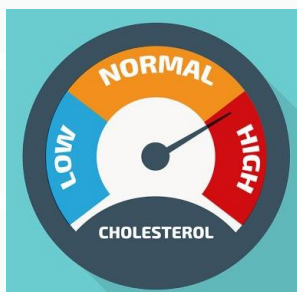
in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Increases in serum
cholesterol and low-density
lipoprotein (LDL) can
increase the risk of
cardiovascular and other
diseases.



in adults

in children

in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Decreased antibody responses to
vaccines

in adults

in children

in pregnant
women



Health effects linked to PFOS exposure



Human studies suggest
PFAS exposure may...

Decreased responses to
vaccines may decrease
protection from the
vaccine but also may
indicate that other parts of
the immune system are
suppressed.



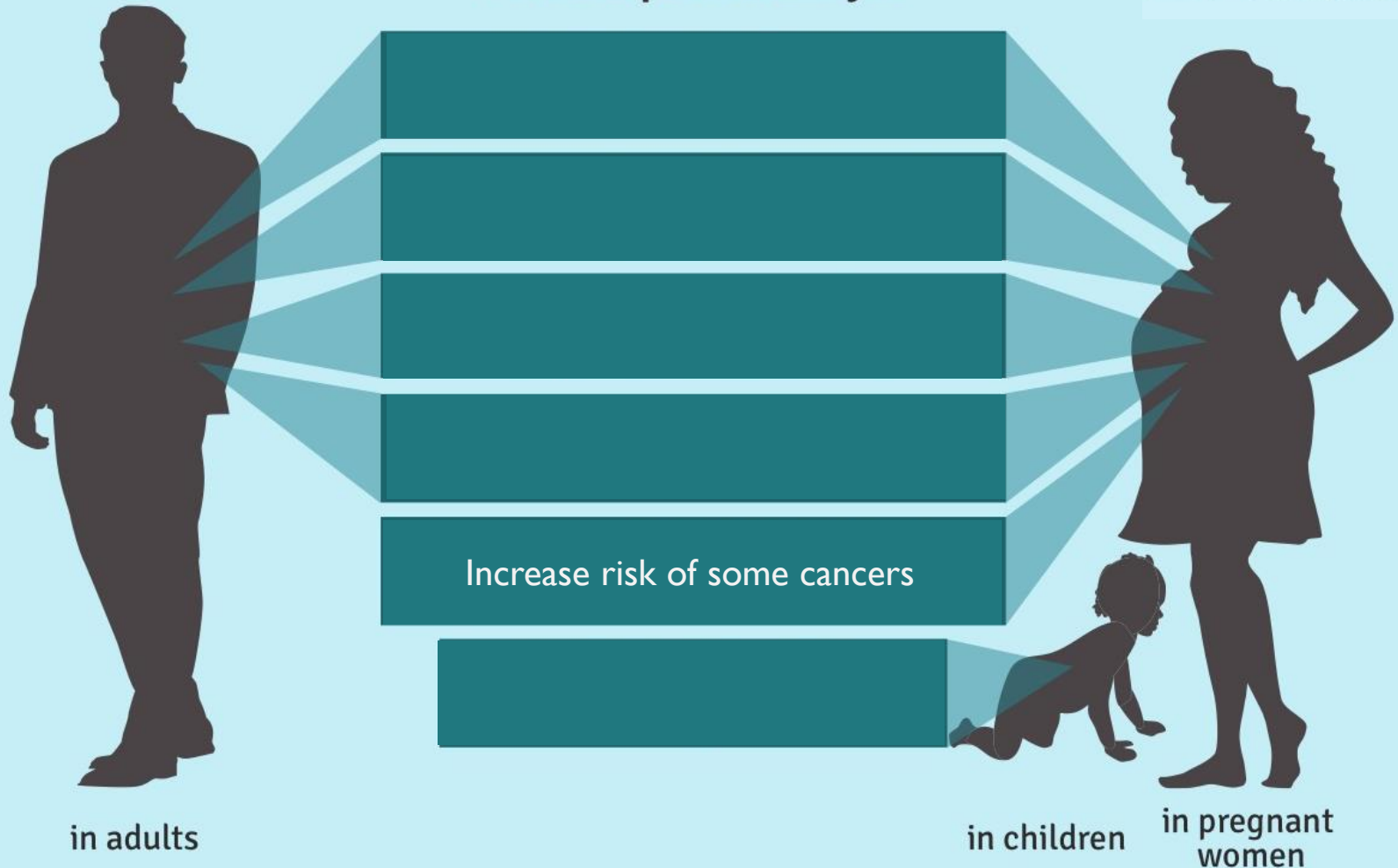
in adults

in children

in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Some studies have found associations between PFOS exposure and bladder cancer, and others have reported increases in prostate and breast cancer. Numbers of studies are limited to date.



in adults

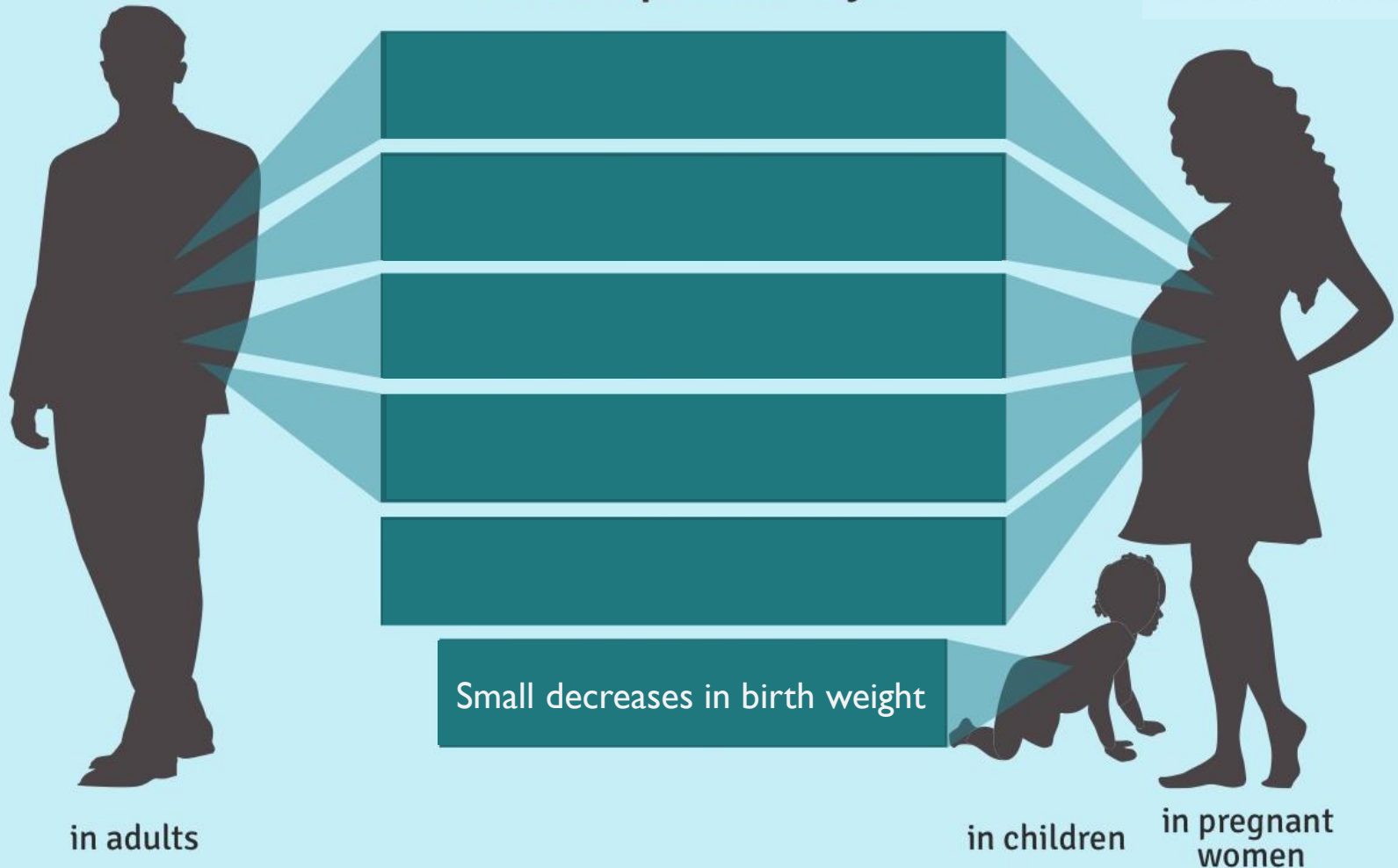


in children

in pregnant
women

Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Health effects linked to PFOS exposure

Human studies suggest
PFAS exposure may...



