Pollution and health

Virissa Lenters, Assisstant Professor
Vrije Universiteit Amsterdam

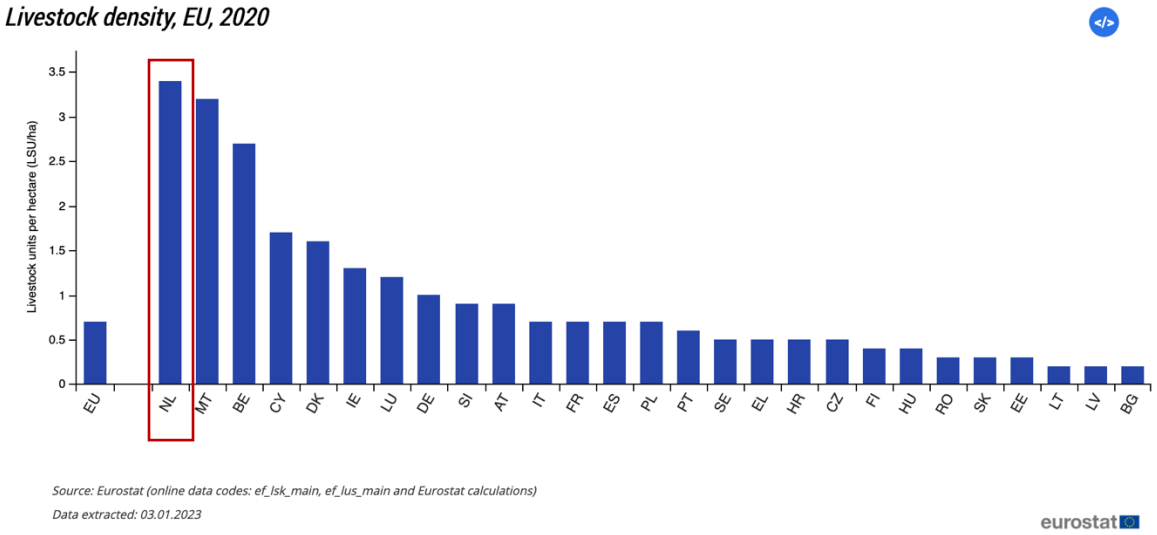
Norwegian Epidemiological Association (NOFE) conference
Oslo, Oct. 16, 2024

- Prof. Majorie van Duursen
- Prof. Marja Lamoree
- Prof. Pim Leonards
- Eva Sugeng
- Prof. Roel Vermeulen
- Runyu Zou
- Amanda Durken
- Anran Cai

“God created the earth, but the Dutch created the Netherlands”

Edward Burtynsky, Polders, Grootschermer, The Netherlands, 2011; Sentinel-1 image © ESA processed by e-Geos

The Netherlands: intensively used



NL TIMES

Vegetation along the Maas river in Roermond - Credit: eurotravel / DepositPhotos - License: DepositPhotos

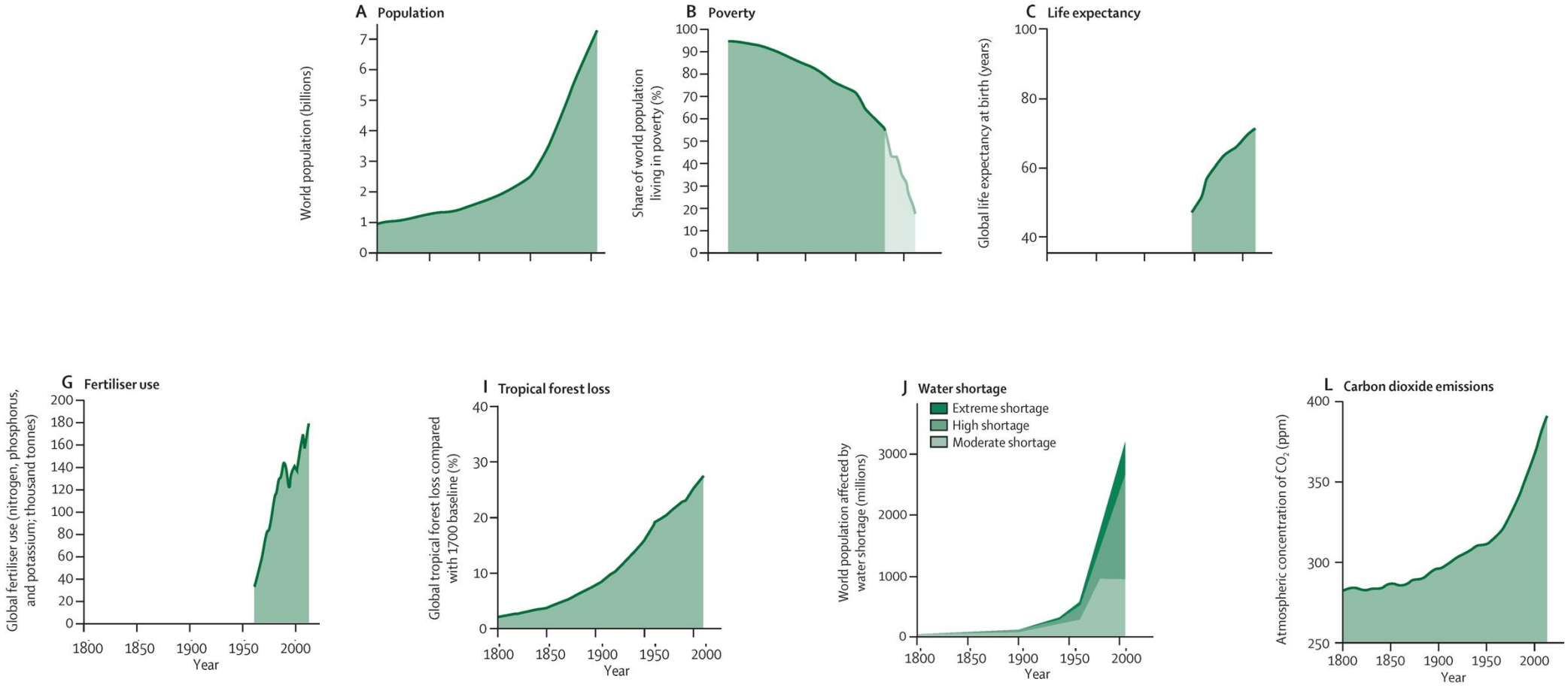
NATURE NATUURMONUMENTEN WAGENINGEN UNIVERSITY & RESEARCH
WATER FRAMEWORK DIRECTIVE SURFACE WATER WATER QUALITY » MORE TAGS

THURSDAY, 9 MARCH 2023 - 13:11

Netherlands risking massive fines with dirtiest surface water in Europe

The Netherlands has the dirtiest surface water in Europe, with not even 1 percent getting the “good” label, according to a

Planetary health perspective: healthier but exploiting planet

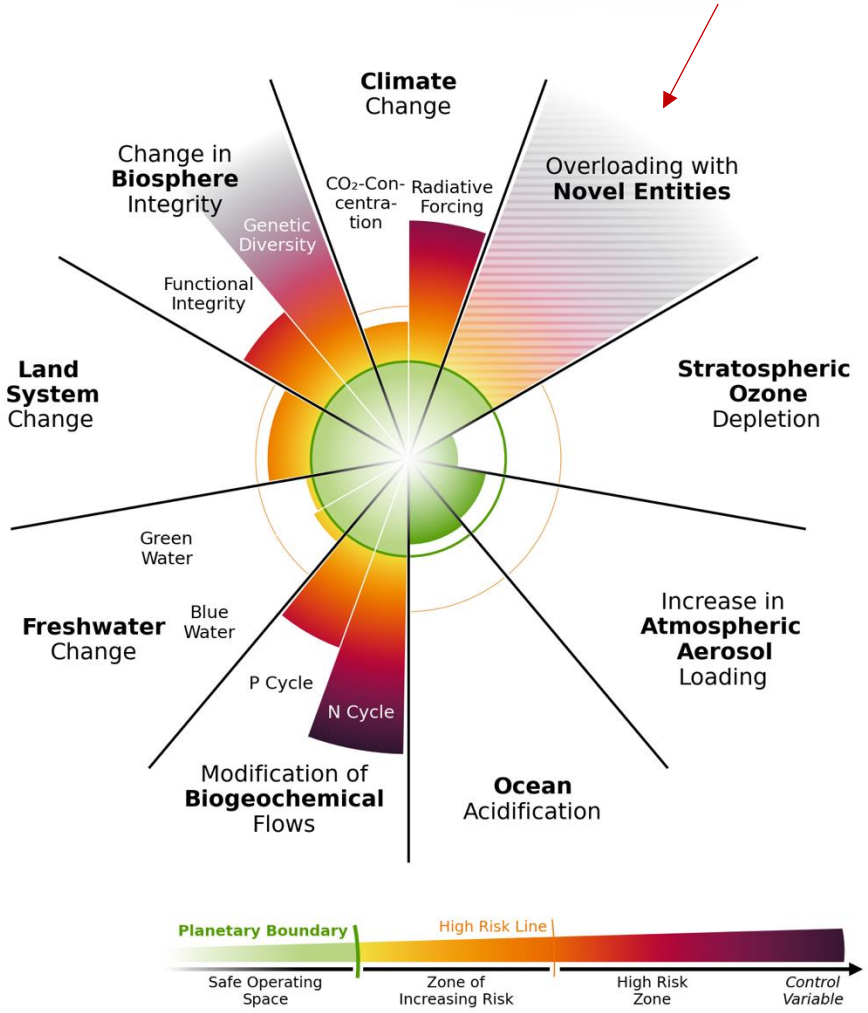


Whtimee et al. Safeguarding human health in the Anthropocene epoch: report of The Rockefeller Foundation–Lancet Commission on planetary health . The Lancet

Planetary health perspective

- Planetary boundaries: 9 processes that are critical for maintaining the stability and resilience of Earth system as a whole
- “suggesting that Earth is now well outside of the safe operating space for humanity”

Includes synthetic chemicals and substances (e.g., microplastics, endocrine disruptors, and organic pollutants)



Steffen et al. Sustainability. Planetary boundaries: guiding human development on a changing planet. Science. 2015
Richardson et al. Earth beyond six of nine planetary boundaries. Science Advances 2023

Impact of pollution

- 1 in 6 premature deaths
  - 92% in LMICs
  - Household air pollution from solid fuels, water pollution, outdoor air pollution, lead, chemicals, occupational fumes…

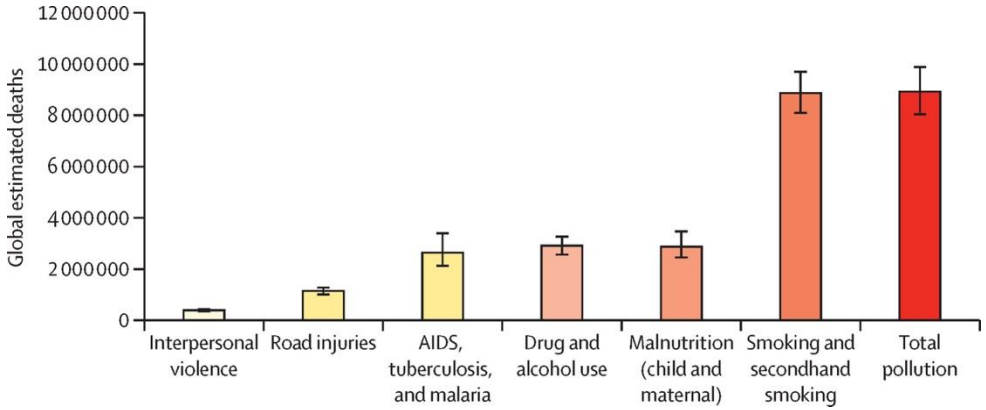
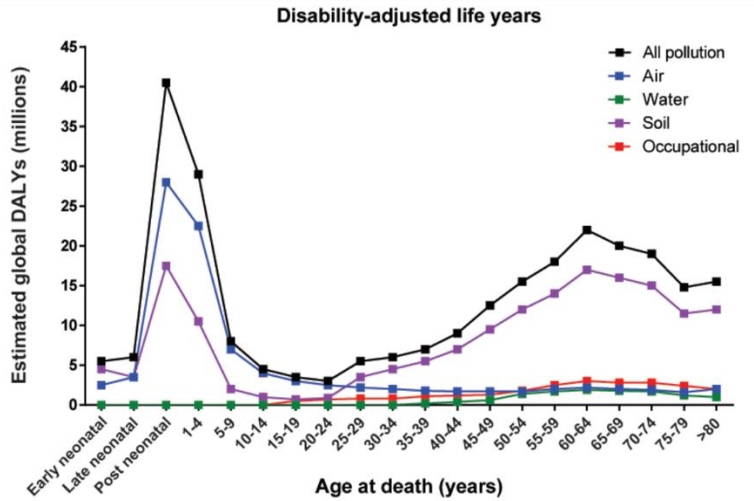
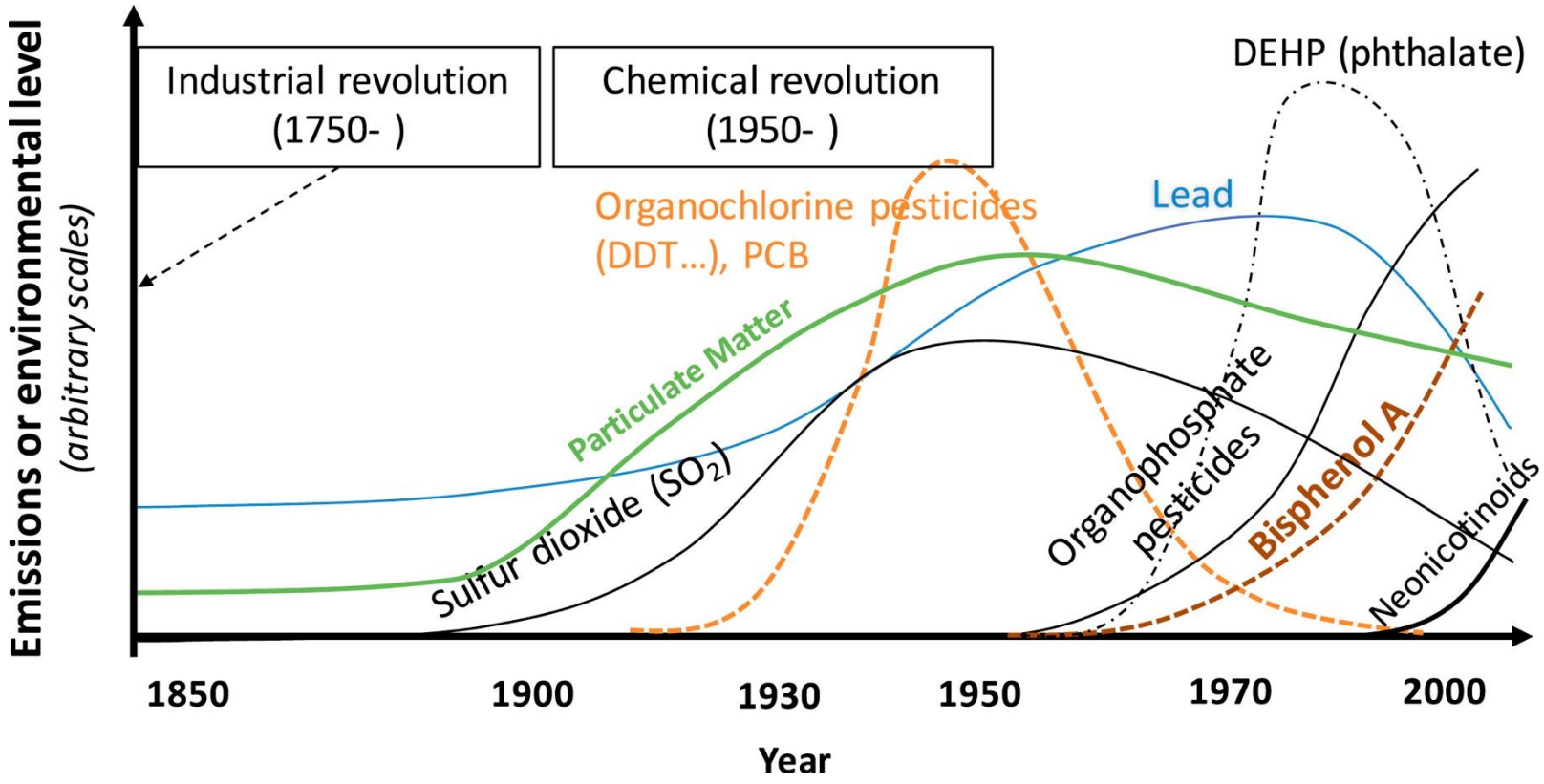


