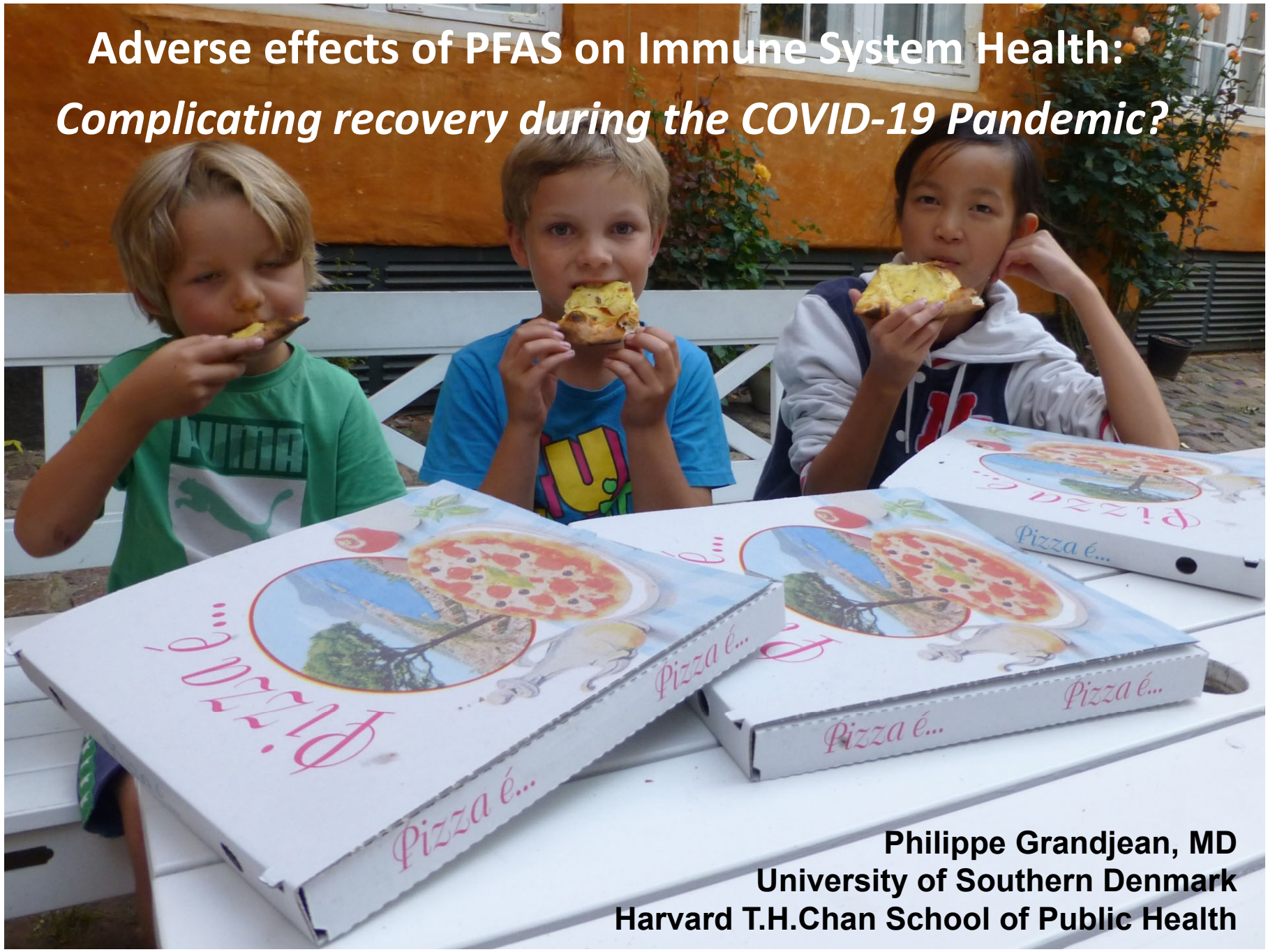
Adverse effects of PFAS on Immune System Health:

Complicating recovery during the COVID-19 Pandemic?



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Professor and chair, Environmental Medicine, University of Southern Denmark

and Adjunct Professor of Environmental Health, Harvard University

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-)

