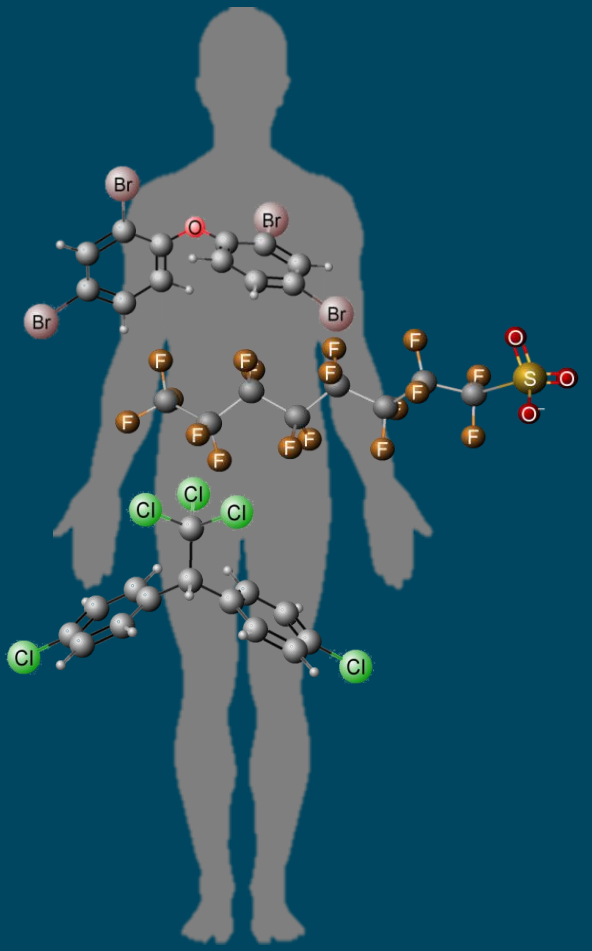
UiT The Arctic University of Norway

Investigating environmental contaminants and health:

Insights from population-based studies in Northern Norway



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NTNU Norwegian University of Science and Technology

Acknowledgements

- Long-term collaborations representing also work lead by colleagues
- Made possible due to that surveys started collecting and biobanking blood in the 1970s
- NILU’s environmental chemistry research group in Tromsø in 1994
- A continuum of research projects

Fram Centre

nilu

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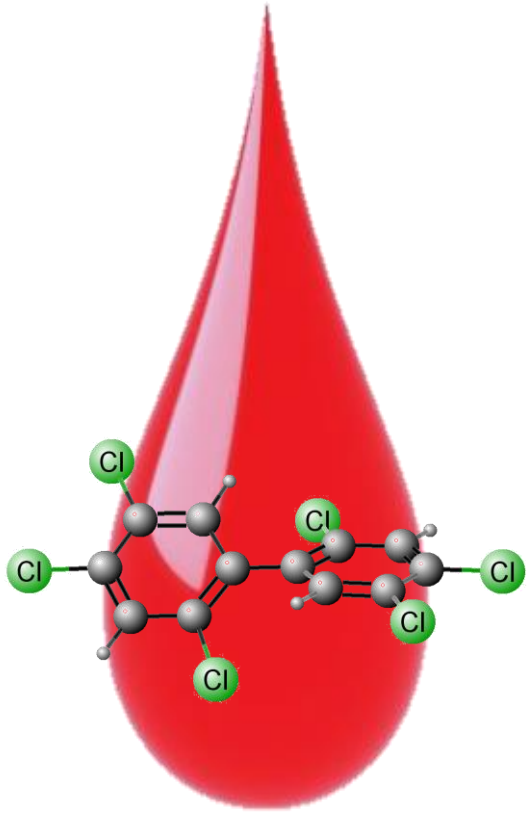
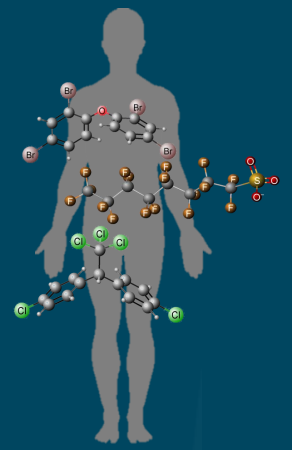
QUALITY SAFETY TEAM PLAY RESPECT UNN

Outline

- Lessons learned in our population-based studies
- Investigation of human exposures
  - Two longitudinal designs
- Investigation of human health effects
  - Specifically: Type 2 Diabetes Mellitus
  - One cross-sectional study
  - One longitudinal study



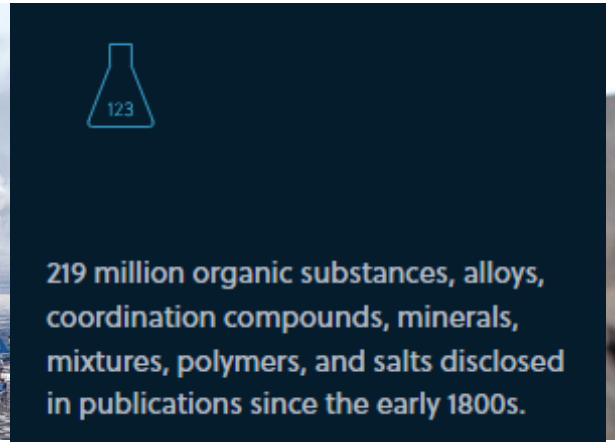
Human exposures to environmental contaminants



Sexton et al. (2004)/American Scientist.

Environmental contaminants

In the past

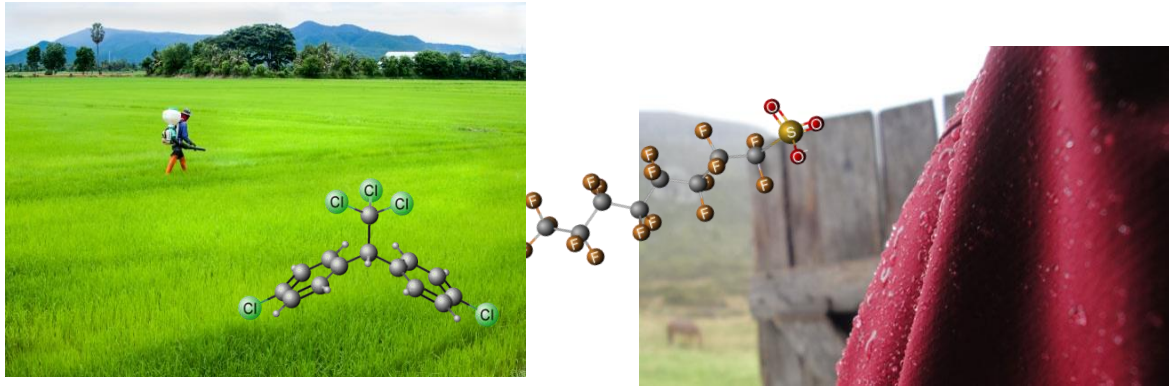


Now

cas.org

Persistent organic pollutants

- Organic chemical substances produced or bi-products of human activity released into the environment and that:
  - remain intact for exceptionally long periods of time;
  - become widely distributed throughout the environment as a result of natural processes involving soil, water and, most notably, air;
  - accumulate in the living organisms including humans, and are found at higher concentrations at higher levels in the food chain; and
  - are toxic to both humans and wildlife.



PCBs= polychlorinated biphenyler,
DDT= 1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane,
PFAS= polyfluoroalkyl substanser

www.pops.int/TheConvention/ThePOPs/tabid/673/Default.aspx

Exposure – who and how?

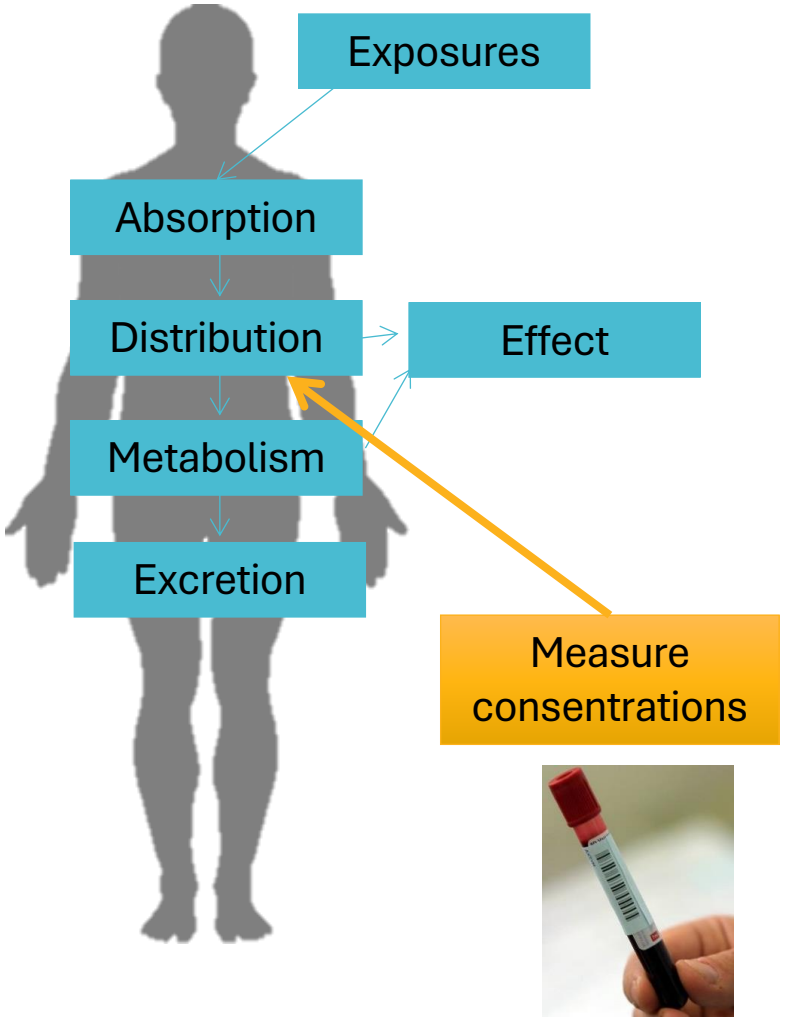
Ingestion

Dermal contact

Inhalation

WHO (2010) WHO Human Health Risk Assessment Toolkit / www.unep.org/topics/chemicals-and-pollution-action/pollution-and-health/

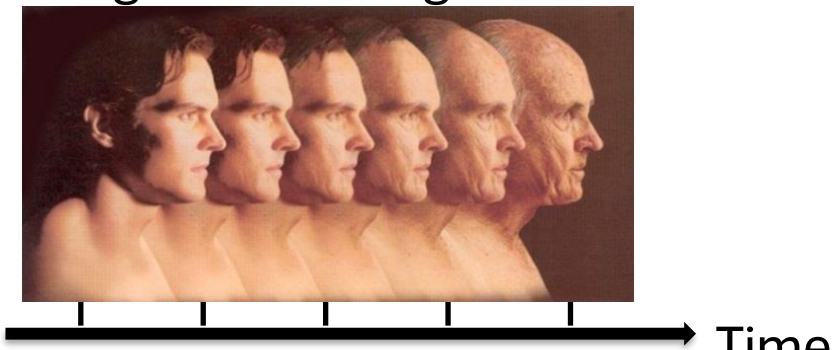
Human monitoring studies



Exposure → Dose → Response

Cross sectional design:

Longitudinal design:



WHO (2010) / WHO Human Health Risk Assessment Toolkit

Population-based surveys at UiT

The Tromsø Study

Tromsø, 45000 at least once, 7 surveys so far

1974 | 1979-80 | 1986-87 | 1994-95 | 2001 | 2007-08 | 2015-06 | 2025-26

The Norwegian Women and Cancer Study

National, 174000

1991 - | 2017 | 2025

The Saminor Study

Sami municipalities, 28000 at least once, 2 surveys so far

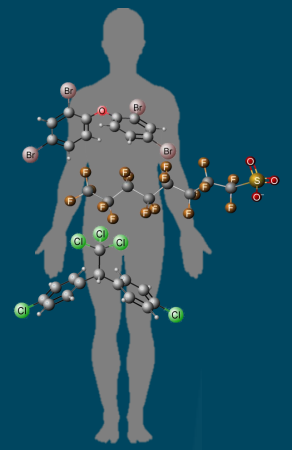
2003-04 | 2012-14 | 2023-25

The Fit Futures Study

Troms county, youth, 1200, 3 surveys

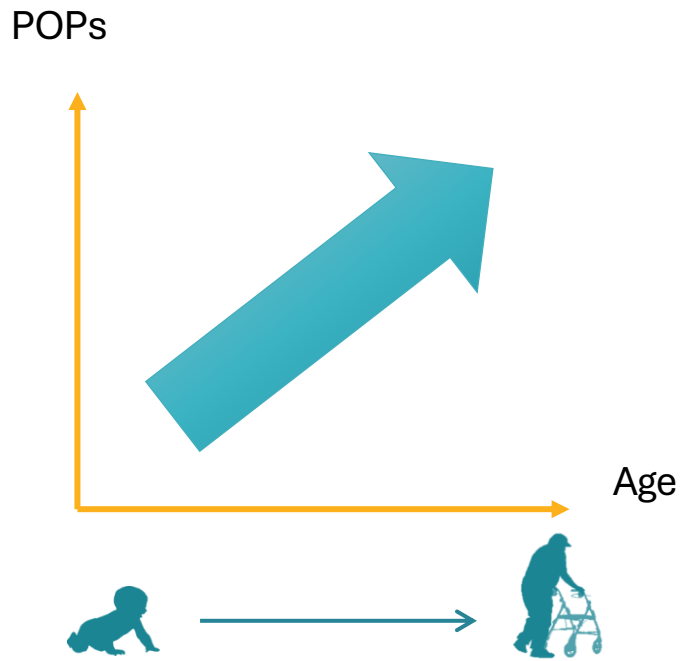
2010-11 | 2012-13 | 2021-22

Time trends of environmental contaminants in Northern Norway



Human exposures and age

- Trends of POPs in humans with respect to time

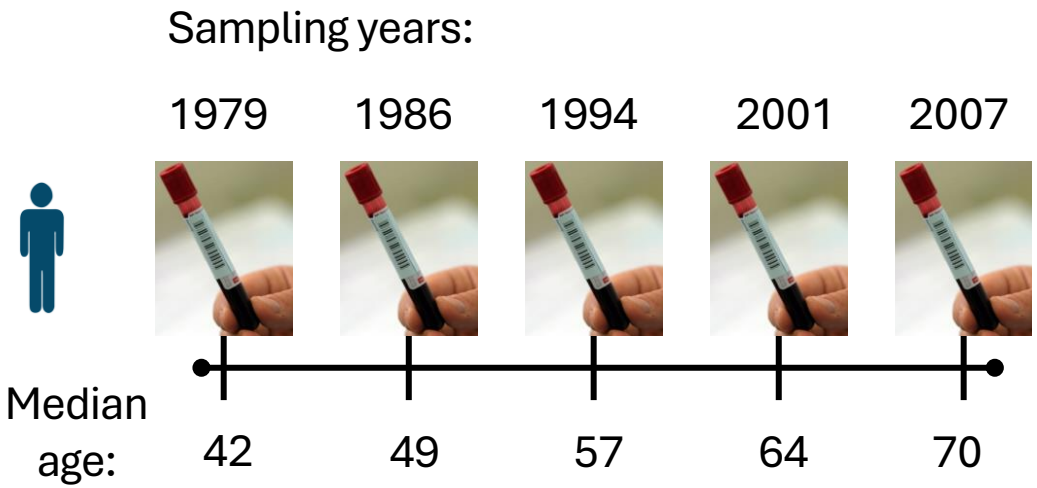


- «Increase with age»
- «Effect of age»
- «Positively correlates with age»

- Longitudinal study - Intraindividual changes
- Analyze a broad range of POPs in blood samples in the period 1979-2007
- Examine trends with respect to age, birth cohort and exposure history
- Validation of human exposure model

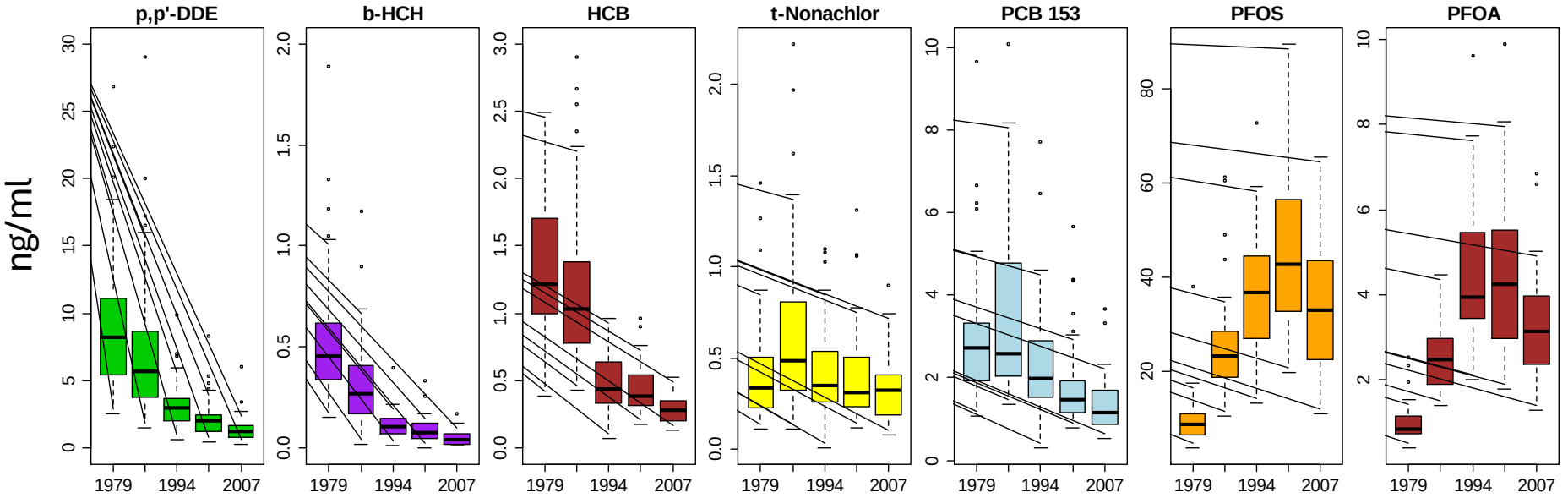
The Tromsø Study 1979-2007 - Study 1

- Archived serum samples of high quality in the Tromsø Study
- 5 repeated blood samples from 54 men over a 30 year period