Fig. Global estimated deaths by major risk factor or cause



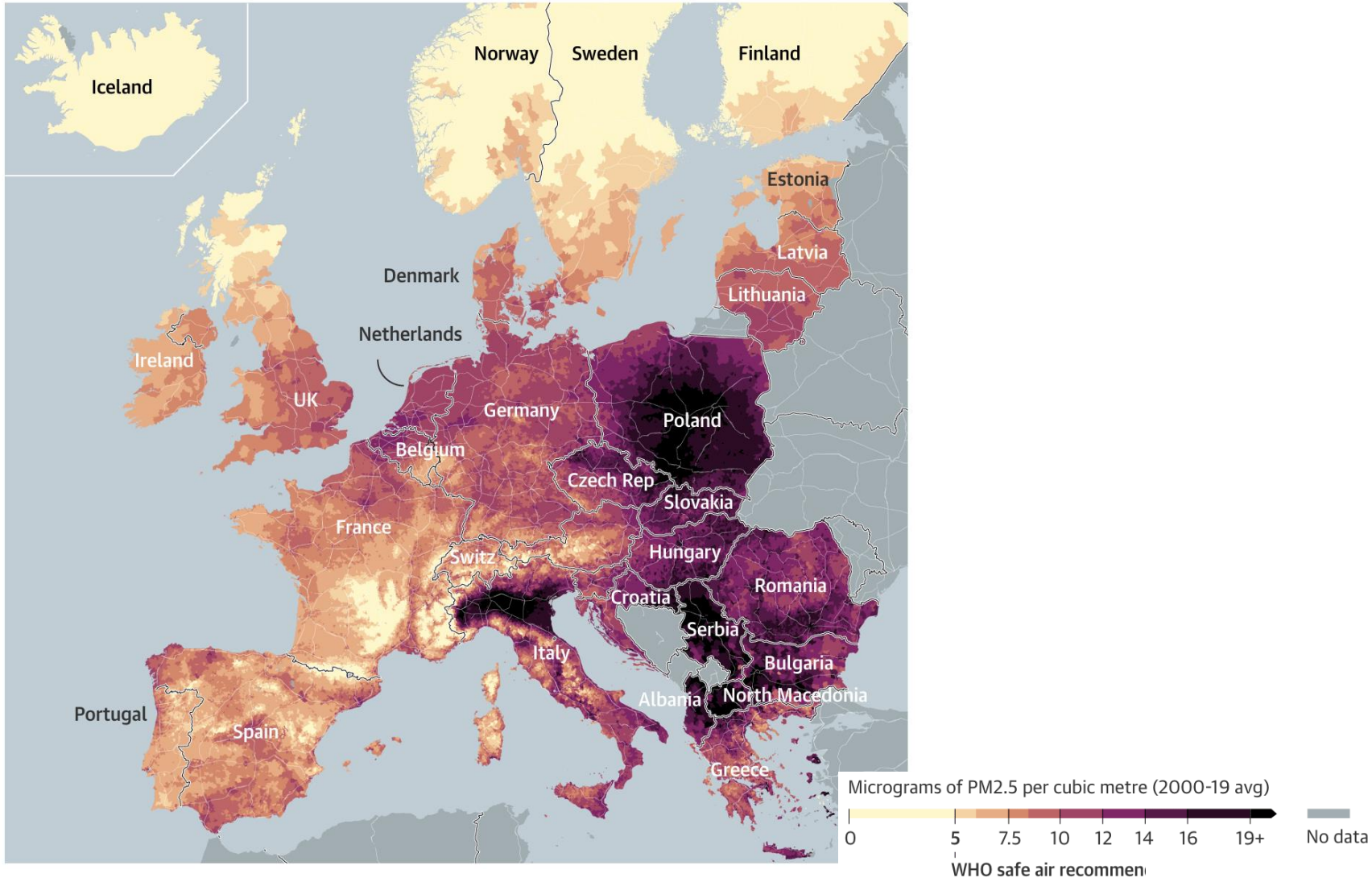
Fuller et al. Pollution and health: a progress update. Lancet Planet Health. 2022 (based on Global Burden of Diseases (GBD) data)

Chemical pollution: a modern phenomenon



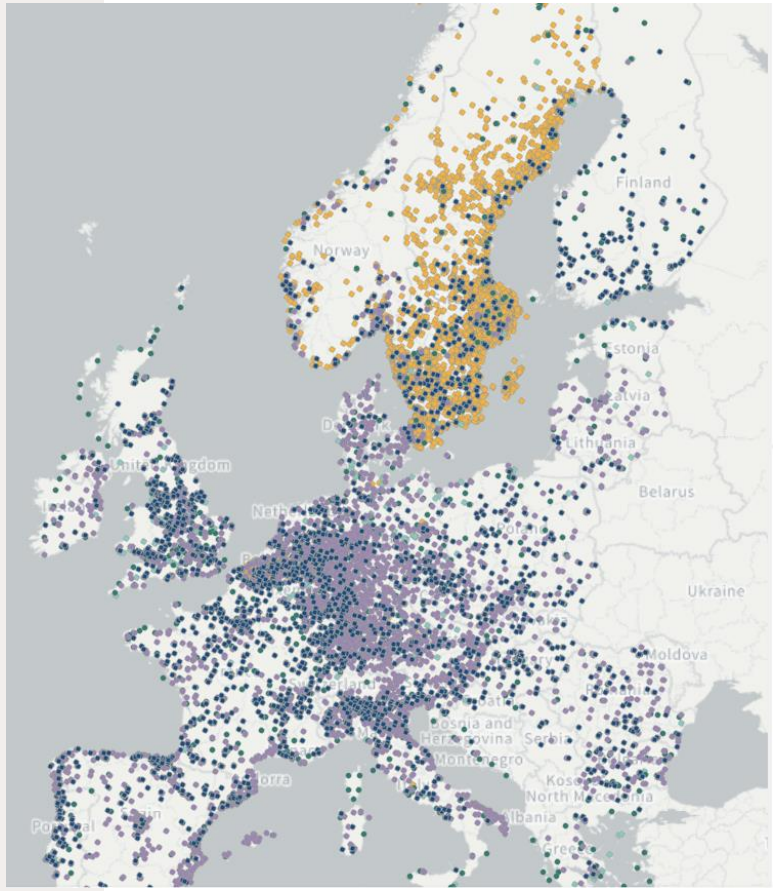
Slama et al. 2017 Characterizing the effect of endocrine disruptors on human health: The role of epidemiological cohorts. Comptes Rendus Biologies

Air pollution: $PM_{2.5}$



EXPANSE project (Coordinator: Prof R Vermeulen, Utrecht University); with The Guardian

PFAS (“Forever chemicals”) contamination

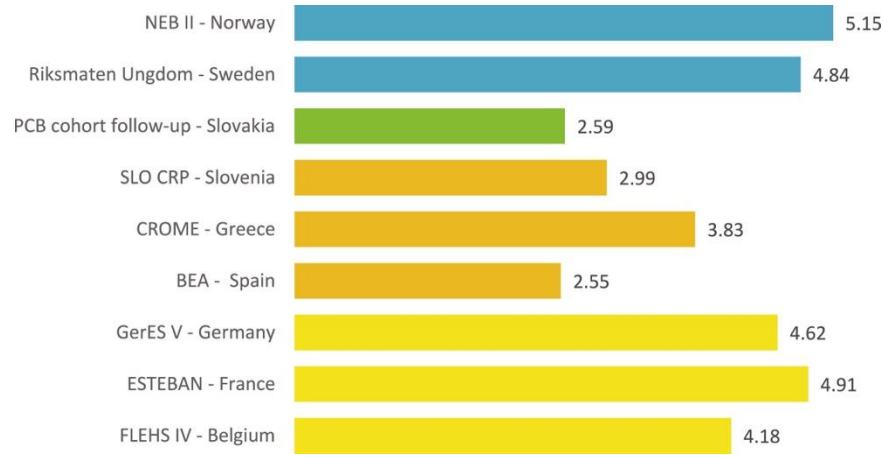


Presumptive contamination

Presumptive contamination sites

- Industrial site
- Waste management site
- Airport
- Military site
- Firefighting incident or training

- 20 PFAS producers
- 23,000 contamination sites (soil, water, organisms >10ng/mL)
- 232 commercial users (plastics, paints, waterproof textiles, varnishes, etc.)
- 21,500 presumptive contamination sites



Median PFAS (PFOS + PFHxS + PFOA + PFNA) in plasma/serum (µg/L) of teenagers in Europe

→ 17.5% Norwegian teenagers exceed EFSA health-based guidance value

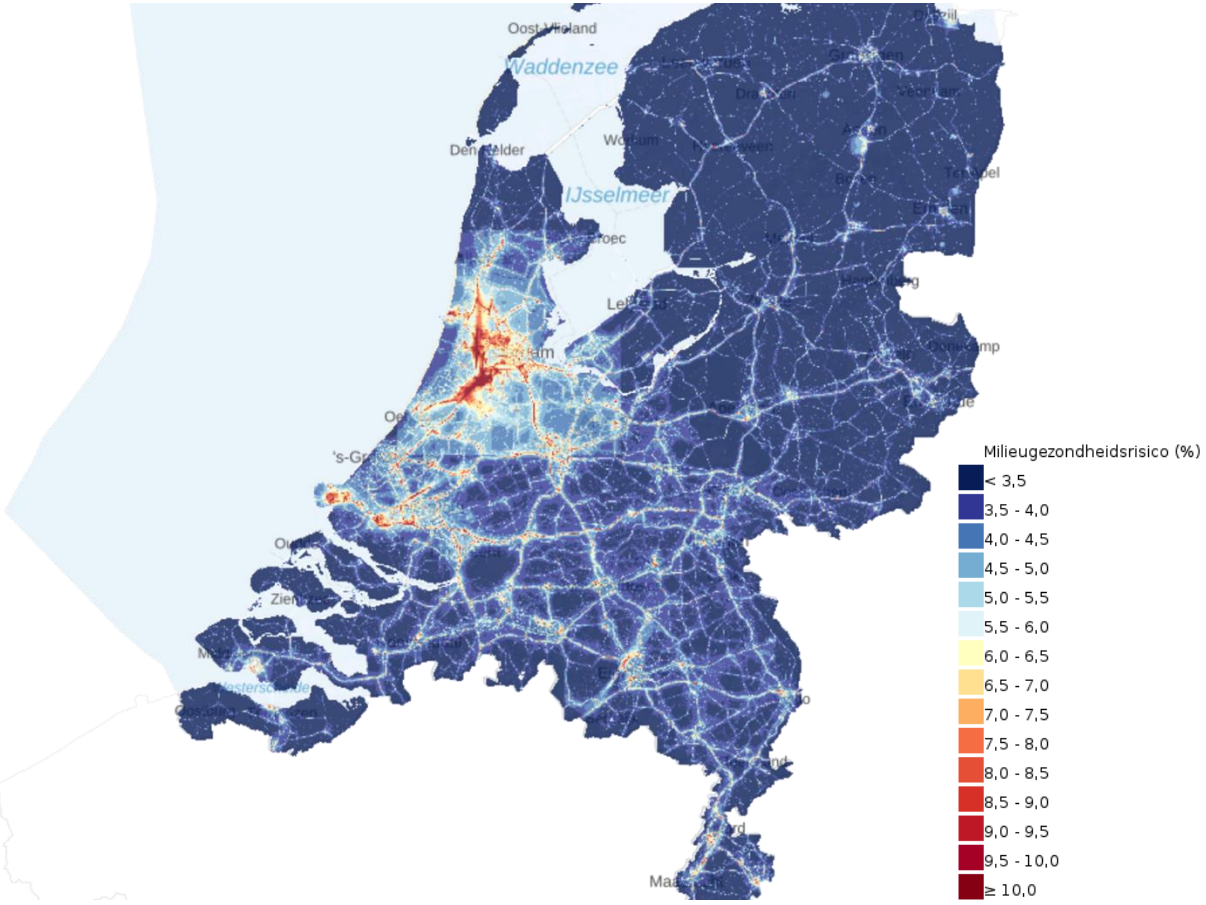
Le Monde 2023; European Environment Agency. Treatment of drinking water to remove PFAS; 2024
HBM4EU Aligned Studies (with 177 tenagers of the Norwegian Environmental Biobank Study): Richterová et al. PFAS levels and determinants of variability in exposure in European teenagers - Results from the HBM4EU aligned studies (2014-2021). Int J Hyg Environ Health. 2023; Uhl et al. PFASs: What can we learn from the European Human Biomonitoring Initiative HBM4EU. Int J Hyg Environ Health. 2023

The cumulative impact of environmental risk factors: 5% of DALY's in NL

Environmental Health Risk

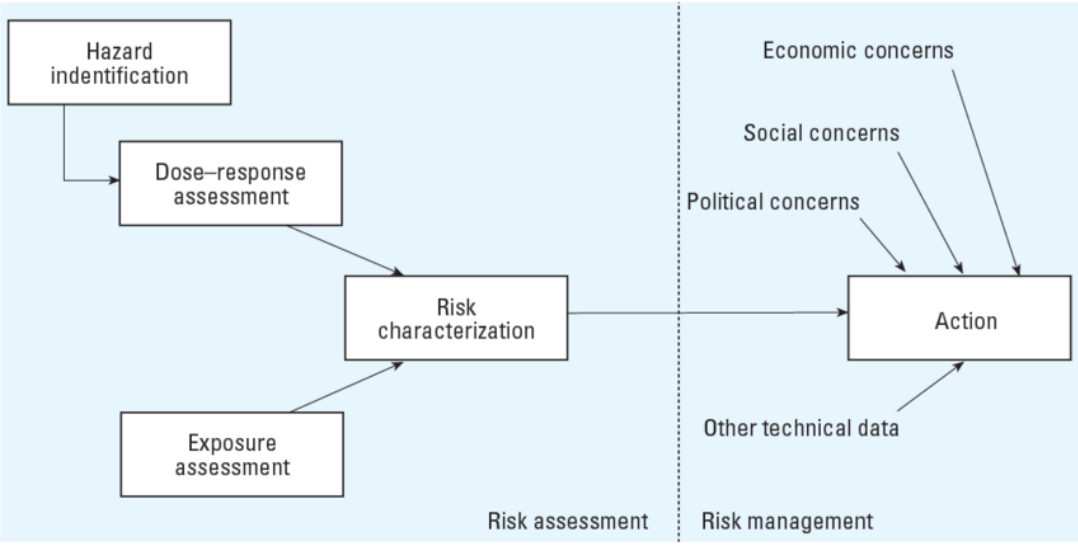
% of total disability-adjusted life years (DALYs)