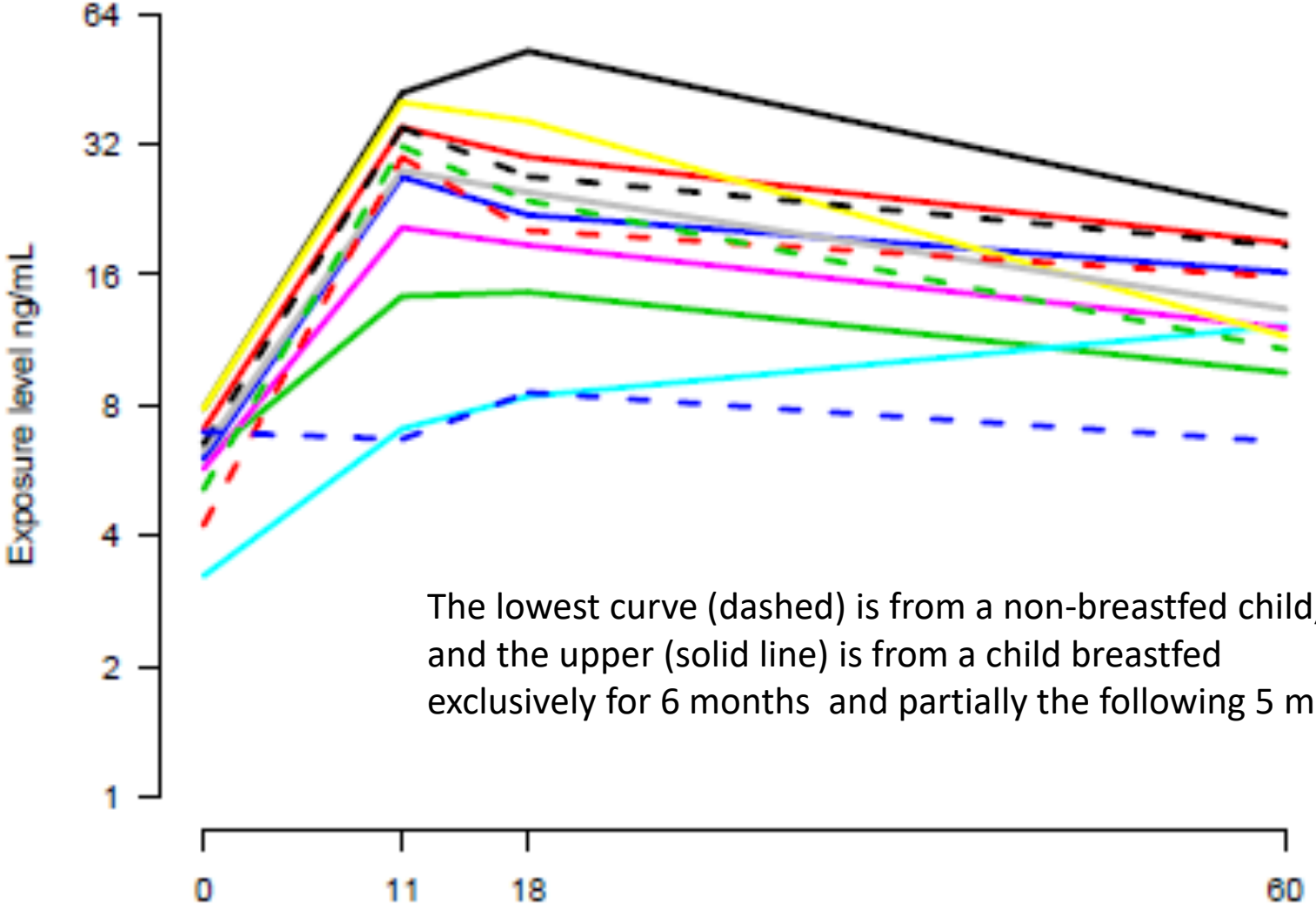
Service as health expert on PFASs for State of Minnesota and exposed communities

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

I declare that my research is funded by public sources only and that I have no conflicts of Interests to declare.

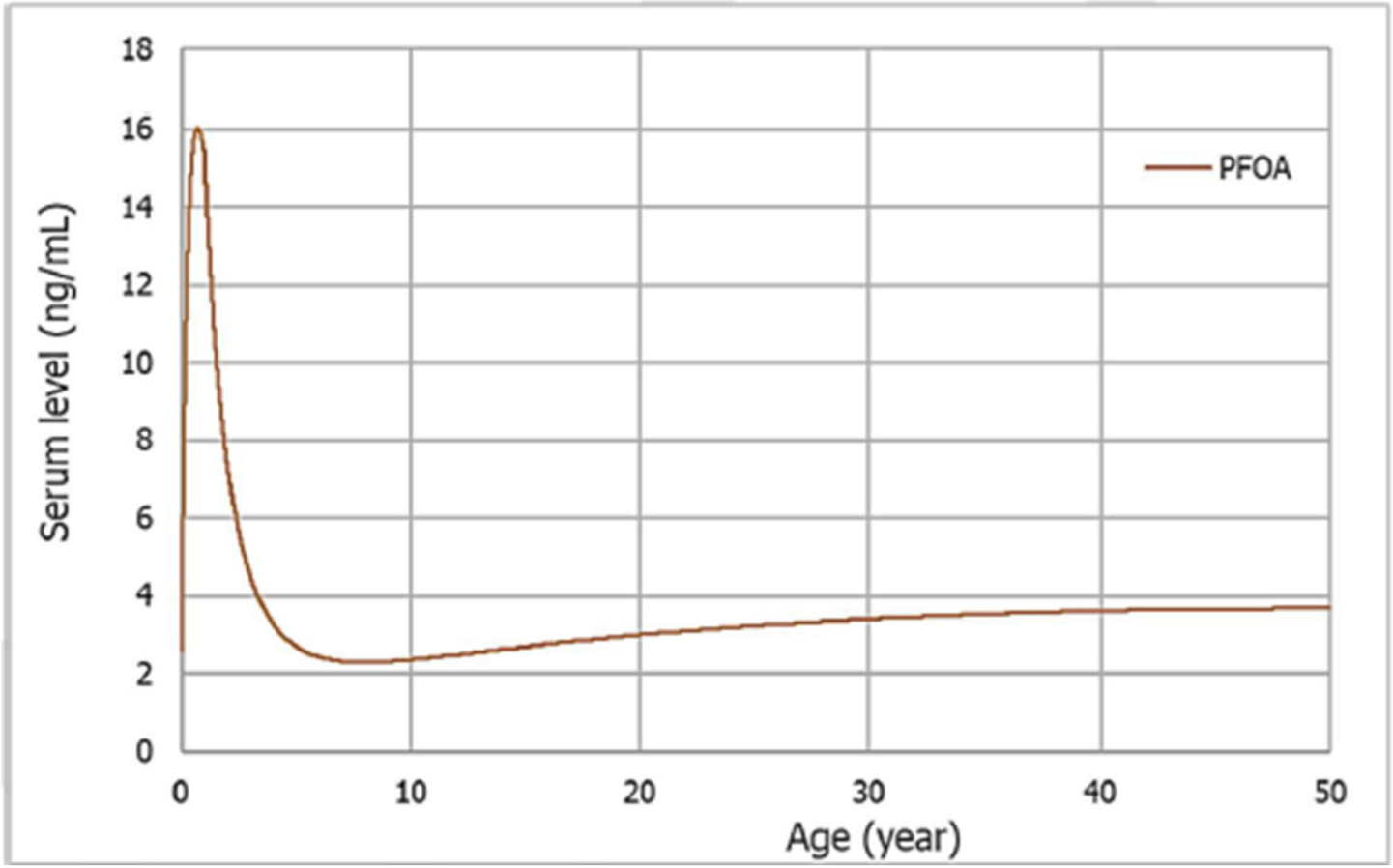
Year	Exposure evidence	Unpublished
1968	Organofluoride compounds in human blood	
1976	Organofluorines in workers' blood	
1981	PFOA found in cord blood (female worker)	
1993	Transfer into milk observed in goats	
1998	PFOS found in general population blood	
2004	PFAS detected in human milk	
2015	Breastfeeding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