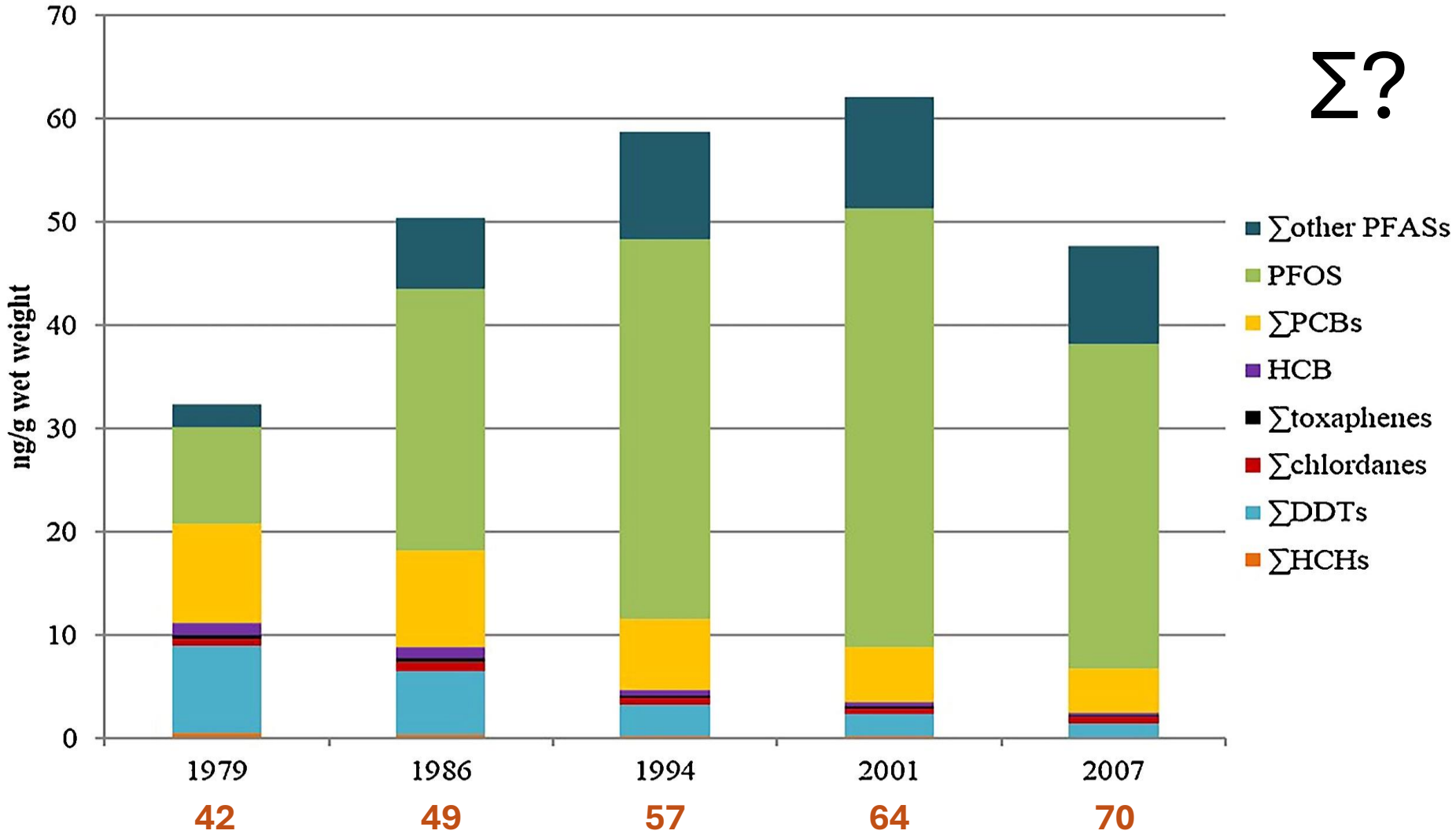
Time trends for over 50 components

- Different trends for different components



Nøst et al. Environ Health Perspect 121 2013 / Nøst et al. Environ Int 67 2014

Dynamic serum POP burden



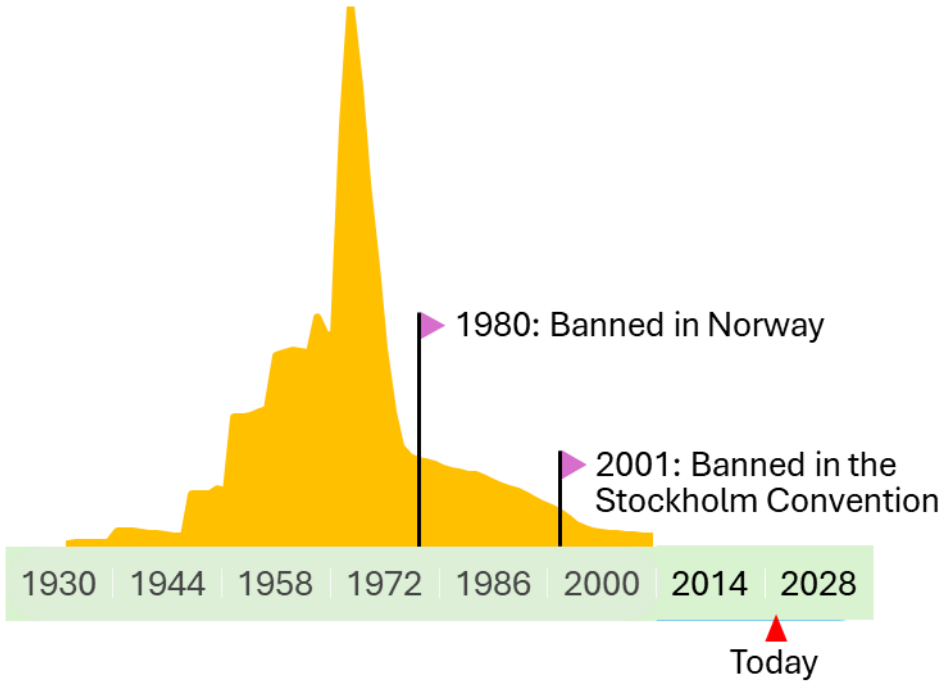
Σ?

Nøst et al. Int J Hyg Environ Health 220 2017

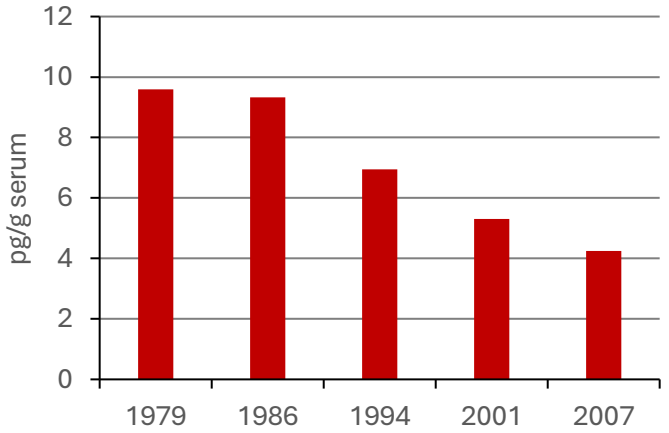
Good news about old sins

- PCB-153

Emissions



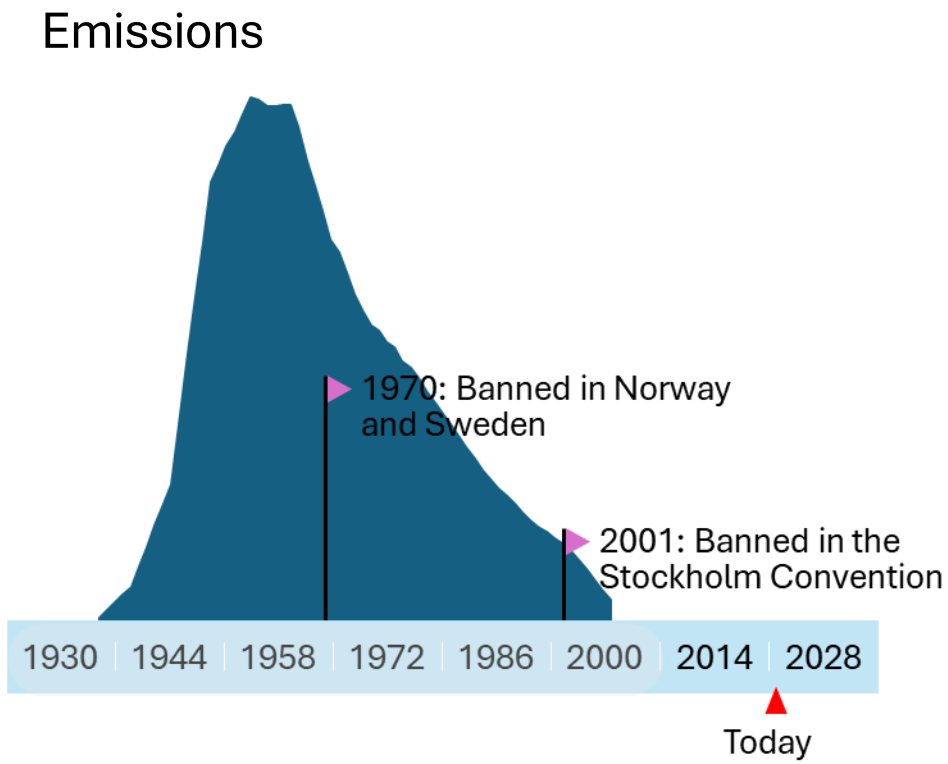
The Tromsø Study blood samples



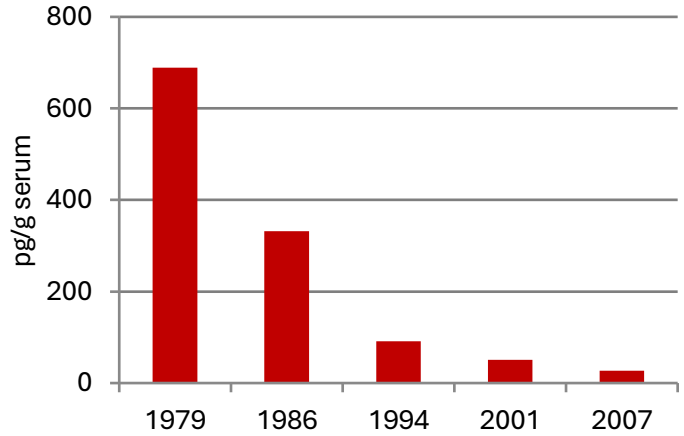
Breivik et al. 2010 Environ Int

Good news about old sins

- DDT



The Tromsø Study blood samples

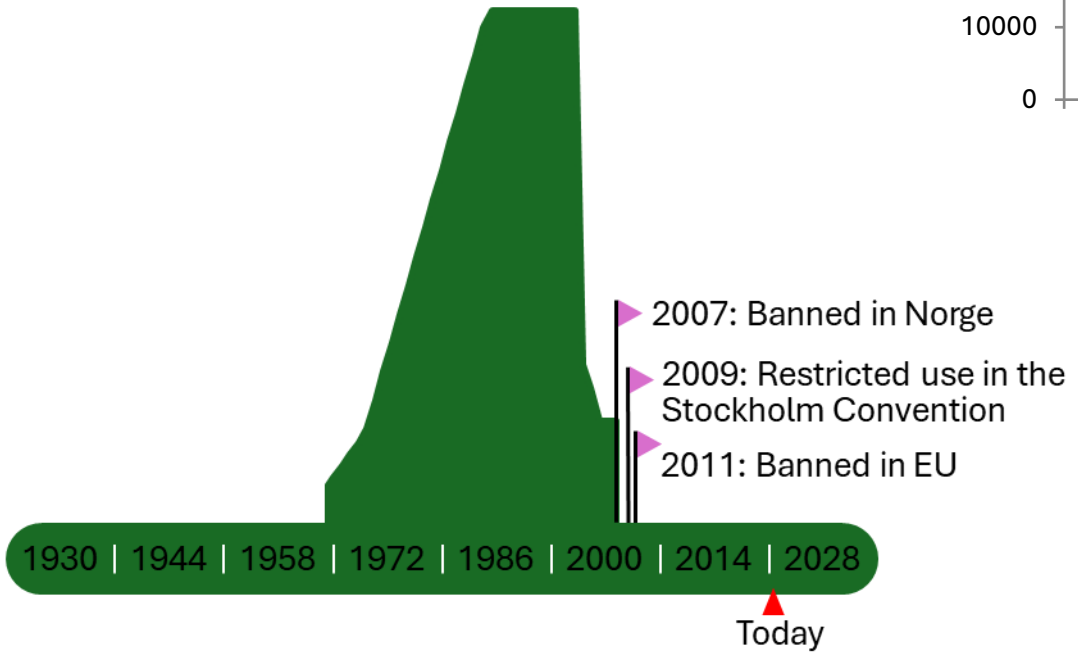


Schenker et al. 2008 ES&T

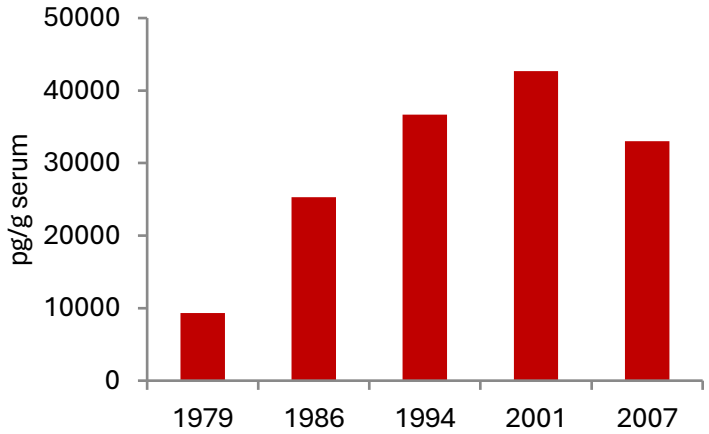
Good news also about more recent sins

- PFOS

Emissions



The Tromsø Study blood samples

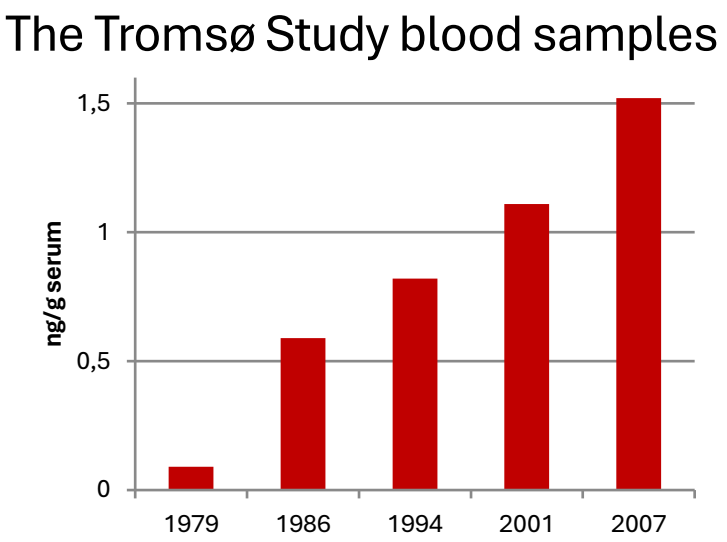


Paul et al. 2009 ES&T

Not good news for newer sins

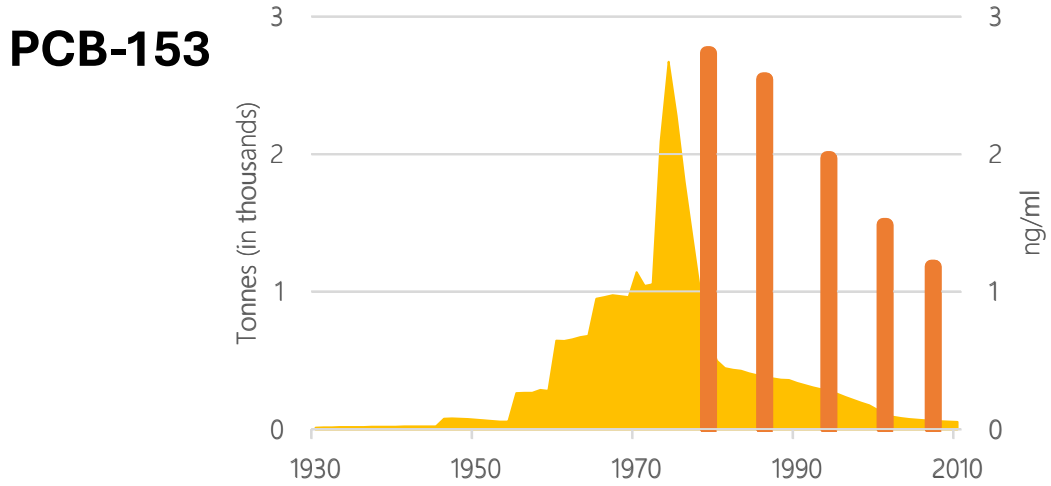
- PFNA

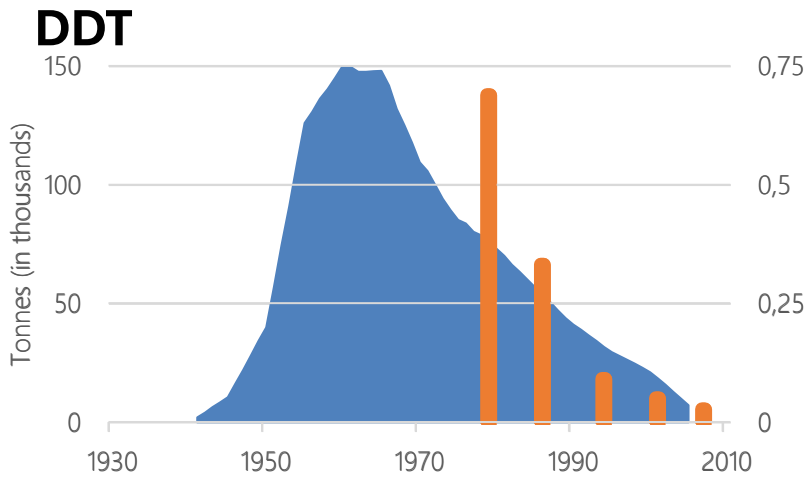
- Emission history not quantified
- Not banned at the time

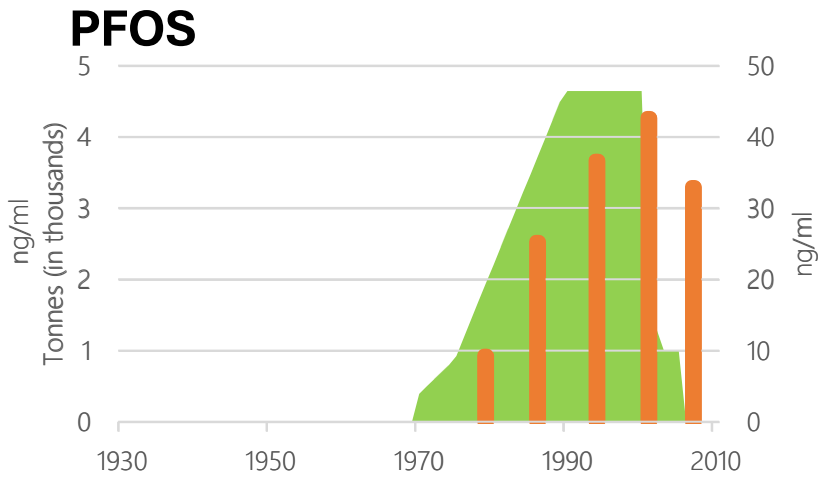


Paul et al. 2009 ES&T

Dynamic and complex burden reflects trends in emissions?



