Everywhere All At Once: The Prenatal Chemical Exposome and Influences on Health and Health Inequities

Tracey J Woodruff

Professor UCSF

June, 20024

Nothing to Declare

Healthier Environments for Healthier People
Targeted Research * Improved Clinical Care * Just Public Policy

Latest Story
Overview
Key Stories
Resources

'Heroine' of FDA Keeps Bad Drug Off Market

By Morton Mintz
Washington Post Staff Writer
July 15, 1962

In this 1962 photo, President Kennedy signs a bill to tighten governmental control over drugs. The legislation was largely due to Thalidomide and its severe side effects on babies. Dr. Frances Oldham Kelsey is second from the left. (UPI/Corbis-Bettman)

This is the story of how the skepticism and stubbornness of a Government physician prevented what could have been an appalling American tragedy, the birth of hundreds or indeed thousands of armless and legless children.

The story of Dr. Frances Oldham Kelsey, a Food and Drug Administration medical officer, is not one of inspired prophesies nor of dramatic research breakthroughs.

Public Law 87-781

October 10, 1962
[S. 1552]

AN ACT

To protect the public health by amending the Federal Food, Drug, and Cosmetic Act to assure the safety, effectiveness, and reliability of drugs, authorize standardization of drug names, and clarify and strengthen existing inspection authority; and for other purposes.

Drug Amendments of 1962.

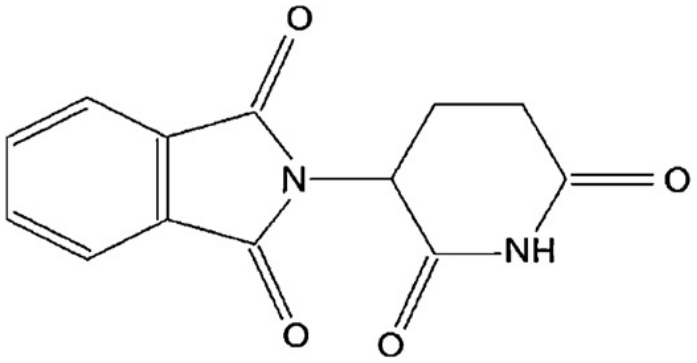
Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That this Act, divided into titles and sections according to the following table of contents, may be cited as the "Drug Amendments of 1962".