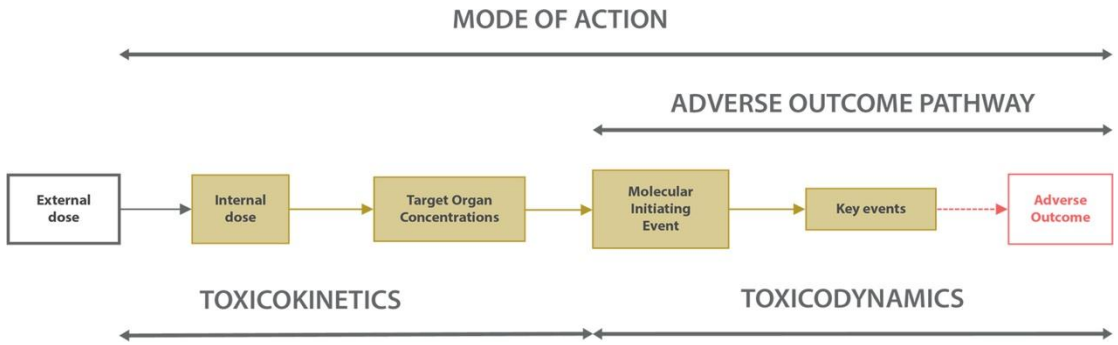
- Air + noise pollution



RIVM 2023 Atlas Leefomgeving

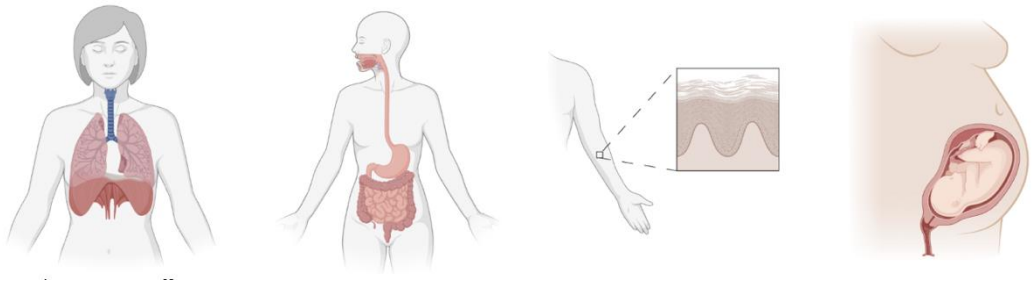
Why environmental epidemiology?

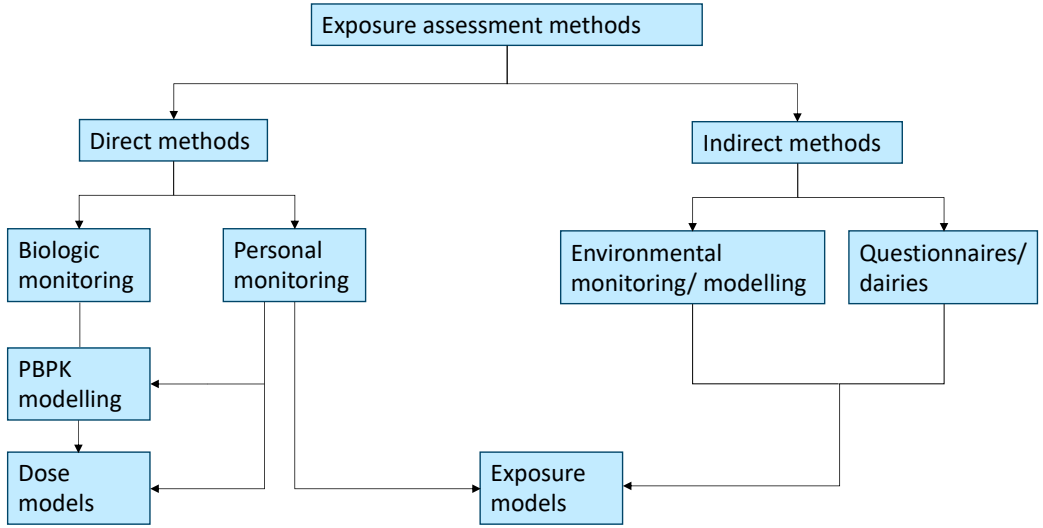


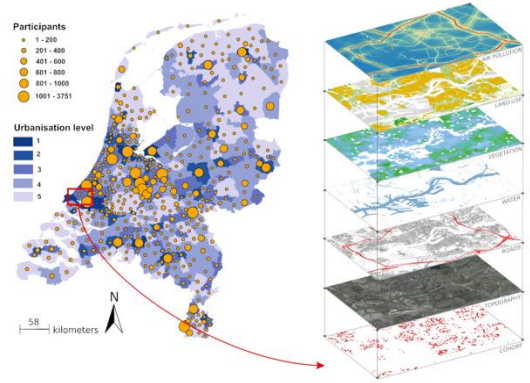


Rigaud et al. The methodology of quantitative risk assessment studies. Environ Health 2024
EFSA Scientific Committee; More et a.. Guidance Document on Scientific criteria for grouping chemicals into assessment groups for human risk assessment of combined exposure to multiple chemicals. EFSA J. 2021

Assess exposures



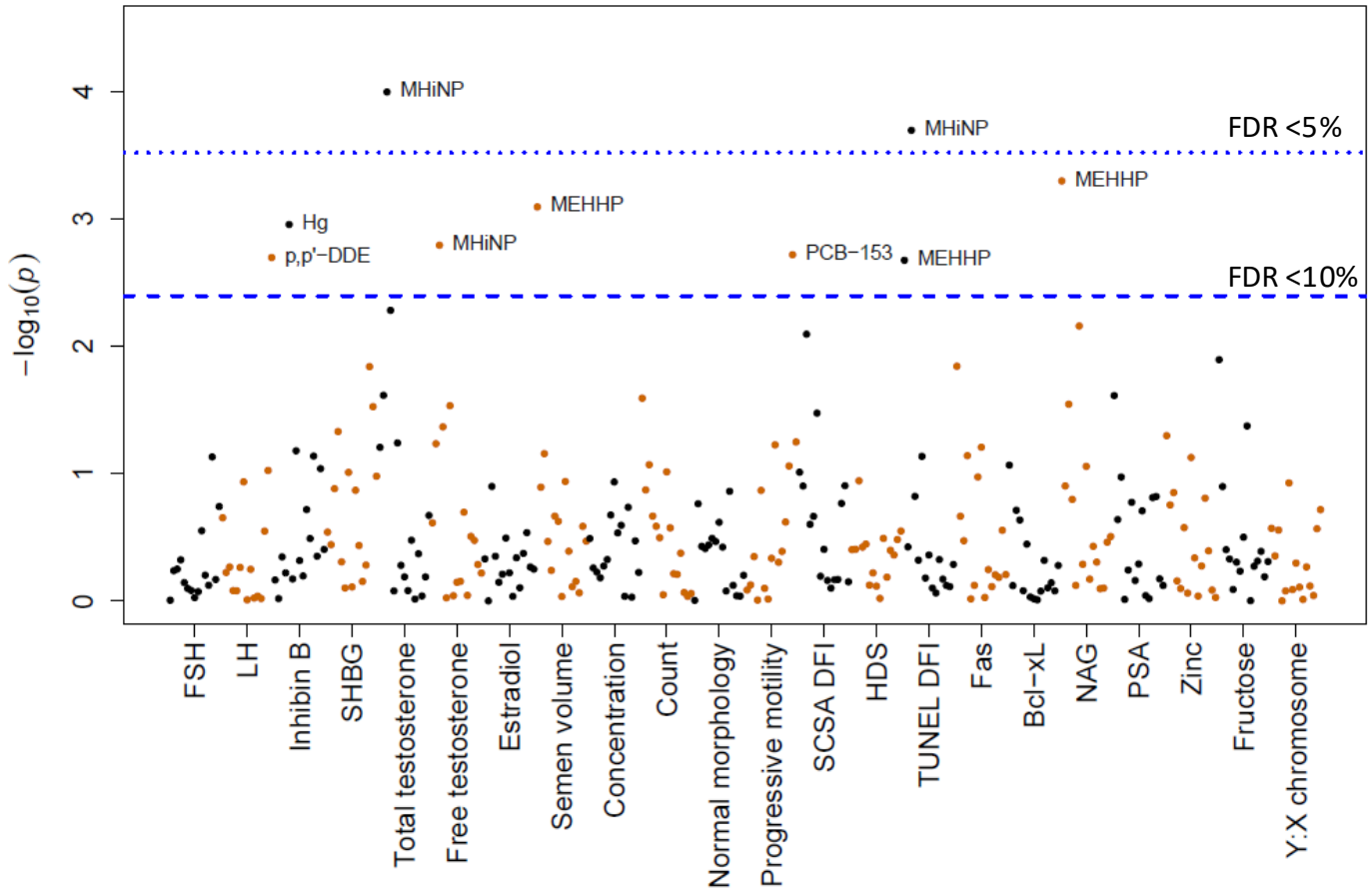




Adapted from US National Academy of Sciences (NAS) 1991

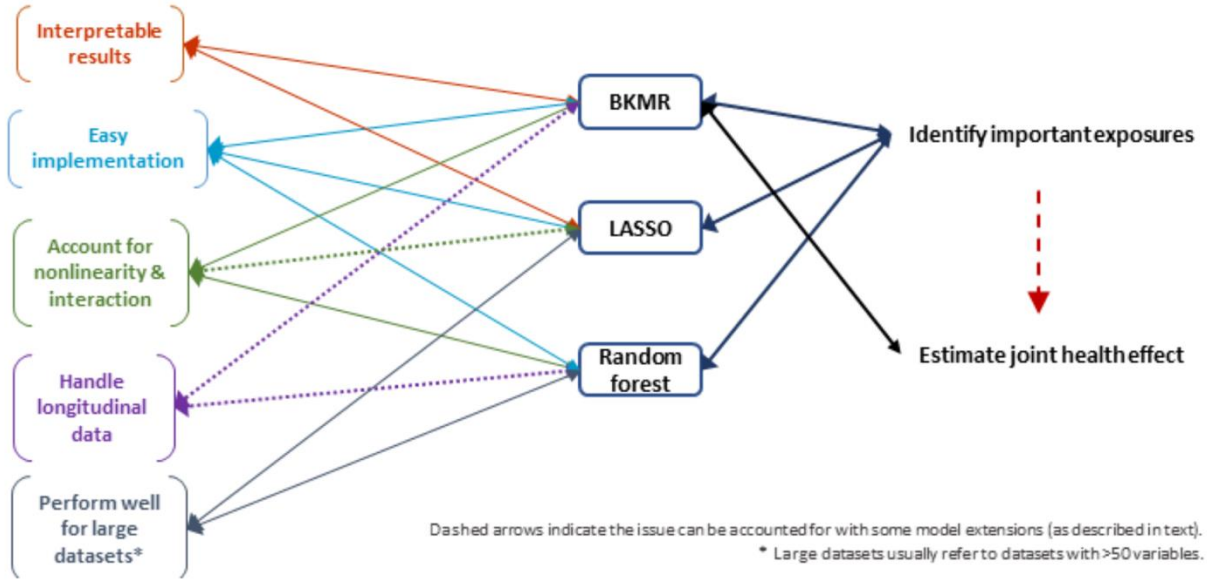
Nieuwenhuijsen et al. New developments in exposure assessment: the impact on the practice of health risk assessment and epidemiological studies. Environ Int. 2006

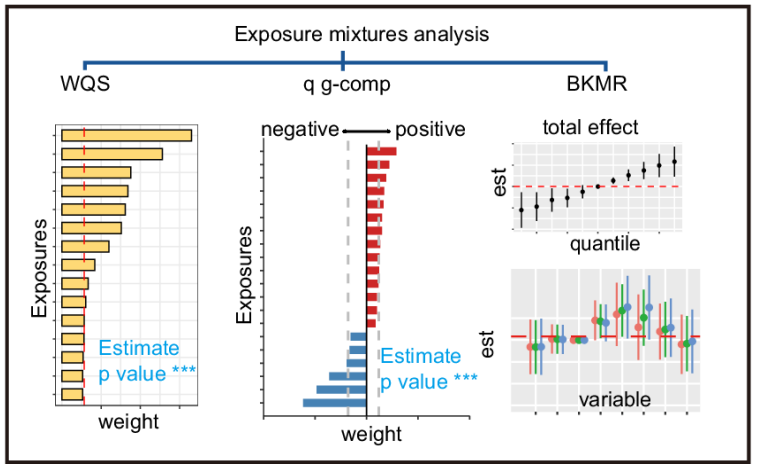
Hazard identification: chemicals → male reproductive health

