

**Adverse effects of PFAS on Immune System Health:  
*Complicating recovery during the COVID-19 Pandemic?***



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Professor and chair, Environmental Medicine, University of Southern Denmark  
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Fellow, American Association for the Advancement of Science (1994)

Bernardino Ramazzini Award, Collegium Ramazzini (2015)

John R. Goldsmith Award, International Society for Environmental Epidemiology (2016)

European Environment Agency: Member, Scientific Committee (2012-2020)

Founding Editor, Environmental Health (2002-)

Service as health expert on PFASs for State of Minnesota and exposed communities

Co-Director, STEEP SRP Center; Co-Director ATSDR PFAS study in New England

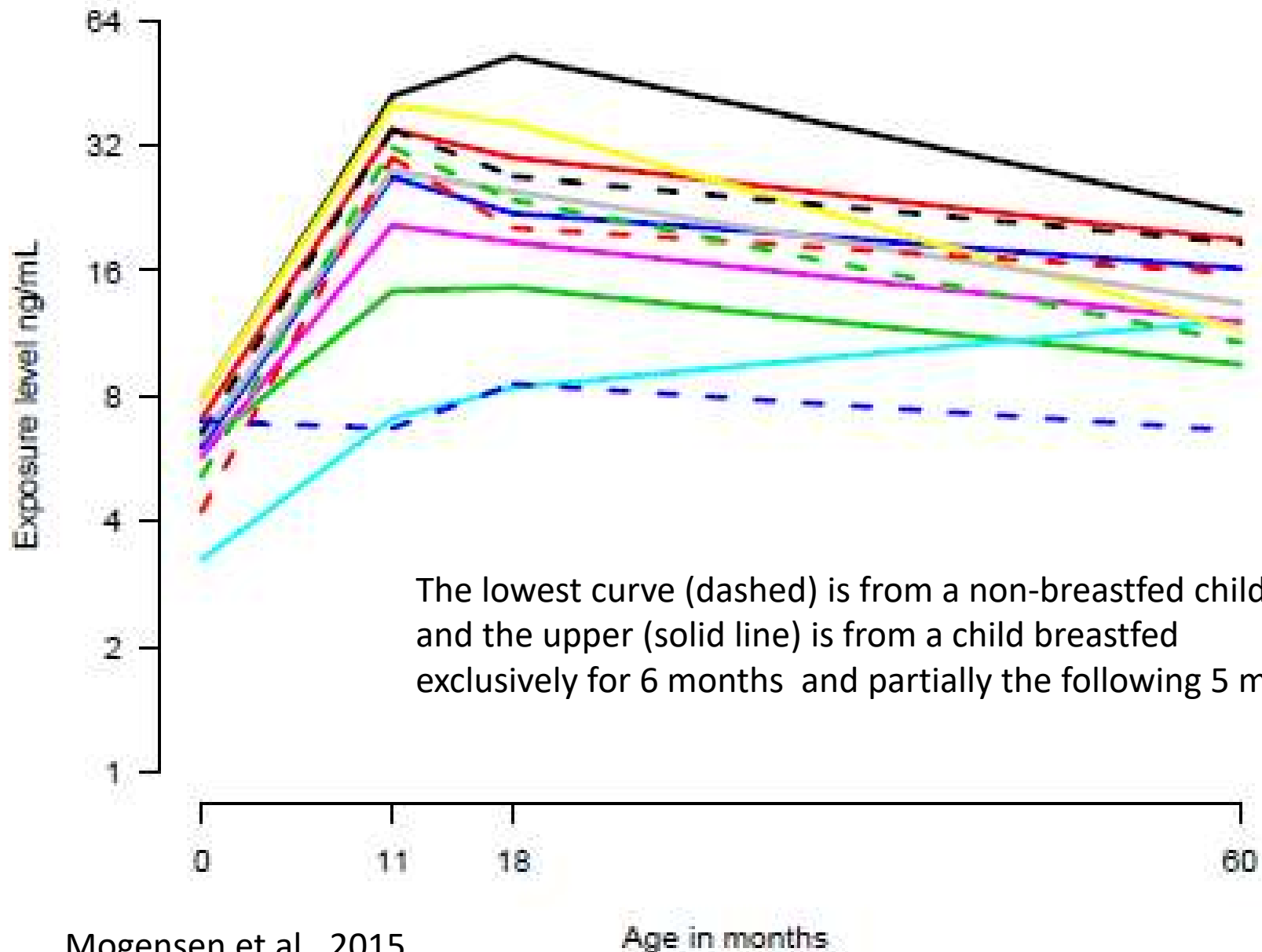
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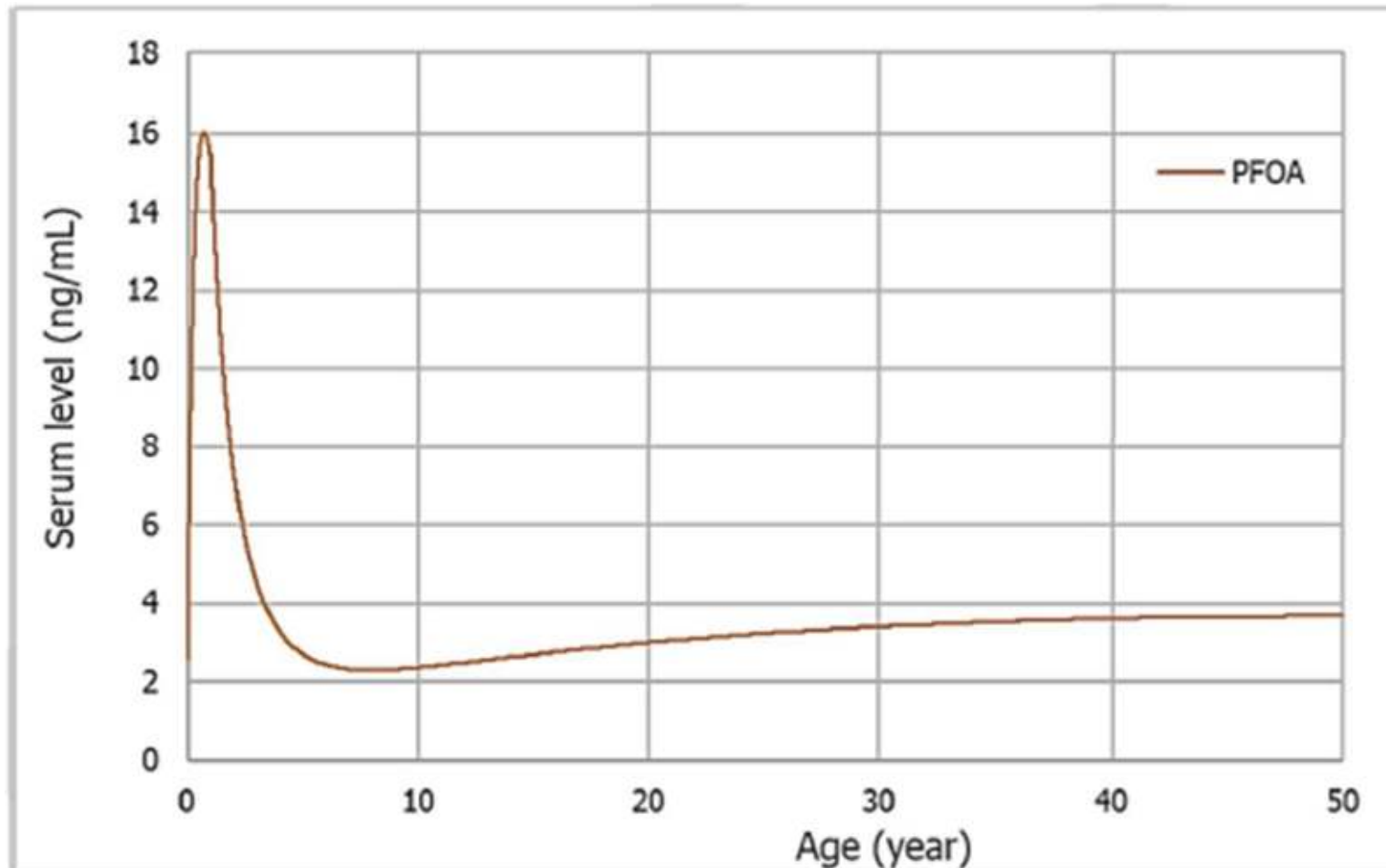
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<b>Year</b>	<b>Exposure evidence</b>	<b>Unpublished</b>
1968	Organofluoride compounds in human blood	
1976	Organofluorines in workers' blood	
1981	PFOA found in cord blood (female worker)	
1993	Transfer into milk observed in goats	
1998	PFOS found in general population blood	
2004	PFAS detected in human milk	
2015	Breastfeeding shown to be major source of PFAS exposure in infants	