TABLE OF CONTENTS

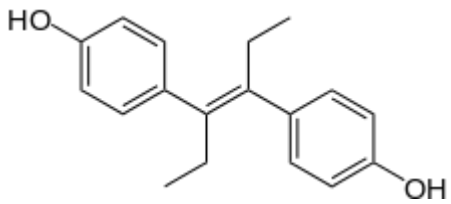
TITLE I—DRUGS

PART A—AMENDMENTS TO ASSURE SAFETY, EFFECTIVENESS, AND RELIABILITY

Manufactured Chemicals and Pharmaceuticals

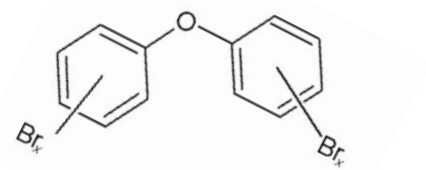


Thalidomide

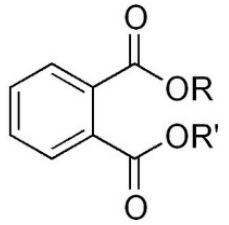


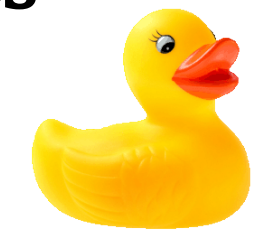
Diethylstilbestrol

PBDEs

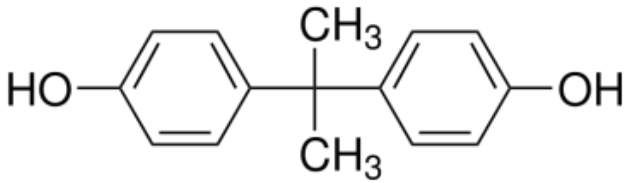


Phthalates





BPA

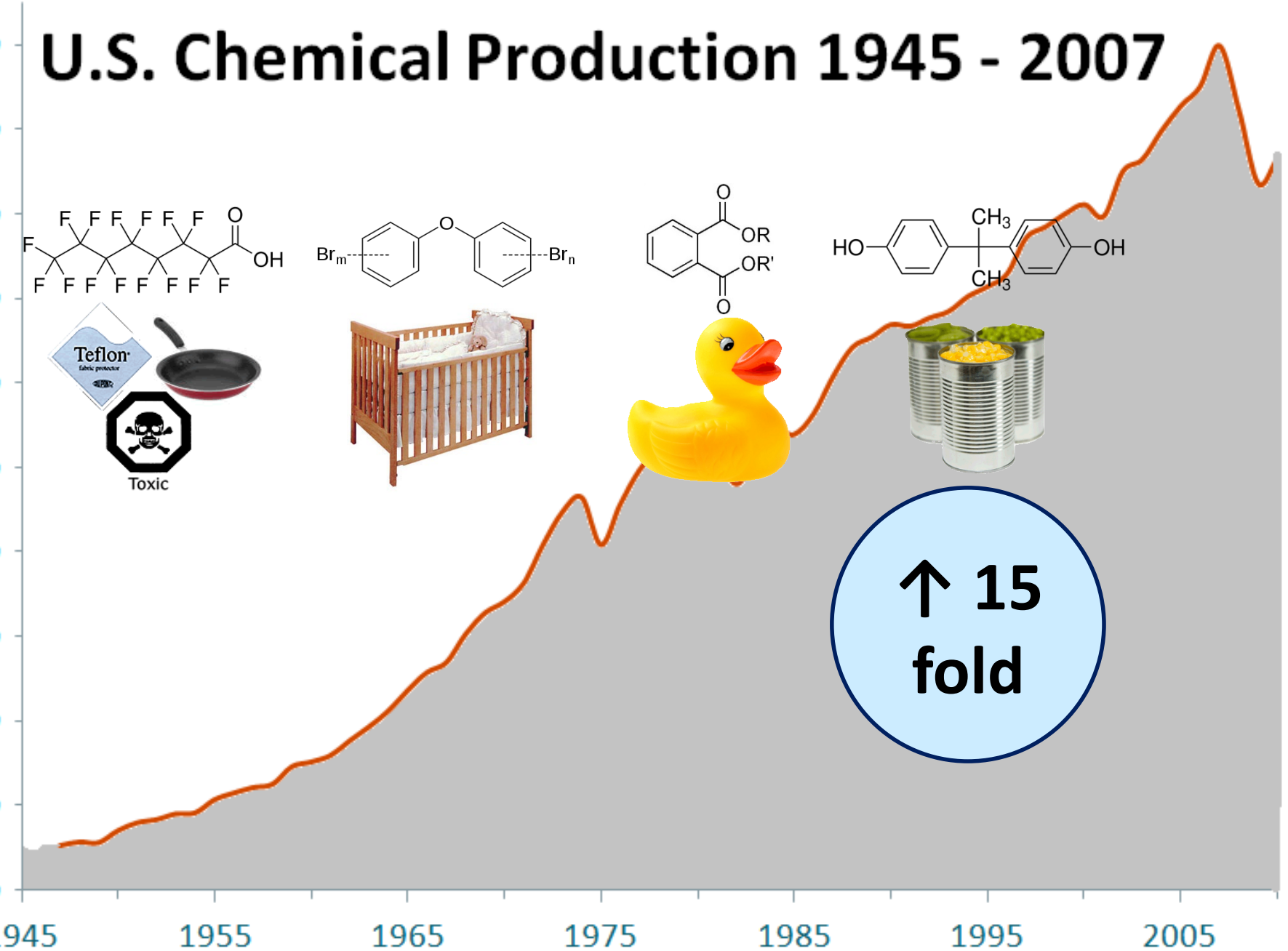


Manufactured pharmaceuticals have to have **safety** data before use

Manufactured chemicals do **NOT**

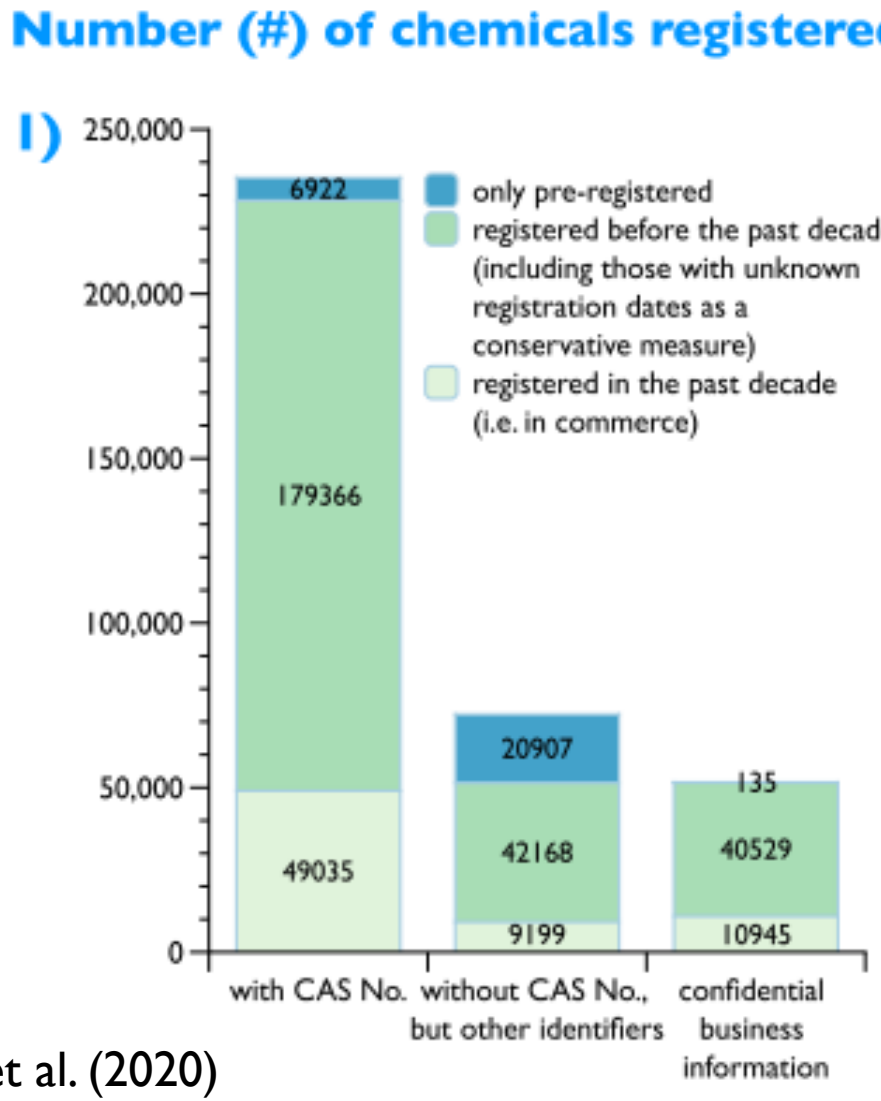
U.S. Chemical Production 1945 - 2007

Production compared to the year 2007



Source: U.S. Federal Reserve Board, Division of Research and Statistics

Globally - 350,000 Chemicals and mixtures registered for production and/or used



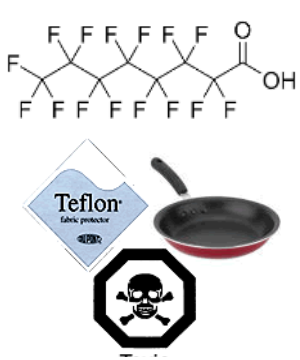
Wang et al. (2020)

235k chemicals are registered

120k chemicals and mixtures without CAS #s or other identifiers

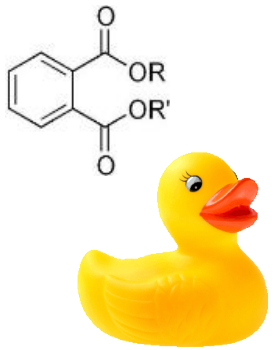
50k chemicals

~30,000 lbs of industrial chemicals produced for each person in the U.S. each year

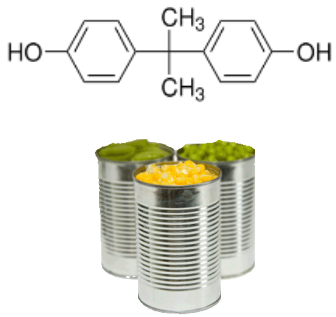


PFAS

Flame Retardants



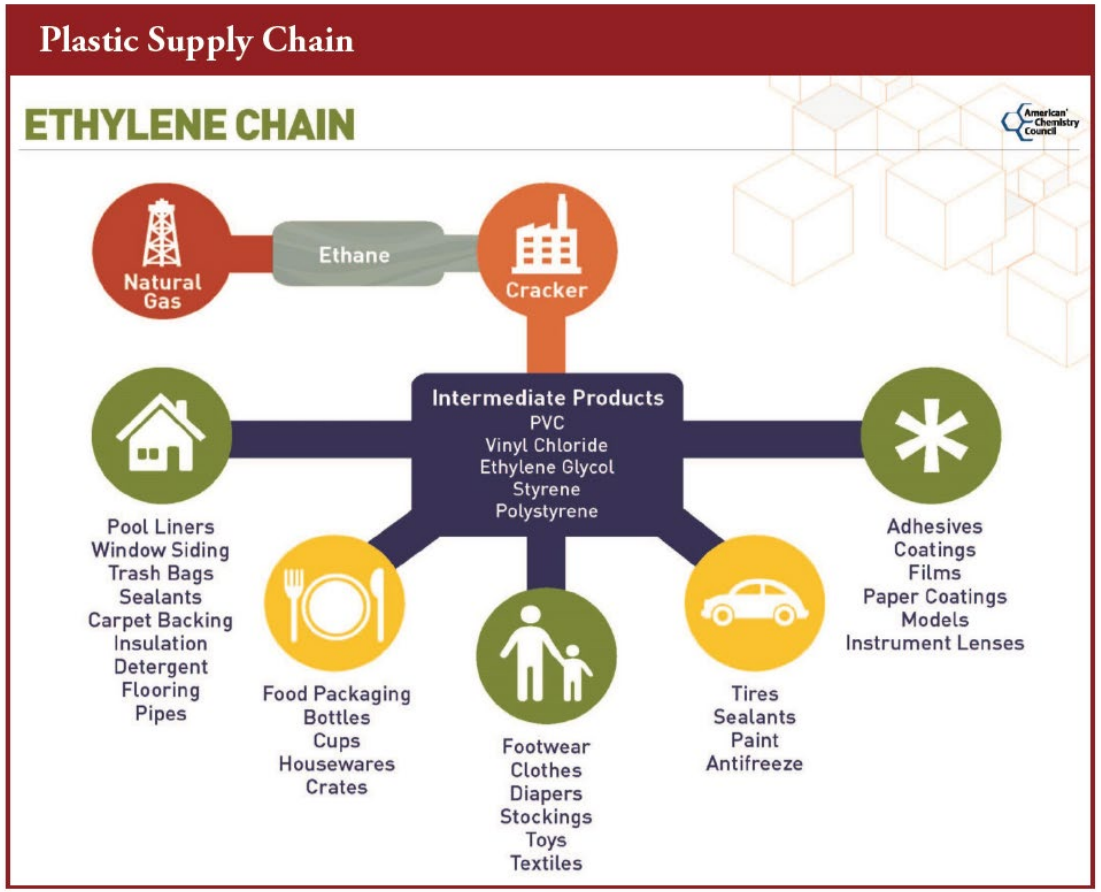
Phthalates



Phenols/BPA

EPA Chemical Data Repor

Petro-chemical connection



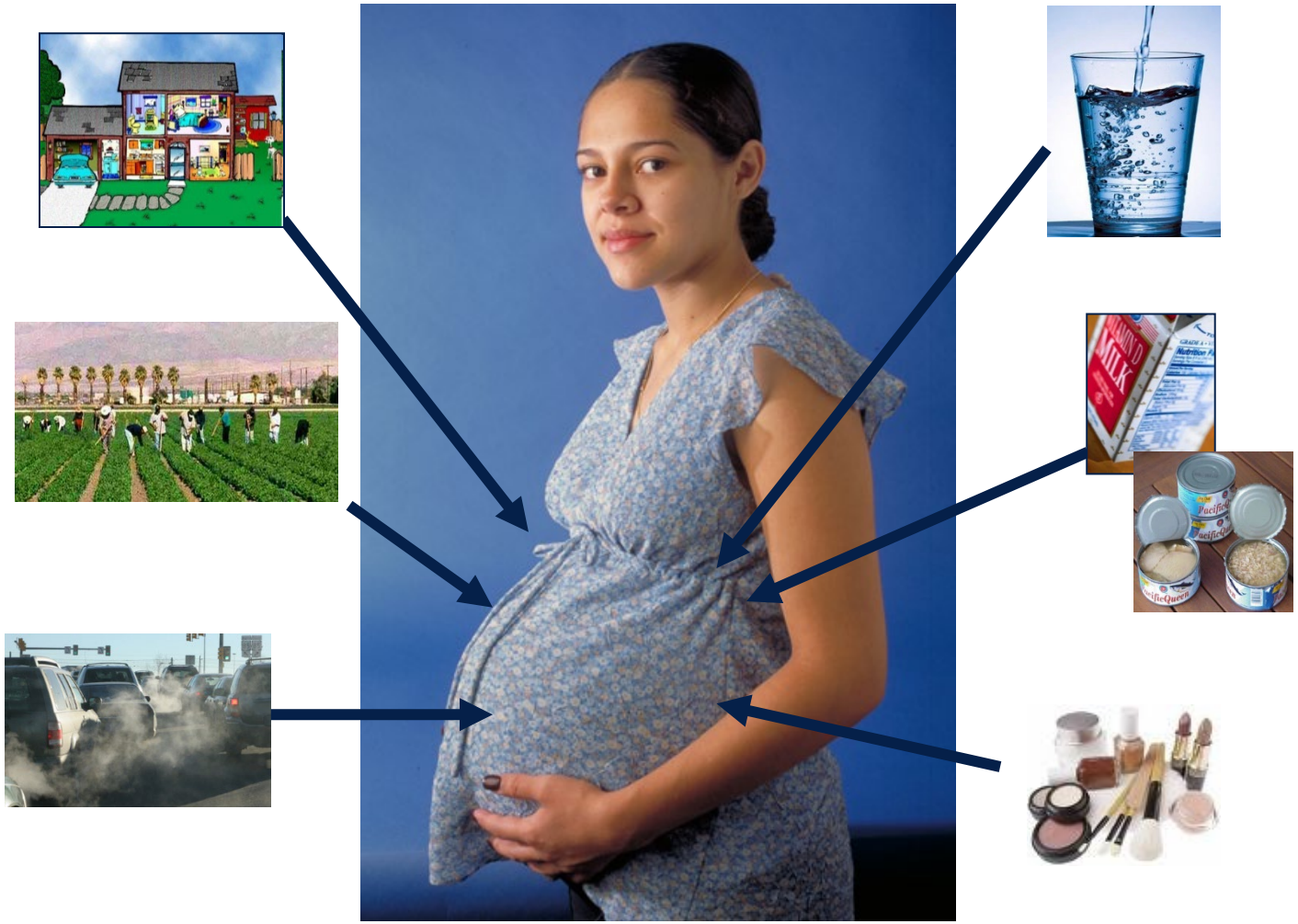
Production of ethylene as a feedstock is more lucrative than the sale of methane and ethane for fuel, heat, or electricity