PFOS transfer via human milk impacts infant serum levels



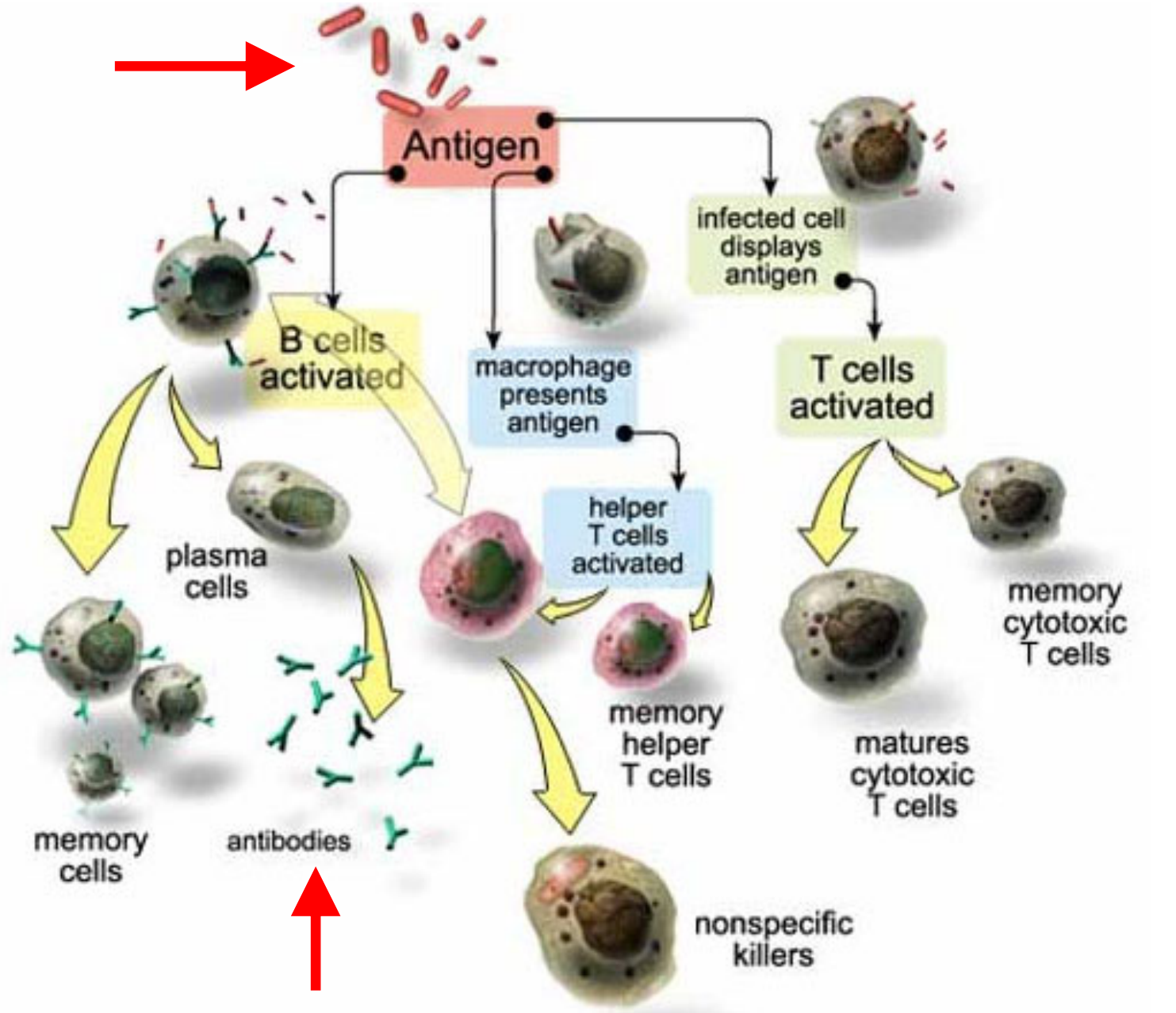
The lowest curve (dashed) is from a non-breastfed child, and the upper (solid line) is from a child breastfed exclusively for 6 months and partially the following 5 months.