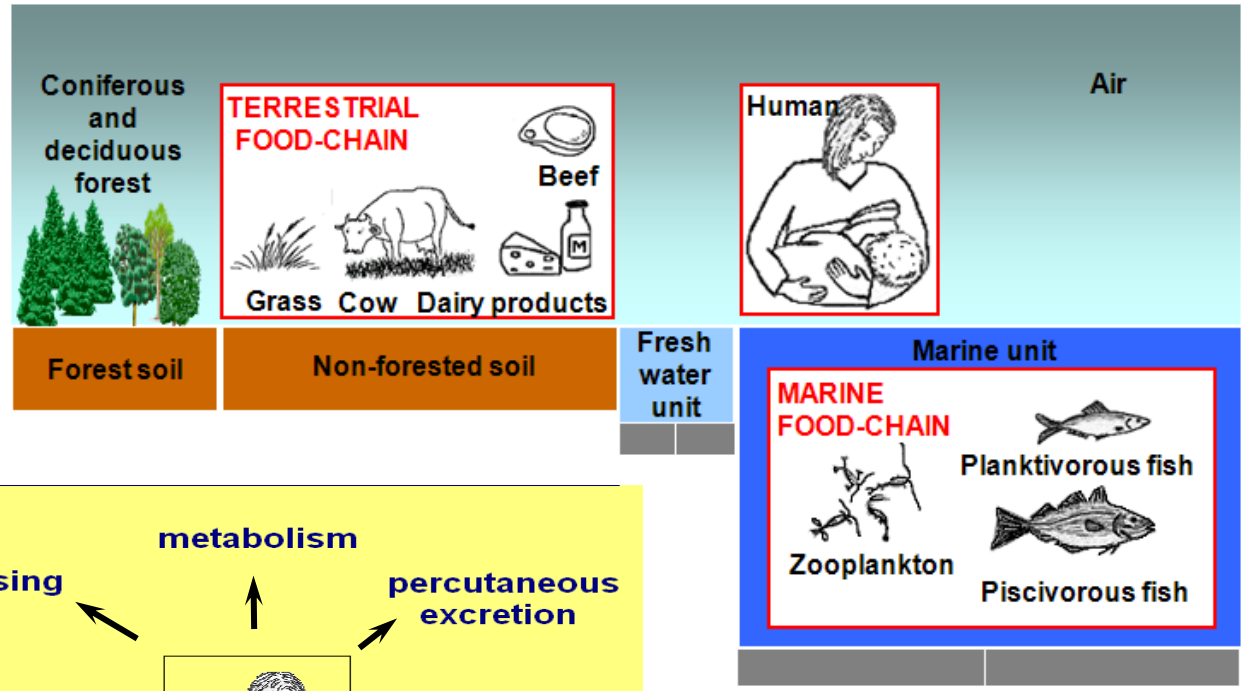


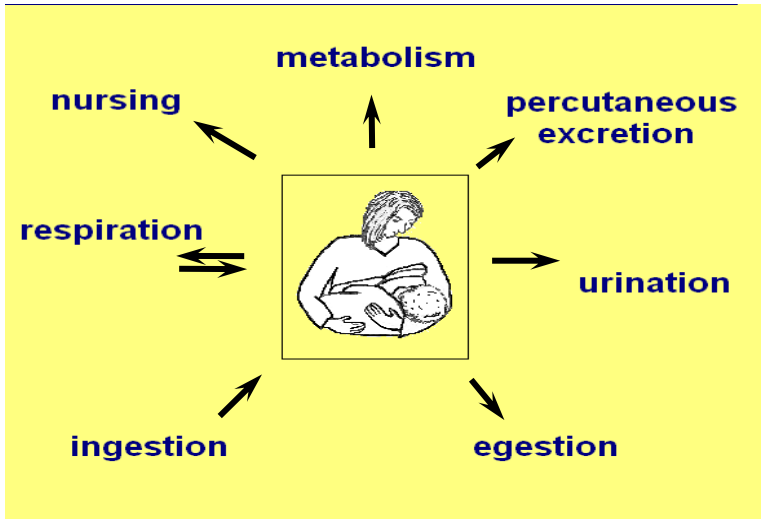


Breivik et al. 2010 Environ Int / Schenker et al. 2008 ES&T / Paul et al. 2009 ES&T / Nøst et al. Int J Hyg Environ Health 2017

Emission-based modelling

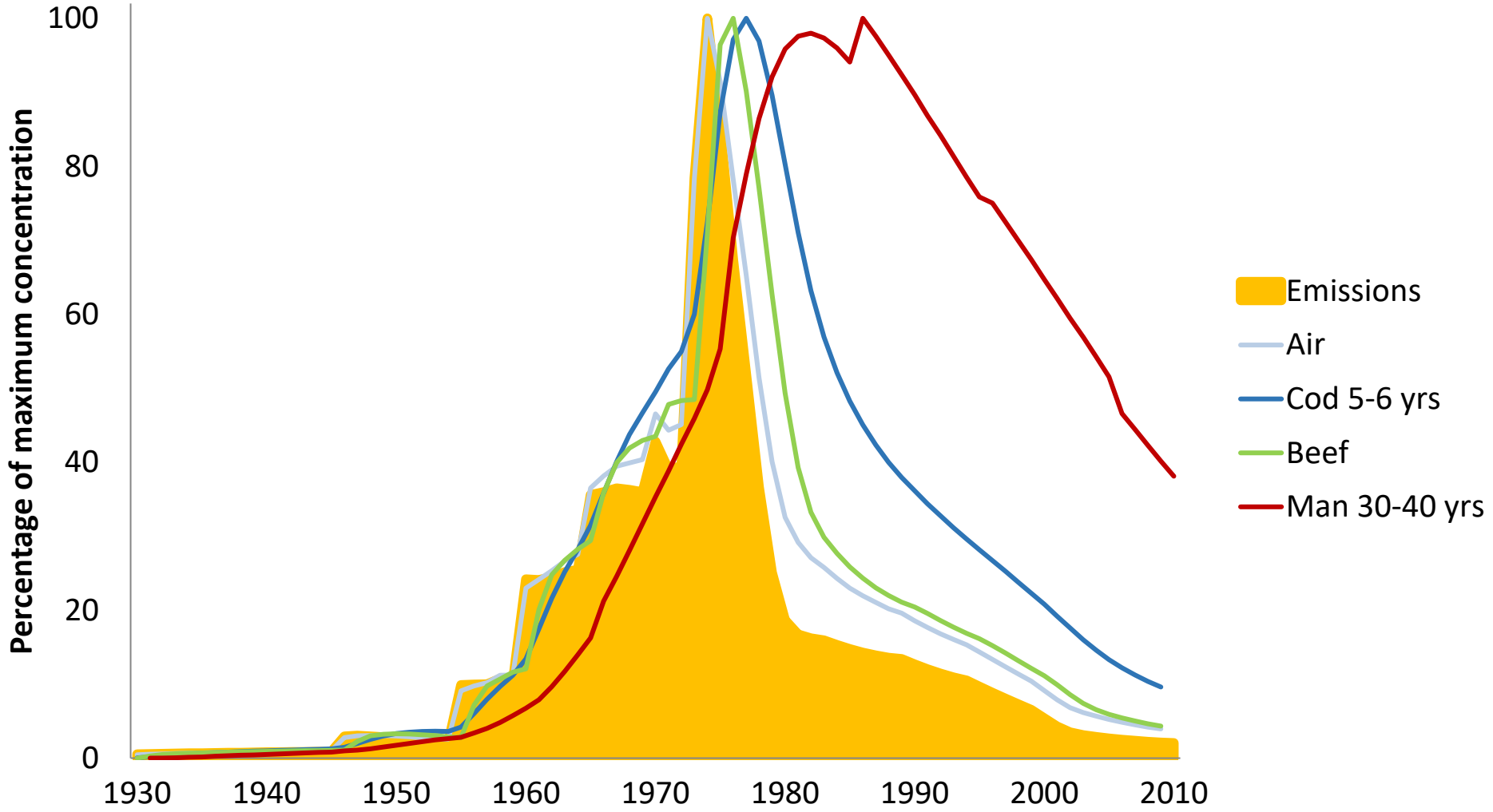
- CoZMoMAN, NILU
- Inventories of global emissions