About half of the petrochemical sector's energy consumption consists of fuels used as raw materials to make chemicals for products

Petrochemicals are becoming the largest driver of global oil consumption. And will account for more than a third of the growth in oil demand to 2030, and nearly half to 2050

“We live in a chemical soup.”

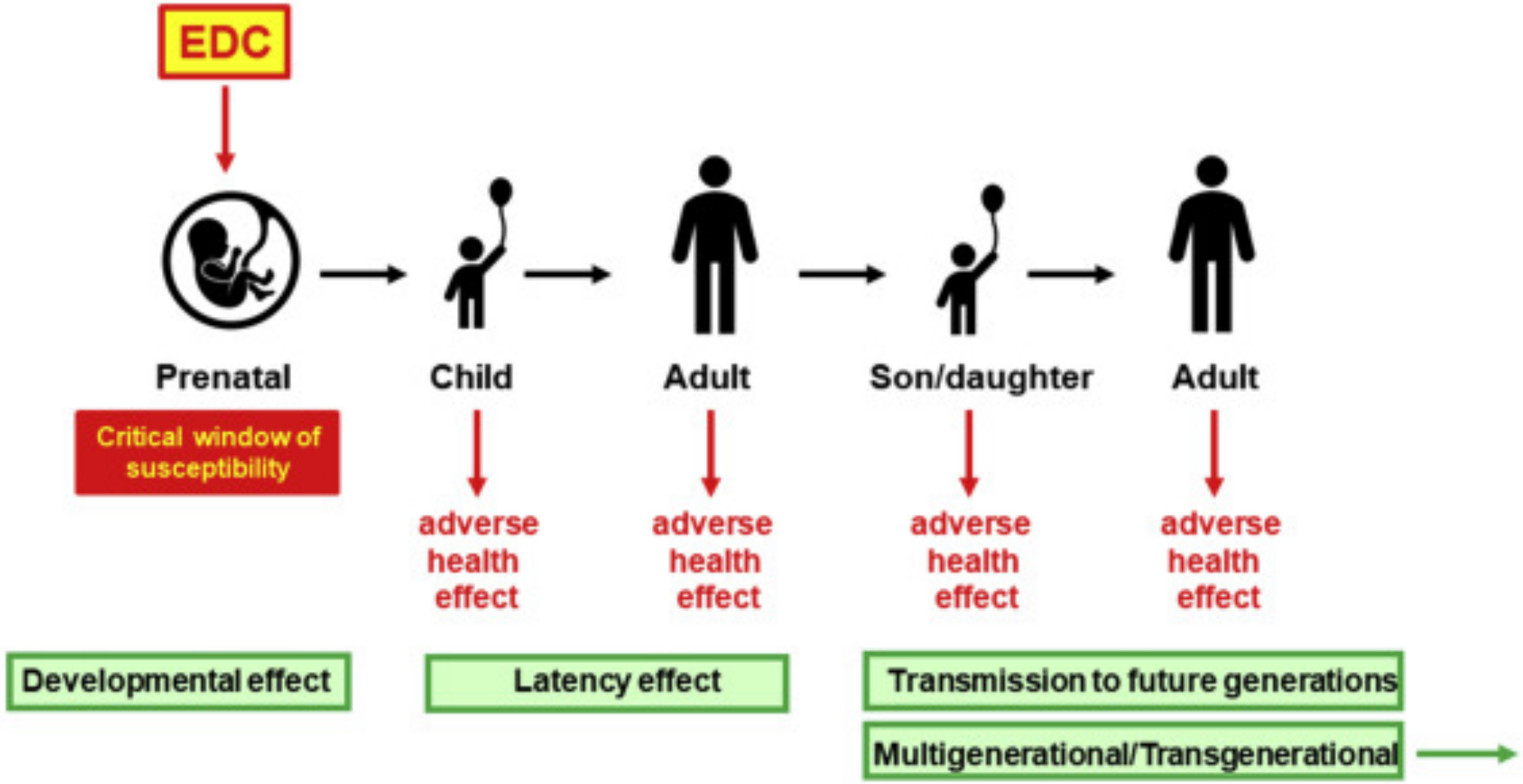
- Linda Birnbaum
Former Director, NIEHS



Toxic chemical exposures start *in utero*

… “ to a disturbing extent, babies are born pre-polluted.”

National Cancer Institute


EDC
Prenatal
Child
Adult
Son/daughter
Adult
Critical window of susceptibility
adverse health effect
adverse health effect
adverse health effect
adverse health effect
Developmental effect
Latency effect
Transmission to future generations
Multigenerational/Transgenerational

WHY DO ENDOCRINE DISRUPTING CHEMICALS MATTER?

EDCs ARE EVERYWHERE

EDCs are mostly man-made chemicals that we encounter in our daily life. EDCs interfere with the normal function of our hormones and as a result cause health problems.

VERY LOW DOSES CAN CAUSE HARM

Amounts which are usually considered "safe" for consumers are based on traditional risk assessment methods that often do not capture effects on hormones.

POTENTIAL DELAYED EFFECTS

Effects can occur years after exposure. Moreover, adverse health effects may affect multiple generations.

IRREVERSIBLE HEALTH DAMAGE

During windows of high vulnerability, a woman's health can be damaged beyond repair.

EFFECTS LARGELY OVERLOOKED

Current regulatory testing strategies lack adequate test methods to identify EDCs.

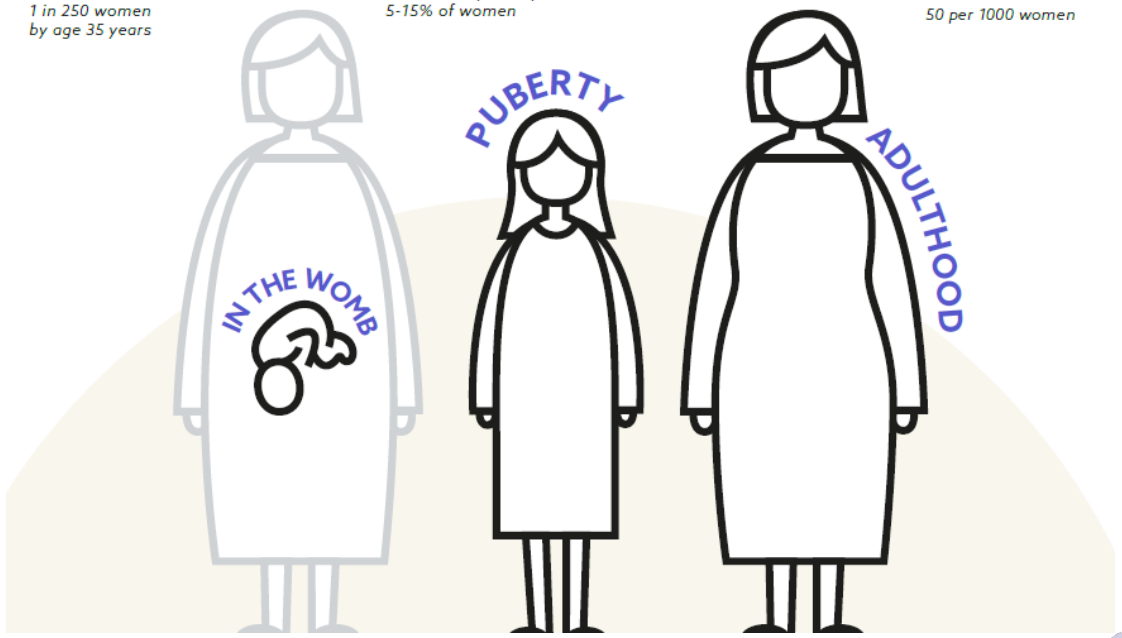
EXAMPLES OF KNOWN AND SUSPECTED EDCS

- BISPHENOL A
- SOME PESTICIDES AND BIOCIDES
- SOME PHTHALATES SUCH AS DEHP
- SOME PERFLUORINATED CHEMICALS SUCH AS PFOA AND PFOS

HOW CAN EDCs AFFECT FEMALE REPRODUCTIVE HEALTH?