Babies with low birth weight are more likely to develop health problems later in life.

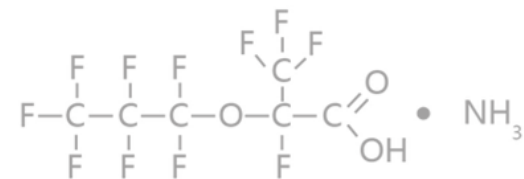
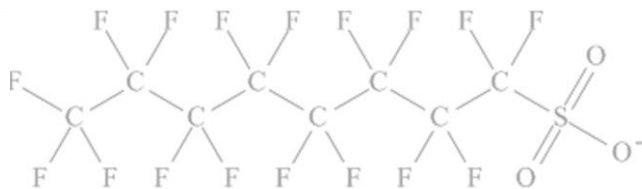
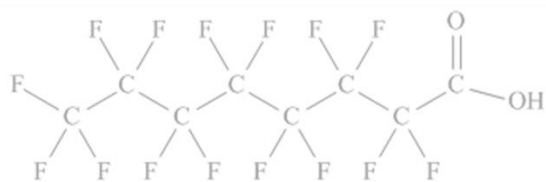


in adults

in children

in pregnant
women

Brief summary of PFOS toxicological findings



Toxicological findings in experimental models exposed to PFOS



Animal studies suggest
PFAS exposure is linked to...



damage to the immune
system

liver damage

birth defects, delayed
development, and newborn
deaths

Information sourced from Agency for Toxic Substances and Disease Registry

Toxicological findings in experimental models

Studies in non-human models allow scientists to:

- 1) confirm what has been seen in human studies;
- 2) establish *causality* between exposure to known concentrations of single PFAS and specific kinds of toxicity;
- 3) explore the molecular (mechanistic) changes that produce toxicity.



From models to people



Epidemiological findings

Liver toxicity
Immunotoxicity
Developmental/reproductive toxicity

Supportive animal studies

Liver toxicity
Immunotoxicity
Developmental/reproductive toxicity



Consistency in observed health effects between studies of people and experimental models *increases our confidence in the strength of the link between exposure and health effects.*

Molecular changes are multiple and varied

Nuclear receptor activation

PPAR α , PPAR γ , PPAR β/δ , CAR, PXR, LXR α and Er α to modify signaling pathways.

Gap junction intercellular communication (GJIC)

Putative mechanism for hepatomegaly and tumor production.

Interference with protein binding

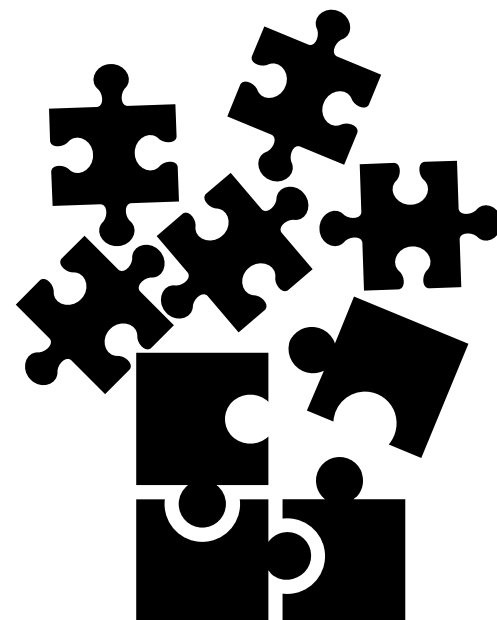
Binding with albumin, liver fatty acid binding protein, transthyretin, and others to alter cell signals and/or functions.