## PFOS transfer via human milk impacts infant serum levels





Serum-PFOA in a woman exposed in utero, via breastfeeding for 12 months and then via diet at 0.33 ng/kg bw per day (EFSA 2020).

## Immunotoxicity

Unpublished

1978 Monkey study: PFOA immunotoxicity

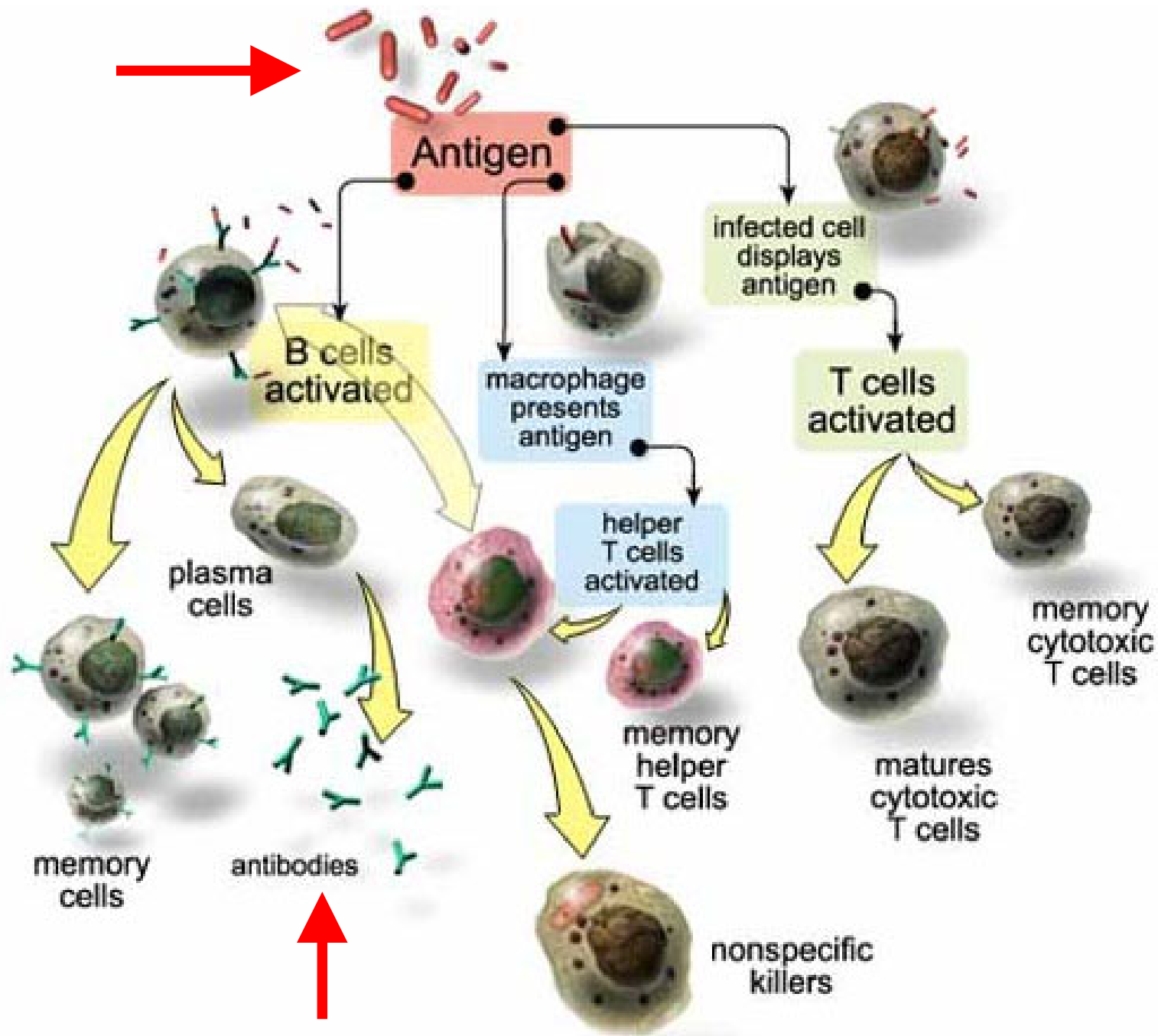
1992 Leukocyte changes in workers

2008 Mouse immunotoxicity at serum PFAS concentrations similar to humans

2012 PFAS immunotoxicity in children

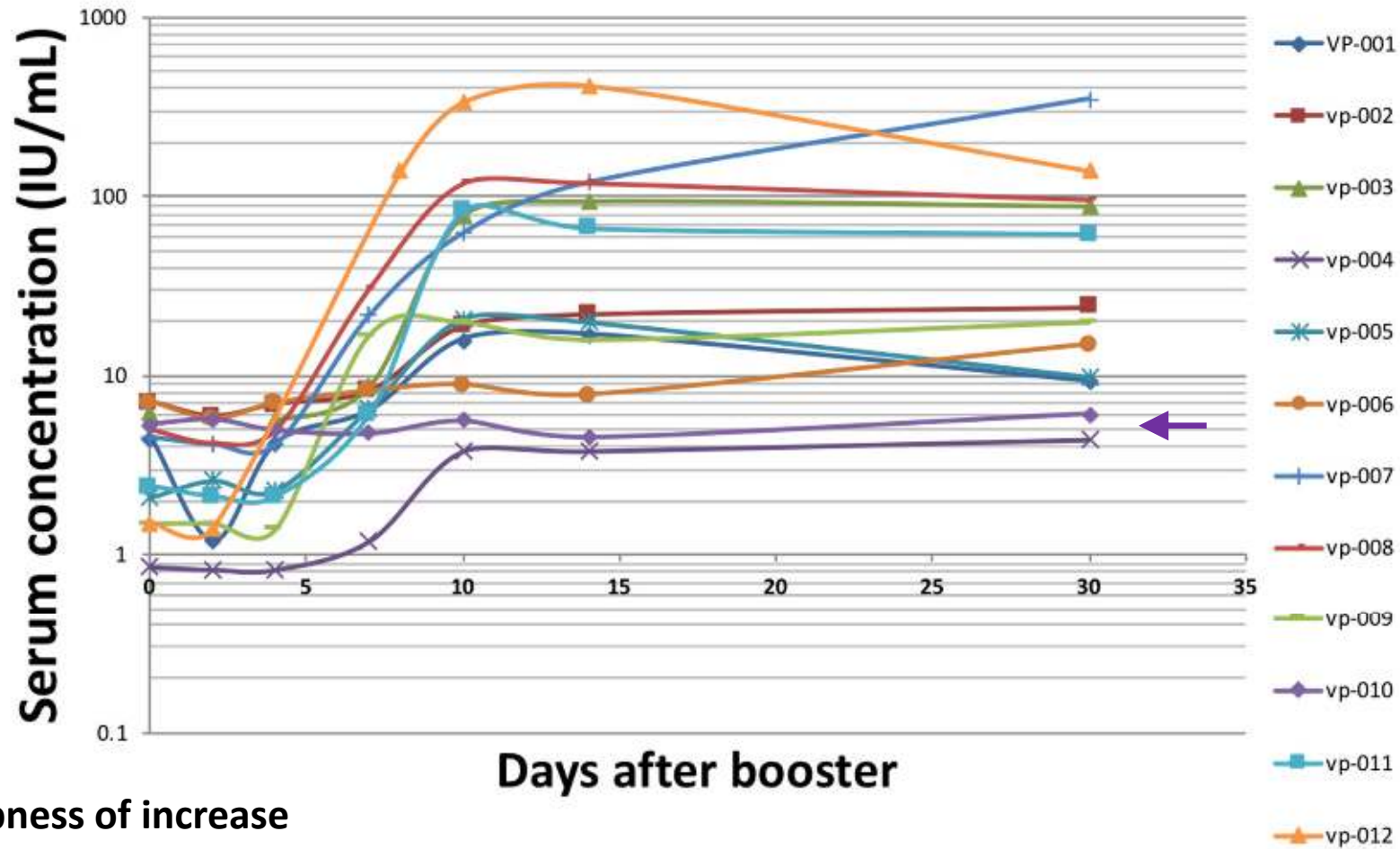
2013 Benchmark Dose calculations suggest that guidelines are far from protective

2020 EFSA considers immunotoxicity the critical effect and lowers tolerable dose



(Source: the Human Immune Response System [www.uta.edu/chagas/images/immunSys.jpg](http://www.uta.edu/chagas/images/immunSys.jpg))

# Change in tetanus antibody concentration after booster in 12 adult volunteers



Steepness of increase  
inversely associated  
with serum-PFAS

Days after booster  
(Kielsen et al., 2015)



> [J Occup Environ Med.](#) 1998 Apr;40(4):311-6. doi: 10.1097/00043764-199804000-00004.