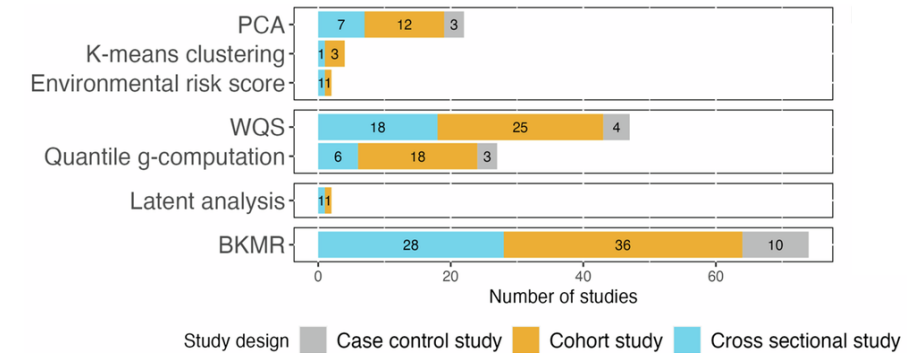


Lenters et al. OEM 2015

Assessing chemical mixtures



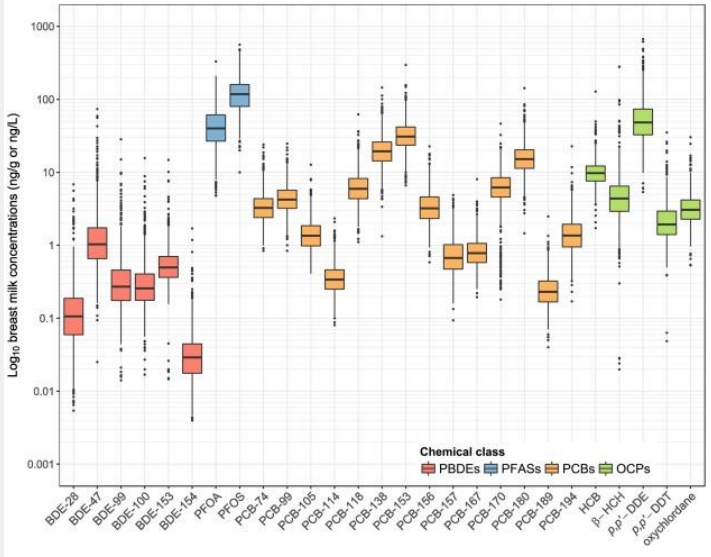


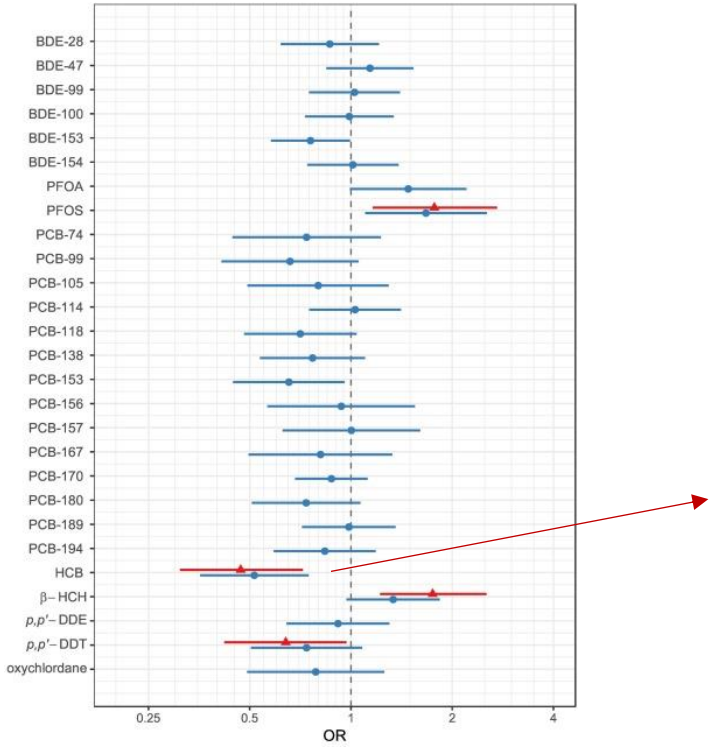


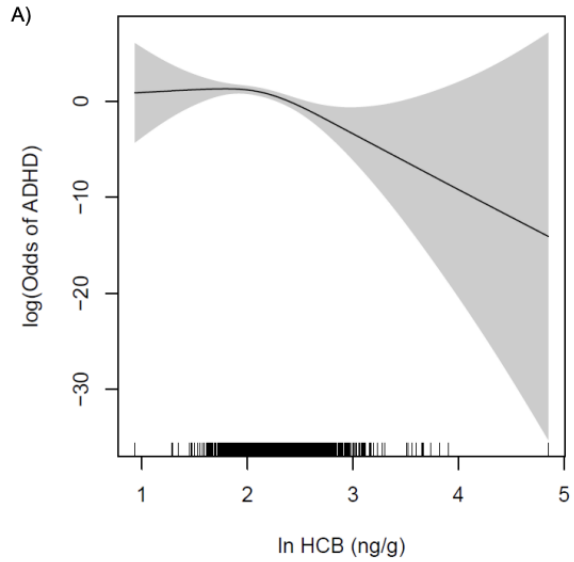
Review of which methods used in studies of chemical mixtures

Lenters et al. OEM 2018; You et al. An exposome atlas of serum reveals the risk of chronic diseases in the Chinese population. Nat Commun 2024; Pan et al. Applications of mixture methods in epidemiological studies investigating the health impact of persistent organic pollutants exposures: a scoping review. J Expo Sci Environ Epidemiol. 2024

Assessing associations: chemicals → ADHD





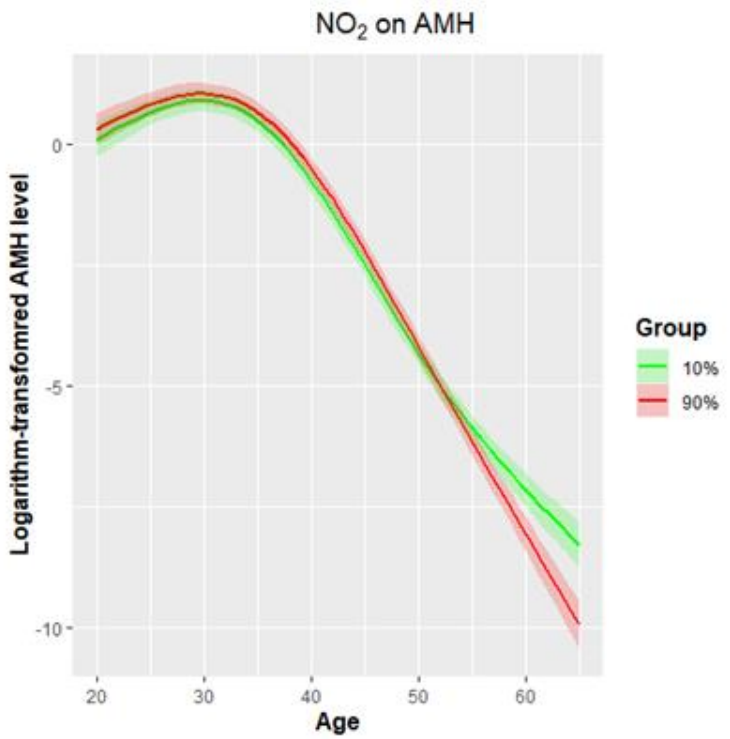


Odds ratios (OR) and 95% CIs for ADHD per interquartile range increase in ln-transformed exposure concentrations.

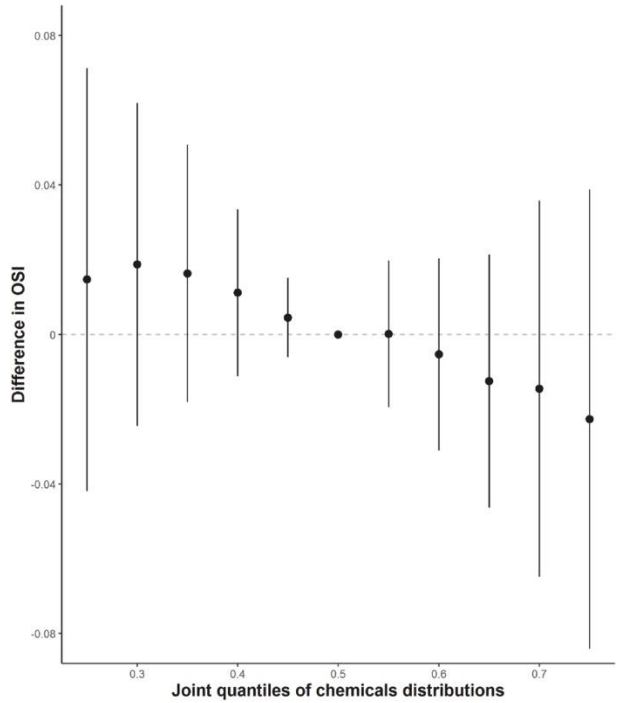
Coefficients from single-exposure logistic regression models (blue); & elastic net logistic regression-selected subset (red)

Early-life exposure to persistent organic pollutants (OCPs, PBDEs, PCBs, PFASs) and attention-deficit/hyperactivity disorder: A multi-pollutant analysis of a Norwegia
Environ Int. 2019

Pollutants → female fertility



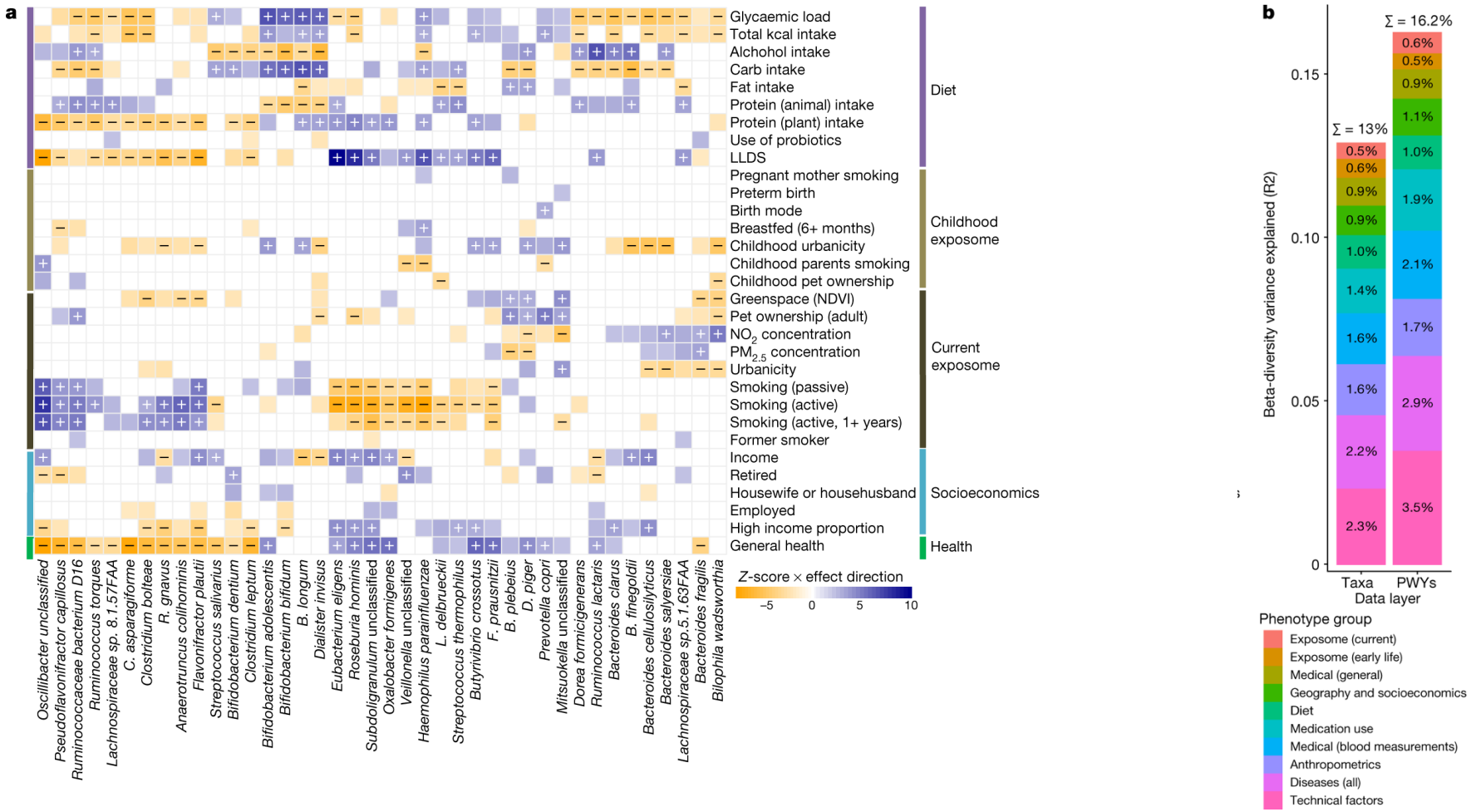
Air pollution → repeated anti-Mühllerian hormone



Overall mixture effect of chemicals → Ovarian Sensitivity Index (OSI)

Zou … Lenters. Air pollution and anti-Müllerian hormone: the Doetinchem Cohort Study. Under review.
Association between chemical mixtures and female fertility in women undergoing assisted reproduction in Sweden and Estonia. Environ Res. 2023

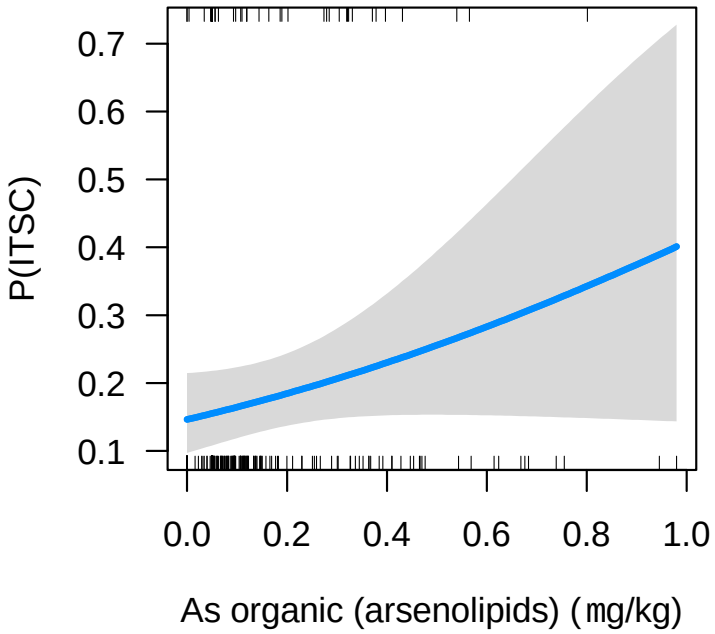
Mechanisms: Environmental factors shaping the gut microbiome



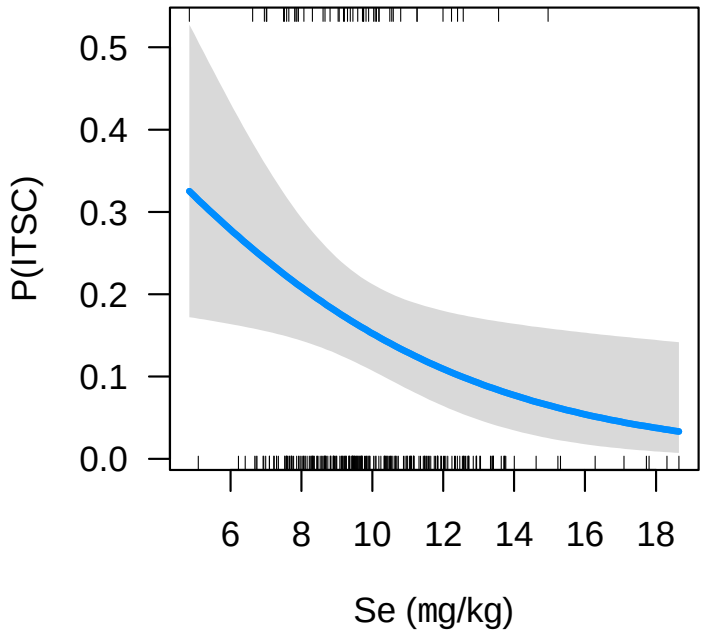
Gacesa…. Lenters… Weersma. Environmental factors shaping the gut microbiome in a Dutch population. *Nature* 2022