Mitochondrial dysfunction

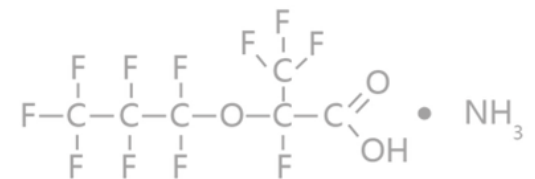
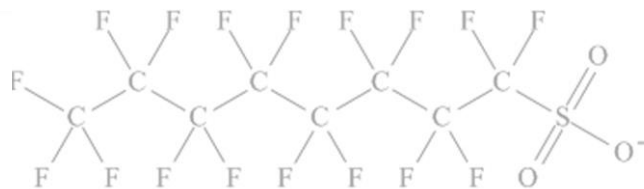
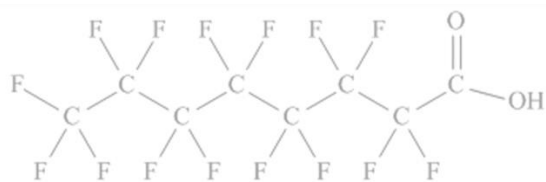
Dysfunctions observed in carbohydrate, lipid and amino acid metabolism as well as oxidative stress. PFAS therefore appear to share features in common with the metabolic syndrome.

Direct cytotoxicity

Partitioning into lipid bilayers, altered calcium homeostasis, and other interactions may lead to cell toxicity.



Other information about PFOS and other PFAS



U.S. National Toxicology Program review of immunotoxicity



National Toxicology Program
U.S. Department of Health and Human Services

SYSTEMATIC REVIEW OF
IMMUNOTOXICITY ASSOCIATED WITH EXPOSURE TO
PERFLUOROOCTANOIC ACID (PFOA) OR PERFLUOROOCTANE
SULFONATE (PFOS)

PFOA and PFOS suppress antigen-specific antibody responses in experimental models (high level of evidence) and humans (moderate level of evidence).

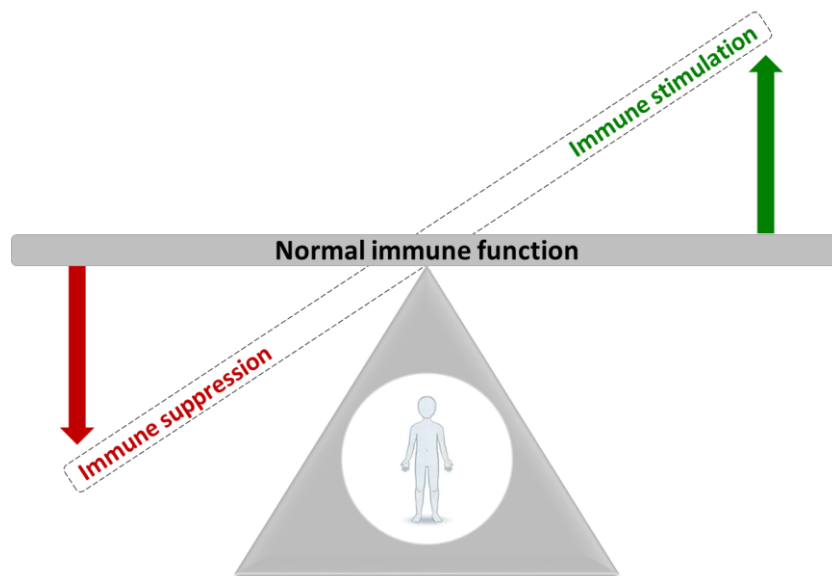
Other immune effects supporting this weight-of-evidence classification:

- Increased hypersensitivity-related outcomes.
- Suppression of innate immune responses (i.e., NK cell function).
- Alterations in disease resistance/infectious disease outcomes.
- Findings of autoimmunity.

NTP conclusion: PFOA and PFOS are presumed to be immune hazards to humans.