## **Absenteeism among employees who participated in a workplace influenza immunization program**

[G W Olsen](#)<sup>1</sup>, [J M Burris](#), [M M Burlew](#), [M E Steinberg](#), [N V Patz](#), [J A Stoltzfus](#), [J H Mandel](#)

Affiliations – collapse

### **Affiliation**

<sup>1</sup> Medical Department, 3M Company, 3M Center, St. Paul, MN 55144, USA.

PMID: 9571521 DOI: [10.1097/00043764-199804000-00004](#)

*No information on absenteeism  
among PFAS-exposed 3M employees*



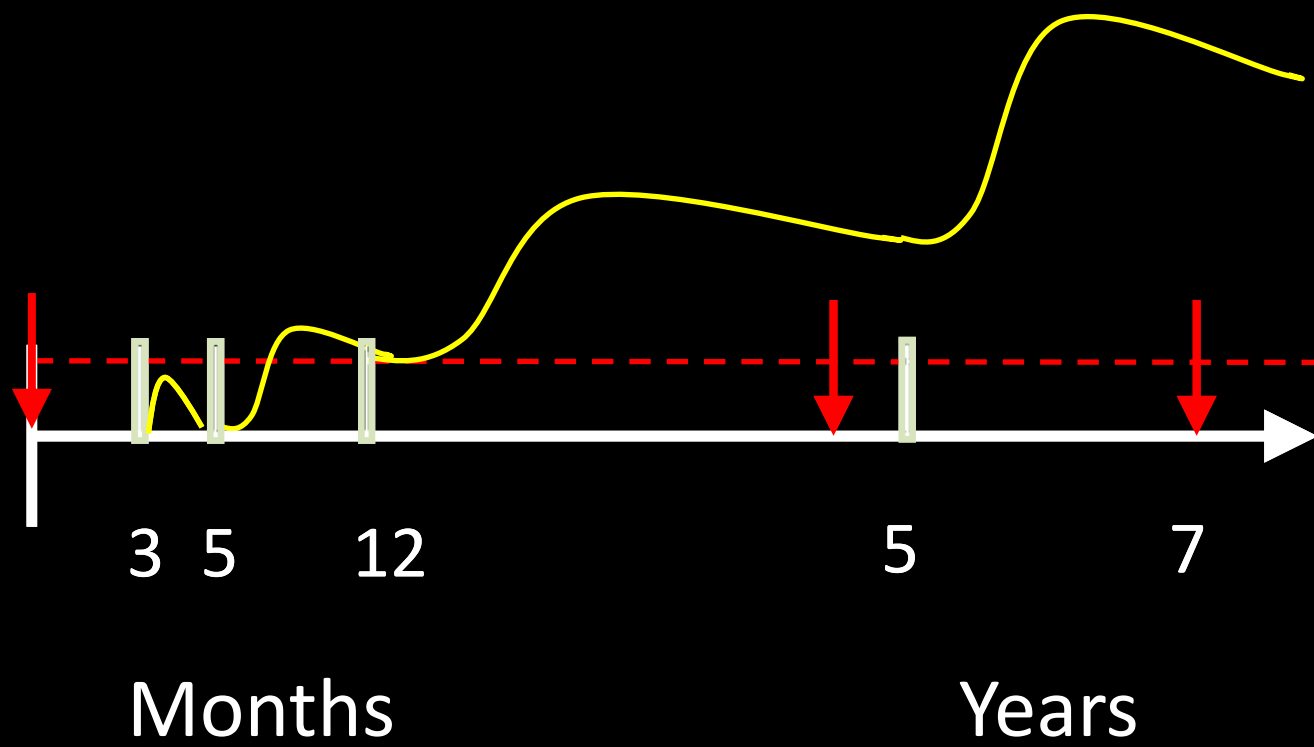
# Faroe Islands

- **Homogeneous, western culture**
- **High participation rate in prospective studies**
- **Fishing community with high seafood intake (+ whale)**
- ***Wide range of exposures from traditional food (pilot whale)***
- **Total population - 48,000**