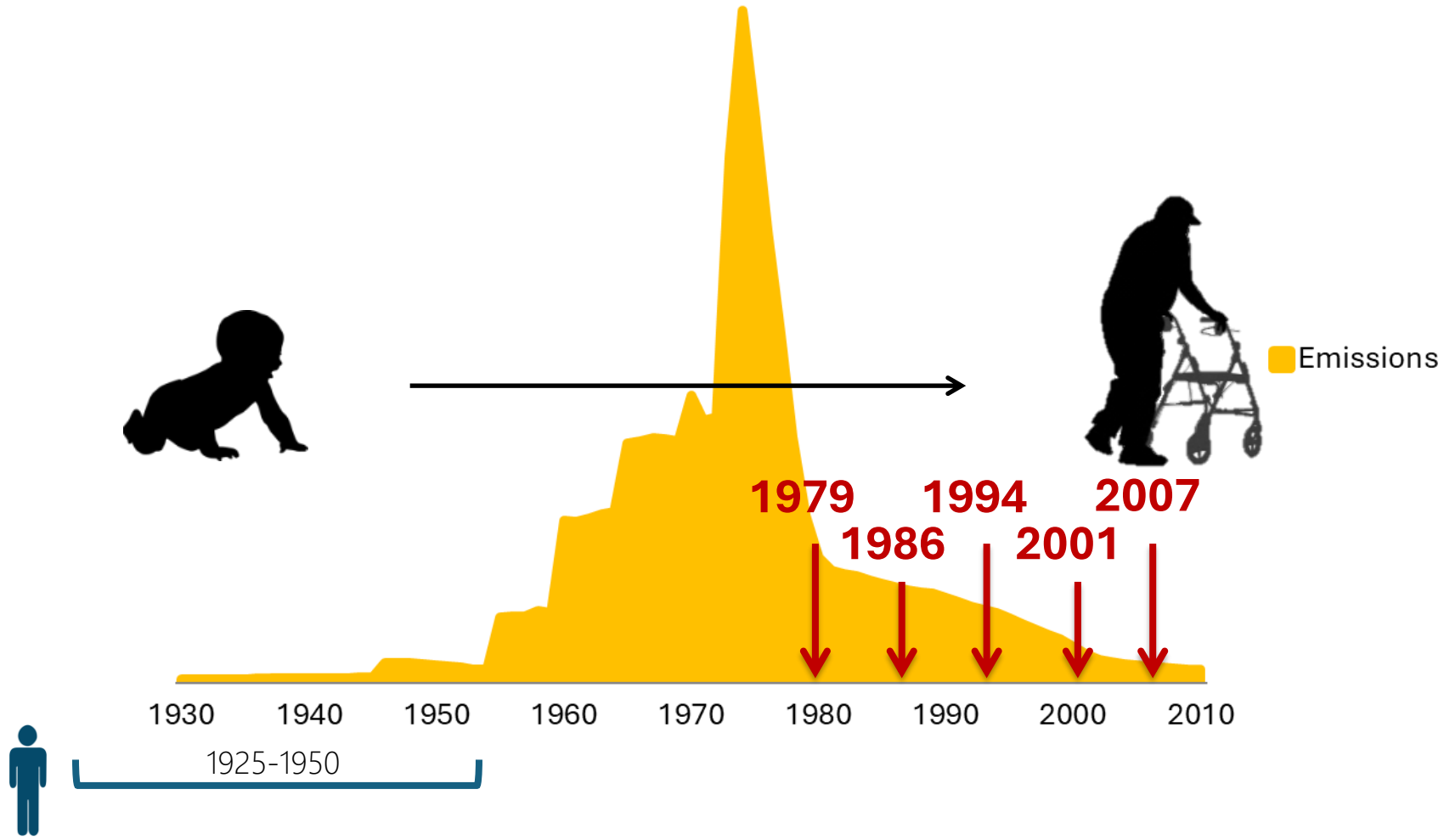
Breivik et al. 2010 Environ Int

Environmental concentrations follow emissions



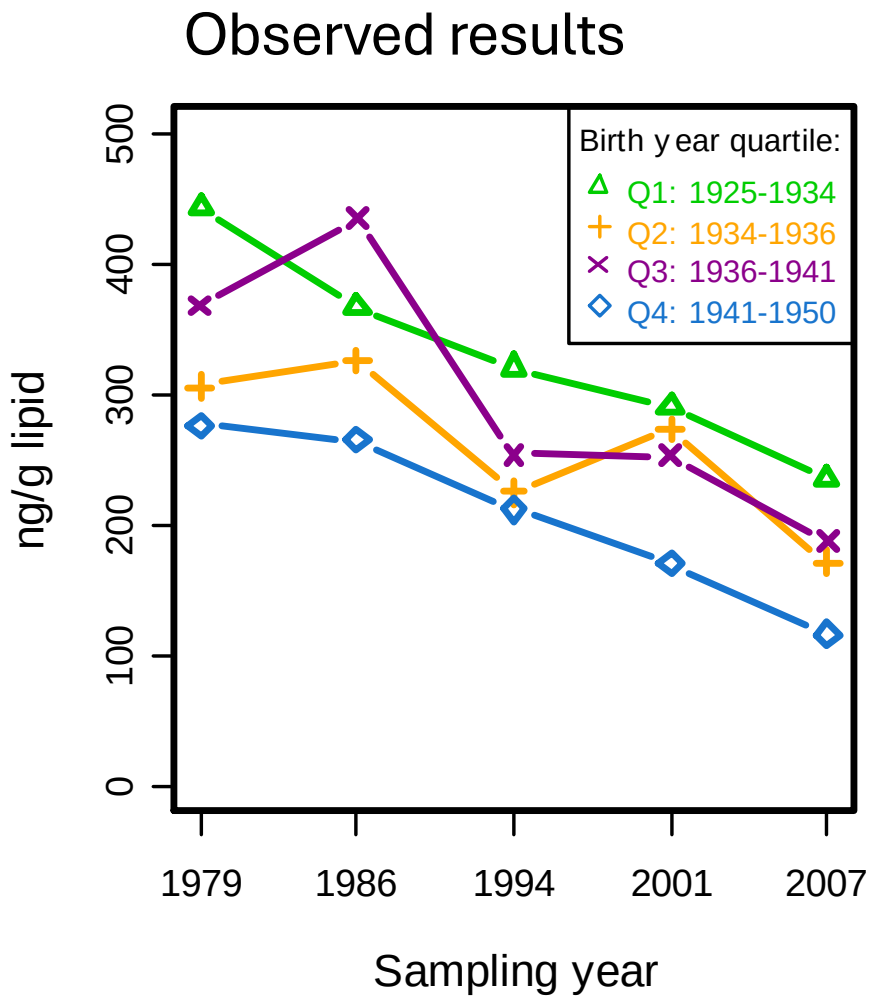
Breivik et al. 2010 Environ Int

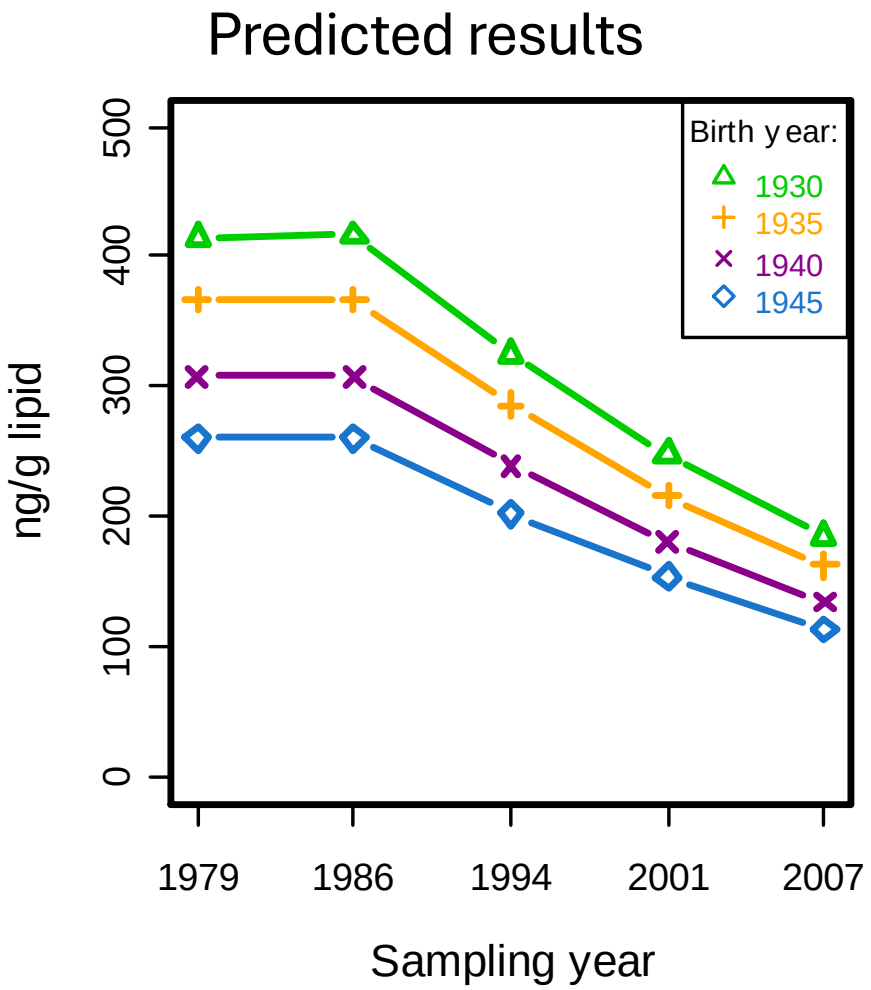
Time trends, lifetime exposure and age



Breivik et al. 2010 Environ Int

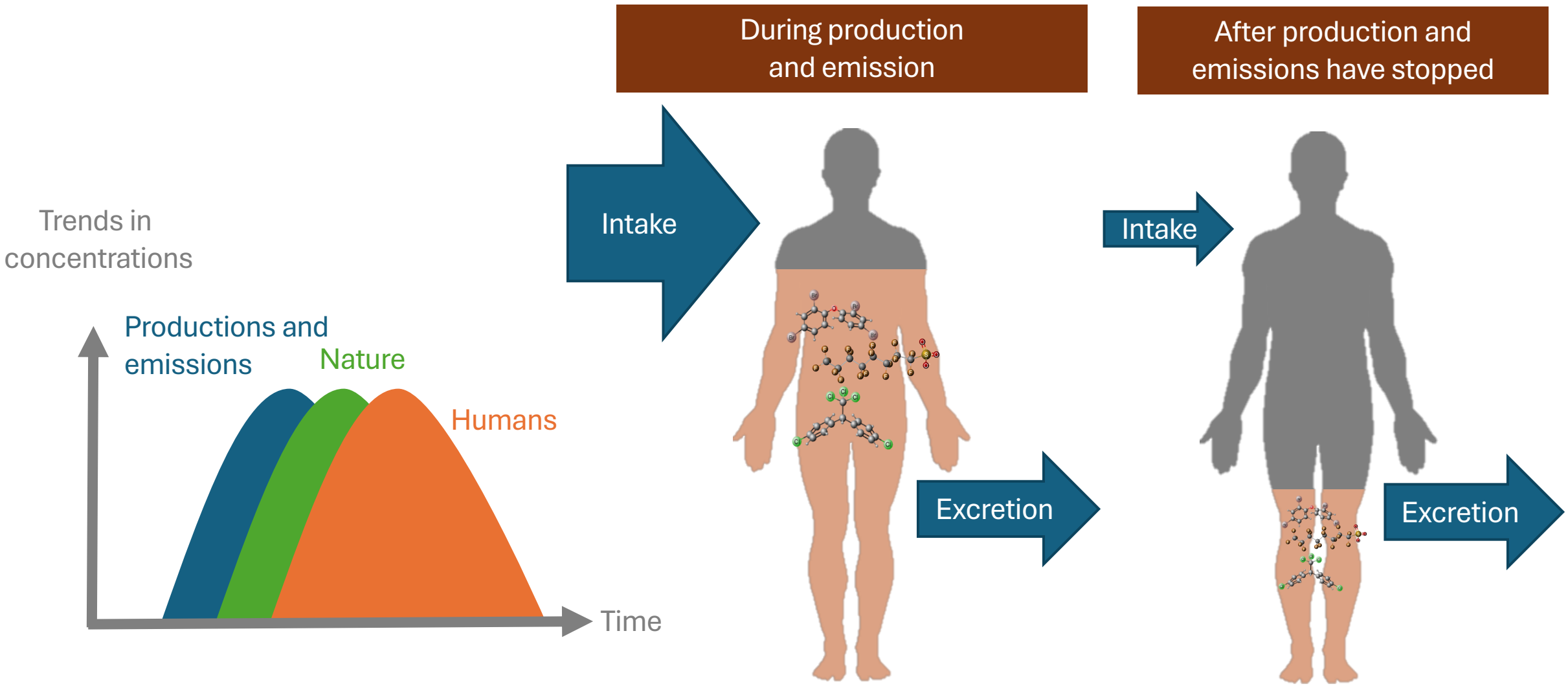
Model predictions for the Tromsø men



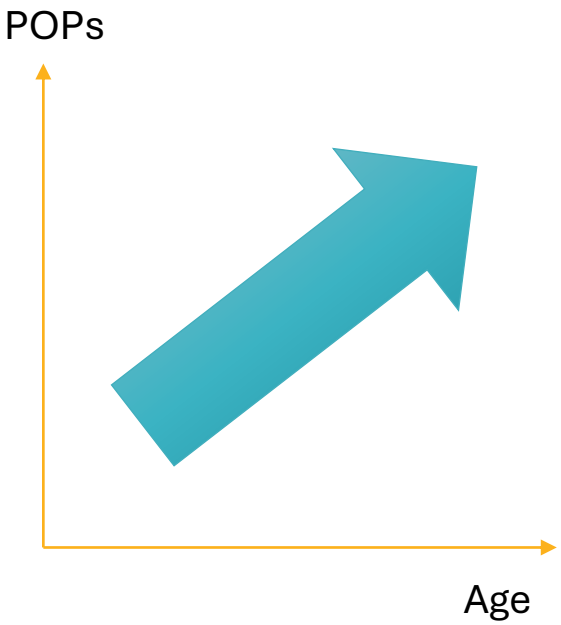


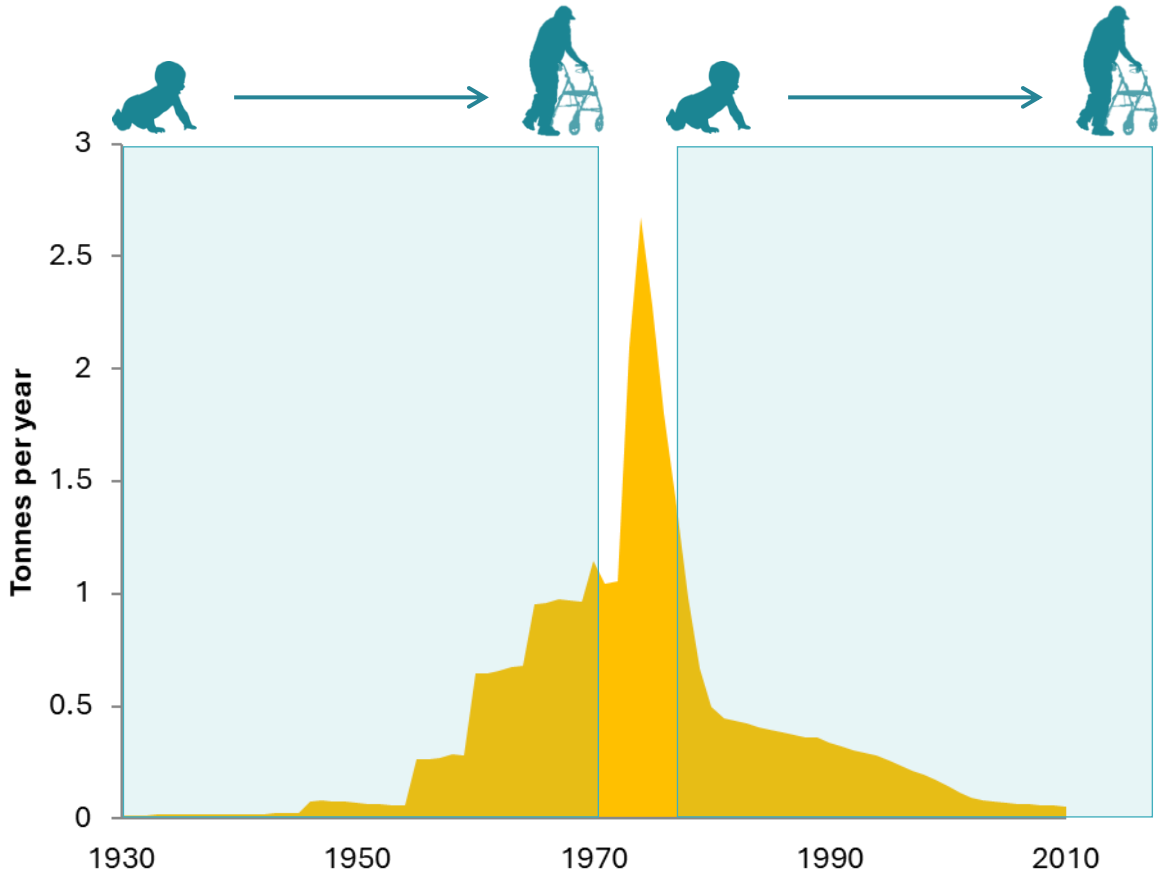
Nøst et al. Environ Health Perspect 121 2013

Human burden reflects trends in emissions



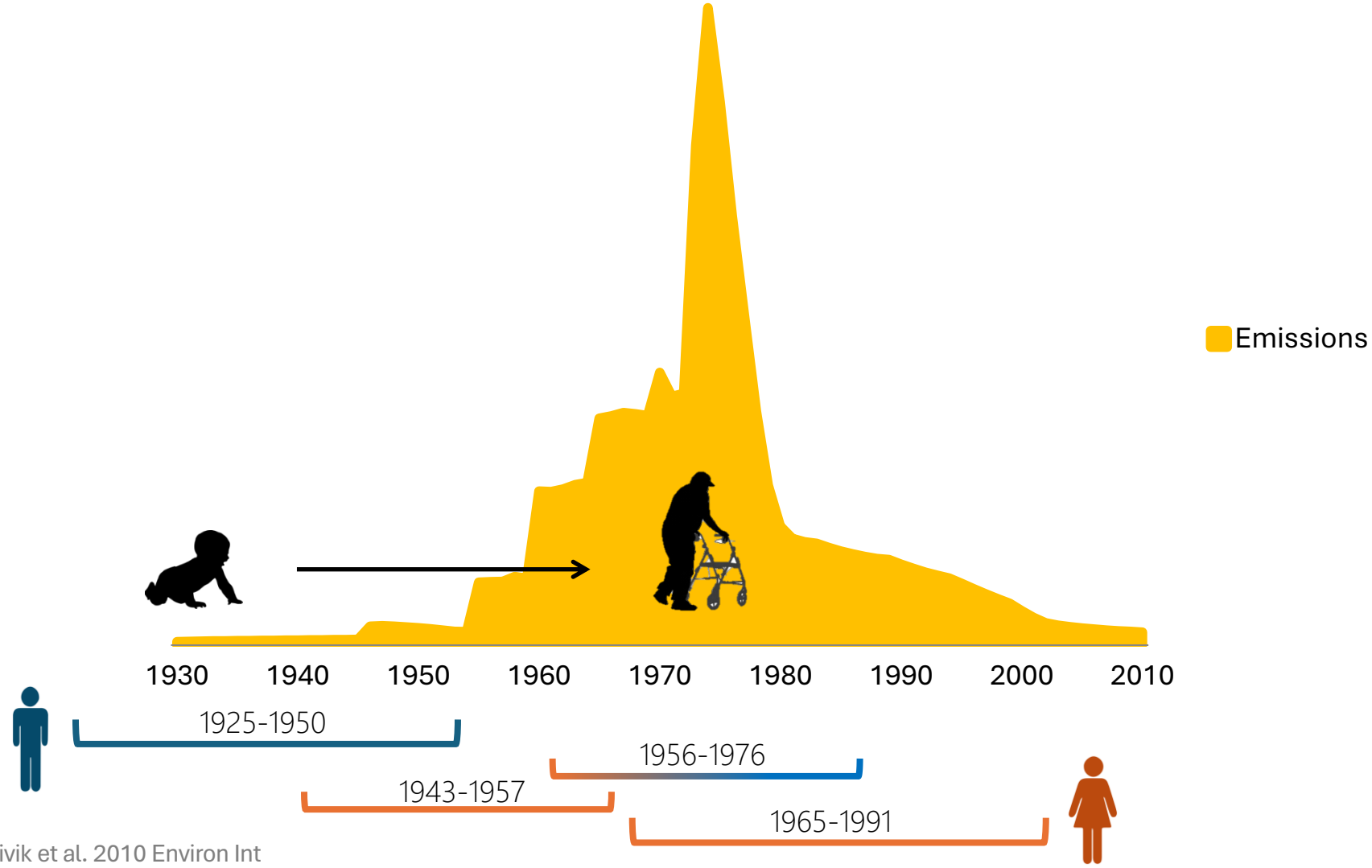
Time trends, lifetime exposure and age





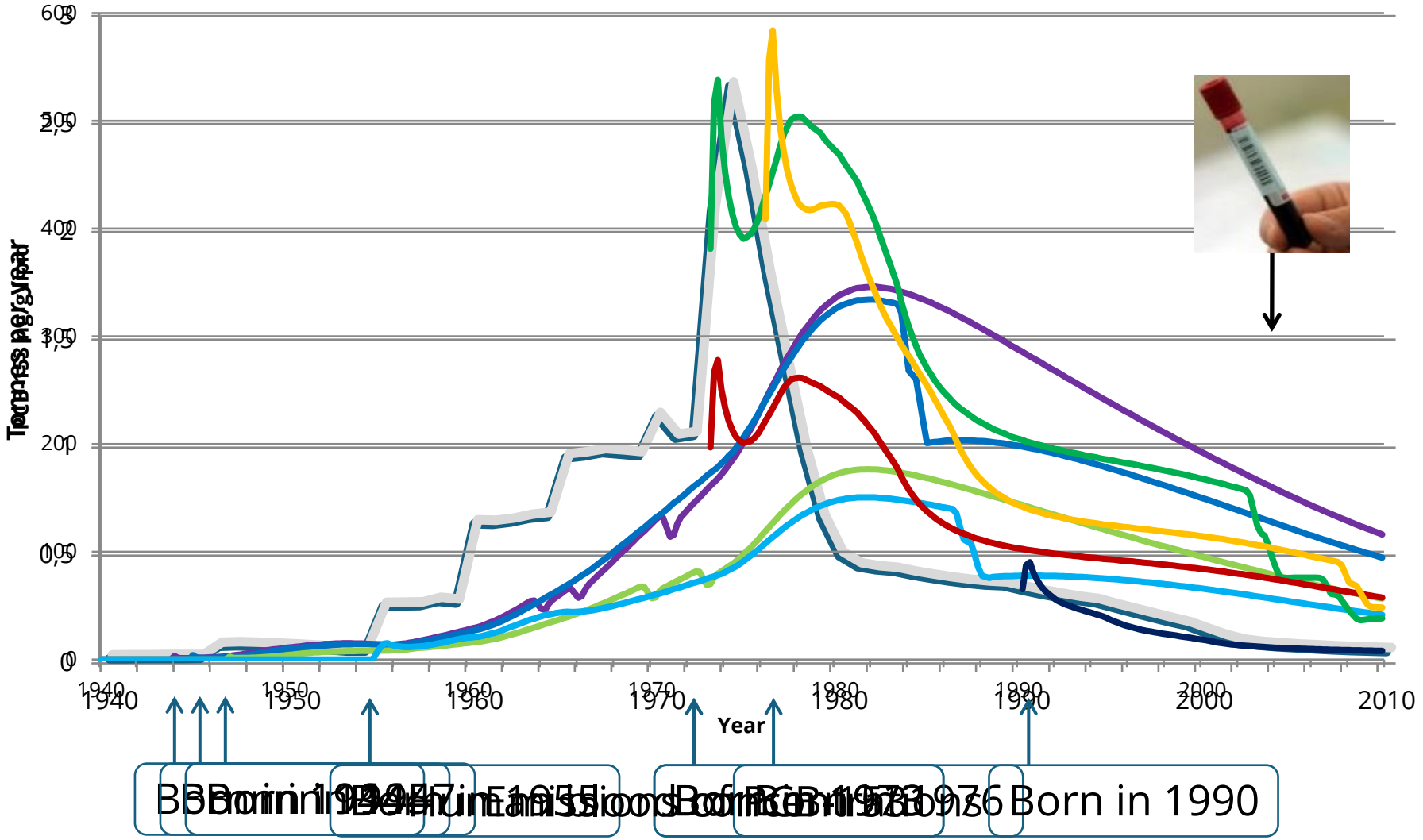
Breivik et al. 2010 Environ Int

Time trends, lifetime exposure and age



Breivik et al. 2010 Environ Int

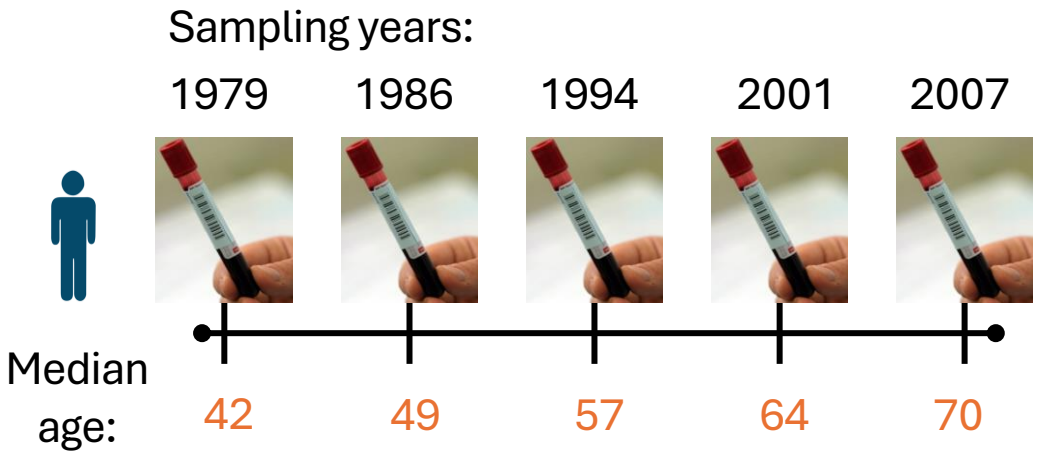
Time trends, lifetime exposure and age



Nøst et al. Environ Health Perspect 2016

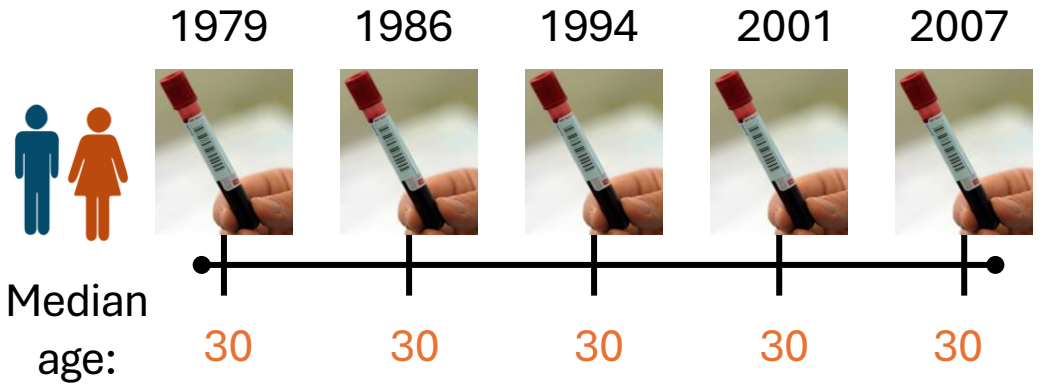
The Tromsø Study – Study 1&2

Study 1:



- Age – within and between persons

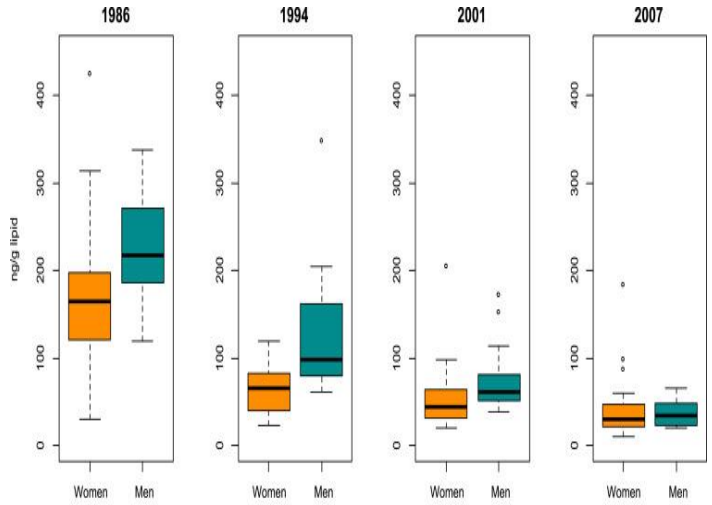
Study 2:



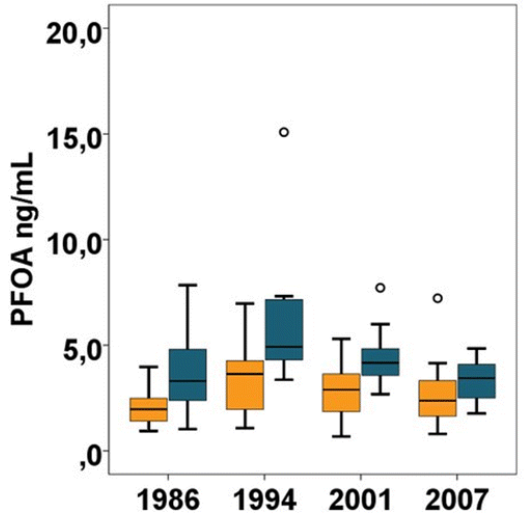
The Tromsø Study – Study 2

Female
Male

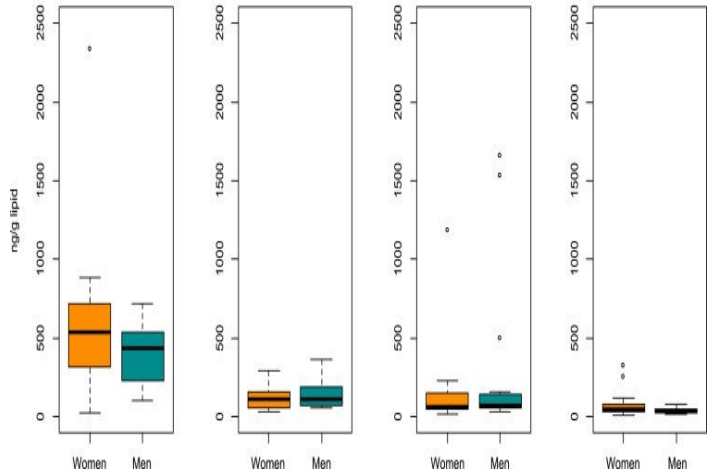
PCB-153



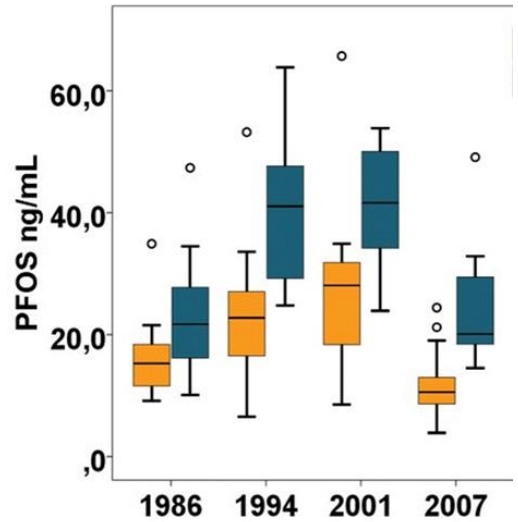
PFOA



DDT

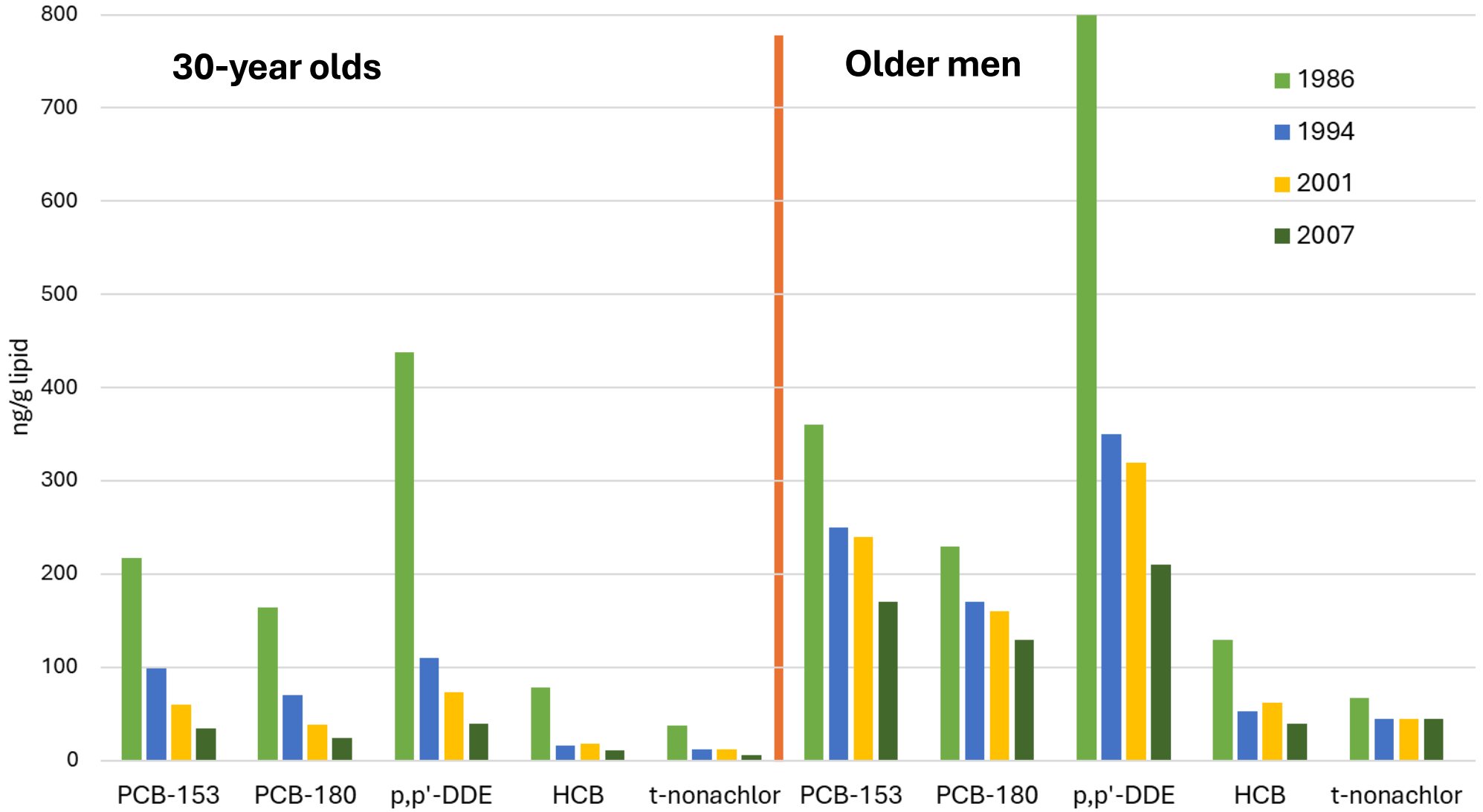


PFOS



Nøst et al. Environ Res 2019 / Berg et al. Environ Sci Pollut Res 2021

The Tromsø Study – Study 1&2



Nøst et al. Environ Res 2019

The Tromsø Study – Longitudinal study 1&2

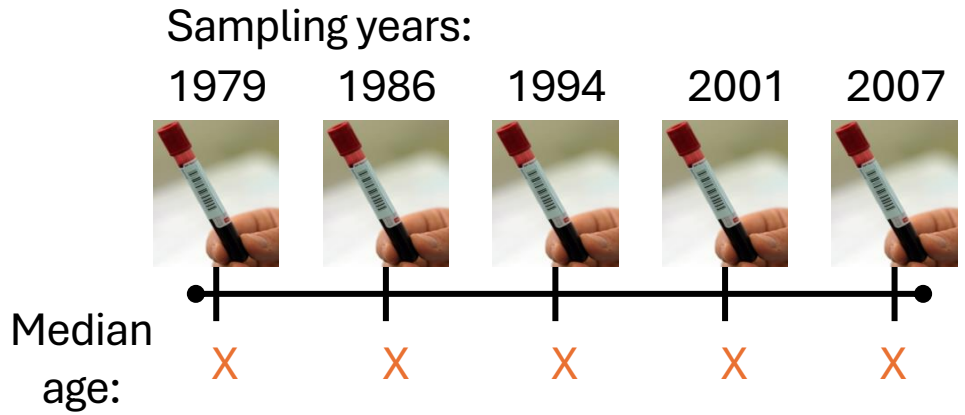
- Study designs:
  - Longitudinal studies – repeated observations
  - Same overall trends, different design and age groups

- Components of time in human studies

Age

Birth cohort

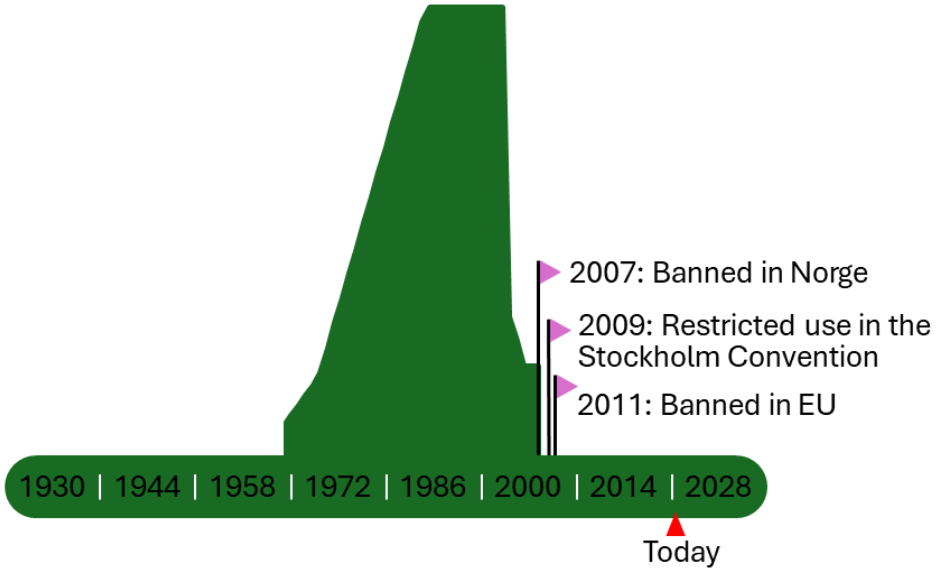
Sampling year



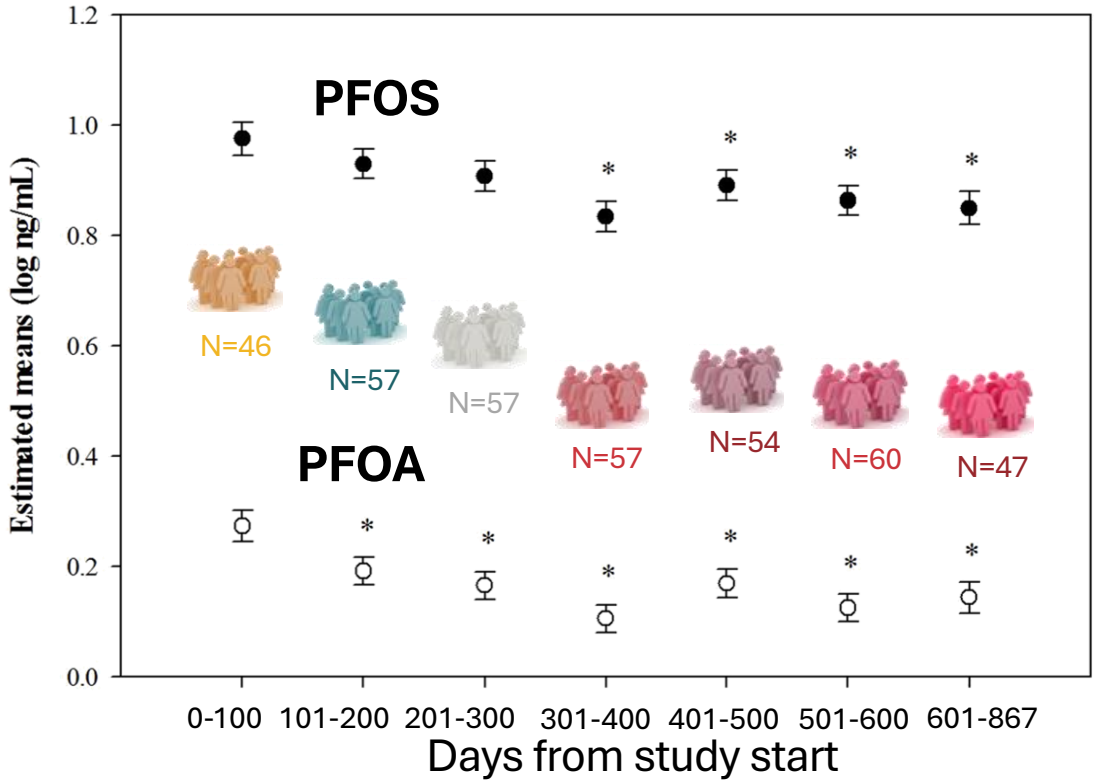
Emissions are time-variant and compound-specific

Time trends in cross-sectional studies?

- The Northern Norway mother and child contaminant cohort study
  - Recruitment period: 2007-2009
  - 2nd trimester (n=391)
  - Blood sampling period: 2.3 years



Berg et al. 2014 Env Int / Illustration by Vivian Berg, UiT.



POPs exposures and ‘omics data

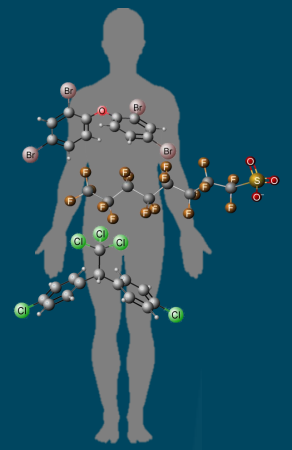
- Study designs:
- Cross-sectional studies – one time point

- Genetic variants associated with 57 essential and non-essential trace elements in HUNT, some also in MoBa and PIVUS
  - Among the non-essensial: Arsenic, cadmium, and lead

- DNA methylation and gene expression profiles and PFAS concentrations
  - Few strong markers consistently indicated across comparisons

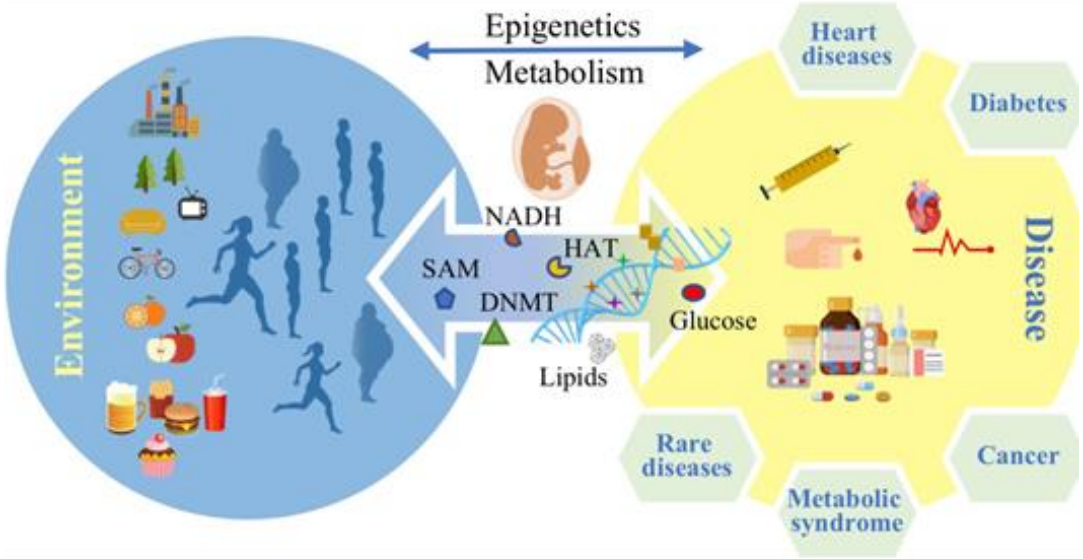
Moksnes et al. 2024 Commun Biol / Coelho et al. *in prep*

Human health effects of environmental contaminants



Human health effects of POPs

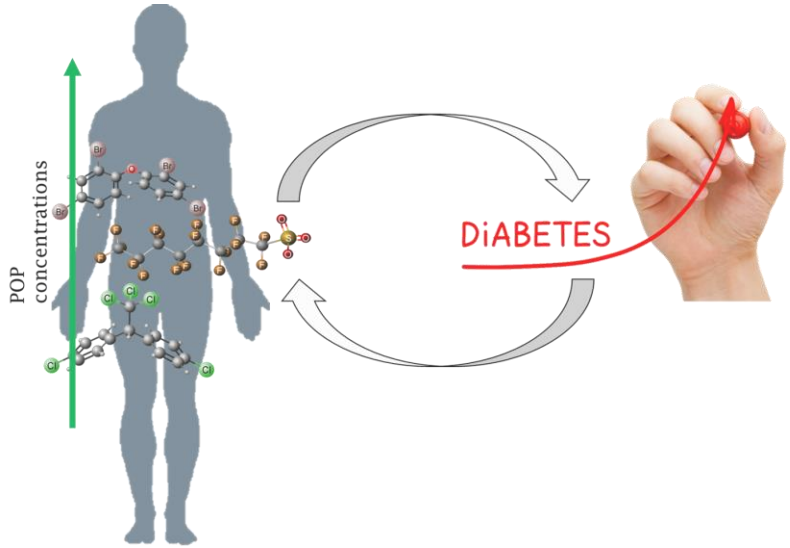
- Most established health effects:
  - Endocrine disruption
  - Increased cancer risks
  - Reproductive disorders
  - Immune system alterations
  - Neurobehavioral impairment
  - Genotoxicity



- Typically:
  - Expensive- limited number of samples
  - Often only one sample = cross-sectional
  - Limited knowledge about molecular mechanisms of POPs and mixtures of POPs
  - Limited knowledge about etiological relevant time periods for exposure

T2DM studies in the Tromsø Study

- An example of research on the relation of POP exposure and risk of Type 2 Diabetes Mellitus (T2DM)
- Rapid increase in T2DM and obesity globally
- T2DM prevalence in Norway: 4.8%

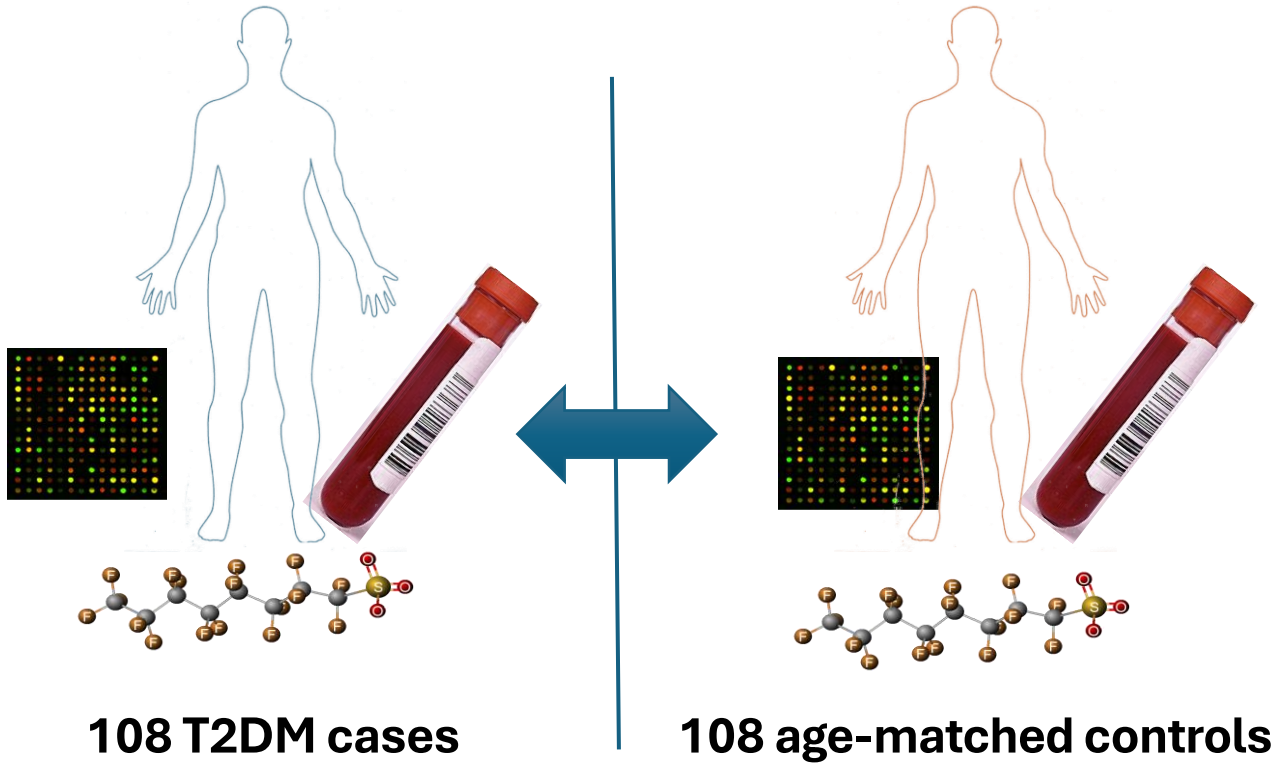


- Strong effect sizes related to POPs in previous studies

- Study 1: Cross-sectional study including mechanistic modelling
- Study 2: Longitudinal study using repeated measurements from the same persons

Study 1: Cross-sectional design - T2DM

- A case-control study of POPs and prevalent T2DM in Norwegian women



Rylander et al. 2015 Environ Res

Associations for many POPs

- Strong associations for prevalent T2DM and β-HCH and p,p'-DDE
- Similar patterns for PCBs and PFAS but lower ORs

- In agreement with prev. studies
- Confounding by lipids?

Crude and adjusted Odds Ratios (OR) for risk of type 2 diabetes mellitus according to lipid-normalized POP concentrations.