Resilience

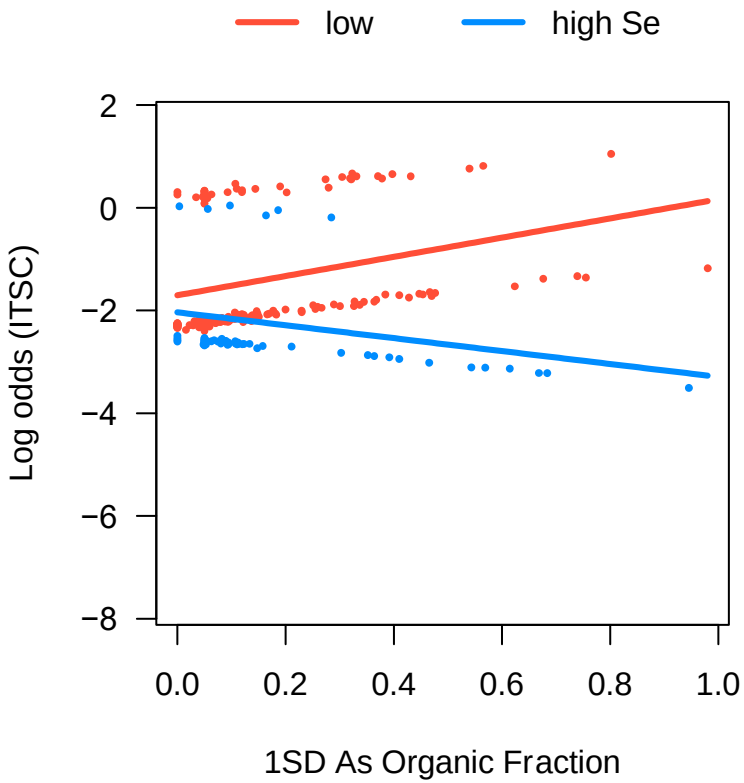
Organic arsenic (pollutant)
neuro-toxic



Selenium (micronutrient)
neuro-protective



Arsenic more toxic if low selenium
'chemoprotection'



Lenters et al. (in preparation)

Risk assessment: Glyphosate

IARC 2015: 2A ‘probable carcinogen’

EFSA 2015; 2017: ‘unlikely to pose carcinogenic hazard to humans’

Panel member: JMPR (FAO/WHO) 2017: ‘unlikely to pose a carcinogenic risk to humans from exposure through the diet’

- *100+ manual with 2 pages of guidelines for considering epi evidence; results of quantitative syntheses not included*

Dutch Health C

The New York Times

GIVE THE TIMES

Glyphosate, Top-Selling Weed Killer, Wins E.U. Approval for 5 Years

Edward Ford on his farm in Brentwood, England, where he relies on the weed killer glyphosate. Mary Turner/Reuters

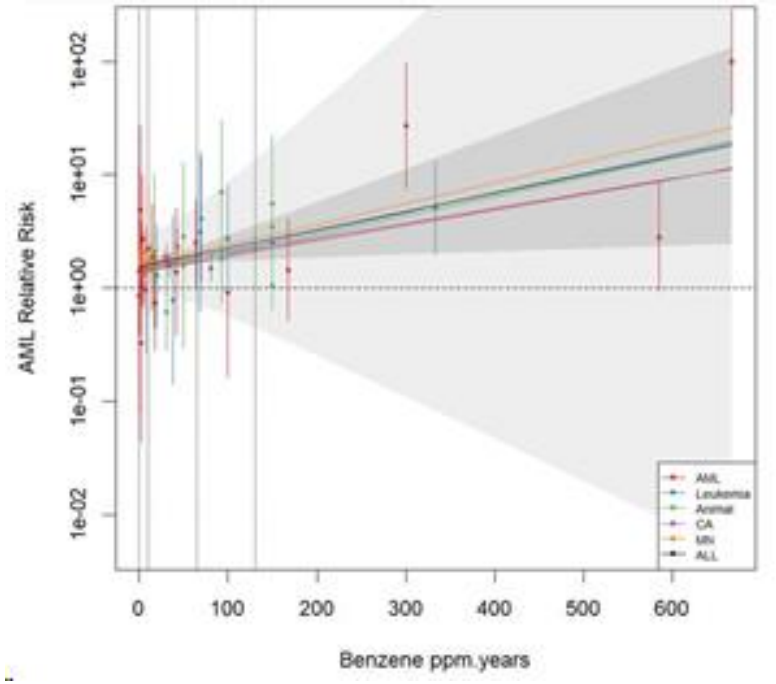
By Danny Hakim

Nov. 27, 2017

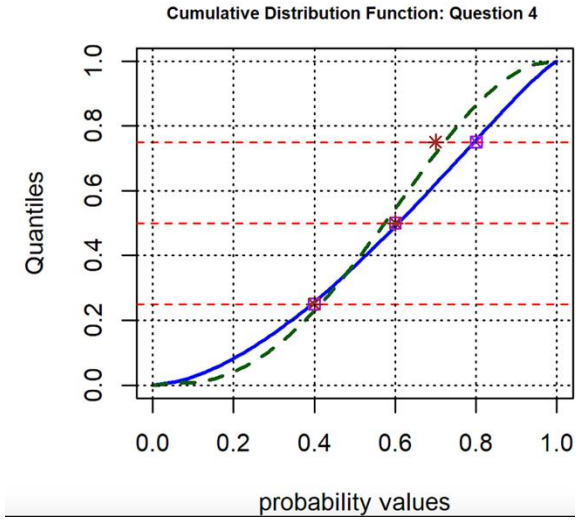
The European Union voted on Monday to extend its authorization for the world’s best-selling herbicide for an abbreviated period of five years, with France and Germany splitting over the move.

Integrated risk assessment: epidemiological + toxicological evidence

Characterizing exposure-outcome association:
Bayesian meta-regression with toxic equivalency factors



Harzard identification:
Expert Knowledge Elicitation of WoE with uncertainty analysis



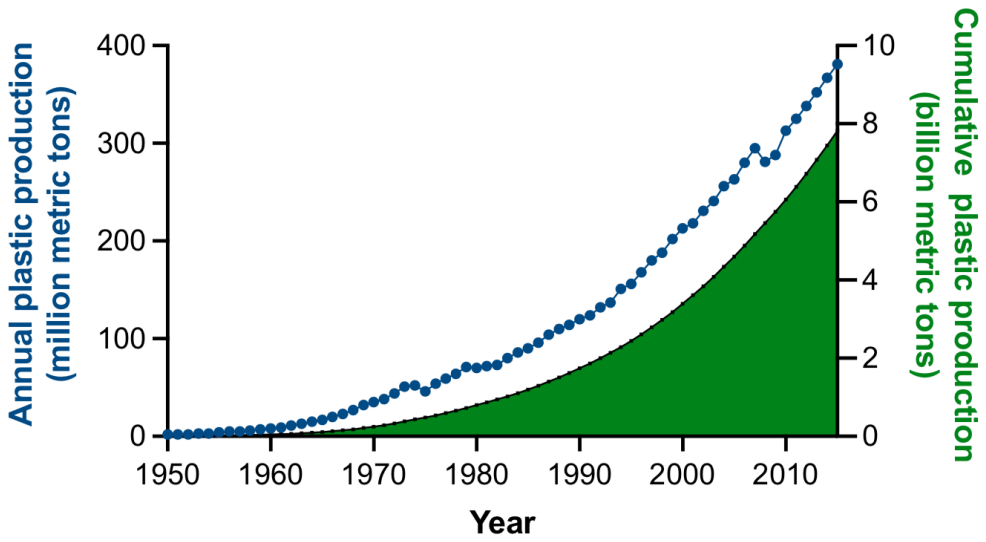
Cumulative probability of expert groups 1 & 2: whether triphenyl phosphate (TPP) is a metabolic disruptor
(MoA: induces obesity/adipogenicity via PPARγ activation)
Conclusion: “suspected ED” (Q50-66)

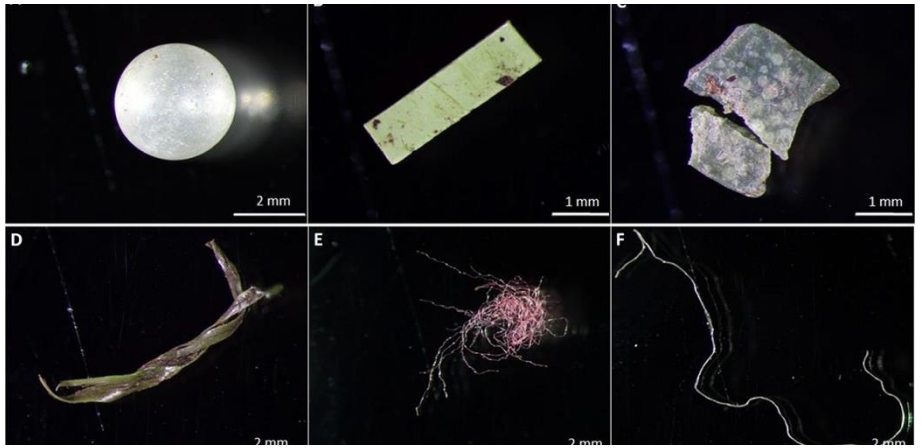
Scholtens et al. Estimation of the Exposure–Response Relation between Benzene and Acute Myeloid Leukemia by Combining Epidemiologic, Human Biomarker, and Animal Data . Cancer Epidemiol Biomarkers Prev. 2022.; Beausoleil et al. Weight of evidence evaluation of the metabolism disrupting effects of triphenyl phosphate using an expert knowledge elicitation approach. Toxicol Appl Pharmacol. 2024

Emerging pollutant of concern: microplastics

“Plastics is the Plan B for the fossil fuel industry”

- 9% recycled, 50% in landfill, 19% incinerated, 22% mismanaged



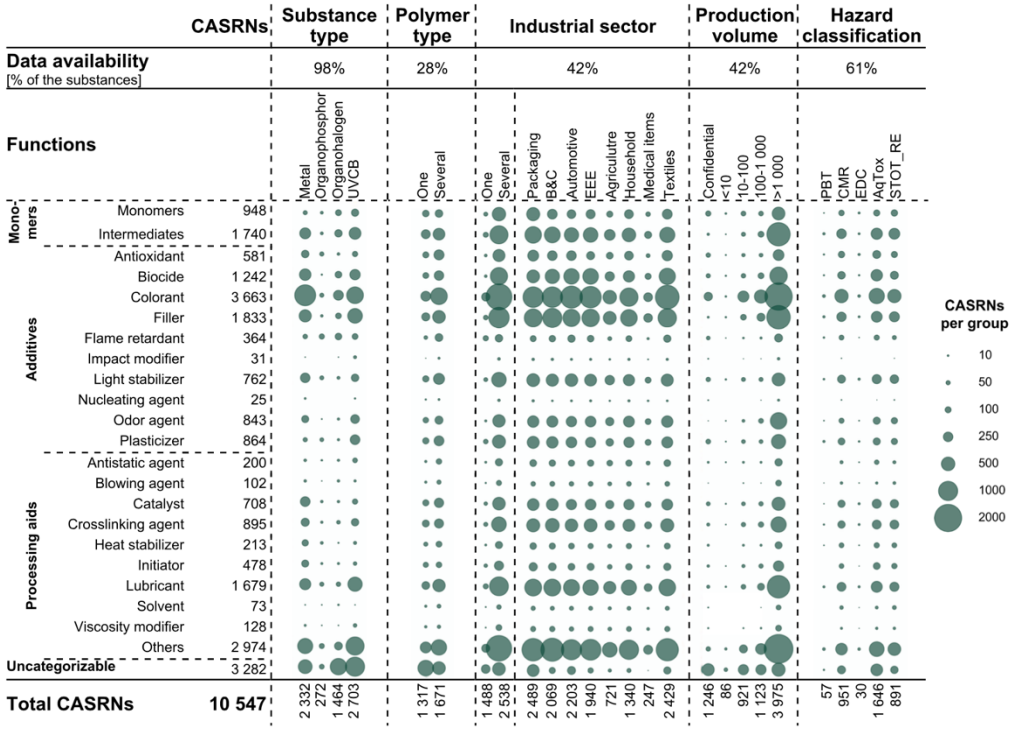


Microplastics (1 µm - 5 mm)
Nanoplastics (<100 nm)

Geyer et al. 2017 Production, use, and fate of all plastics every made. Science Advances; Weithmann et al Science Advances 2018

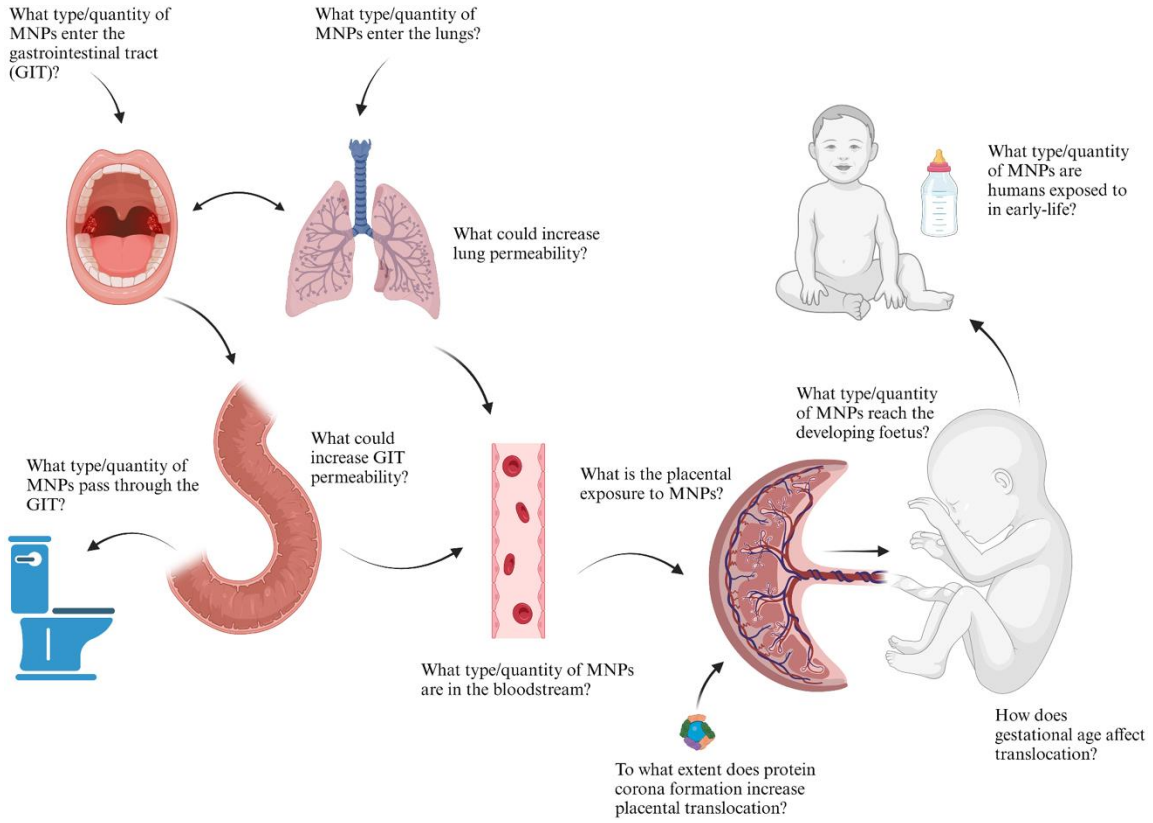
Complex exposure

- Size fractions
- Morphology
  - Fibre, fragment, granule, film, foam…
    - (20% to >90% fibers reported in drinking water)
- Chemical composition
  - 5300 polymer formulations are commercially available
  - Chemical additives (e.g., plasticizers, flame retardants, stabilizers, pigments, biocides) → up to 50% weight
  - Non-intentionally added substances (i.e., impurities, reaction by-products, degradation products)
- Surface chemistry
- Adsorbed/absorbed
  - Microbes/bioflims, chemicals, metals