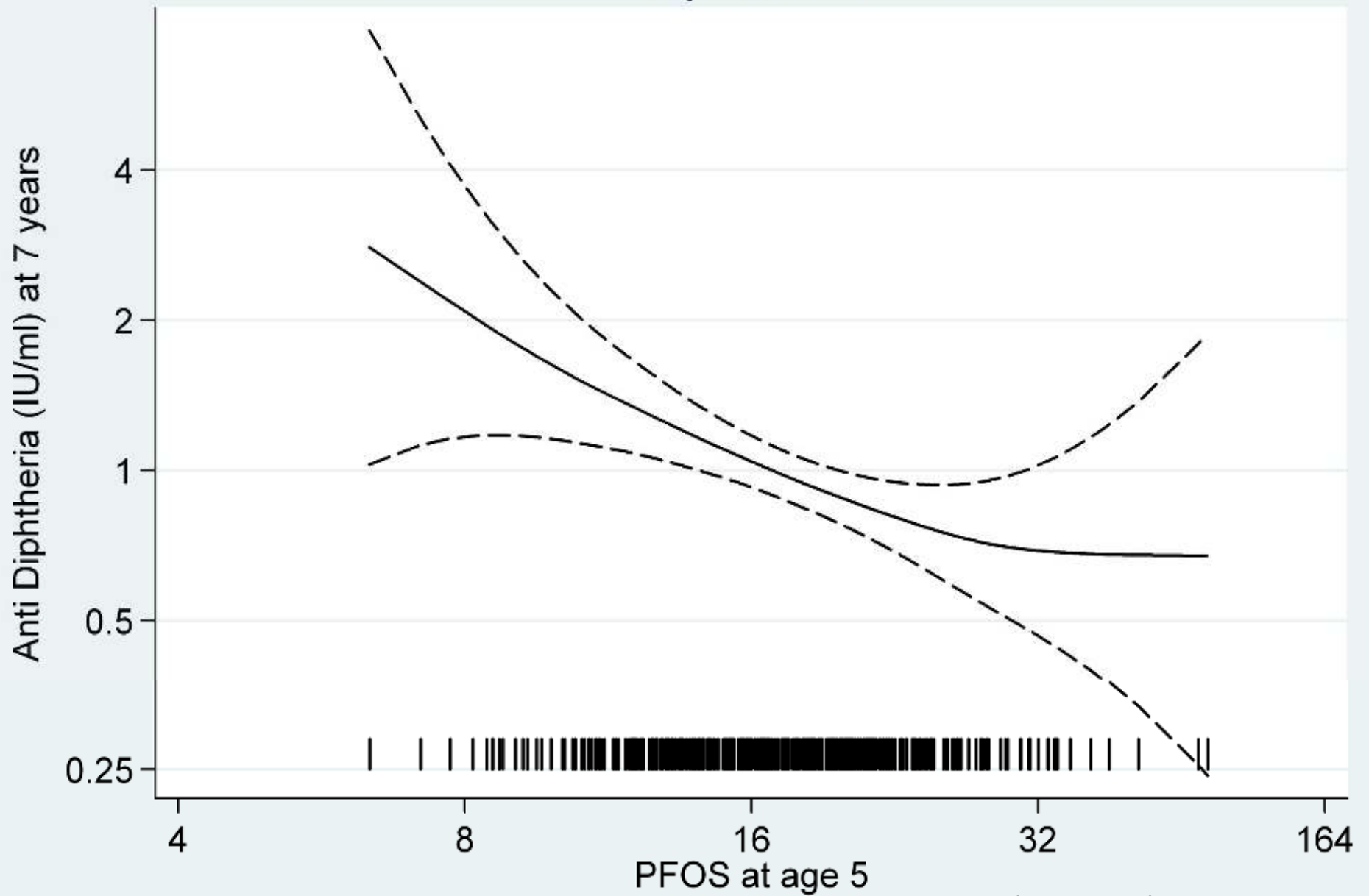
|| Vaccination

↓ Blood sample

Antibody concentration



# Diphtheria



Grandjean et al., JAMA, 2012



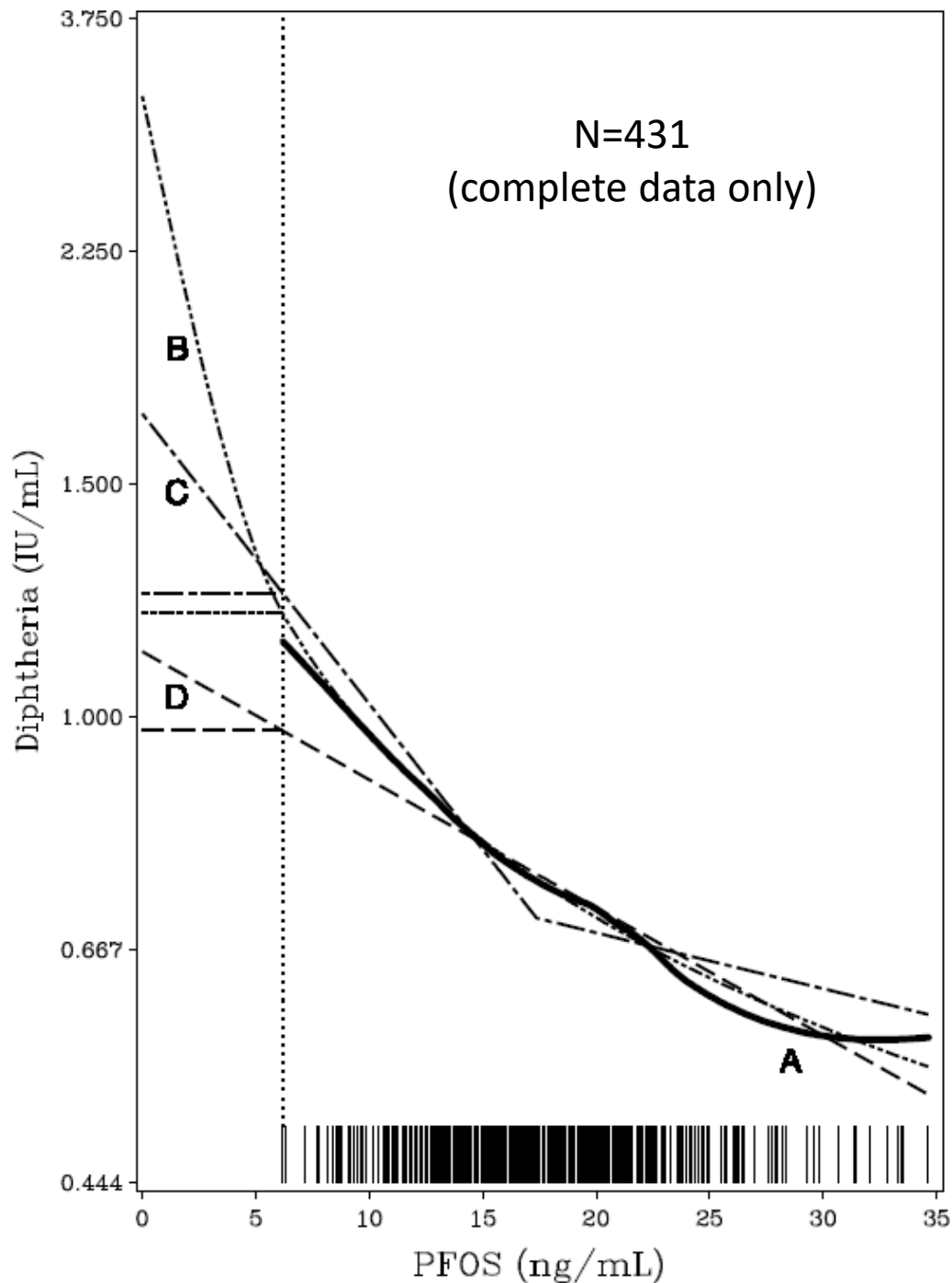
National Toxicology Program  
U.S. Department of Health and Human Services