POP[a]		Crude OR (95% CI)	Adjusted OR[b] (95% CI)
HCB	1Q	1.00	1.00
	2Q	1.34 (0.56, 3.20)	3.03 (0.71, 13.0)
	3Q	3.52 (1.47, 8.43)	3.19 (0.84, 12.1)
	4Q	6.74 (2.47, 18.4)	7.00 (1.59, 30.8)
β-HCH	1Q	1.00	1.00
	2Q	4.21 (1.38, 12.9)	3.63 (0.67, 19.7)
	3Q	18.8 (4.44, 79.7)	16.8 (2.00, 141)
	4Q	136.2 (21.0, 882)	203.8 (11.5, 3620)
t-NC	1Q	1.00	1.00
	2Q	1.80 (0.81, 4.02)	2.22 (0.53, 9.35)
	3Q	2.39 (1.11, 5.15)	5.06 (1.21, 21.1)
	4Q	4.11 (1.65, 10.2)	6.56 (1.57, 27.5.)
oxy-CD	1Q	1.00	1.00
	2Q	1.02 (0.47, 2.23)	1.33 (0.37, 4.8)
	3Q	2.64 (1.16, 6.01)	3.61 (0.96, 13.6)
	4Q	4.12 (1.64, 10.31)	7.22 (1.60, 32.58)
p,p'-DDE	1Q	1.00	1.00
	2Q	2.68 (1.05, 6.83)	1.58 (0.44, 5.63)
	3Q	4.68 (1.74, 12.6)	3.44 (0.87, 13.66)
	4Q	15.4 (5.06, 46.6)	11.3 (2.55, 49.9)

Rylander et al. 2015 Environ Res

Modelling applied in health effect study

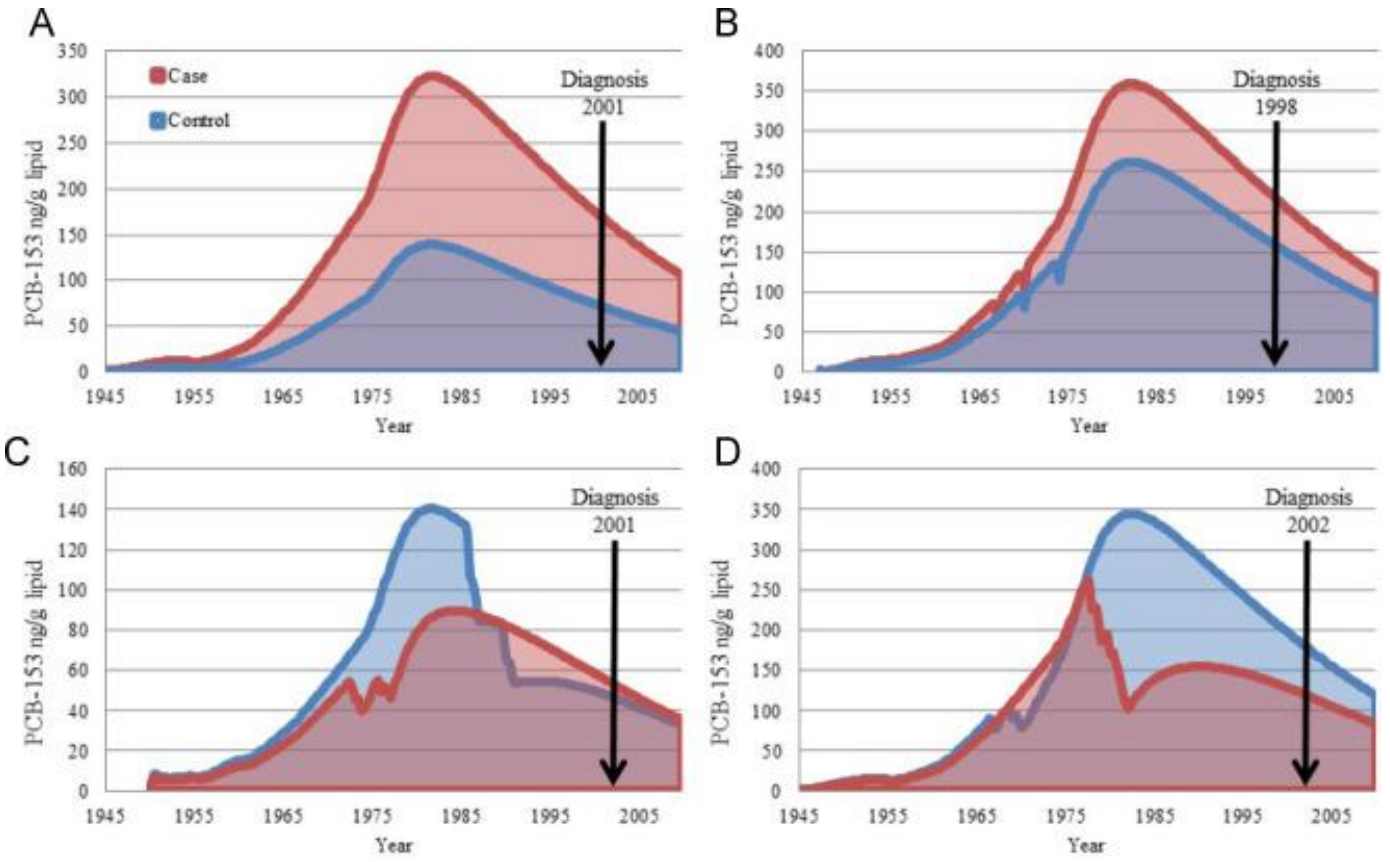
- Combined cross-sectional plasma measurements PCB-153 with emission-based modeling

Early life ($AUC_{0\text{-}18}$)

1Q	1.00	1.00
2Q	1.95 (0.78, 4.89)	7.93 (1.72, 36.6)
3Q	0.67 (0.24, 1.89)	2.12 (0.5, 9.06)
4Q	1.83 (0.49, 6.77)	4.21 (0.51, 34.8)

Total life ($AUC_{0\text{-}diagnosis}$)

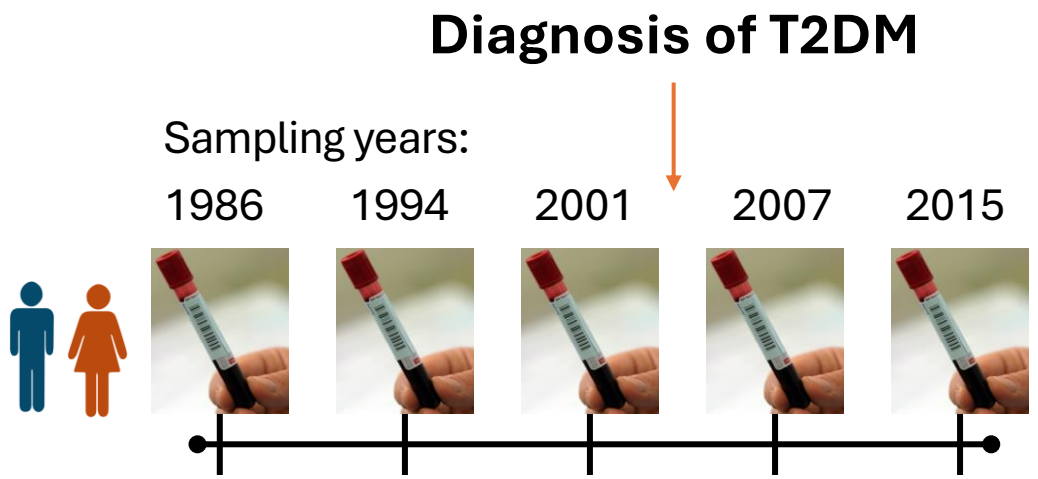
1Q	1.00	1.00
2Q	0.8 (0.33, 1.9)	0.36 (0.08, 1.53)
3Q	1.93 (0.76, 4.93)	3.37 (0.65, 17.4)
4Q	1.97 (0.76, 5.09)	2.45 (0.46, 13.2)



Rylander et al. 2015 Environ Res

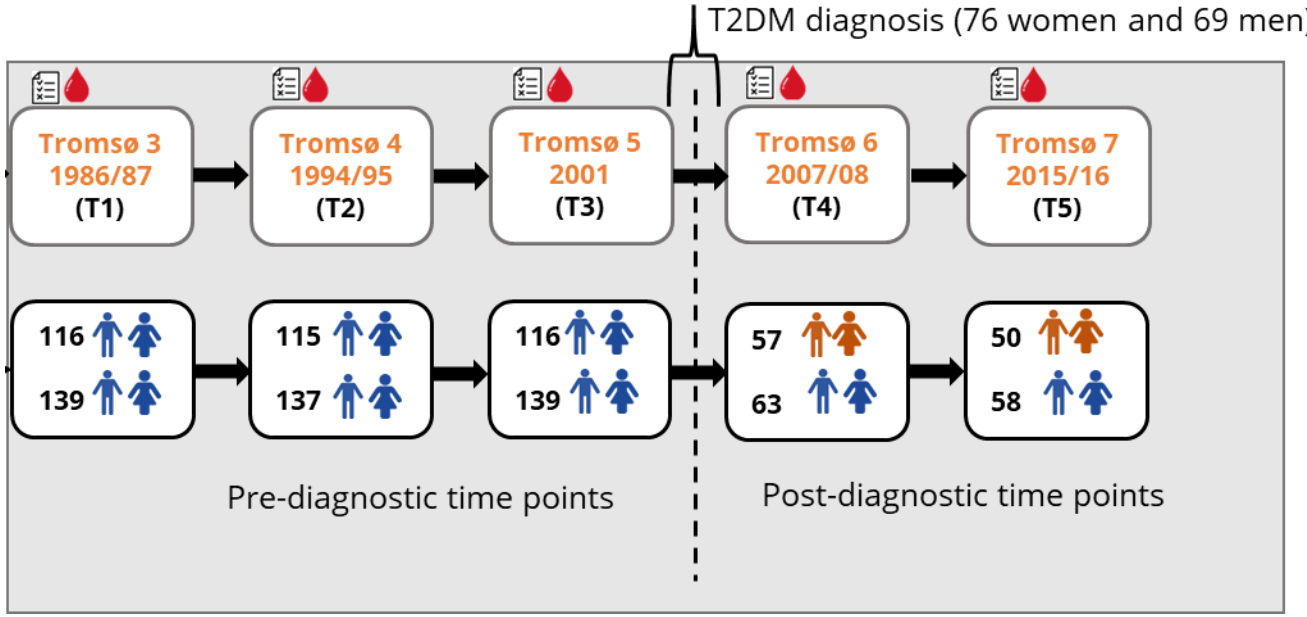
Study 2: Longitudinal design - T2DM

- A longitudinal, nested case-control study with samples before diagnosis
- Examine the associations with T2DM prospectively and cross-sectionally in the same individuals
- Compare the time trends of PCBs, OCPs, PFAAs, and PBDEs between T2DM cases and controls



Charles et al. 2022 Environ Res

Study 2: Longitudinal design - T2DM

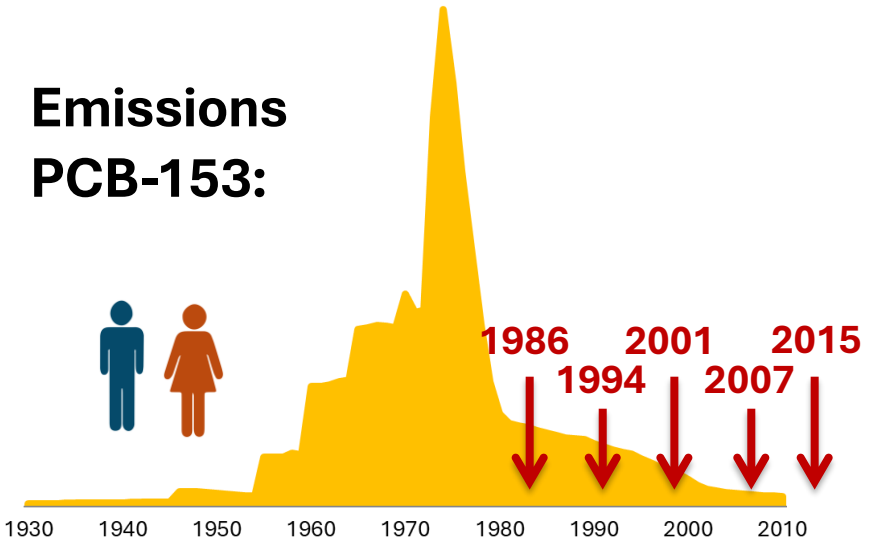


Diabetes status:

- T2DM free

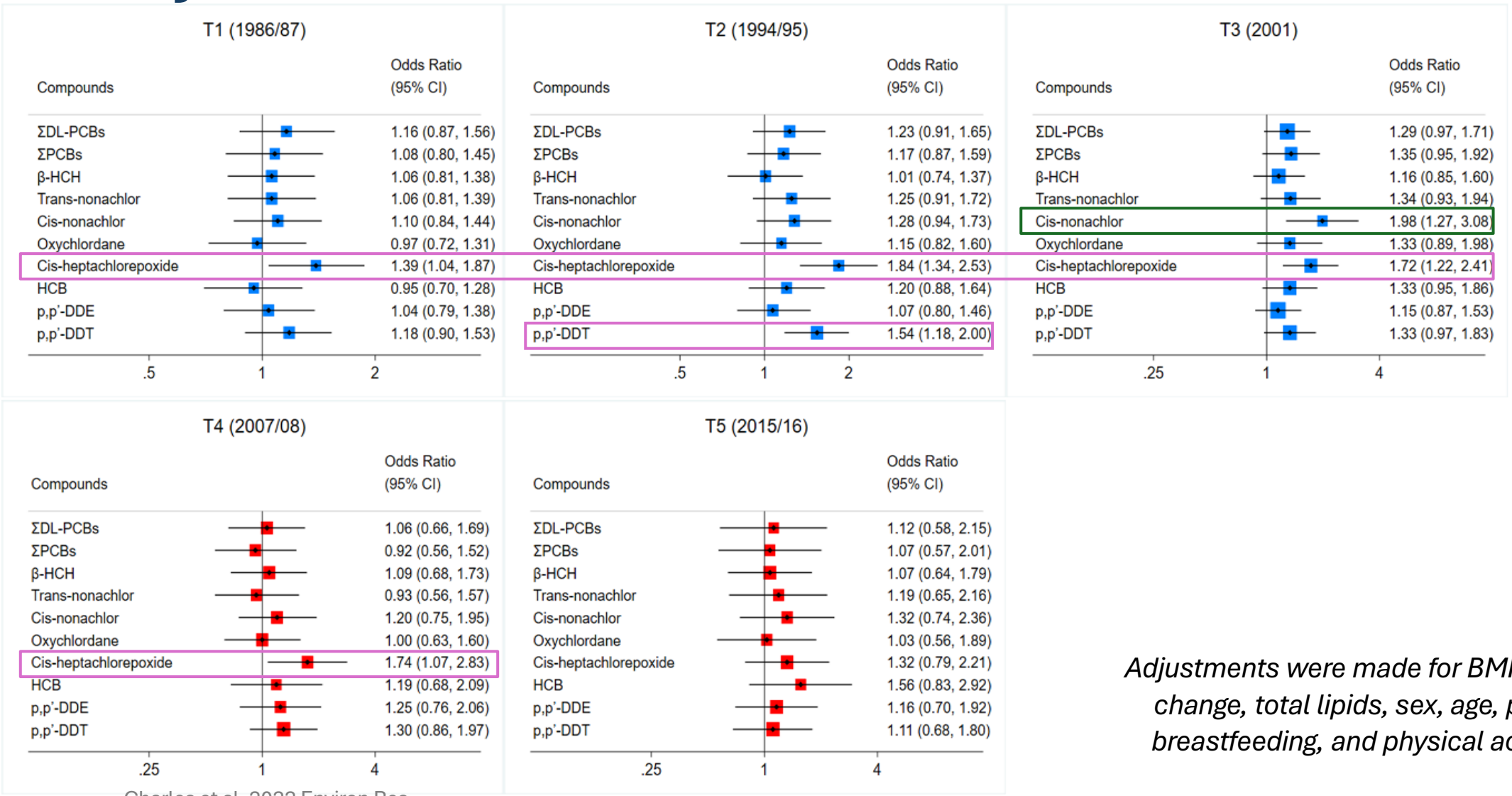
- Diagnosed with T2DM

Total serum samples
N=990



Charles et al. 2022 Environ Res

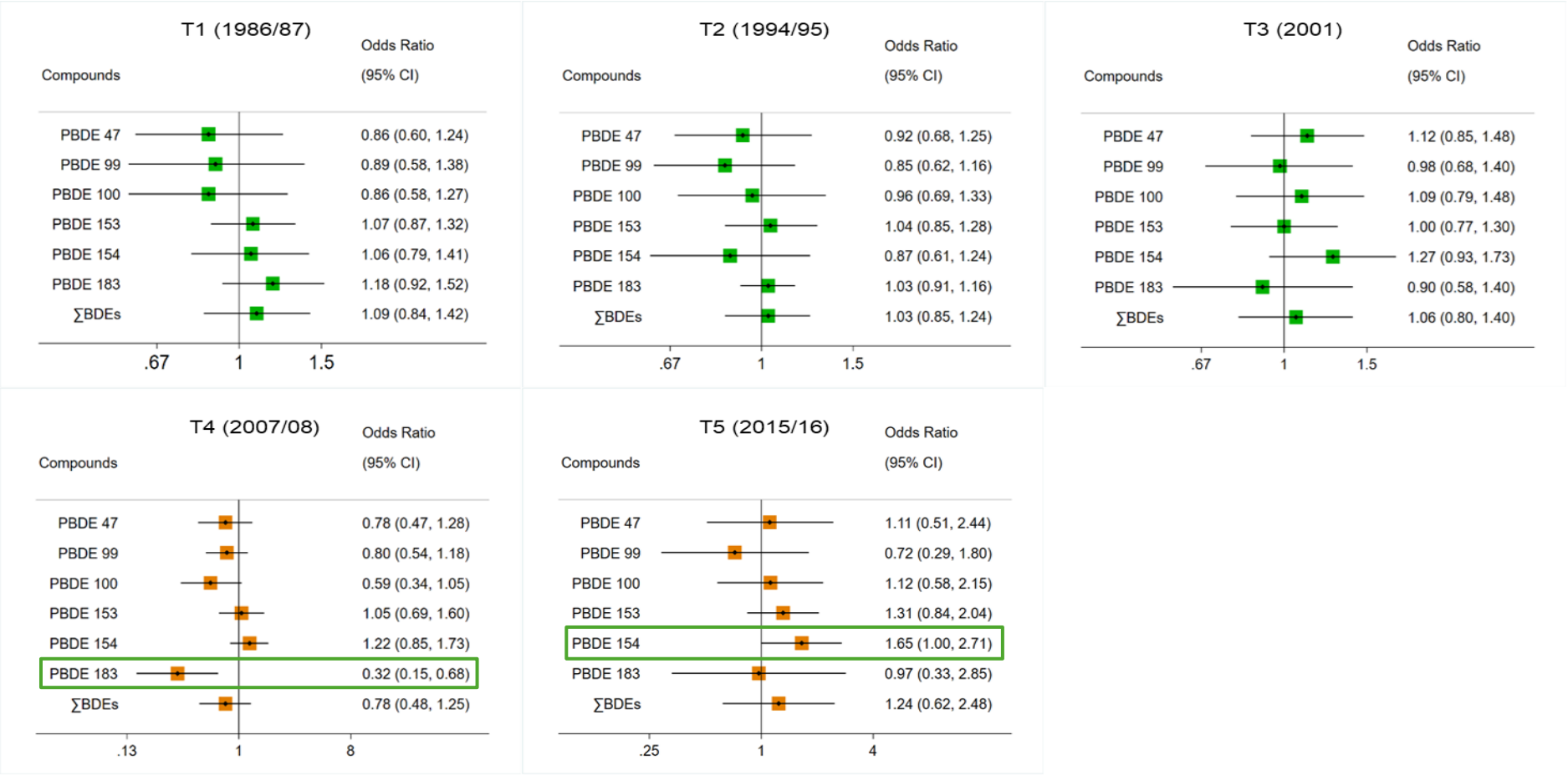
Study 2: Associations to T2DM



Adjustments were made for BMI, weight change, total lipids, sex, age, parity, breastfeeding, and physical activity.