Weithmann et al Science Advances 2018

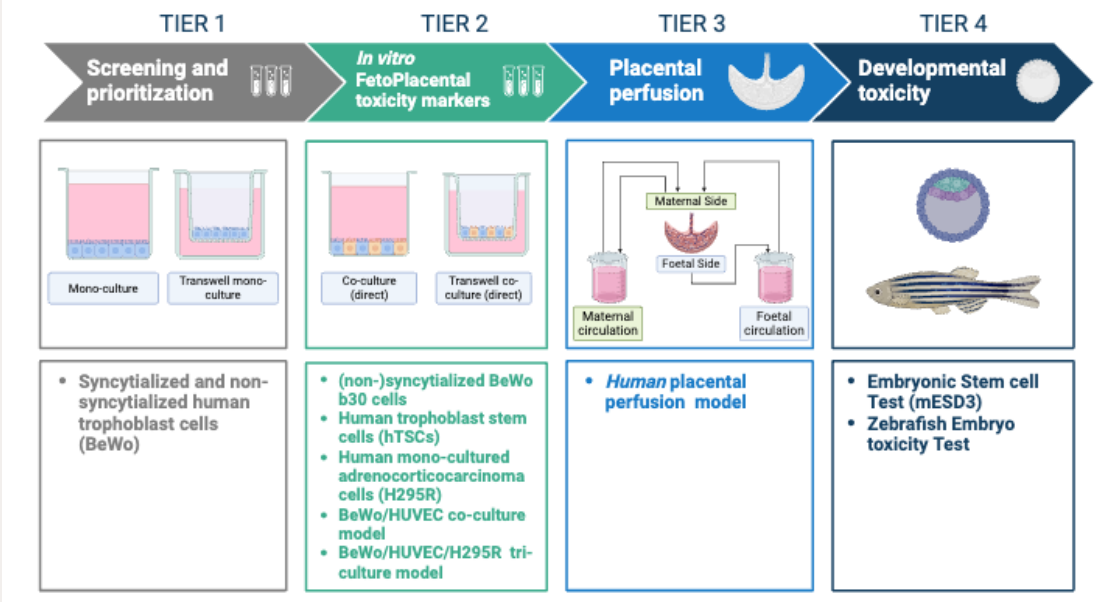
Assessing the early-life health effects micro/nanoplastics



Durkin … Lenters V, Vermeulen R. 2024. Investigating Exposure and Hazards of Micro- and Nanoplastics During Pregnancy and Early Life (AURORA Project): Protocol for an Interdisciplinary Study. JMIR Res Protoc 2024

Assessing the early-life health effects micro/nanoplastics

Toxicological assays



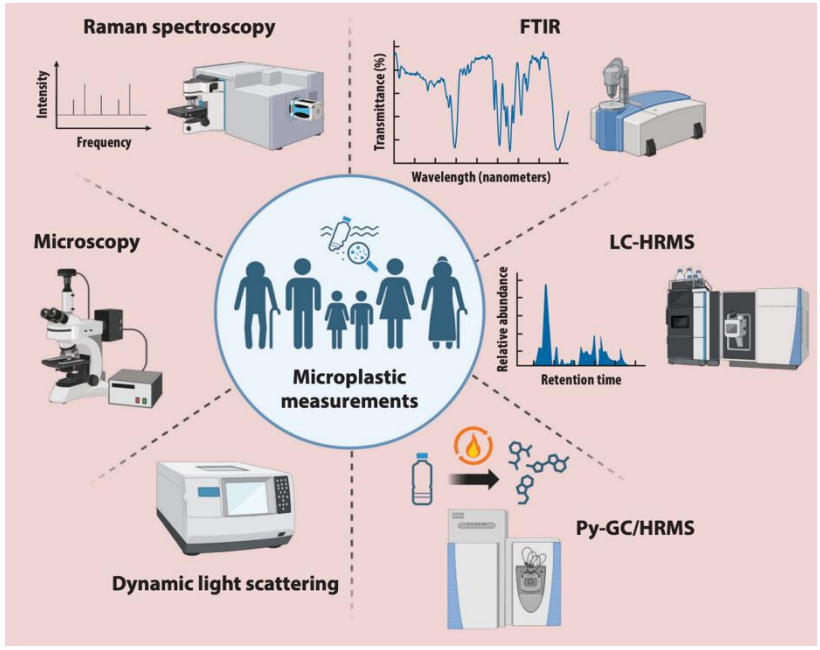
Epidemiological assessments

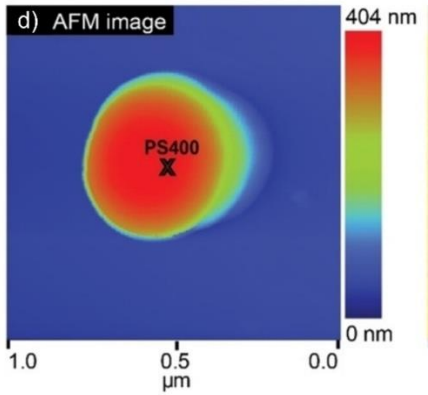
Assessments		Participant		Age				
		Maternal	Child	Pregnancy	Birth	1 year	4-6 years	9-10 years
Exposure to MNPs	Placenta	✓	✓		✓			
	Cord Blood		✓		✓			
	Whole Blood	✓			✓			
	Urine	✓			✓			
Placental Function	Placental blood flow • *Including uterine, umbilical, and middle cerebral artery pulsatility index, aortic isthmus pulsatility index, and cerebroplacental ratio*	✓		✓				
System Homeostasis	Immune-inflammatory responses		✓		✓		✓	✓
	Oxidative stress		✓		✓		✓	✓
	Accelerated ageing biomarkers		✓		✓			✓
	Endocrine function		✓		✓			
	Metabolomics		✓		✓			
Early Life Development	Fetal and child growth		✓	✓	✓	✓	✓	✓
	Metabolic markers		✓		✓		✓	
	Asthma & allergies		✓			✓	✓	✓
	Respiratory health		✓			✓		

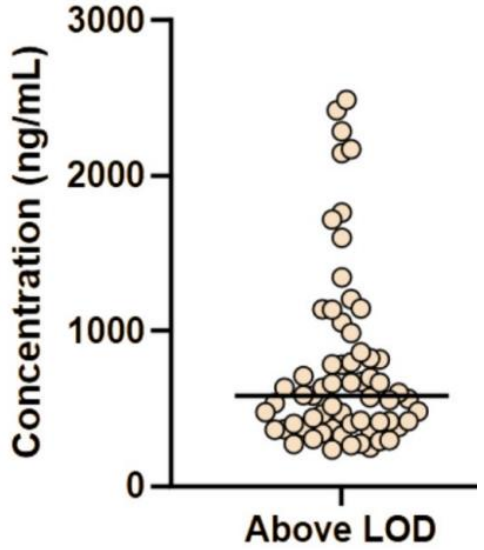
Durkin … Lenters V, Vermeulen R. 2024. Investigating Exposure and Hazards of Micro- and Nanoplastics During Pregnancy and Early Life (AURORA Project): Protocol for an Interdisciplinary Study. JMIR Res Protoc 2024

AURORA

Measuring micro- and nanoplastics



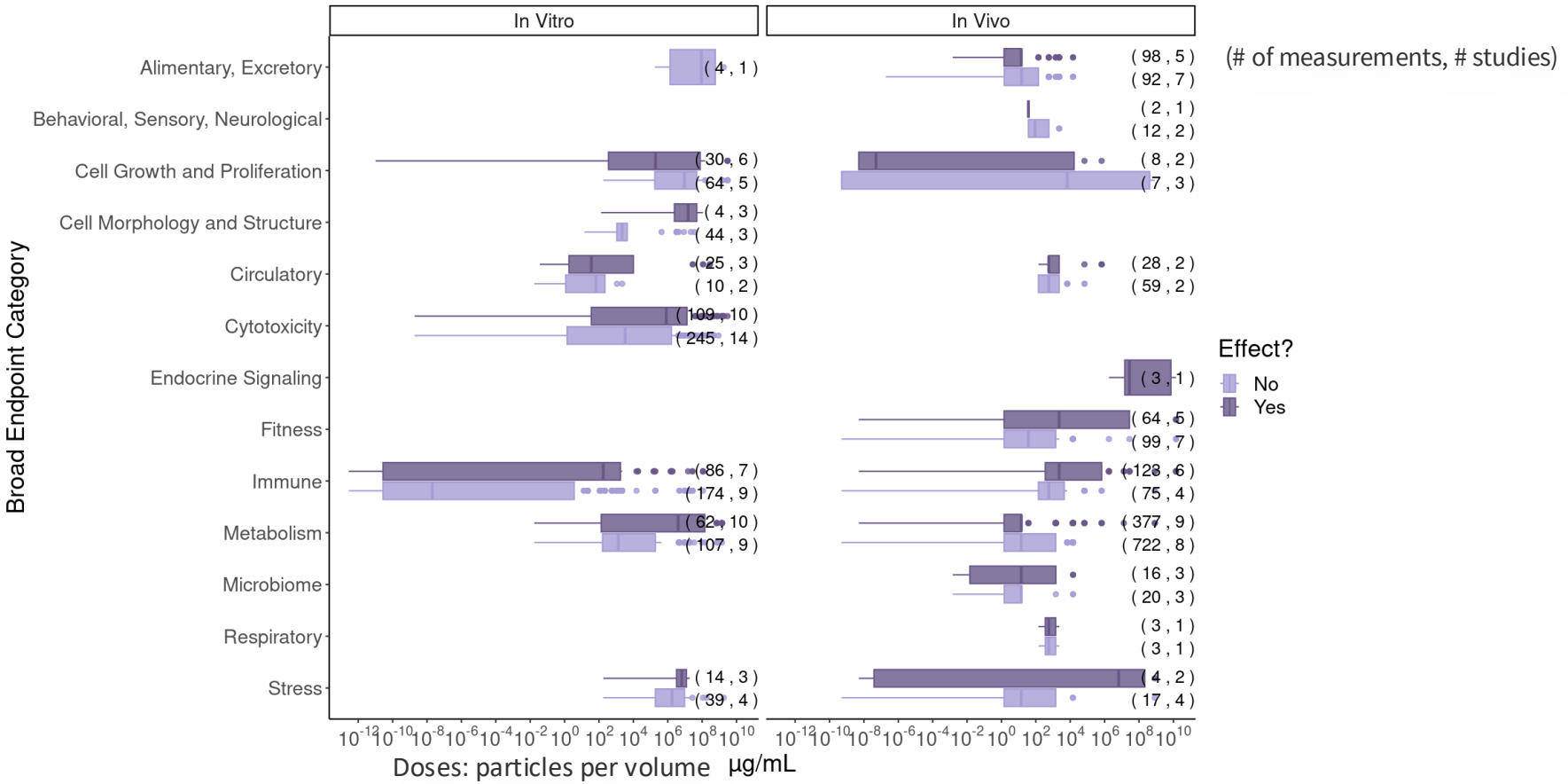


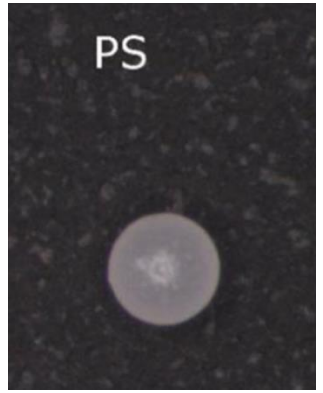


Relevant exposure metrics: mass concetrations, count *(quantification);* polymer/composition, particle size, volume, surface area, morphology *(characterisation)*

Shao et al. Advancements in Assays for Micro- and Nanoplastic Detection: Paving the Way for Biomonitoring and Exposomics Studies. Ann Rev of Pharmacol and Toxicol. 2024; Mandemaker et al. 2023. Spectro-microscopic techniques for studying nanoplastics in the environment and in organisms. Angewandte Chemie International Edition

Toxicological assessments





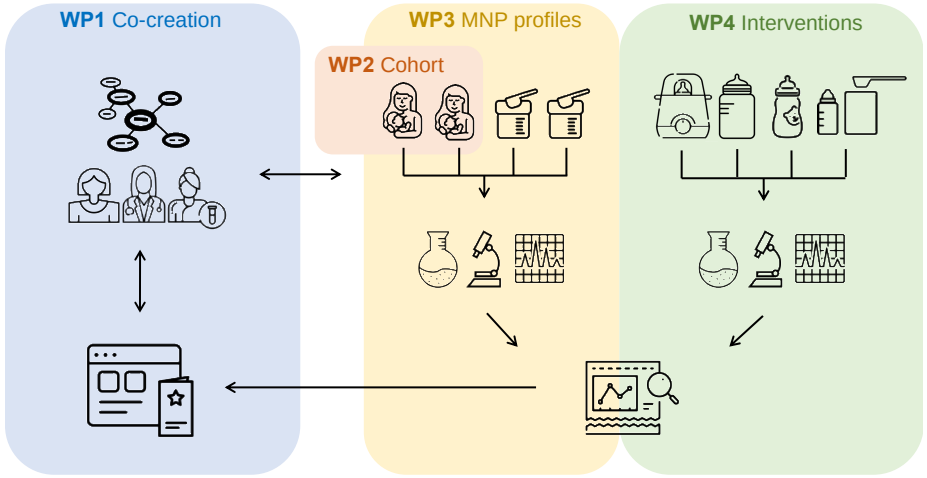
Test with beads

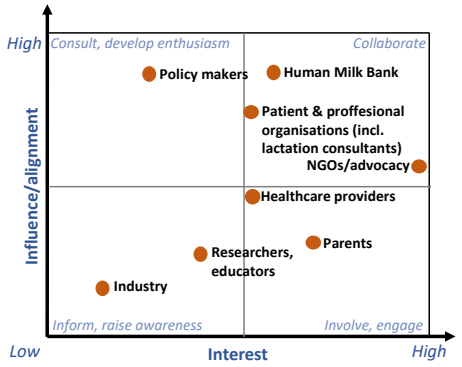
Real-life observed in human samples

ToxMex: Toxicity of Microplastics Explorer 2024

Thornton Hampton, L.M., Lowman, H., Coffin, S. et al. A living tool for the continued exploration of microplastic toxicity. Micropl.&Nanopl. 2022

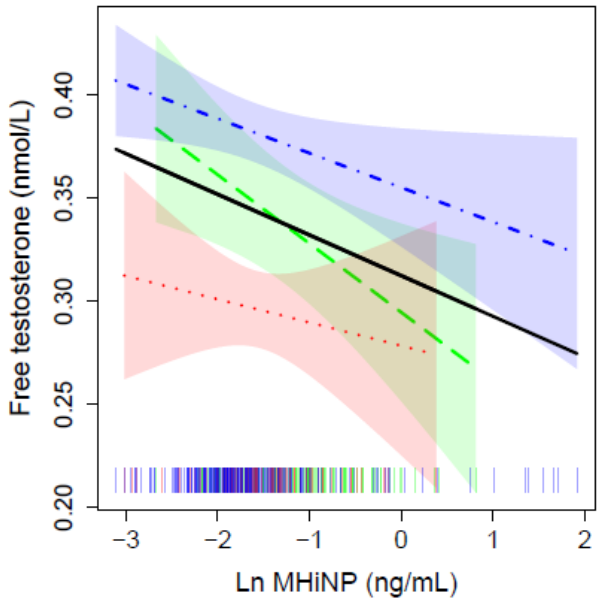
Micro/nanoplastic exposure assessment & reduction interventions

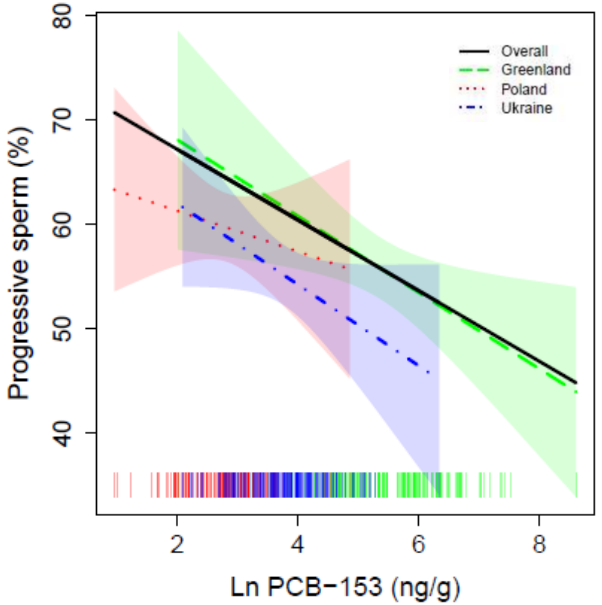




FLES project: Fed with a side of microplastics: interventions to reduce plastic exposure via infant formula and human milk . PI: Virissa Lenters

Male reproductive health → risk communication





Phthalates, perfluoroalkyl acids, metals and organochlorines and reproductive function: a multipollutant assessment in Greenlandic, Polish and Ukrainian men. Occup Environ Med. 2015

FOX NEWS Login Watch TV

FOX NATION

Tucker Carlson's Fox Nation special 'The End of Men' explores science behind testosterone, fertility decline

The 'Tucker Carlson Originals' episode exploring the chemical war on America's men is streaming now on Fox Nation

By Bailee Hill · Fox News

Get Fox Nation

Published October 6, 2022 2:14pm EDT

Interest

The New York Times

Oct. 7, 2024

How Can I Get 'Forever Chemicals' Out of My Life?