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

(July 2016)

“The NTP concludes that **PFOS** is presumed to be an immune hazard to humans...”

“The NTP concludes that **PFOA** is presumed to be an immune hazard to humans...”



## BMC calculations

### Serum-PFAS at age 5

### Serum antibody at age 7

BMCL at BMR = 5%  
 ~1.3 ng PFOS/mL serum  
 ~0.3 ng PFOA/mL serum  
 for linear curve

Lower for log curve  
 Higher for BMR = 10%  
 (2.6 and 0.6 ng/mL)

*Environmental Health* 2013, 12:35

# Exposure error in simple linear regression

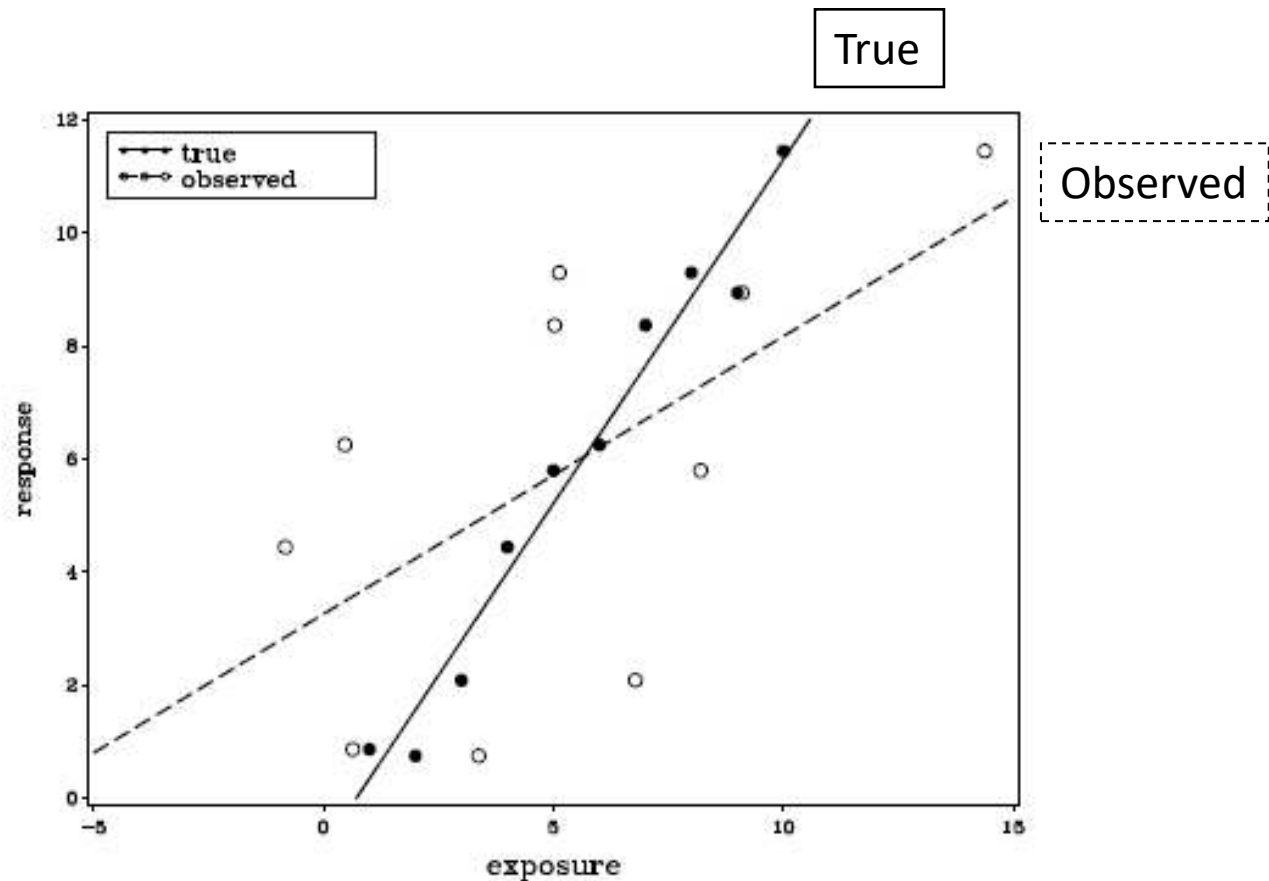
$X$ : true exposure,  $W$ : measured exposure

Classical additive error:  $W = X + U$  with  $U$  independent of  $X$

$Y = \alpha + \beta \cdot X + \epsilon$ , Naive Analysis: replace  $X$  by  $W$

Standard regression analysis assumes no imprecision of the independent variables

Courtesy:  
Esben Budtz-Jorgensen



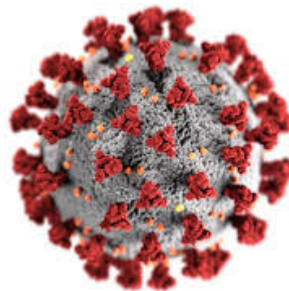
Change (in %) of tetanus and diphtheria antibody concentration at age 5 years associated with a doubling in *calculated* serum-PFOA concentrations in infancy (95% confidence intervals)