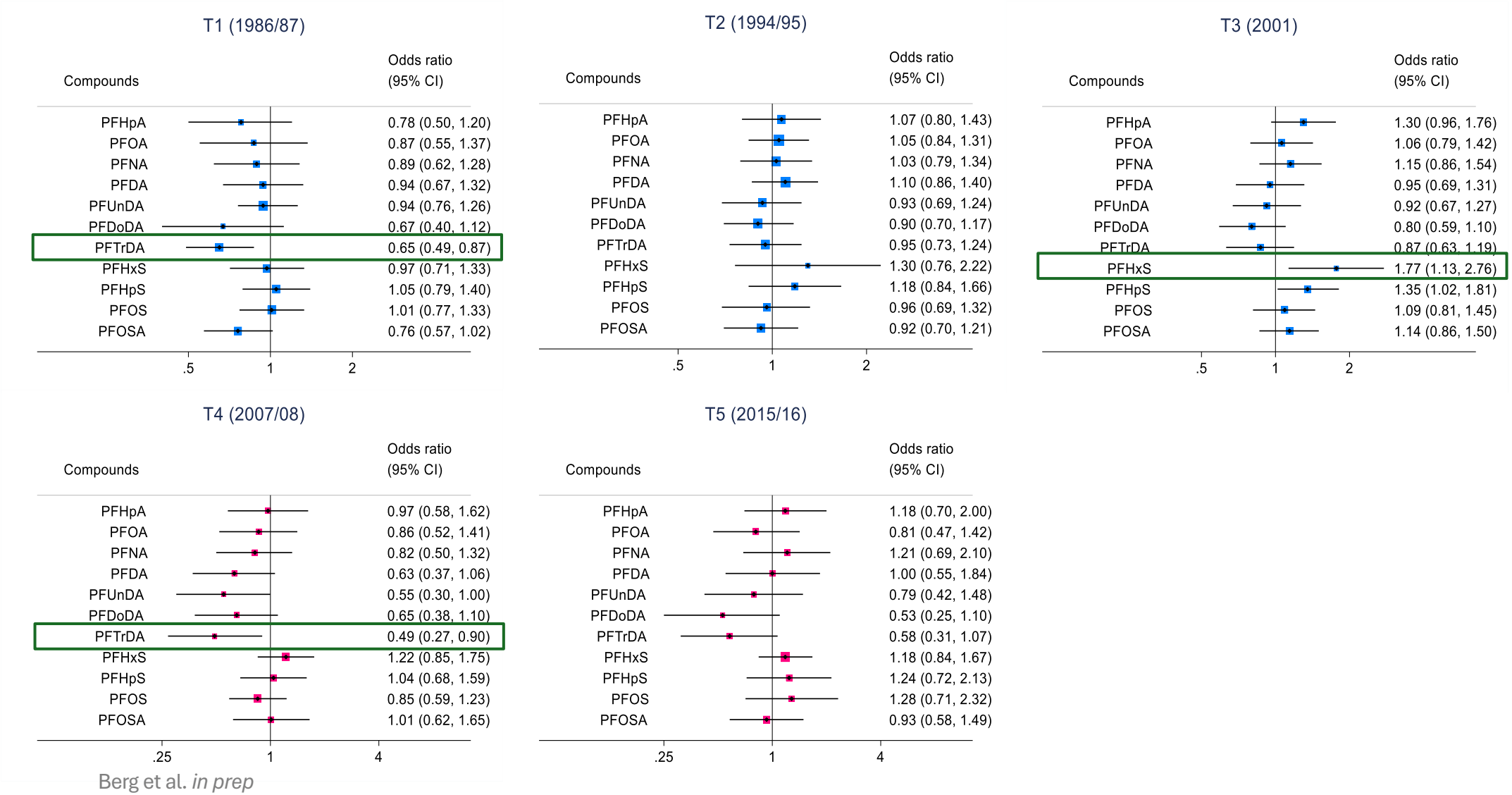
Charles et al. 2022 Environ Res

Study 2: Associations to T2DM



Charles et al. 2023 Int J Hygiene Environ Health

Study 2: Associations to T2DM

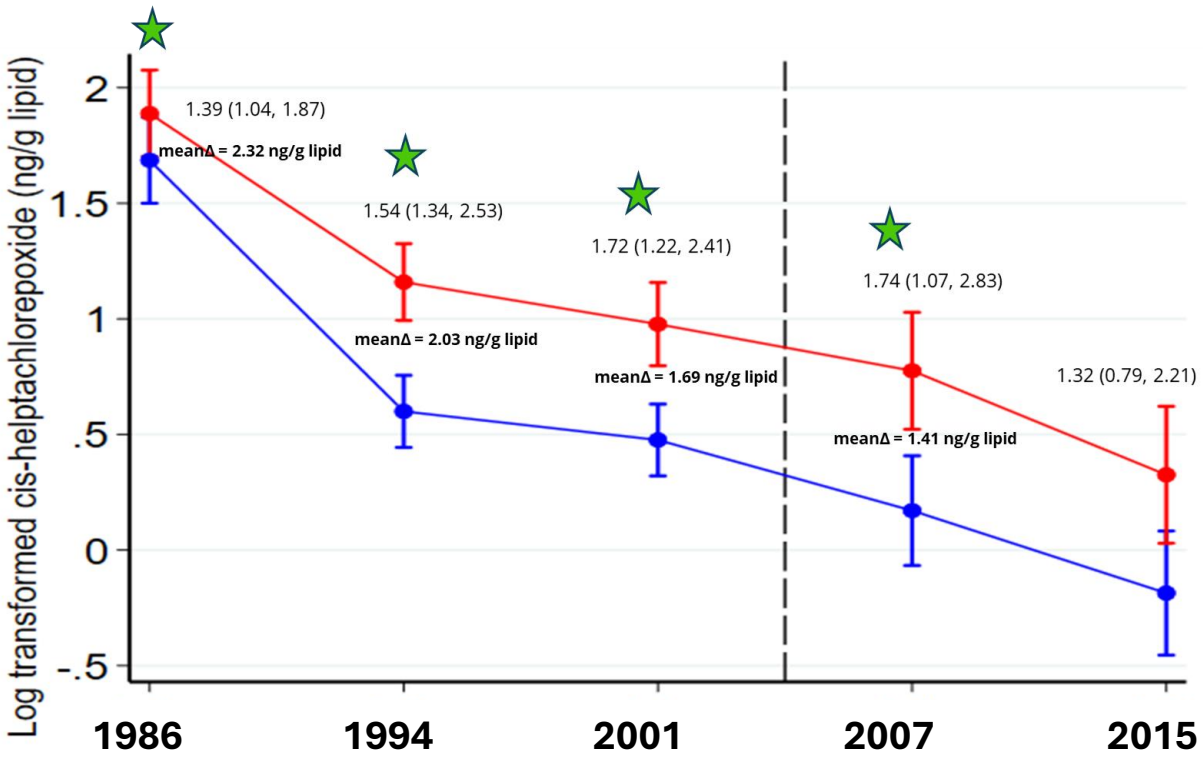


Berg et al. *in prep*

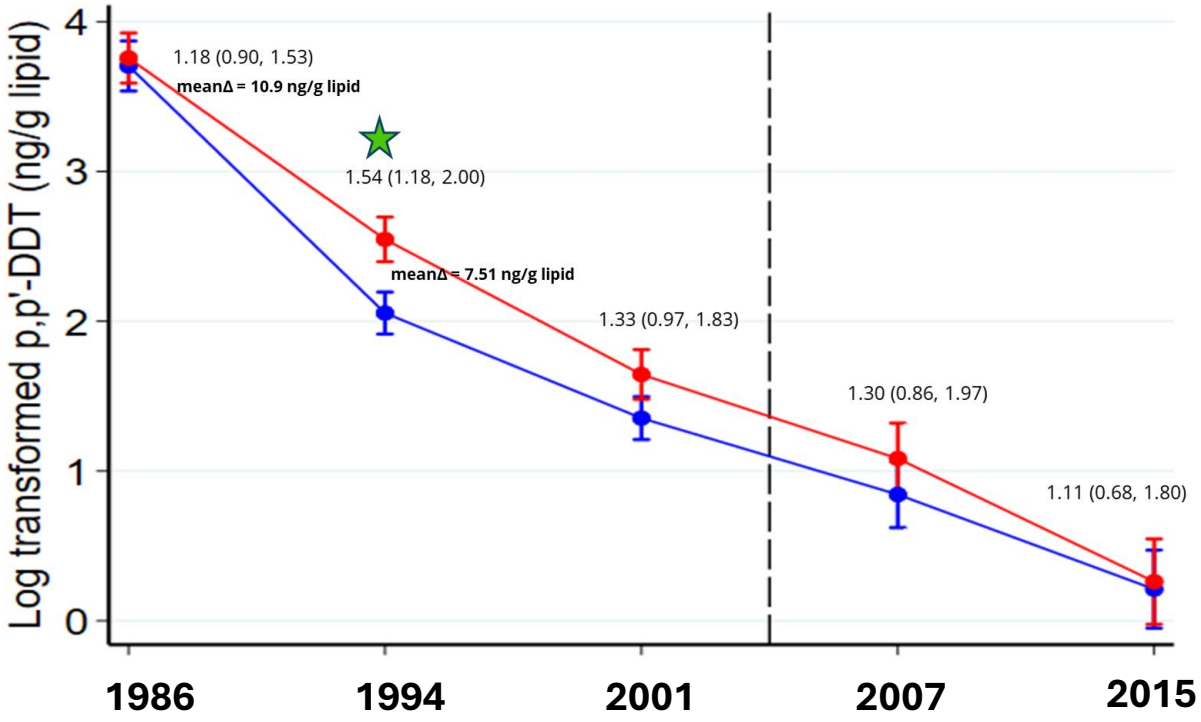
Study 2: Time trends in cases and controls

- Cases
- Controls

cis-heptachlorepoxide

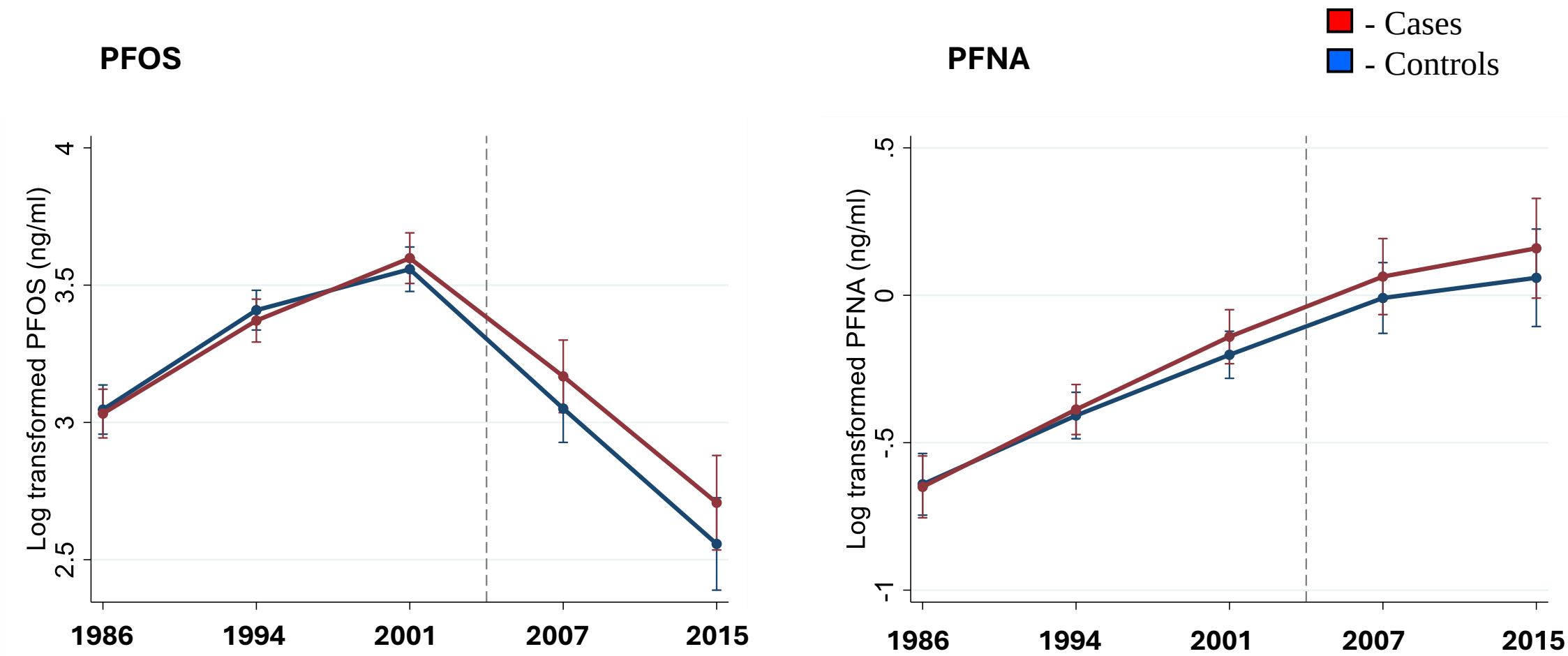


DDT



Charles et al. 2023 Int J Hygiene Environ Health

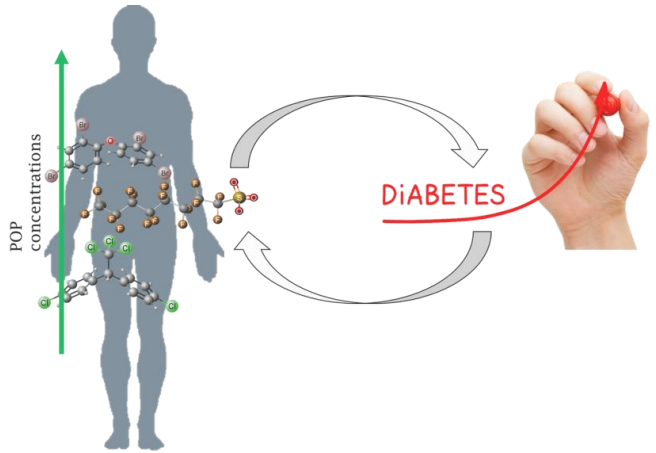
Study 2: Time trends in cases and controls



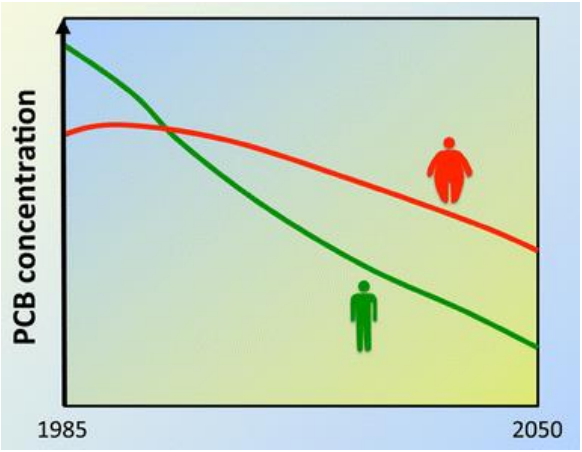
Berg et al. *in prep*

The Tromsø Study – T2DM study 1&2

- Study designs:
- Cross-sectional study – one time point
- Longitudinal study – repeated observations



- Up to three measurements before clinical diagnosis of T2DM in cases.
- The observed consistently strong associations between cis-heptachlor epoxide and T2DM
  - Higher in cases compared to controls and slower declines in cases in pre-diagnostic time points



Wood et al. 2016 ES&T

Recent simulation study

Environment International 192 (2024) 109056

Contents lists available at ScienceDirect

Environment International

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

Short communication

How well does a single blood sample represent long-term exposure for epidemiological studies of PFOA among men in the general population?

Scott M. Bartell [a,*], Mark P. Purdue [b], Jongeun Rhee [b], Therese H. Nøst [c,d], Jennifer Rusiecki [e], Kyle Steenland [f]

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[b] Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics
[c] Department for Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway
[d] HUNT Research Centre, NTNU Norwegian University of Science and Technology, Trondheim, Norway
[e] Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Scie
[f] Dept. of Environmental Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA

"Using data based on studies of men, single baseline serum samples … were not always reliable surrogates for average exposure over 3 decades, during which time PFOA exposure levels in the general population have changed substantially."

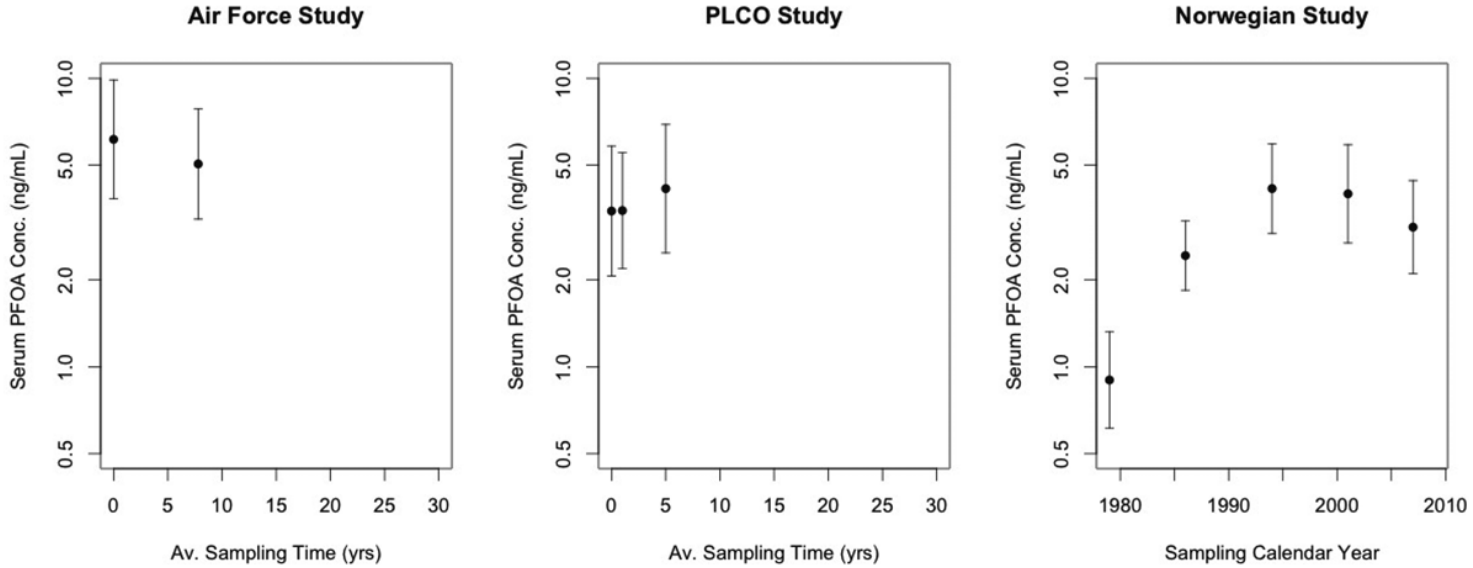
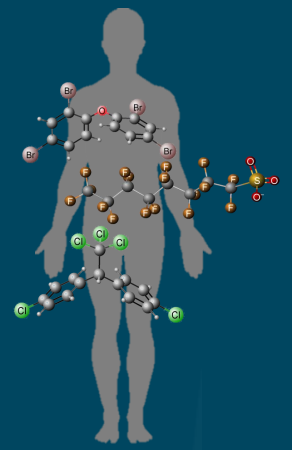


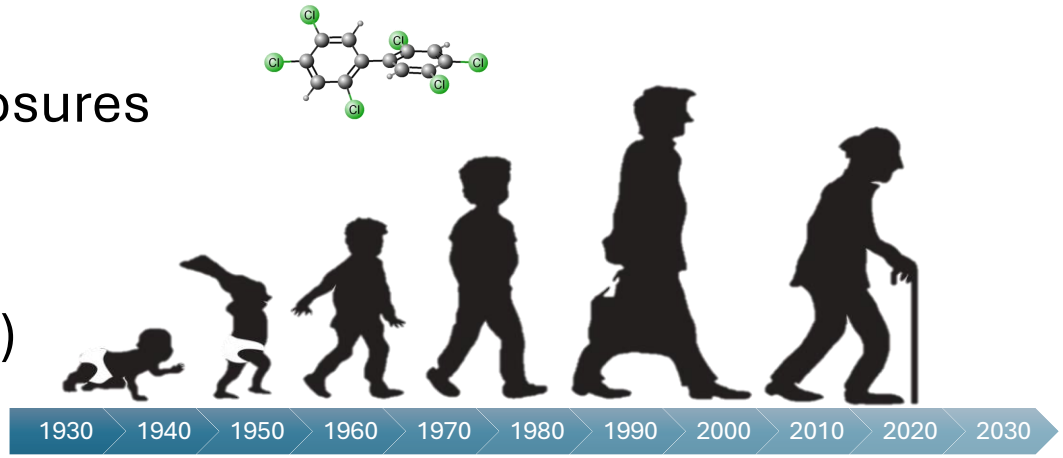
Fig. 1. Temporal patterns in serum PFOA concentrations for the 3 studies (PLCO, Air Force, and Norwegian). Geometric mean serum PFOA concentration (points) with 1 geometric standard deviation (error bars) are shown for each time point.