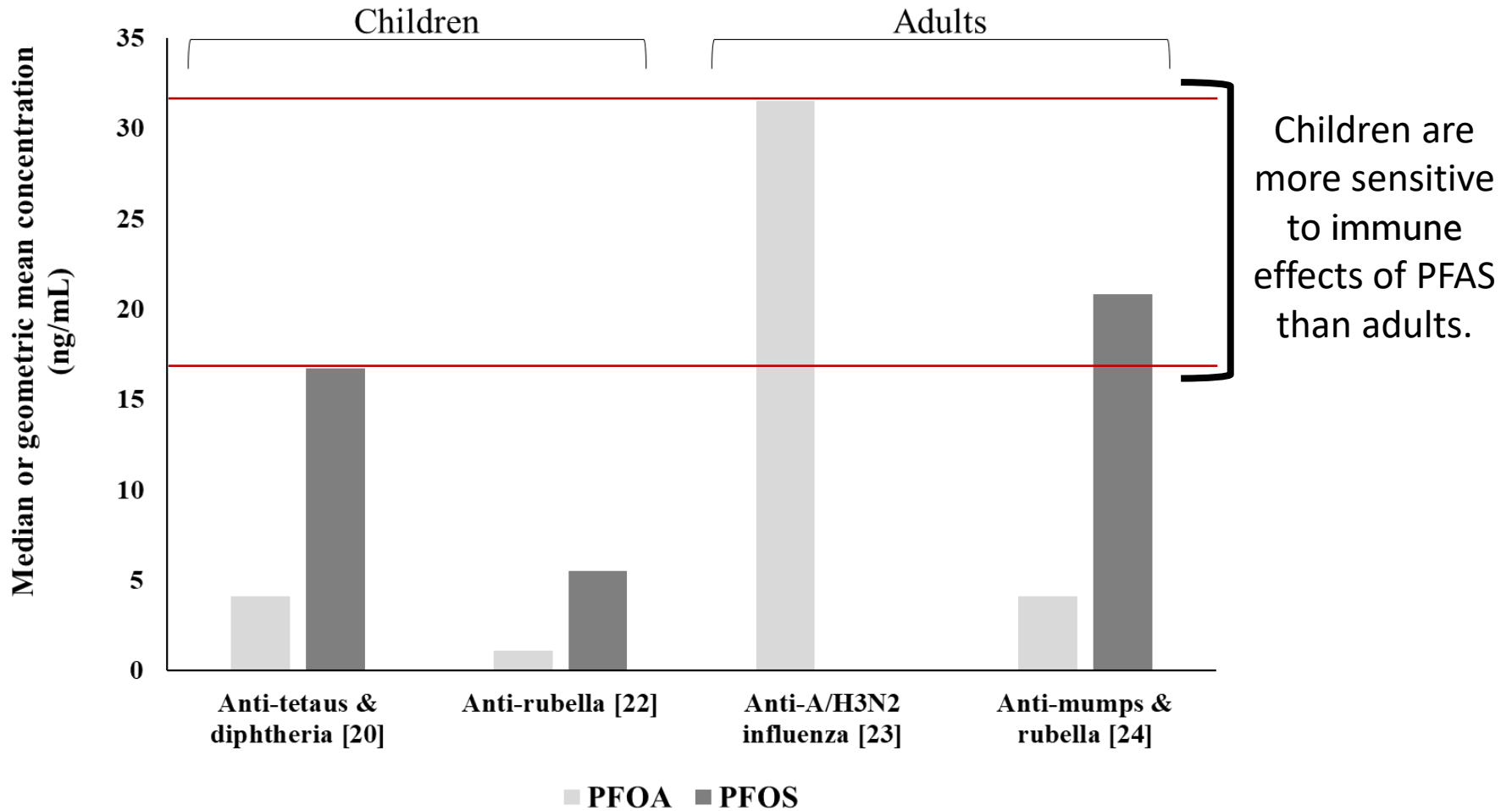
Decisions based on PFOS immunotoxicity

- States of New Jersey and Michigan maximum contaminant level for PFOS in drinking water is based on immunotoxicity
 - NJ PFOS MCL: 13 ng/L (parts per trillion)
 - MI PFOS MCL: 16 ng/L
- European Food Safety Authority (EFSA) revised tolerable weekly intake for PFOS based on immunotoxicity
 - EFSA TWI: 4.4 ng/kg/bw (for PFOS, PFOS, PFNA, and PFHxS)



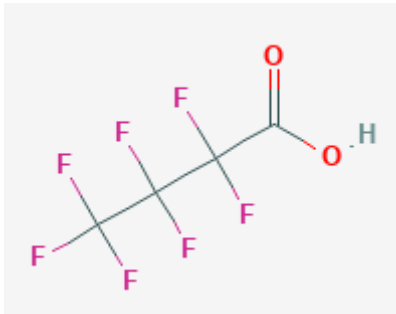
Risks from PFOS exposure to the immune system are real.