Age (months)	Tetanus		Diphtheria	
	Change	95% CI	Change	95% CI
0	-22.3	-35.3, -6.6	-18.9	-33.2, -1.7
3	-32.8	-47.0, -14.9	-12.7	-31.0, 10.4
6	-25.8	-39.5, -8.9	-6.9	-24.1, 14.1
12	-17.8	-31.1, -1.9	-4.1	-19.4, 14.2



# Risk factors for COVID-19

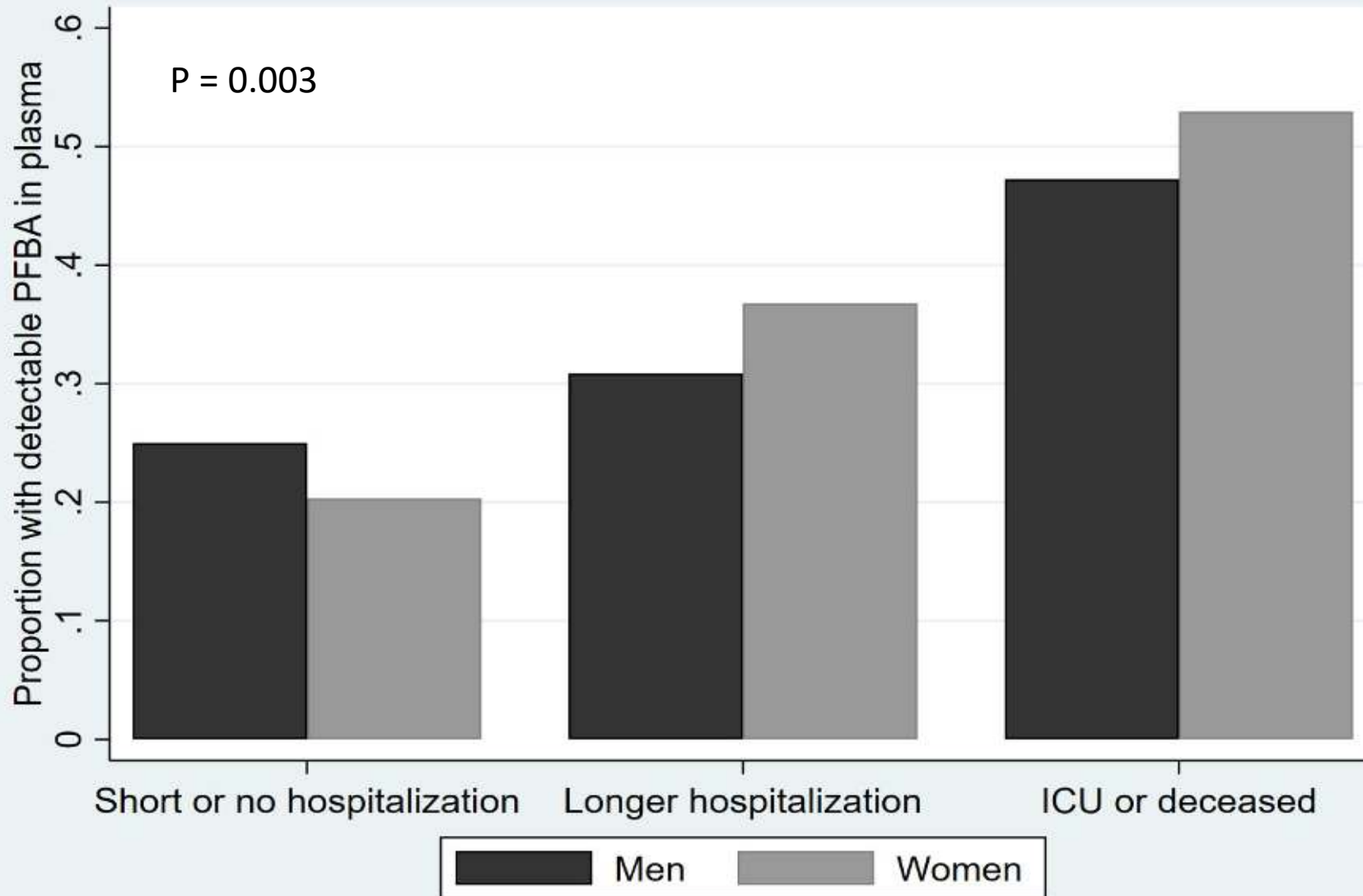
- **Elderly** Have higher accumulated PFAS levels in blood
- **Men** Have higher accumulated PFAS levels in blood
- Existing disease, such as
  - **Diabetes** Occur at increased incidence when PFAS exposure is elevated
  - **Obesity** Occur at increased incidence when PFAS exposure is elevated



# Study design

- Plasma from residual volumes from diagnostic blood tests at hospitals (30-70 years)
- All 323 subjects positive for SARS-CoV-2
- Study conducted without informed consent
- All information anonymous on secure server
- Health and demographic information from existing national registers
- Clinical course: no hospitalization, two weeks, or longer, intensive care, and death
- Adjustment for age, sex, chronic disease, ethnicity