Mogensen et al., 2015



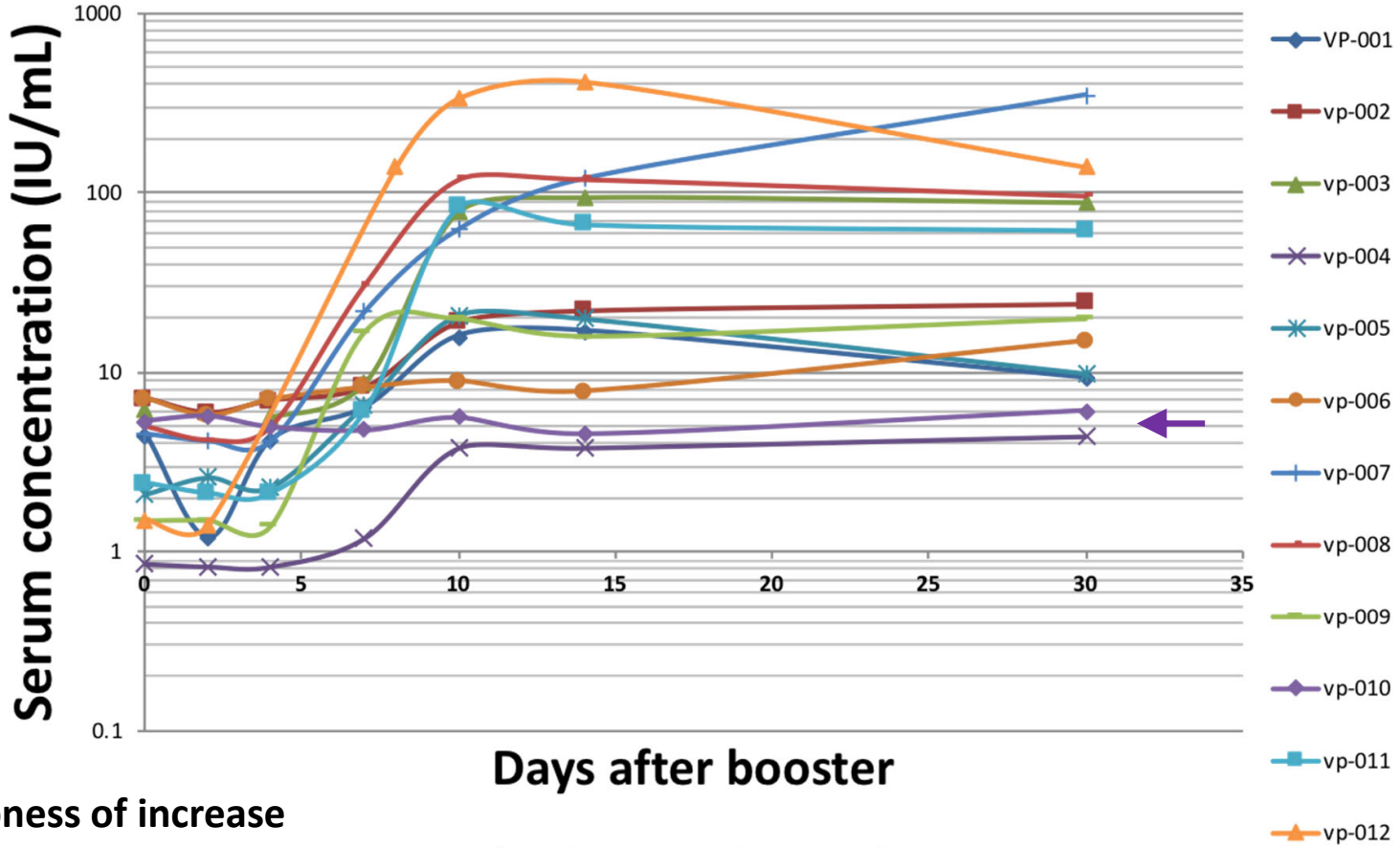
Serum-PFOA in a woman exposed in utero, via breastfeeding for 12 months and then via diet at 0.33 ng/kg bw per day (EFSA 2020).

	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)

Change in tetanus antibody concentration after booster in 12 adult volunteers



Steepness of increase inversely associated with serum-PFAS

(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 [1], J M Burris, M M Burlew, M E Steinberg, N V Patz, J A Stoltzfus, J H Mandel