Reproductive health issues in women are often related to hormonal disbalance. In addition to risk factors such obesity or smoking, EDCs can affect reproductive health. ECDs can disrupt hormones at any life stage, from conception to adulthood, which can lead to a range of health problems.

- EARLY MENOPAUSE *1 in 250 women by age 35 years*
- BREAST CANCER *1 in 8 women*
- POLYCYSTIC OVARY SYNDROME (PCOS) *5-15% of women*
- ENDOMETRIOSIS *10% reproductive-age women*
- INFERTILITY *1 in 6 couples*
- IRREGULAR MENSTRUAL CYCLES *50 per 1000 women*



https://www.env-health.org/wp-content/uploads/2020/03/FREIA-infographic_EN_sm.pdf

Intrinsic and extrinsic risk factors of disease

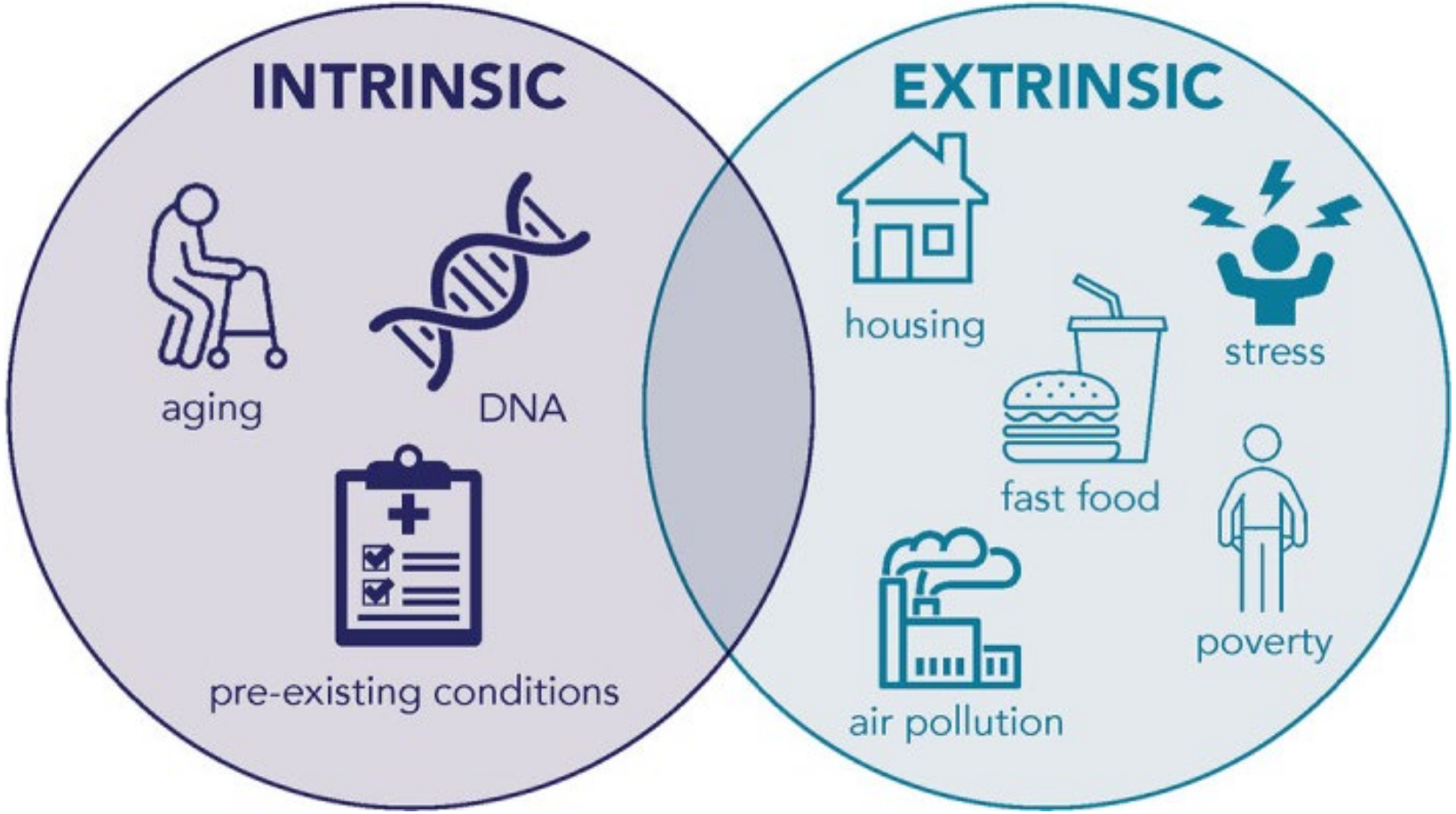


Image source: Varshavsky, J. R., *et al* (2023). Current practice and recommendations for advancing how human variability and susceptibility are considered in chemical risk assessment. *Environmental health : a global access science source*, *21*(Suppl 1), 133. https://doi.org/10.1186/s12940-022-00940-1