<https://doi.org/10.1101/2020.10.22.20217562>

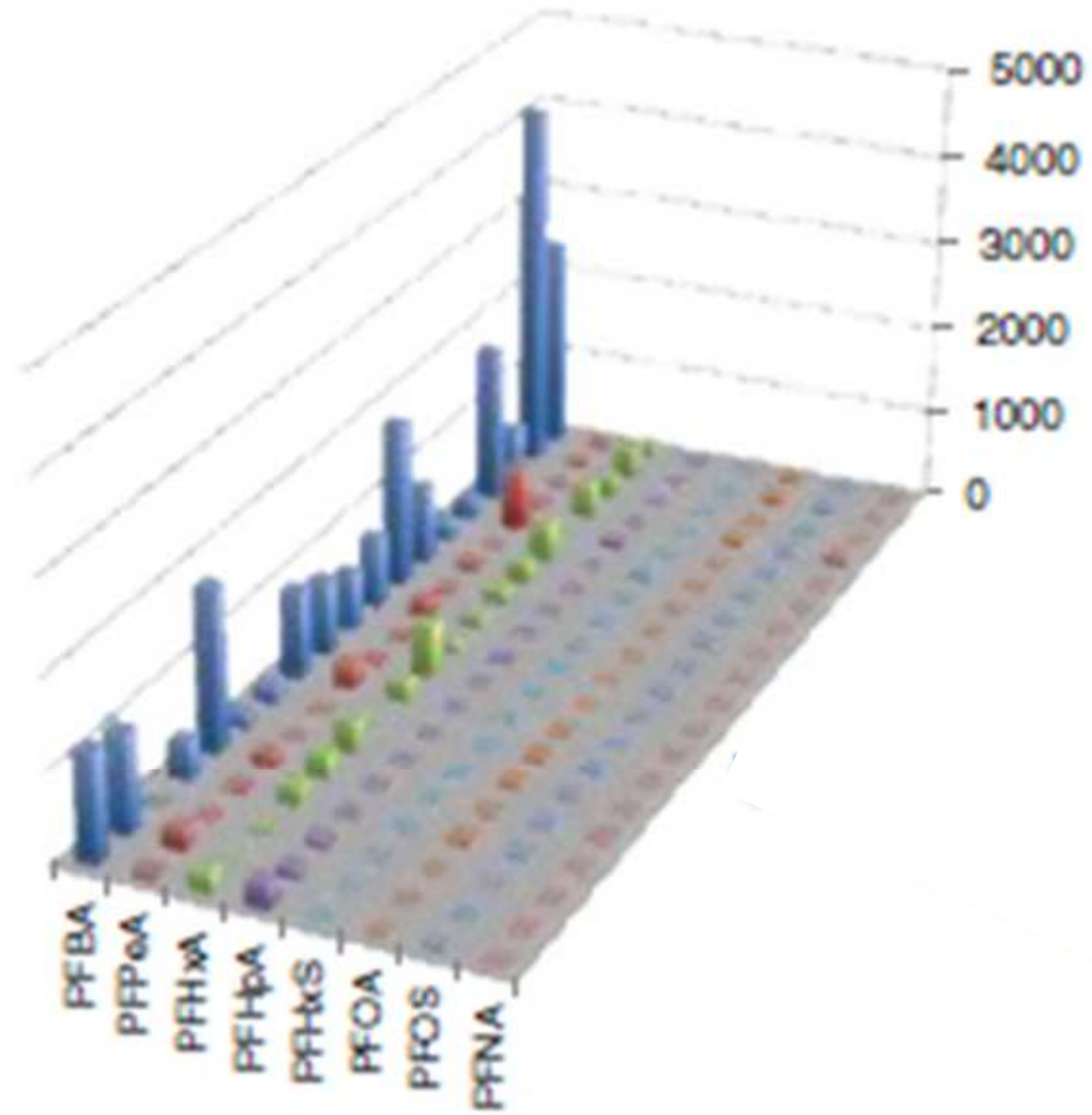


44 men and 64 women with up to two weeks of hospitalization

94 men and 68 women with longer hospitalization

36 men and 17 women admitted to the intensive care unit (ICU) or deceased

Lung



Perez et al., 2013

# PFAS and immune dysfunction

- Lower *antibody response* to some vaccines in children and adults
- More frequent *fever* in children
- ...and *hospitalization* for infection
- Likely increased *severity* of COVID-19
- Possible *autoimmunity/allergy*
- Other adverse outcomes possible

# Challenges in identifying and preventing PFAS-associated adverse effects

- PFASs used for more than 70 years
- Almost no independent PFAS science before 2000
- Immunotoxicity internally known in 1978
- In humans, antibody response to vaccines
- Most focus on PFASs present in blood
- PFBA low in blood, accumulates in lungs
- Blood concentrations may not reflect retention
- PFBA used as precursor/substitute for legacy PFASs
- Prevention focus on PFASs as a group?

# Drinking Water Health Advisory Levels

2009 (U.S.EPA):

Provisional level of 400 ppt for PFOA  
and 200 ppt for PFOS

2016 (U.S.EPA):

Guidance level of 70 ppt for total of PFOA and PFOS

2020: EFSA proposal for 4 PFASs

TWI (for PFOA+PFNA+PFHxS+PFOS) 8 ng/kg bw · wk  
Corresponds to 2.2 ppt in water

# STEEP SRP Center



## STEEP Mission

*Address the ubiquitous human health threat of PFASs through rigorous interdisciplinary science to redefine dose exposure benchmarks, develop novel detection techniques, and prepare communities to expect long-term solutions for contaminated sites.*

## STEEP Vision

*To avert human and environmental health impacts of PFASs exposure and disseminate lessons learned to help avoid similar contamination problems in the future.*

THE  
UNIVERSITY  
OF RHODE ISLAND



SCHOOL OF PUBLIC HEALTH



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More information about STEEP is available at: <https://web.uri.edu/steep/> and [https://tools.niehs.nih.gov/erp/programs/Program\\_detail.cfm?Project\\_ID=P42ES027736](https://tools.niehs.nih.gov/erp/programs/Program_detail.cfm?Project_ID=P42ES027736)