Affiliations – collapse

Affiliation

1 Medical Department, 3M Company, 3M Center, St. Paul, MN 55144, USA.

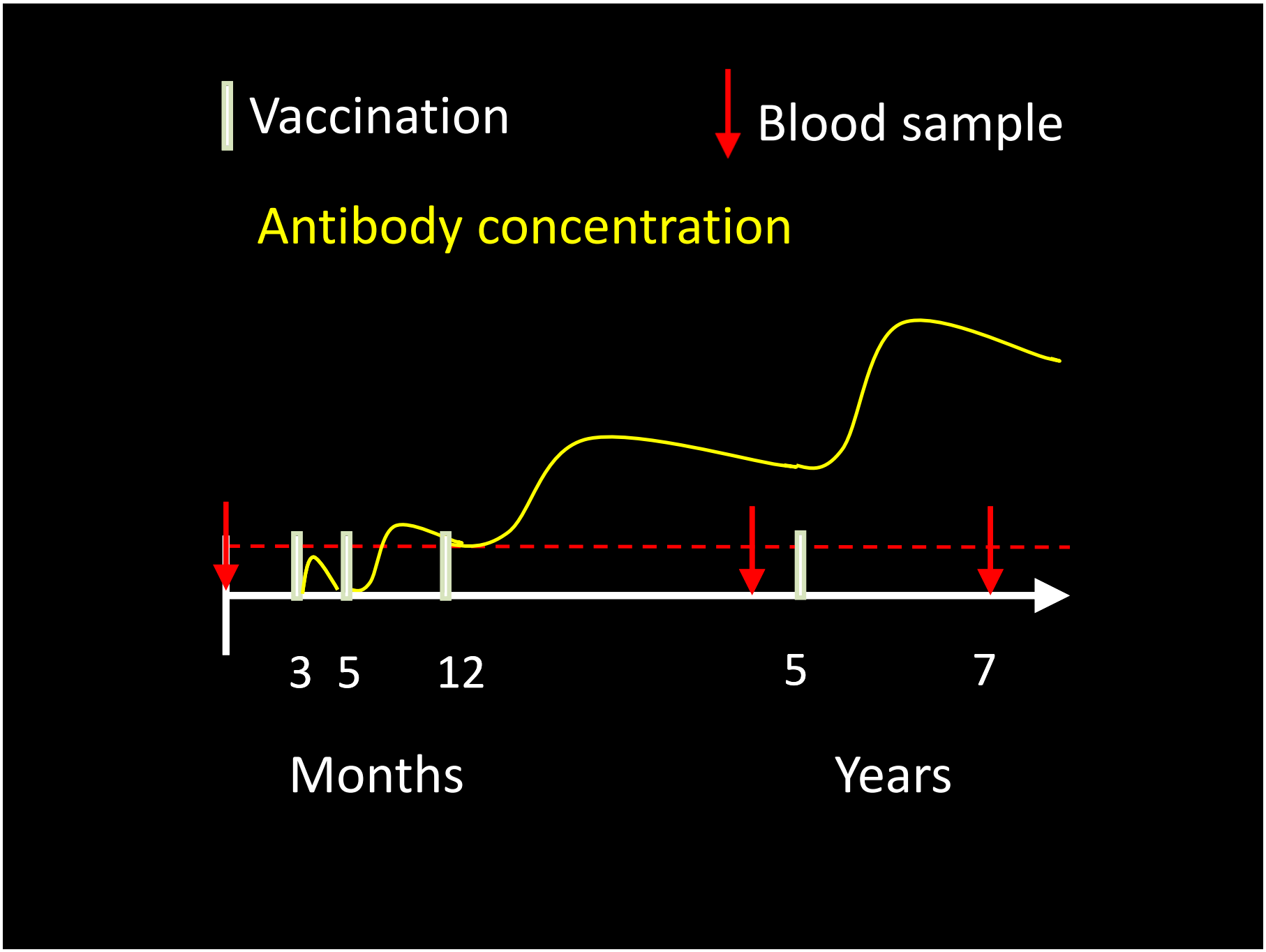
PMID: 9571521 DOI: 10.1097/00043764-199804000-00004

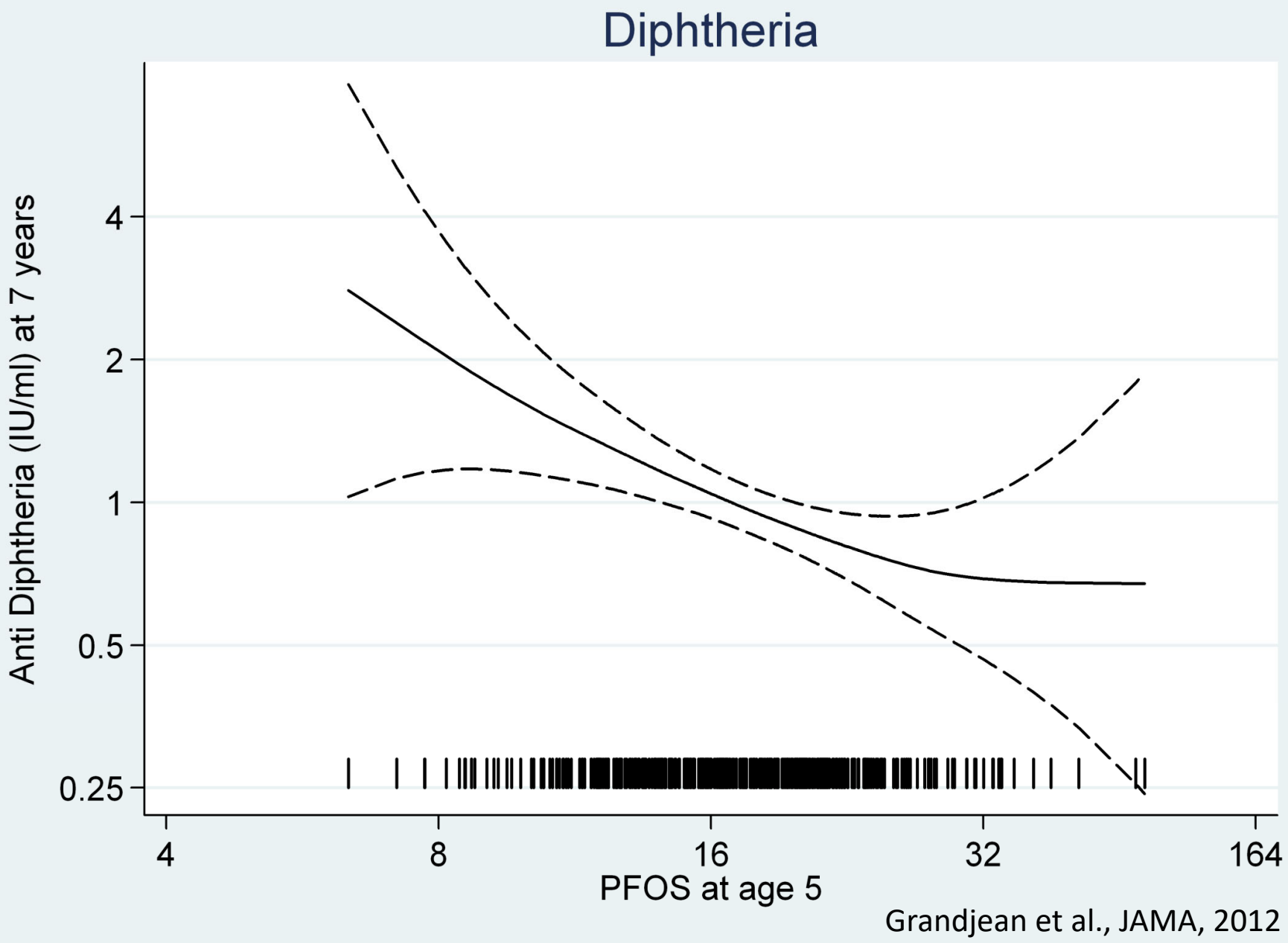
No information on absenteeism among PFAS-exposed 3M employees