Triple Jeopardy of Social Inequality

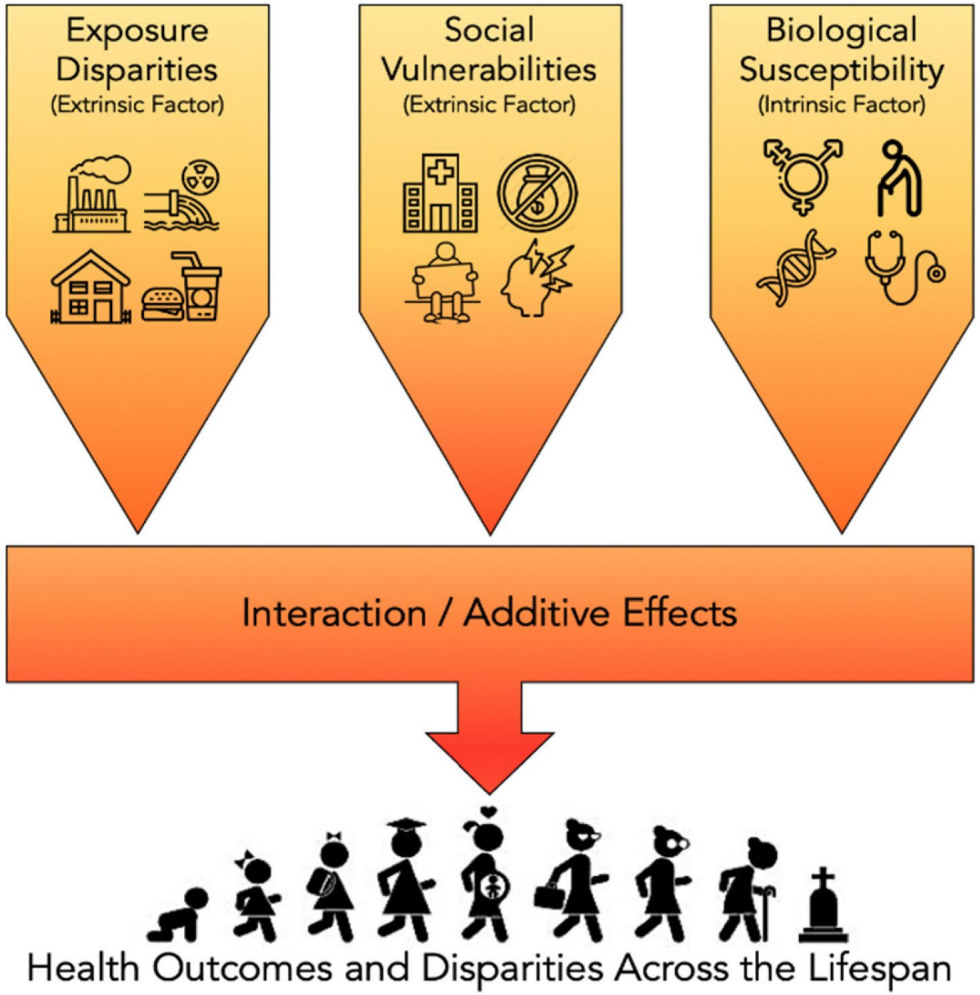
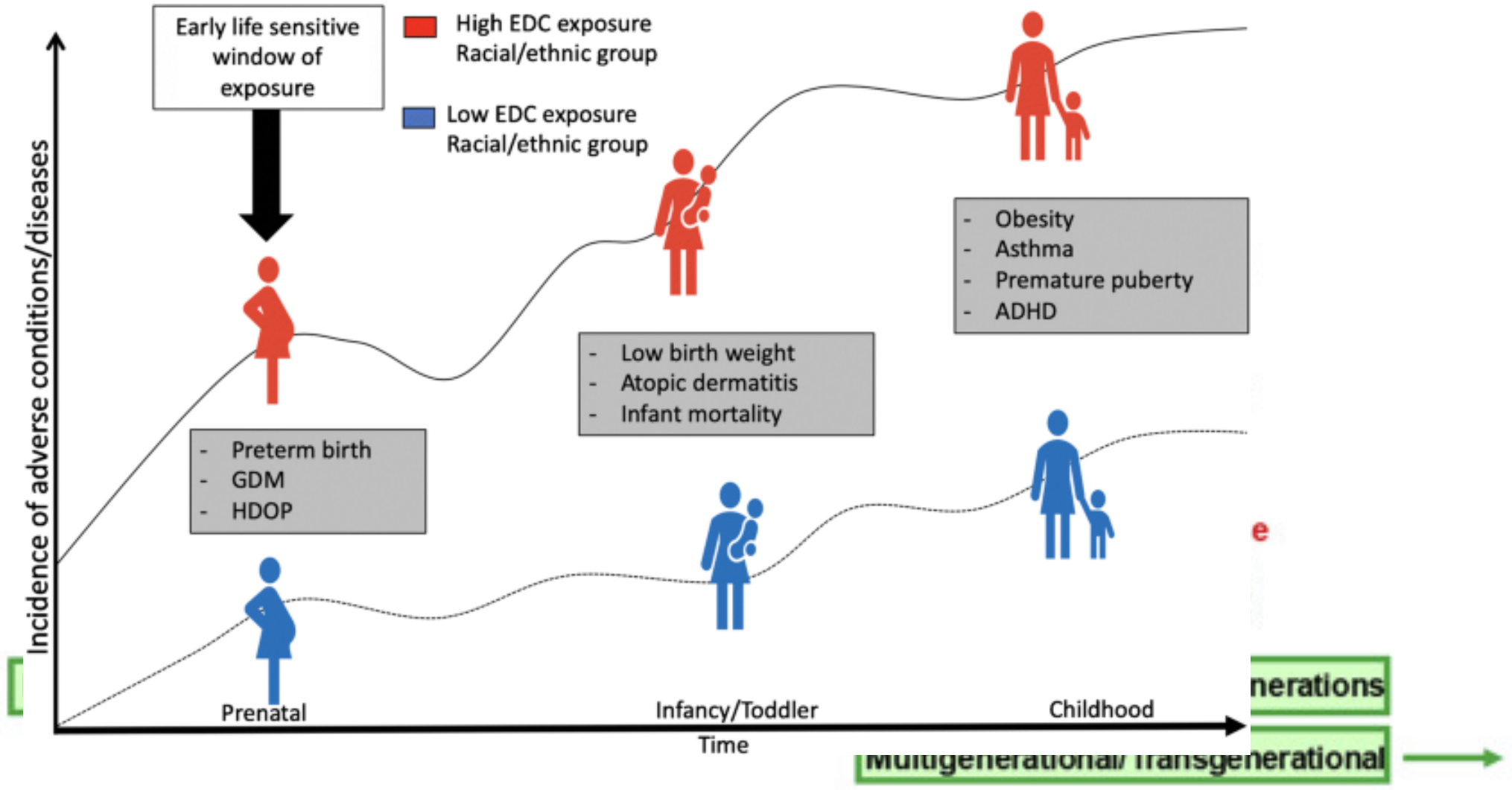
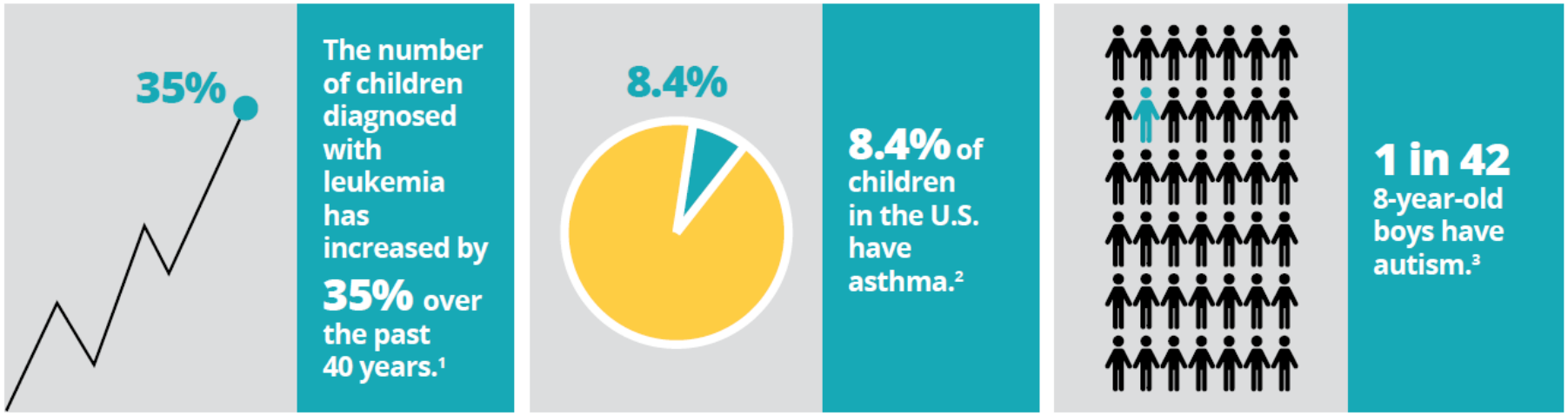


FIGURE 3-1 Triple jeopardy of environmental and social "riskscapes." Environmental justice frameworks encourage scientists and regulators to consider the cumulative impacts of environmental and social stressors and how structural determinants, including segregation and discrimination, drive environmental health inequities across the life course. SOURCE: Swati Rayasam, University of California, San Francisco, Program on Reproductive Health and the Environment. Reprinted with permission; copyright 2023, University of California, San Francisco.


Early life sensitive window of exposure
High EDC exposure Racial/ethnic group
Low EDC exposure Racial/ethnic group
Incidence of adverse conditions/diseases
- Preterm birth
- GDM
- HDOP
- Low birth weight
- Atopic dermatitis
- Infant mortality
- Obesity
- Asthma
- Premature puberty
- ADHD
Prenatal
Infancy/Toddler
Childhood
Time
nerations
Multigenerational/ Transgenerational