Why the immune system matters

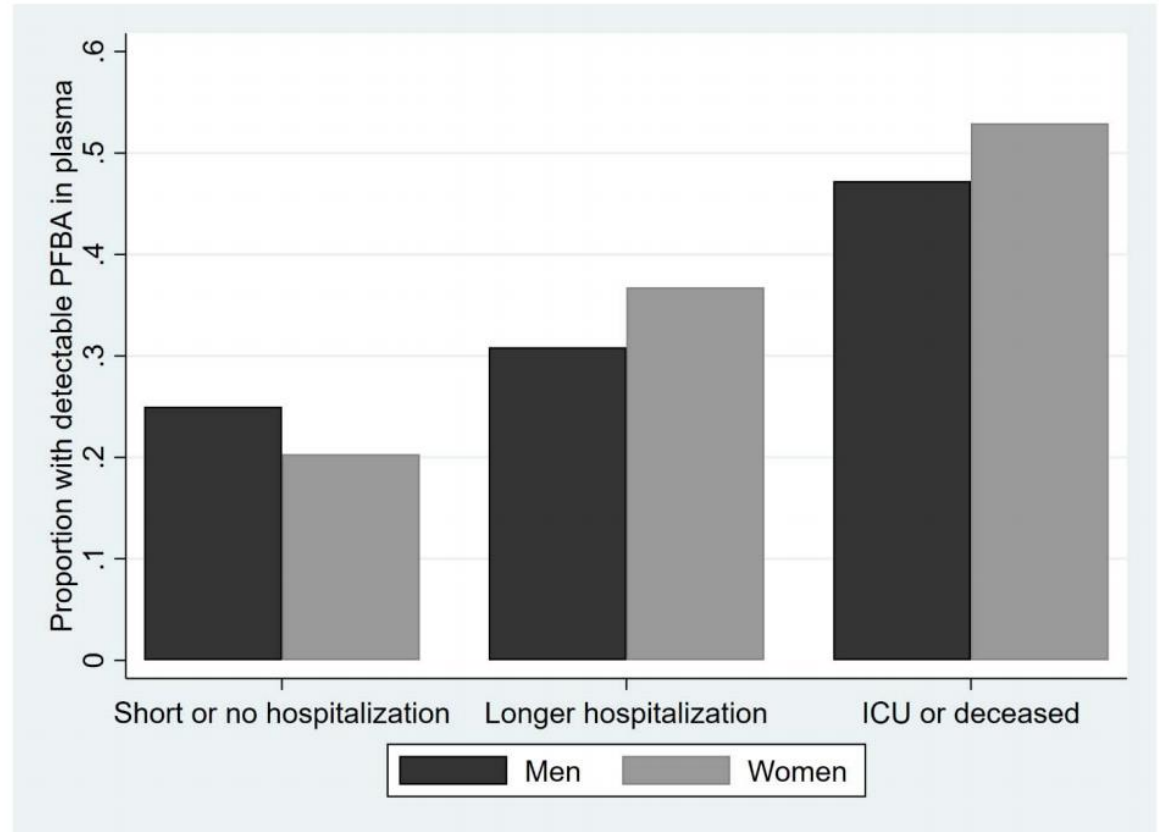


Why the immune system matters

Patients with higher PFBA concentrations in their blood had COVID infections that required longer hospital stays or worse infections.



**This is
PFBA**



Brief conclusions

PFAS

Are detectable in the environment, including water, soil, air, and food.
Some have been detected in people.

Cousins et al. (2019) made a case for characterizing non-essential uses of PFAS.

Eliminate non-essential uses of PFAS and find safe substitutes.

Kwiatkowski et al. (2020) recommended a scientific basis for managing PFAS as a class.

Manage all PFAS as a single class due to concerns about persistence, bioaccumulation, mobility, and/or toxicity.