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**

NASA


Vaccination
Blood sample
Antibody concentration
3
5
12
5
7
Months
Years



Grandjean et al., JAMA, 2012

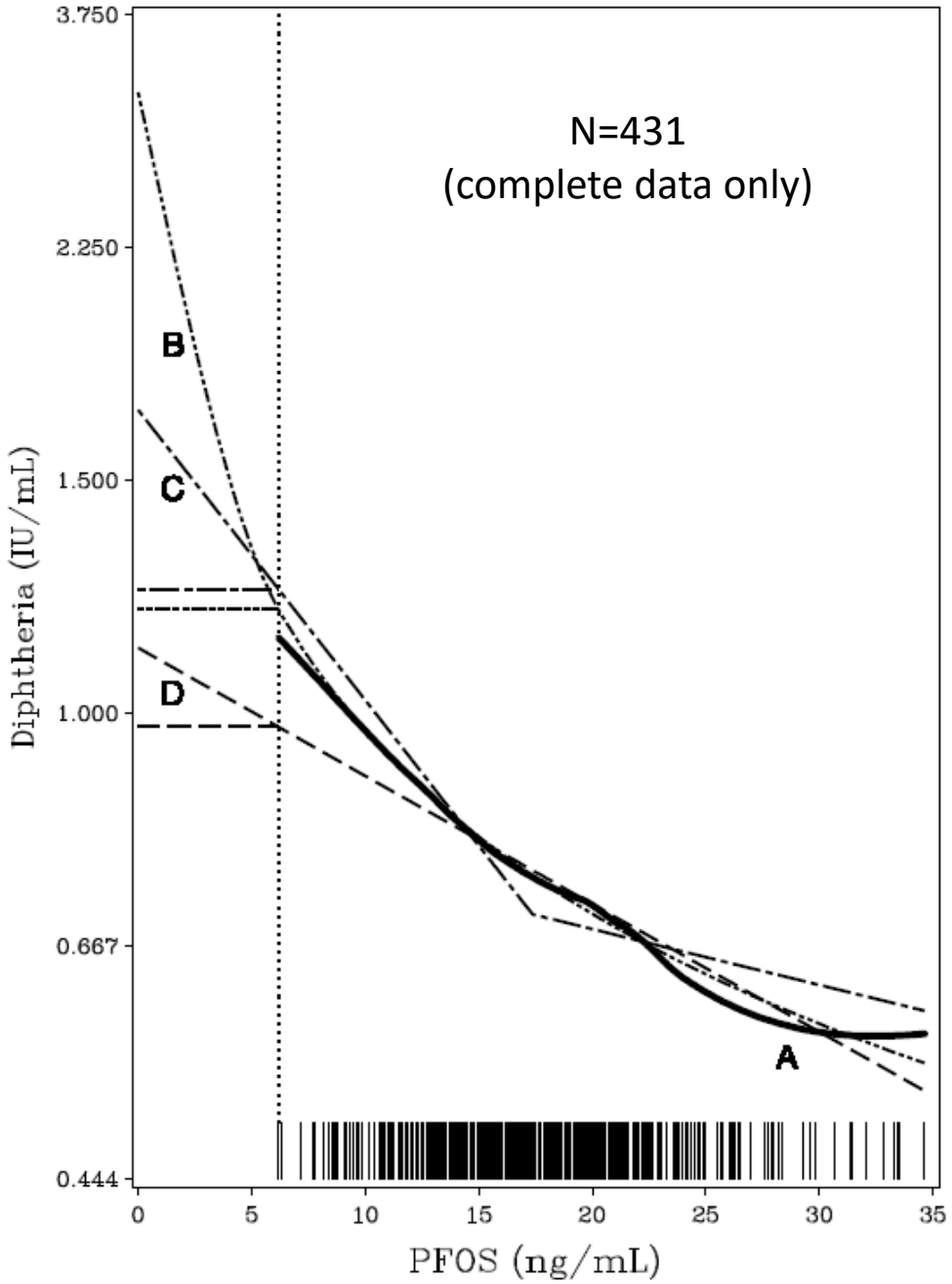
National Toxicology Program
U.S. Department of Health and Human Services