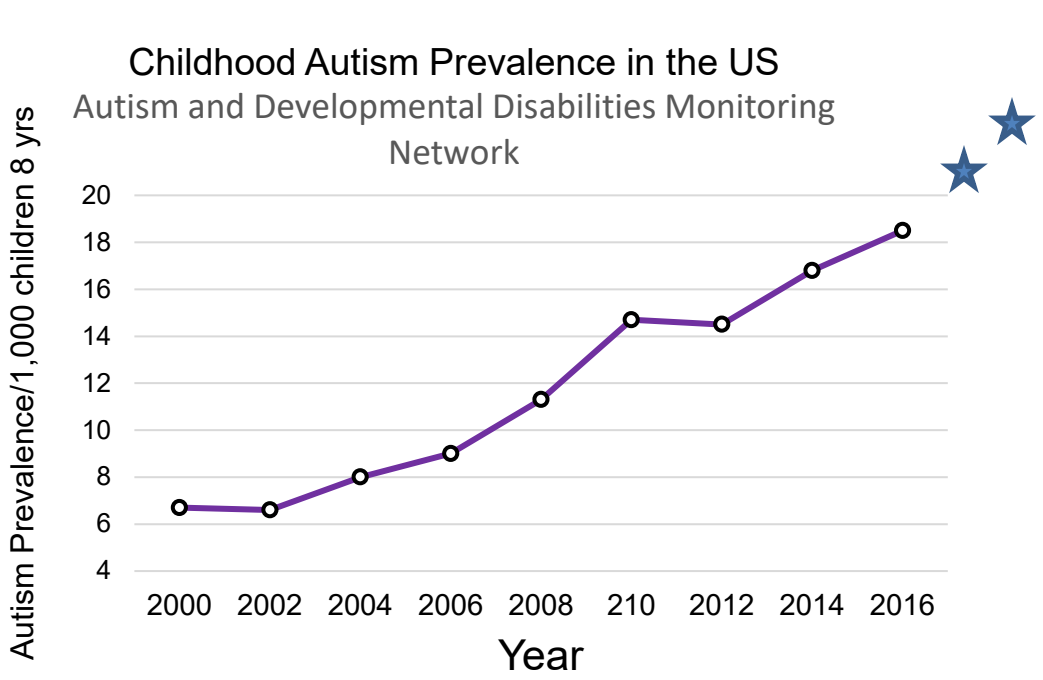
Our children could be healthier

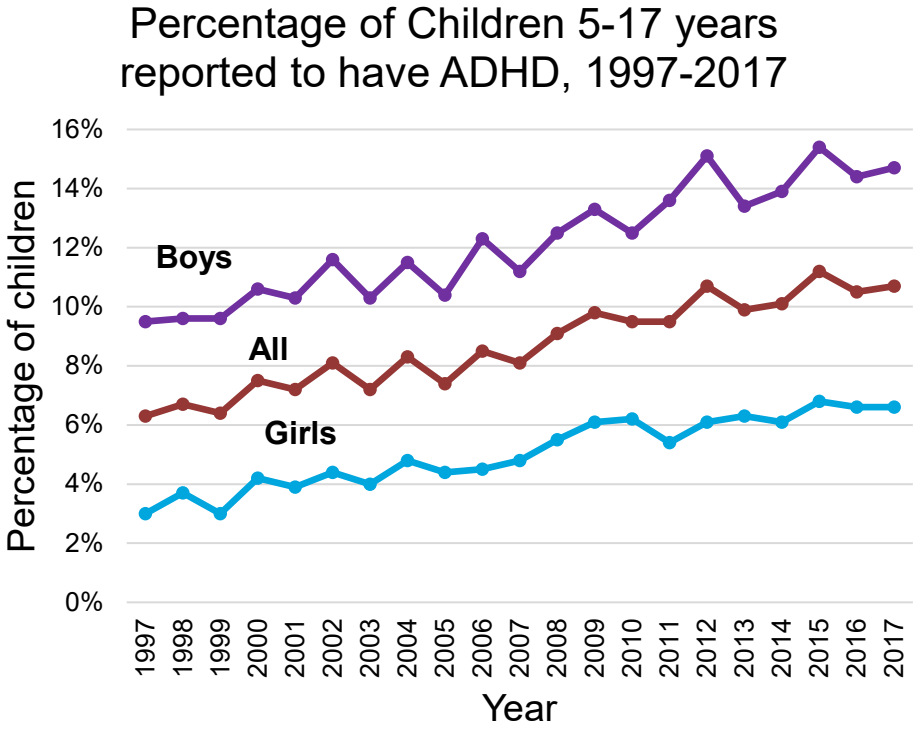


Children in the U.S. are at high risk for chronic disease

U.S EPA/ NIEHS 2017

Increasing Prevalence of Neurodevelopmental Disorders





Among 4-year-old children

•More **Black, Hispanic, and Asian or Pacific Islander children** had autism than **White children**.

•Children **born in 2014** were more likely to be identified with autism by the time they were 4 years old compared to children born in 2010.

•In 2020, rate is 28/1,000 – 1 in 36 children

Comparing the Environment to Other Risk Factors - IQ

Table 2. Estimated FSIQ point losses associated with different risk factors in a population of 25.5 million children.

Risk factor	Total no. of FSIQ points lost
Medical conditions	
Congenital heart disease	104,805
Preterm birth	34,031,025
Type 1 diabetes	185,640
Acute lymphocytic leukemia	135,788
Brain tumors	37,288
Duchenne muscular dystrophy	68,850
Neurodevelopmental disorders	
ASDs	7,109,899
Pediatric bipolar disorder	8,164,080
ADHD	16,799,400
Postnatal traumatic brain injury	5,827,300
Socioeconomic, nutritional, psychosocial factors	
Nonorganic failure to thrive	5,355,000
Iron deficiency	9,409,500
Environmental chemical exposures	
Methylmercury	284,580
Organophosphate pesticides	16,899,488
Lead	22,947,450

34 million

38 million

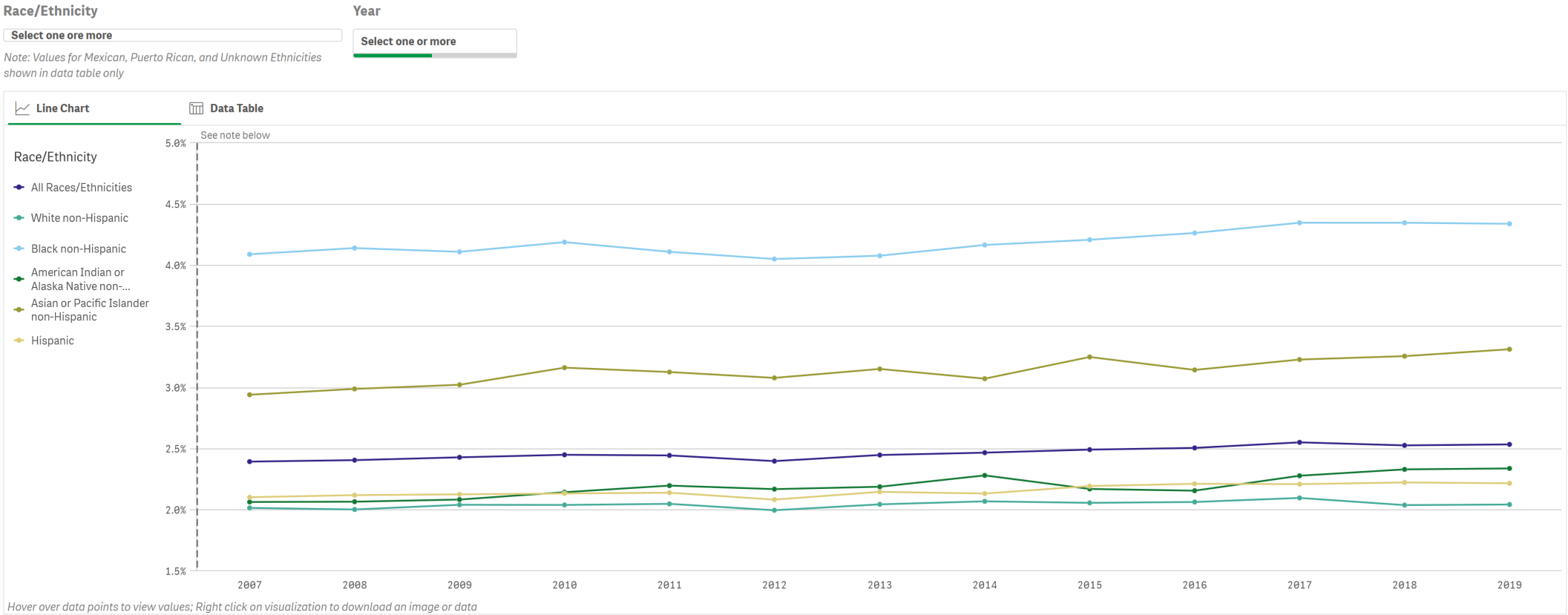
15 million

40 million

Source: Bellinger EHP 2012

UCSF

Percentage of babies born at term with low birth weight, by race/ethnicity, 1993-2019