They're almost everywhere. And they're bad. But there are some things you can do to avoid them.

Be wary of anything in contact with food.

Scrutinize products touching your skin.

Investigate your local water and food supply.

Minimize hidden sources of exposure at home.

Chemical exposure reduction interventions

Intervention studies: dietary, behavioural, residential, healthcare settings

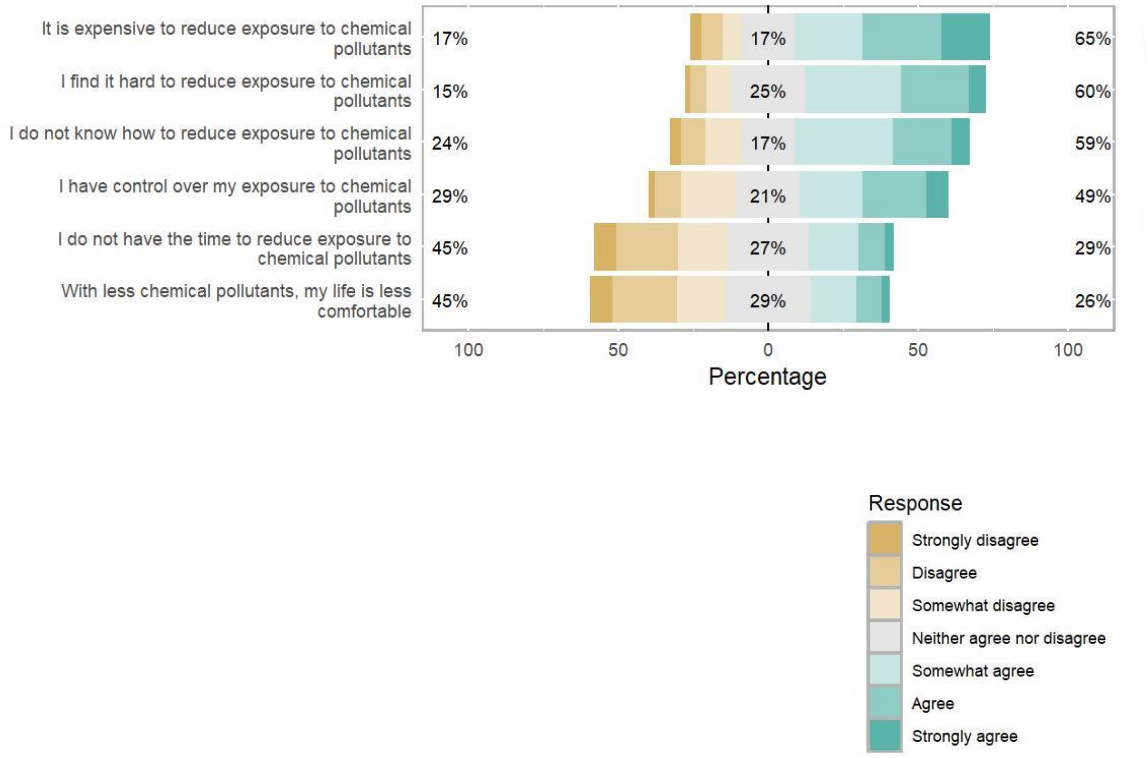
- 28 studies (n>30 participants)
- 12 studies in hospitals

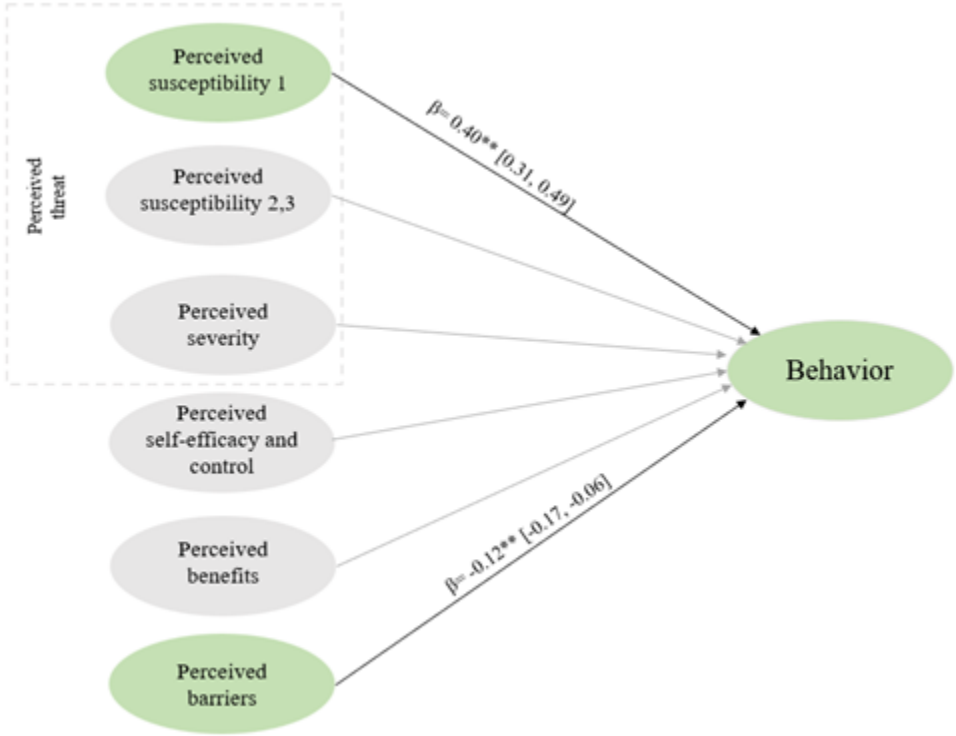
Source	Interventions	Weight of evidence[a]
Personal care products	Use low/no fragrance products	+
	Use eco-labelled personal care products	++
	Frequent hand washing	+
Diet and food packaging	Consume organic food	+
	Avoid canned foods	++
	Avoid plastic food and beverage containers (including re-heating)	+++
	Avoid fast/processed foods	+
	Limit fish intake and avoid higher trophic level predatory fish	+++
Residential	Select lower-chemical materials and furnishings	+
	Avoid chemical pest management	+
	Use eco-labelled cleaning products	+/-
	Frequent vacuuming and cleaning	++
Healthcare settings	Remove EDCs from products/processes	++

[a] Based on the existing scientific literature, the weight of evidence was rated as equivocal (+/-), moderate (+), high (++) or the highest (+++) level of evidence as to whether an intervention action is effective or not. Ratings to not reflect the relative magnitude change in exposure levels expected for interventions.

Lenters VC, Sugeng EJ, van Duursen MBM. Safeguarding women's health against endocrine disrupting chemicals: Paving the way to successful health strategies. Vrije Universiteit Amsterdam. 2024. DOI:10.13140/RG.2.2.27889.29281

Chemicals: perceptions & facilitators/barriers





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Chemicals: perceptions & facilitators/barriers

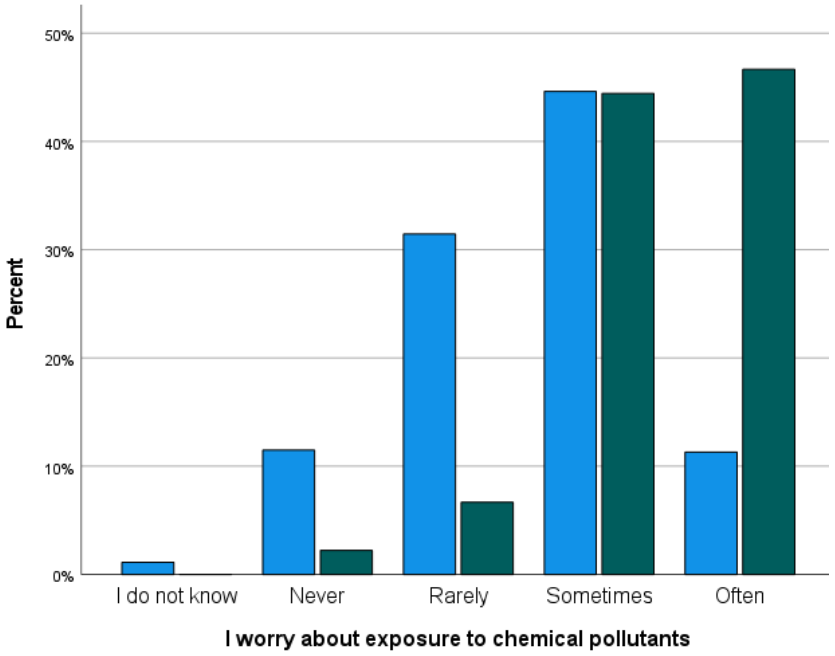
Reviewed surveys of public (8) & health professionals (6)

- Most adults & pregnant women feel **moderately concerned & insufficiently informed** about EDCs, with large variability across countries
- Most obtain information from internet & media; would prefer information from health professionals and government to be responsible
- **Health professionals report limited training in environmental health** & EDCs, including history taking & counselling. Barriers for professionals: lack of knowledge, uncertainties, doubt about individuals' agency to reduce exposures, concerns about increasing anxiety.

Recommendations

- Increase **environmental health literacy** through improved labelling, apps for consumers, counselling during pregnancy/pre-conception
- Increase environmental health **training** for health professionals
- Increase **knowledge** on the effectiveness of exposure reduction interventions & promotion strategies; biomonitoring of population exposure levels

Public (18-45, NL)
With fertility issues



Lenters et al. Safeguarding women's health against endocrine disrupting chemicals: Paving the way to successful health strategies. Vrije Universiteit Amsterdam. 2024. DOI:10.13140/RG.2.2.27889.29281

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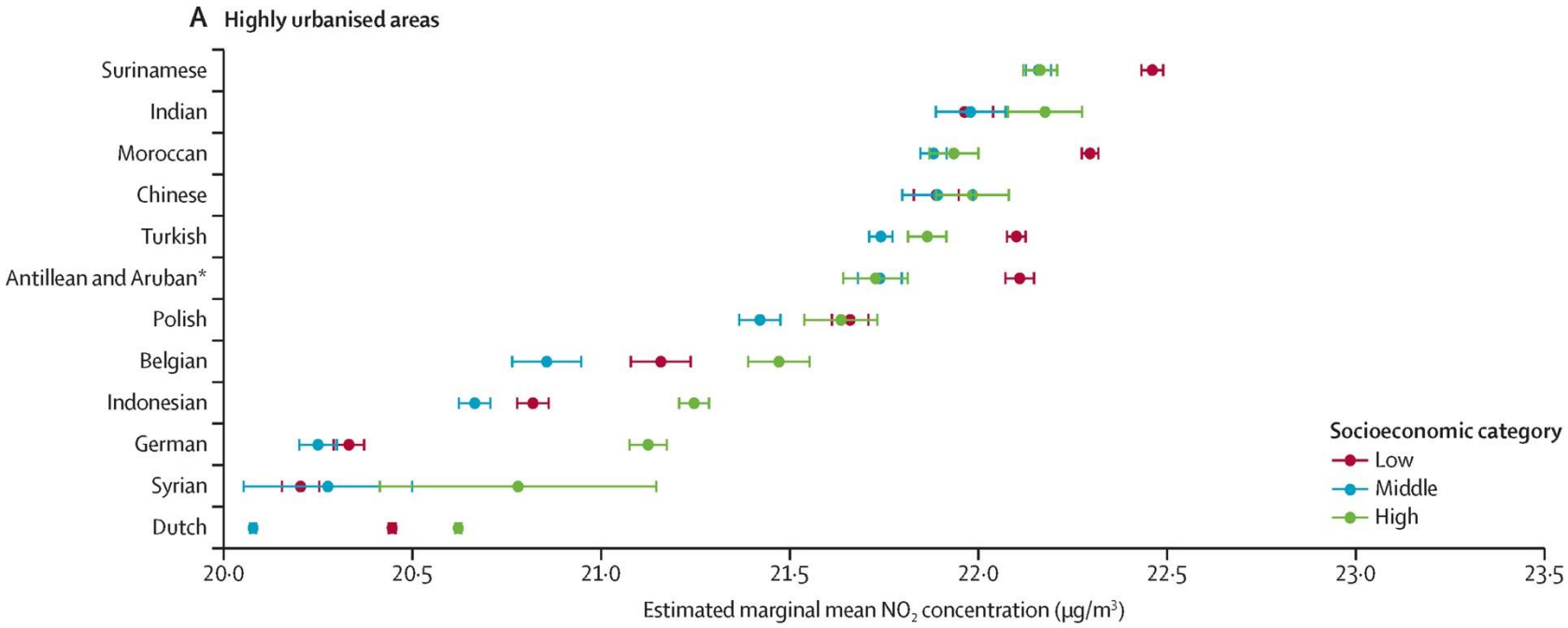
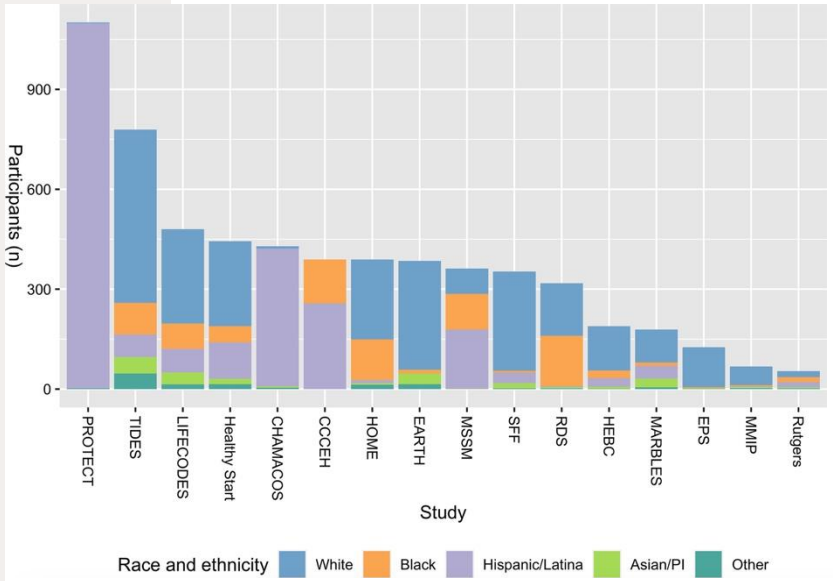
Ethnic & socioeconomic inequalities in air pollution exposure in the Netherlands



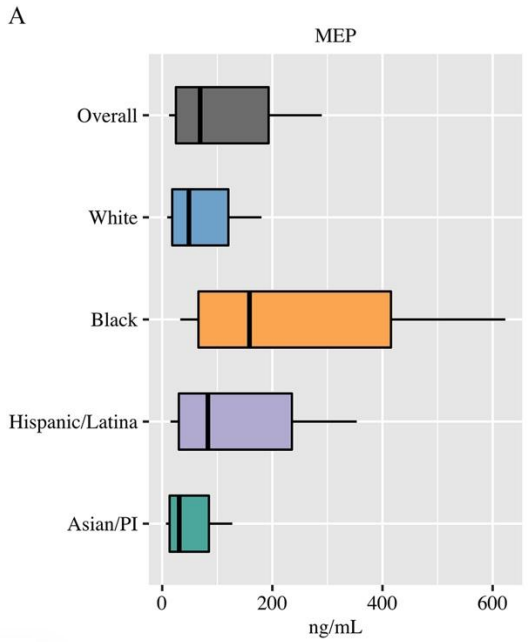
Minority ethnic groups were consistently exposed to higher levels of air pollution (NO_2, $PM_{2.5}$ & elemental carbon/soot) than the ethnic Dutch population; not explained by SEP; both in urban & rural areas.