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

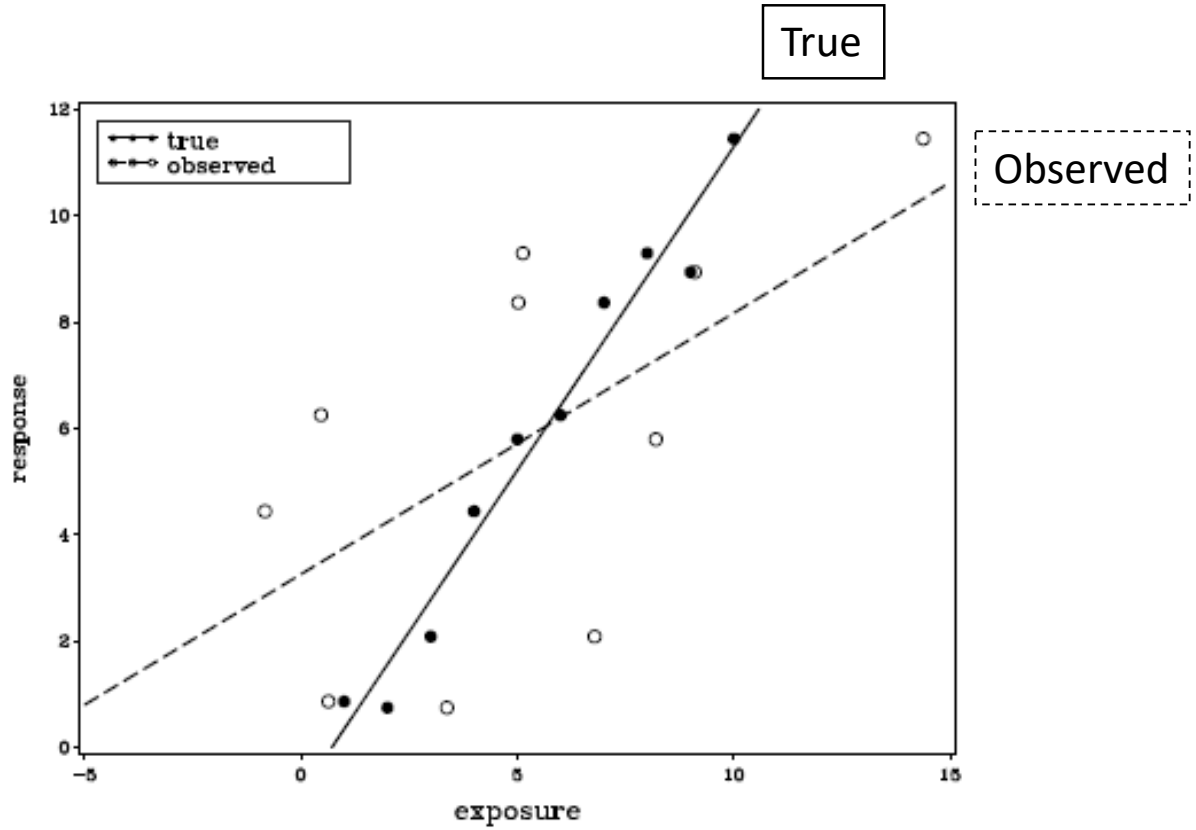
Exposure error in simple linear regression

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	Tetanus		Diphtheria	
(months)	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

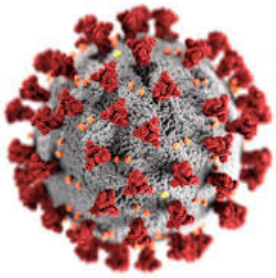
Grandjean et al., 2018

Risk factors for COVID-19

- Elderly
- Men
- Existing disease, such as
  - Diabetes
  - Obesity

Have higher accumulated PFAS levels in blood

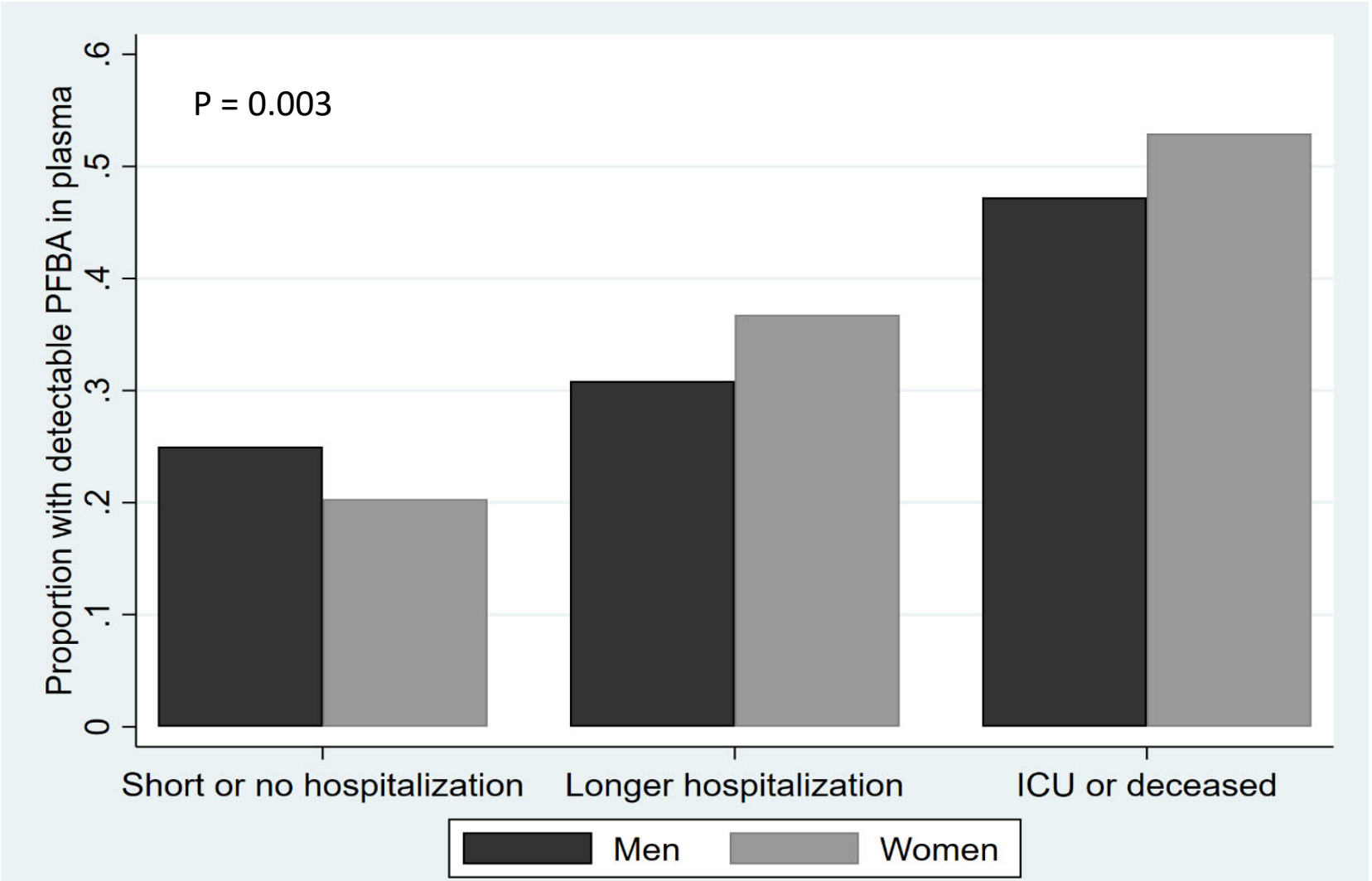
Occur at increased incidence when PFAS exposure is elevated