Black infants 4.3%

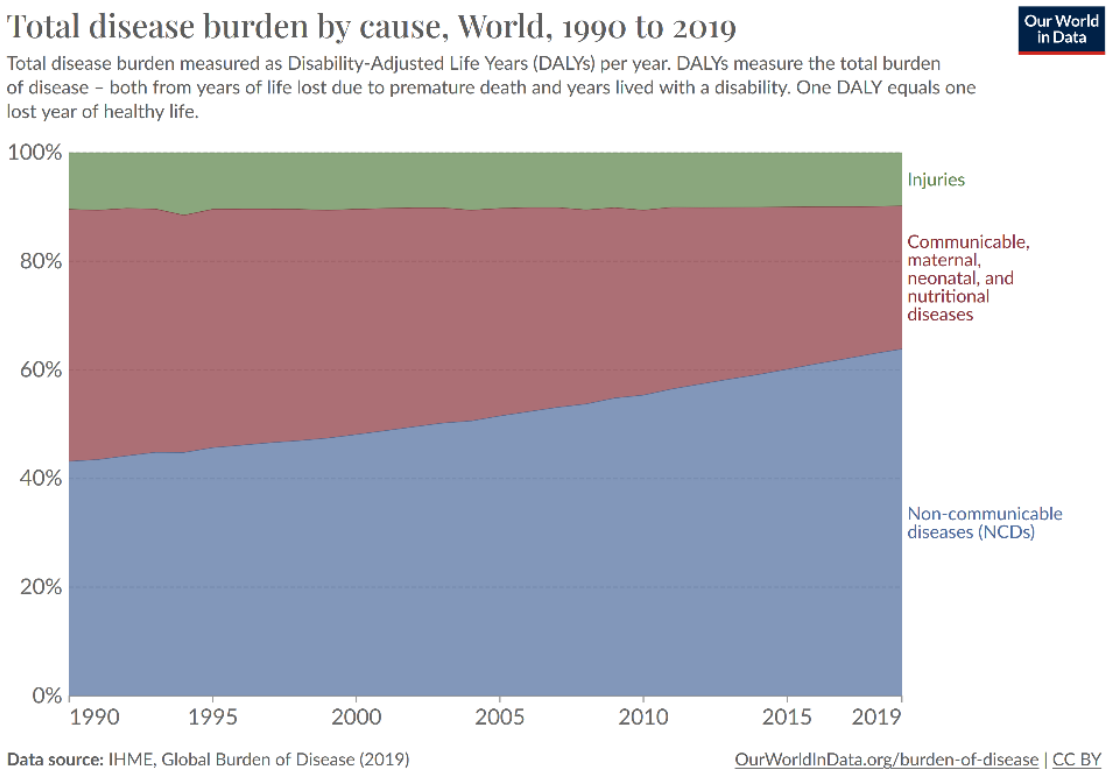
White infants 2%

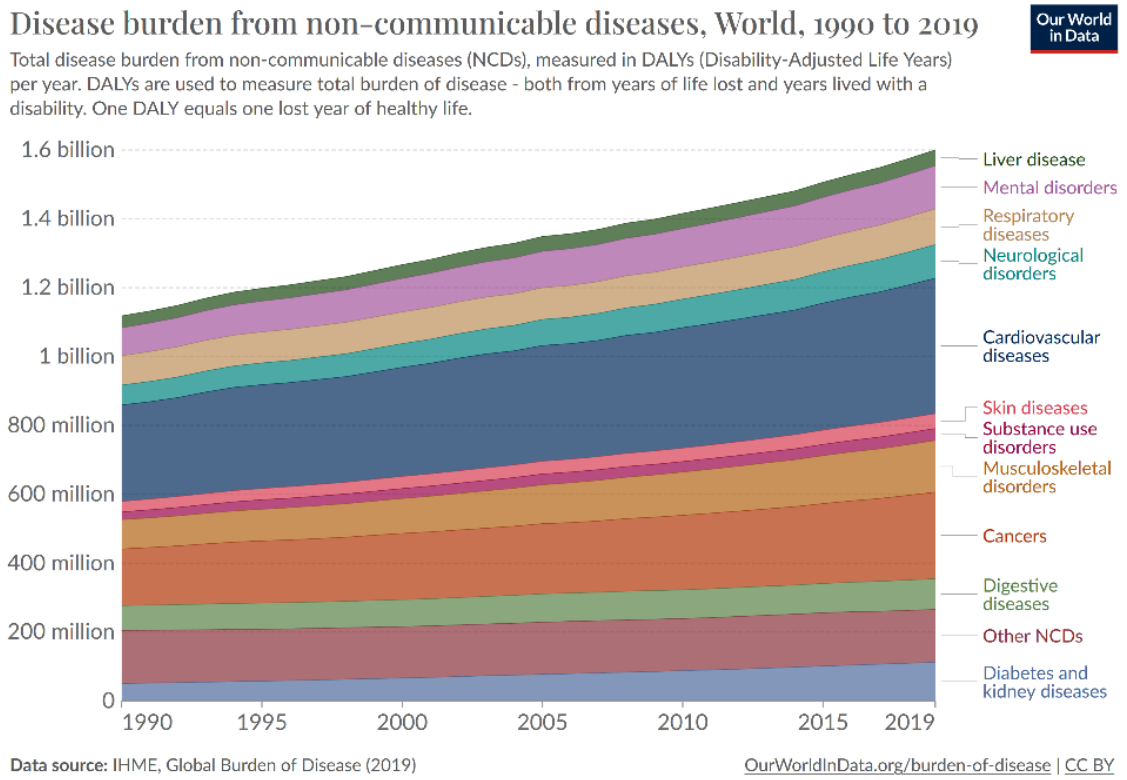
DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System

NOTE: Values from 2007 to the present are not comparable to those for earlier years due to a change in the measure for estimating gestational age. See https://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_05.pdf.

Rate of term low birth weight for women of all race/ethnicities increased from 2.4% to 2.5% between 2007 and 2019. This increasing trend was statistically significant.

Shift from communicable to noncommunicable disease





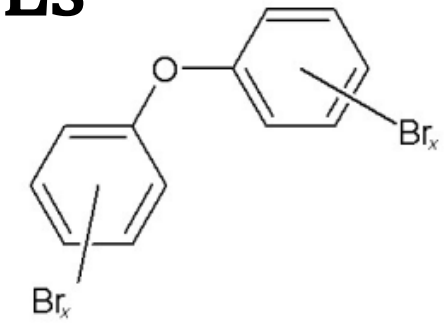
- **1990 - communicable diseases highest share at 46%**
- **2019 - noncommunicable disease now the highest at 64%**
  - Cancer, respiratory, cardiovascular, neurological, metabolic disease

https://ourworldindata.org/burden-of-disease

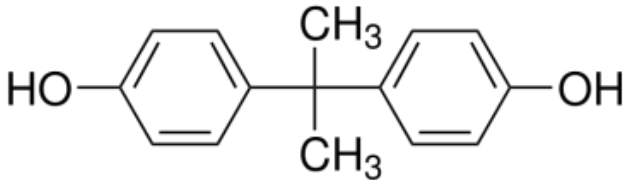
Common Toxic Chemical Classes

PFAS

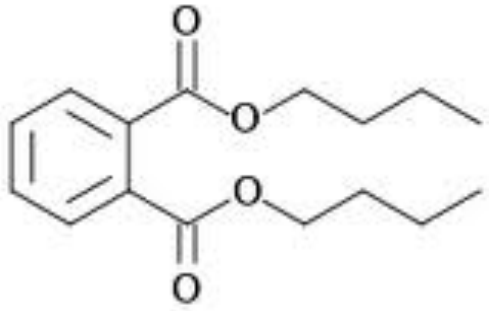
PBDEs

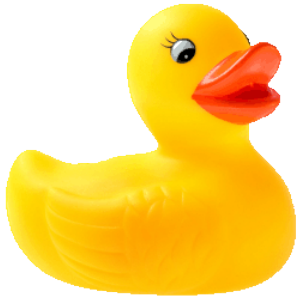


BPA

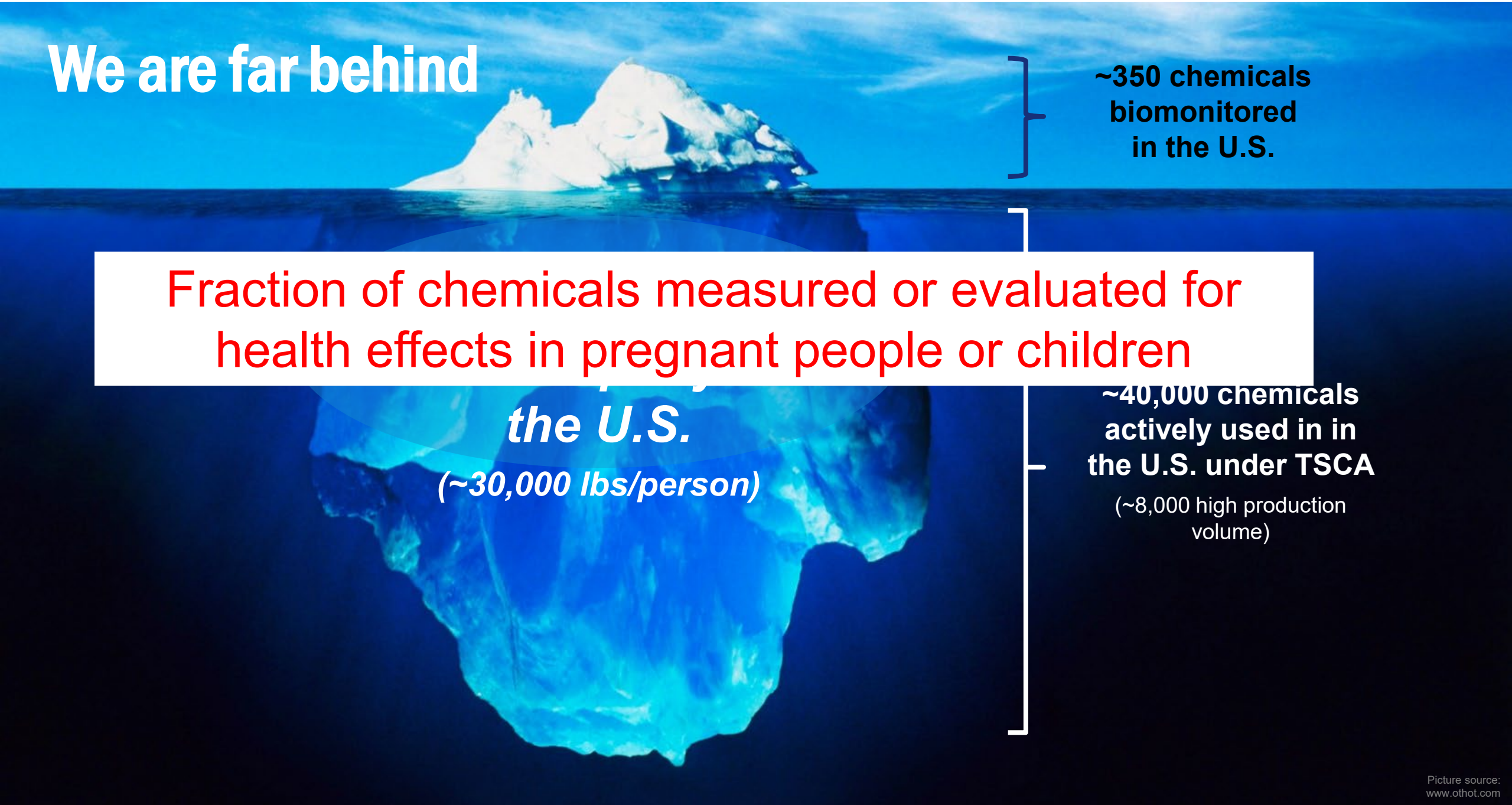


Phthalates





We are far behind



~350 chemicals biomonitored in the U.S.

Fraction of chemicals measured or evaluated for health effects in pregnant people or children

the U.S.