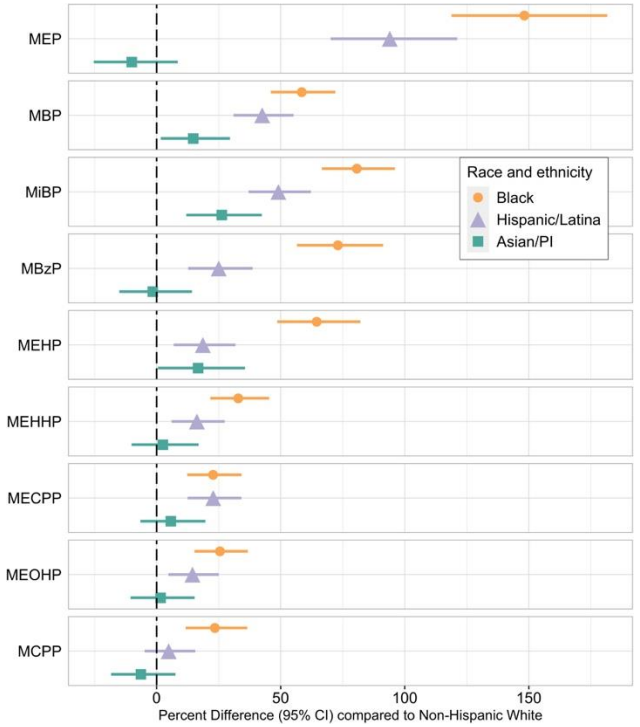
Van den Brekel, Lenters, et al. Ethnic and socioeconomic inequalities in air pollution exposure: a cross-sectional analysis of nationwide individual-level data from the Netherlands. Lancet Planetary Health 2023

Racial/ethnic disparities in phthalate exposure in the US



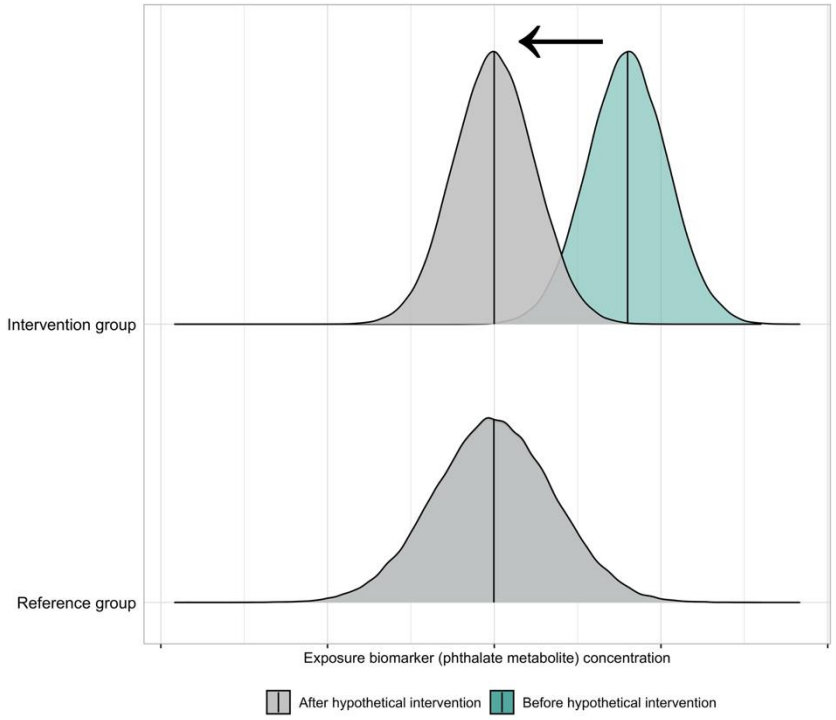
6,045 pregnancies, 16 U.S. cohorts

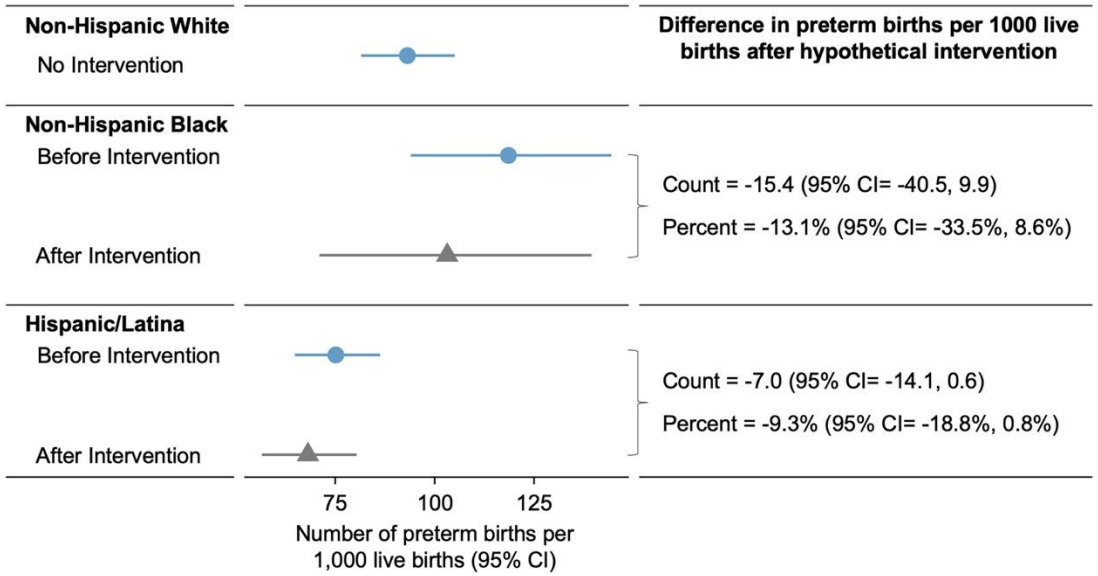




Welch et al. Racial and Ethnic Disparities in Phthalate Exposure and Preterm Birth: A Pooled Study of Sixteen U.S. Cohort. Env Health Perspectives 2023

Quantifying impacts of exposure disparities: phthalate → preterm birth



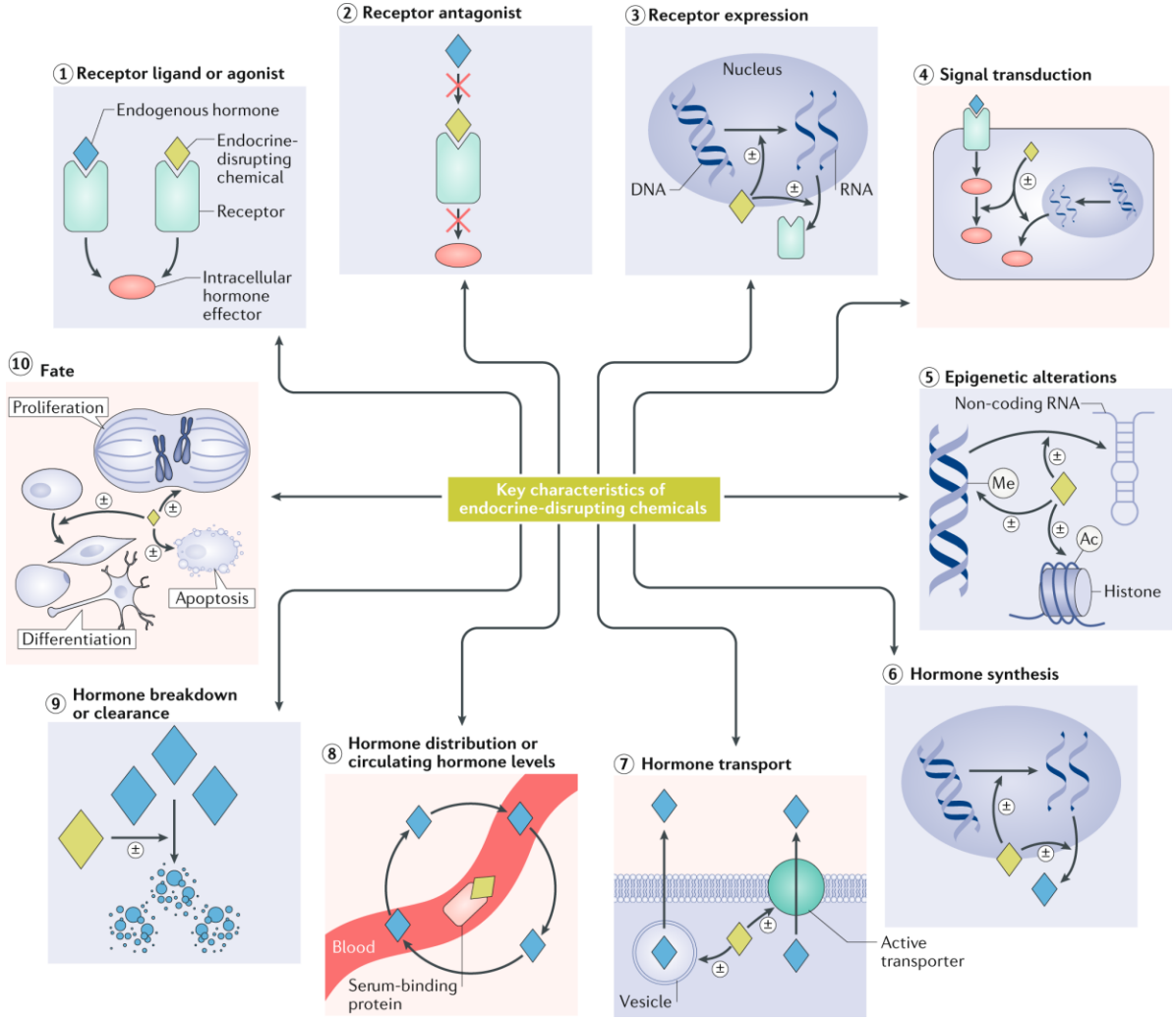


Estimated changes in the probability of preterm birth under hypothetical interventions to eliminate disparities in levels of urinary phthalate metabolites (mixture effect: g-computation) during pregnancy by proportionally lowering average concentrations in Black and Hispanic/Latina participants to be approximately equal to the averages in White participants

Welch et al. Racial and Ethnic Disparities in Phthalate Exposure and Preterm Birth: A Pooled Study of Sixteen U.S. Cohort. Env Health Perspectives 2023

Thank you

Modes of action: EDCs



La Merrill, M.A., Vandenberg, L.N., Smith, M.T. et al. Consensus on the key characteristics of endocrine-disrupting chemicals as a basis for hazard identification. Nat Rev Endocrinol 16, 45–57 (2020)

EFSA 2022

"The Scientific Committee reconfirms that the benchmark dose (BMD) approach is a scientifically more advanced … for deriving a Reference Point... may also apply to data from (observational) epidemiological studies. However, such studies have their own peculiarities with respect to study design and interpretation of data and for these reasons, the application of dose–response analysis of epidemiological data will be addressed in a separate future guidance document."

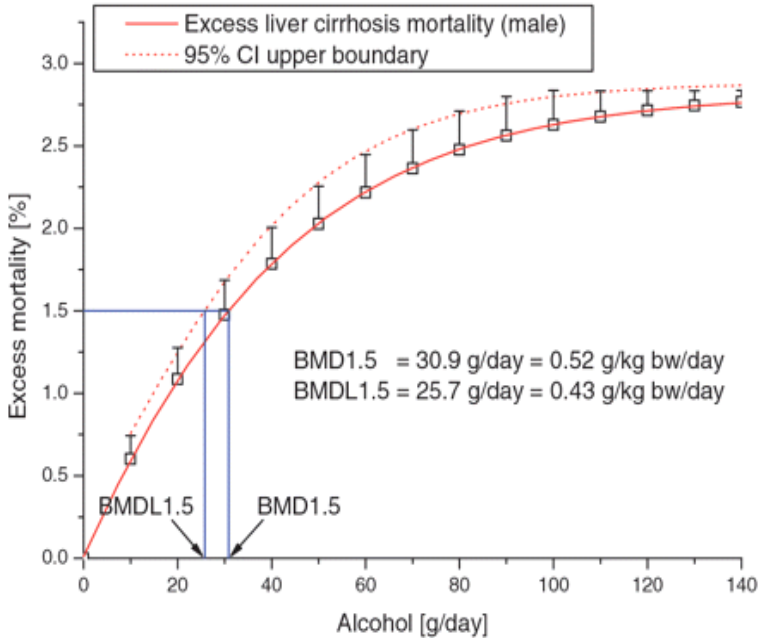


Fig: BMD modelling of excess liver cirrhosis mortality and alcohol intake in the male Canadian population.

Conclude: "'virtually safe guideline' based on our ADI of 2.6 g/day…max. of 6 drinks/month"

Note: 1–5% excess risk pre-defined when using epidemiological data (10% with toxicological data)

EFSA Scientific Committee et al. Guidance on the use of the benchmark dose approach in risk assessment. 2022
Lachenmeier et al. 2011, Epidemiology-based risk assessment using the benchmark dose/margin of exposure approach: the example of ethanol and liver cirrhosis, Int J of Epidemiology