Study design

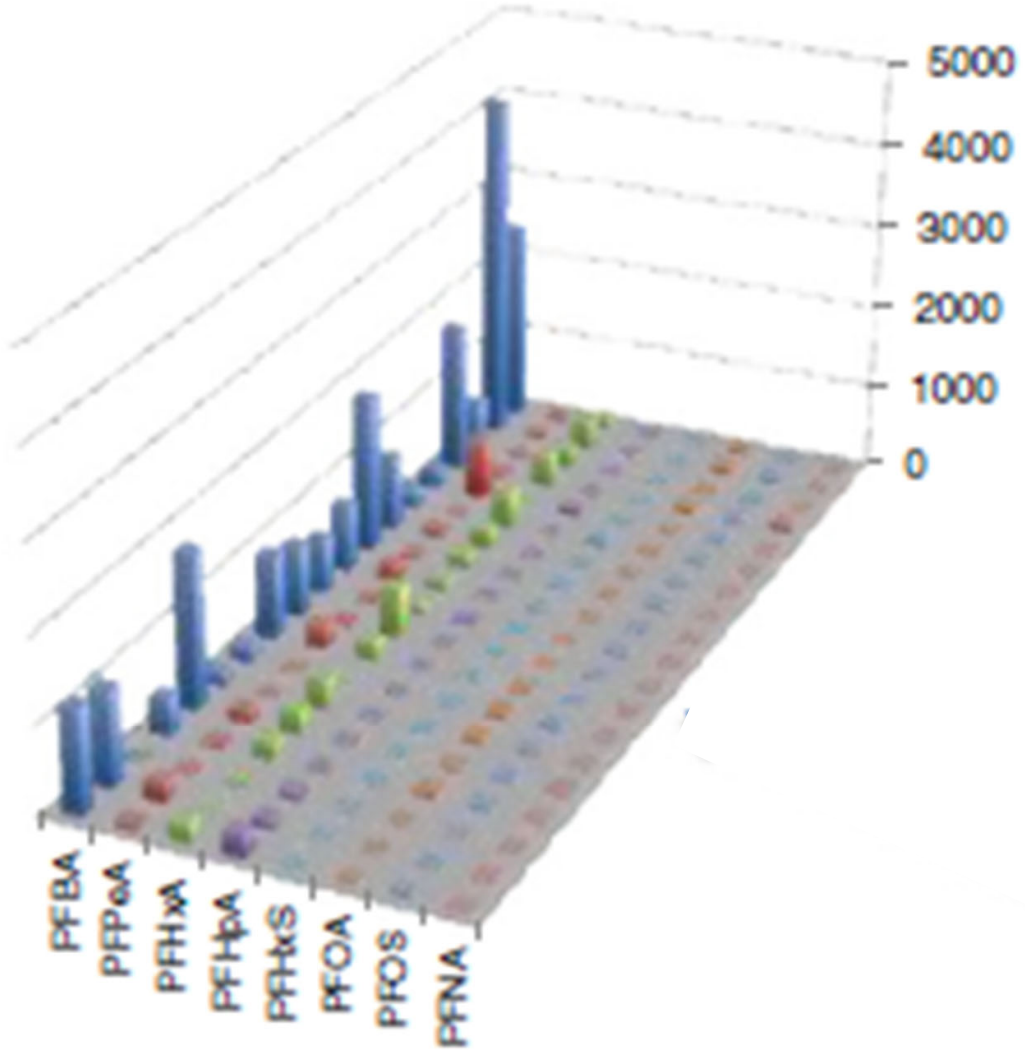
- Plasma from residual volumes from diagnostic blood tests at hospitals (30-70 years)
- All 323 subjects positive for SARS-CoV-2
- Study conducted without informed consent
- All information anonymous on secure server
- Health and demographic information from existing national registers
- Clinical course: 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):

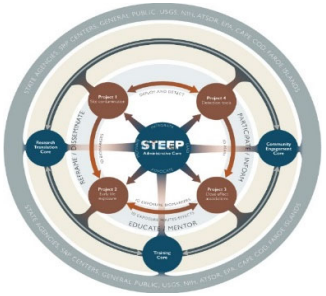
Provisional level of 400 ppt for PFOA
and 200 ppt for PFOS

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

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

SILENT SPRING INSTITUTE
Researching the Environment and Women's Health

NIH NIEHS

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More information about STEEP is available at: https://web.uri.edu/steep/ and https://tools.niehs.nih.gov/srp/programs/Program_detail.cfm?Project_ID=P42ES027706