A summary



Designing human exposure monitoring

- Aspects of time when investigating human exposures
  - Sampling year and emissions
  - Birth cohort
  - Age (inter-individually and intra-individually)



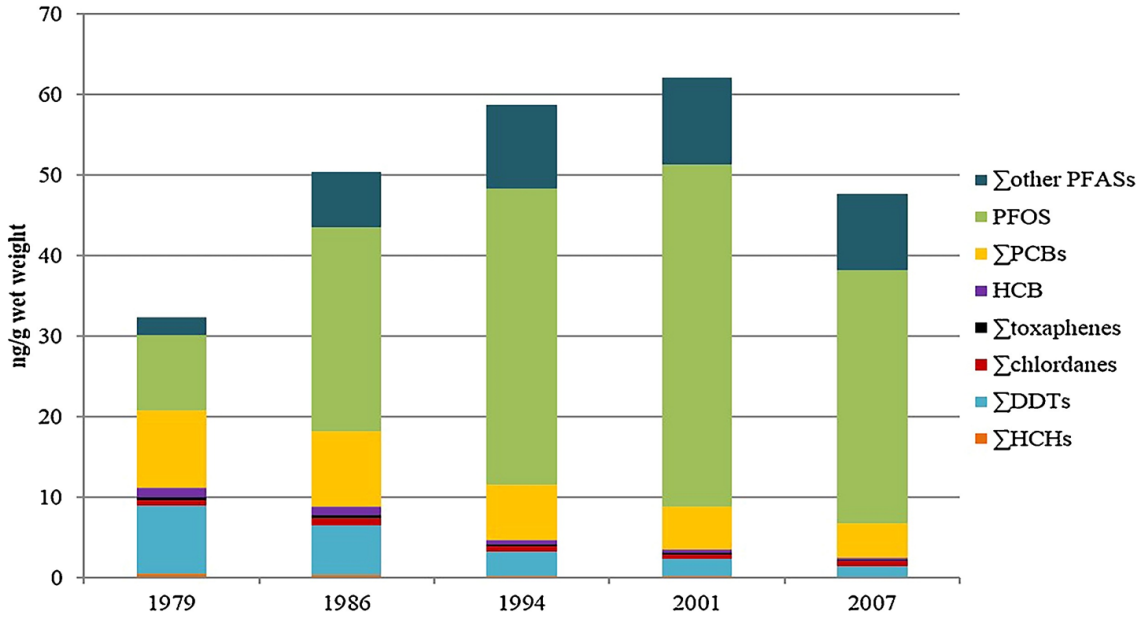
- Longitudinal studies: repeated measurements, long study period
- Cross-sectional studies: good range of birth years

- Exposure misclassification when based on one blood sample
- How much of lifetime exposure is reflected in a blood sample depends on compound-specific past emission histories relative to birth years

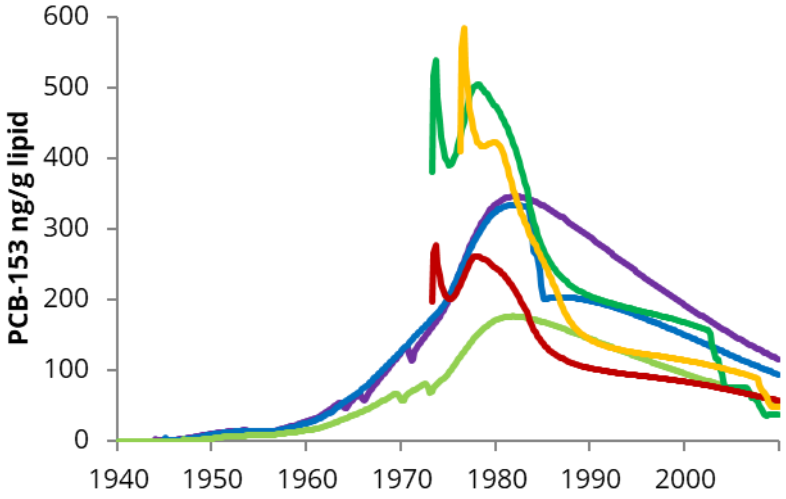
Using both measurements and modelling

- Modelling increased our understanding of human exposure

Measurements

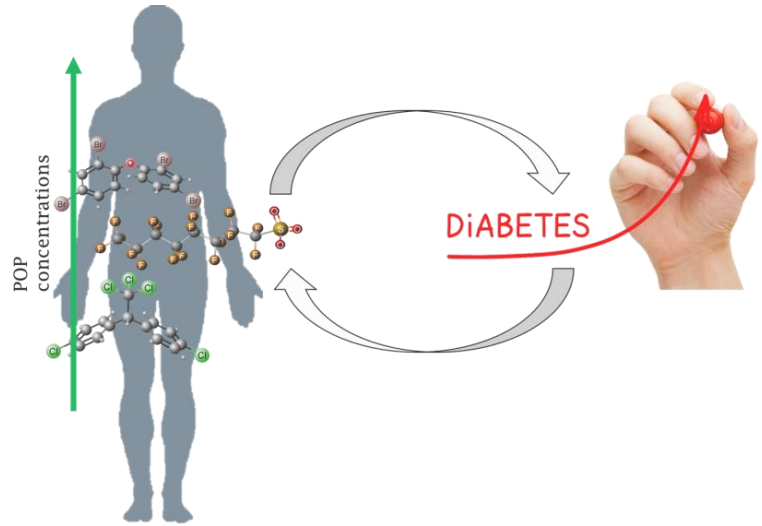


Modeling



Effect studies using repeated measurements

- Prospective associations rarely studied

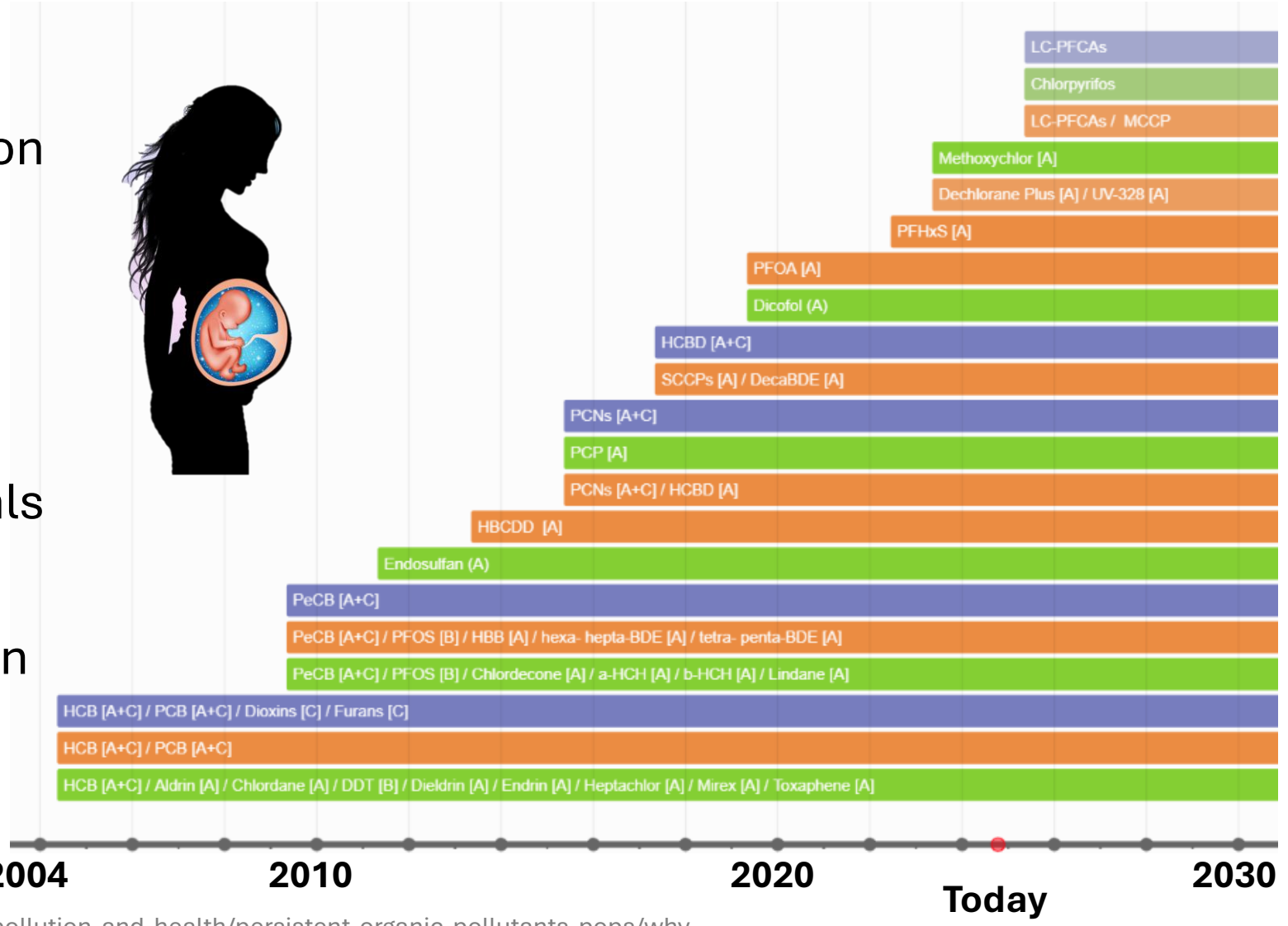


- PCBs and OCPs - slower declines in T2DM cases, strong positive associations with T2DM for some OCPs
- Slower decline → increased POP concentrations → positive associations?
- Complex health endpoints and causality difficult to evaluate

The importance of international regulations

- Currently listings in the Stockholm Convention on POPs:

- The Basel Convention
- The Rotterdam Convention
- EU's European Chemicals Agency (ECHA)
- EU's Registration, Evaluation, Authorisation and restriction of Chemicals (REACH)

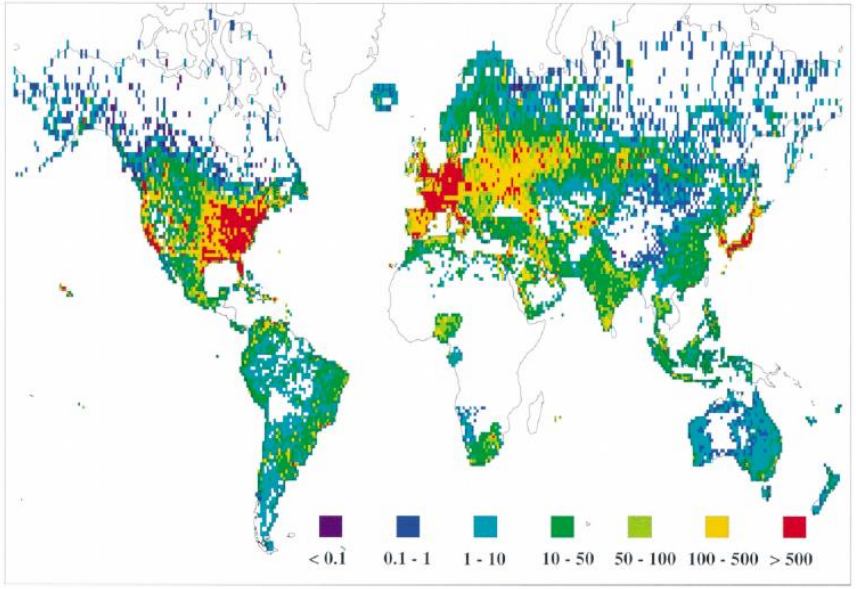


www.unep.org/topics/chemicals-and-pollution-action/pollution-and-health/persistent-organic-pollutants-pops/why

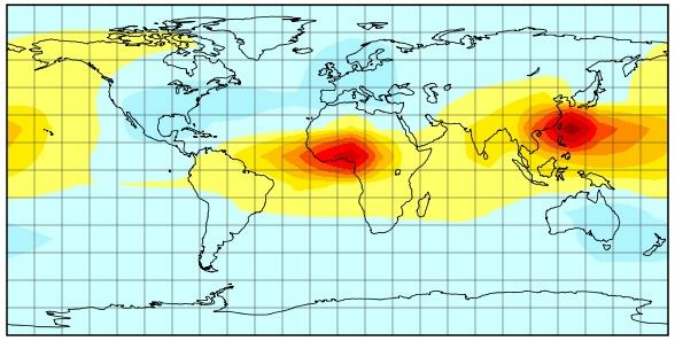
Important to remember

- Focus today: Norwegian studies

Historic use of PCBs



Electronic waste today



Breivik et al. 2010 Environ Int; Breivik et al. 2014 Environ Sci Technol; Asante et al. 2011 EST.

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- Dolley Charles for slides from her work
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- Illustrations cited or from Mostphotos.com

Fram Centre

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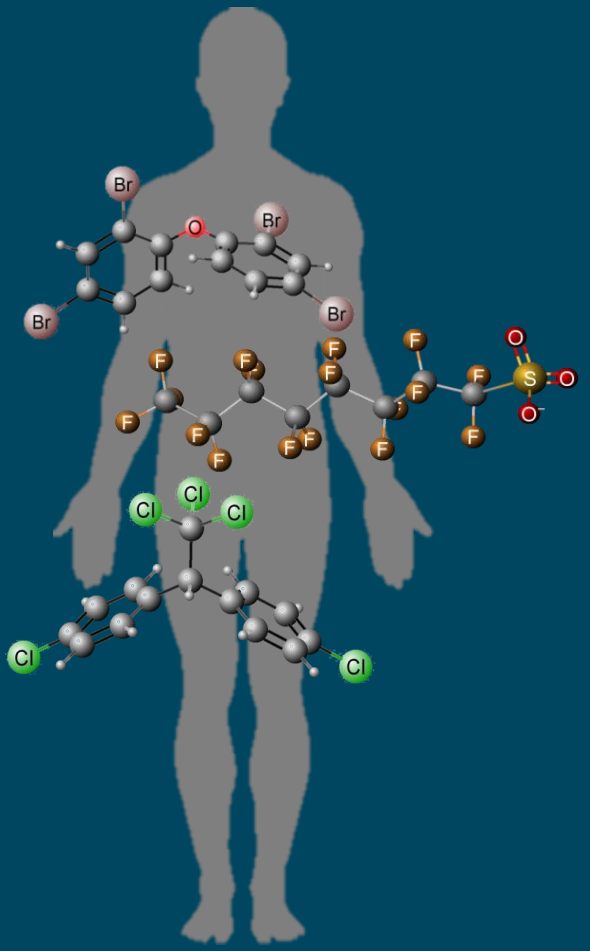
UiT The Arctic University of Norway

Thank you for your attention!



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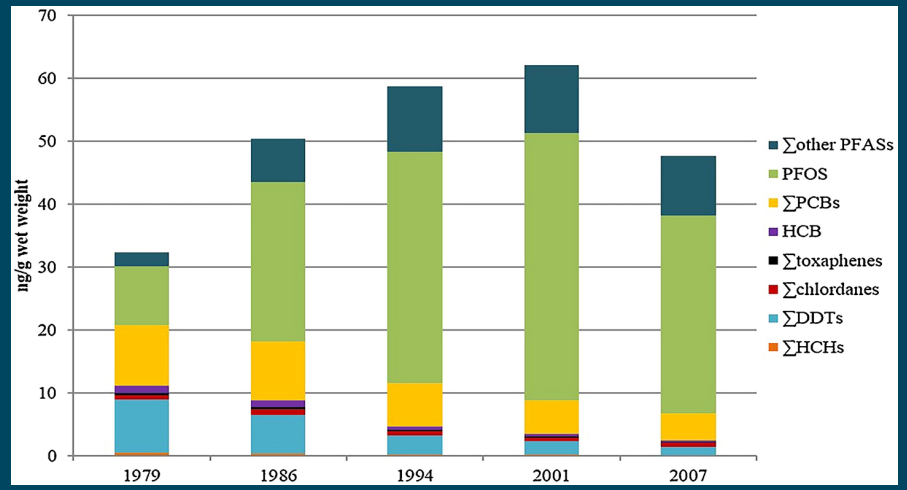
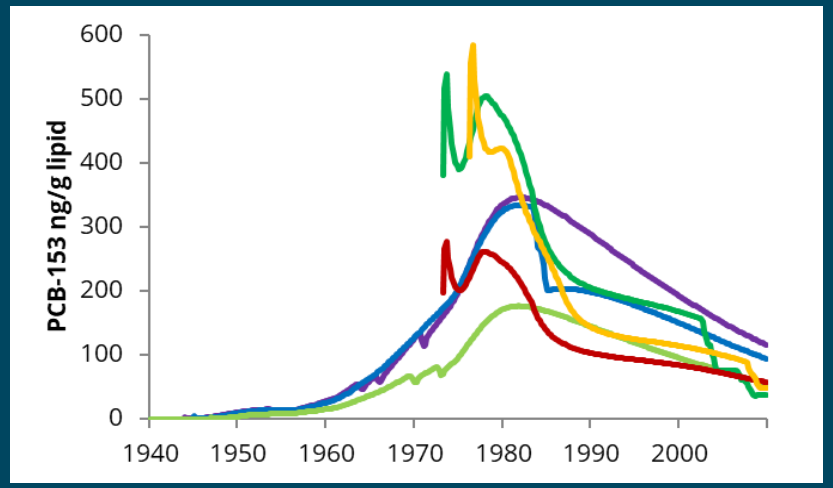
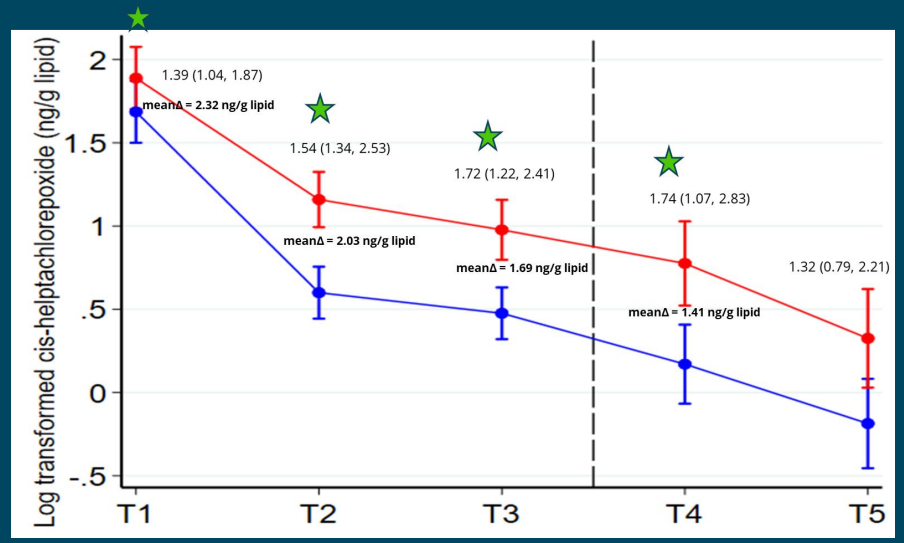
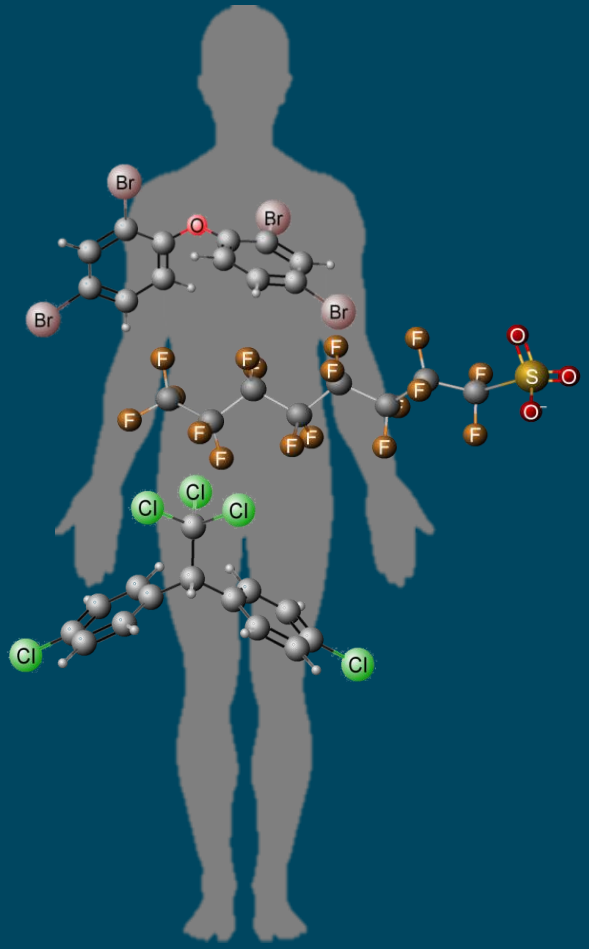
UiT The Arctic University of Norway
Researcher, HUNT Research Centre,
NTNU Norwegian University of Science and Technology

Take home visuals:









Questions?

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