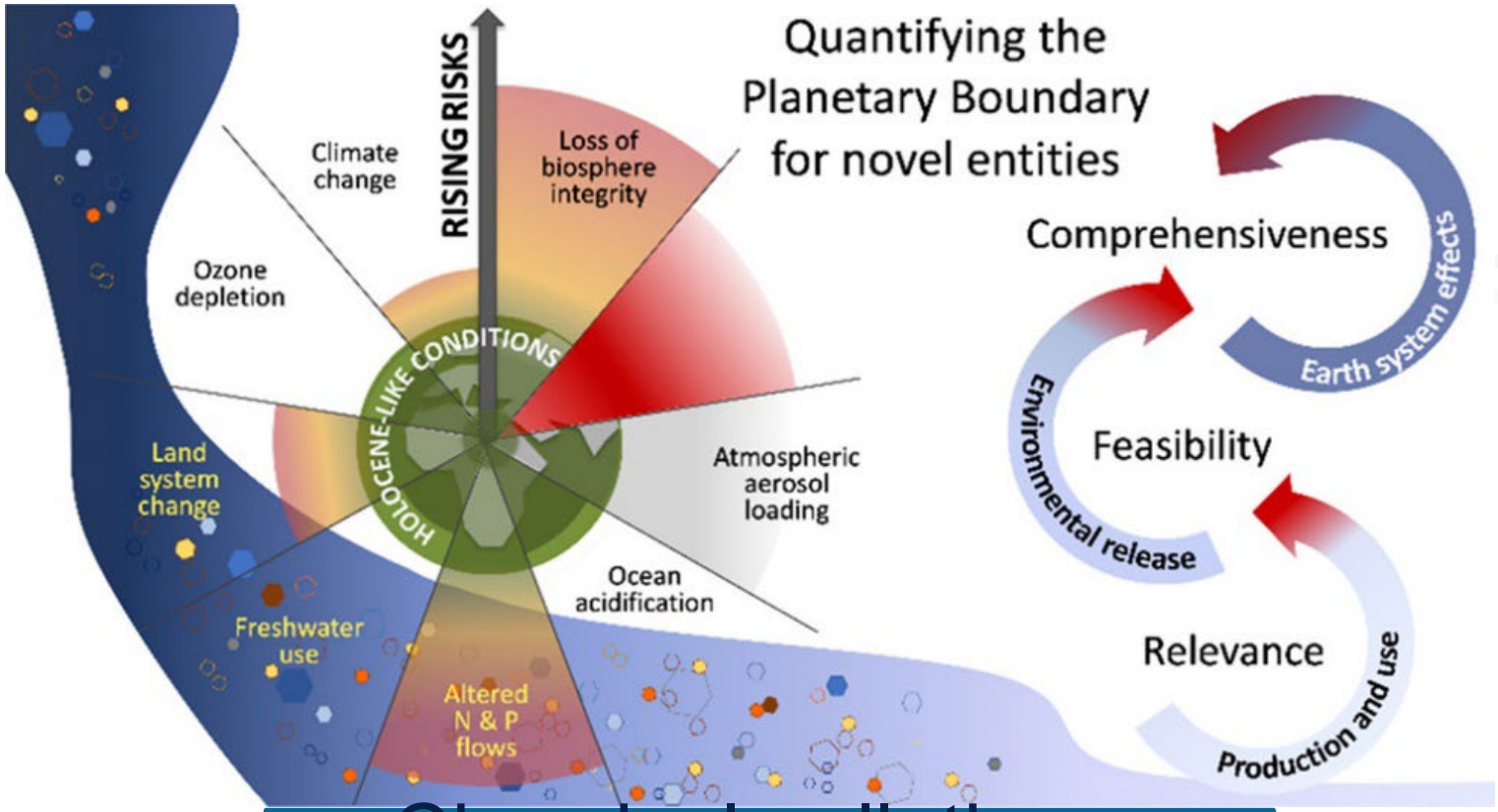
(~30,000 lbs/person)

~40,000 chemicals actively used in in the U.S. under TSCA

(~8,000 high production volume)

Picture source: www.othot.com

Past the Point of No Return?



ENVIRONMENTAL Science & Technology

pubs.acs.org/est

Policy Analysis

Outside the Safe Operating Space of the Planetary Boundary for Novel Entities

Linn Persson,* Bethanie M. Carney Almroth, Christopher D. Collins, Sarah Cornell, Cynthia A. de Wit,* Miriam L. Diamond, Peter Fantke, Martin Hassellöv, Matthew MacLeod, Morten W. Ryberg, Peter Søgaard Jørgensen, Patricia Villarrubia-Gómez, Zhanyun Wang, and Michael Zwicky Hauschild

Cite This: *Environ. Sci. Technol.* 2022, 56, 1510−1521 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

Chemical pollution = Novel Entities

DOI: (10.1021/acs.est.1c04158)


The problem has piled up


Now we have a wicked problem!!

Even I can't clean this up by myself!!

Opportunity to Understand and Address Environmental Contributors to Disease

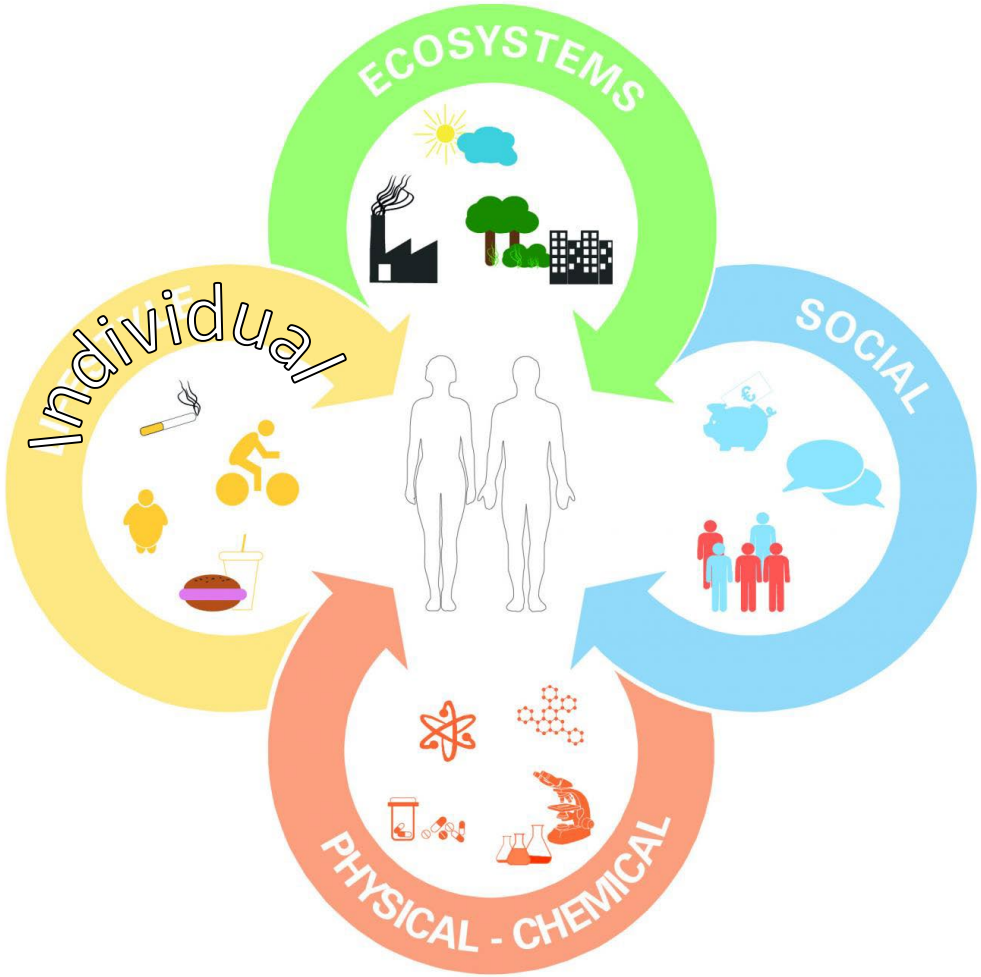
Exposome

Genome

Exposome encompasses:
the ***totality*** of human environmental exposures
from conception onwards

Picture source: D.P. Jones, Yale symposium presentation 2017; Jessica Young's FYC6230 Blog; K. Sainani, BCR 2016

Christopher Wild (2005): Complementing the Genome with an Exposome



The exposome is the sum of all the factors our body is exposed to. Numerous parameters play a role: from what we eat and do, our experiences, to where we live and work.

Based on an illustration by the Utrecht University.

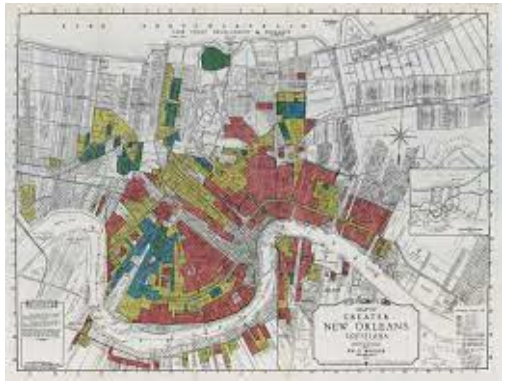
What are cumulative impacts?

"...the totality of exposures to combinations of chemical and non-chemical stressors, and their effects on health, well-being, and quality of life outcomes." –US EPA

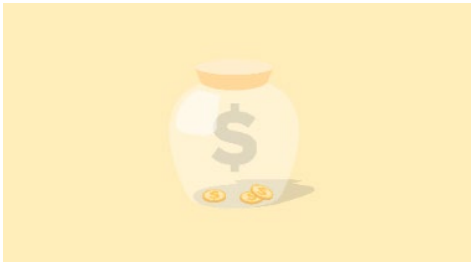
The Lancet Regional Health – Americas 2024 30DOI: (10.1016/j.lana.2023.100666)

Non-Chemical Stressors

Structural



Financial Strain



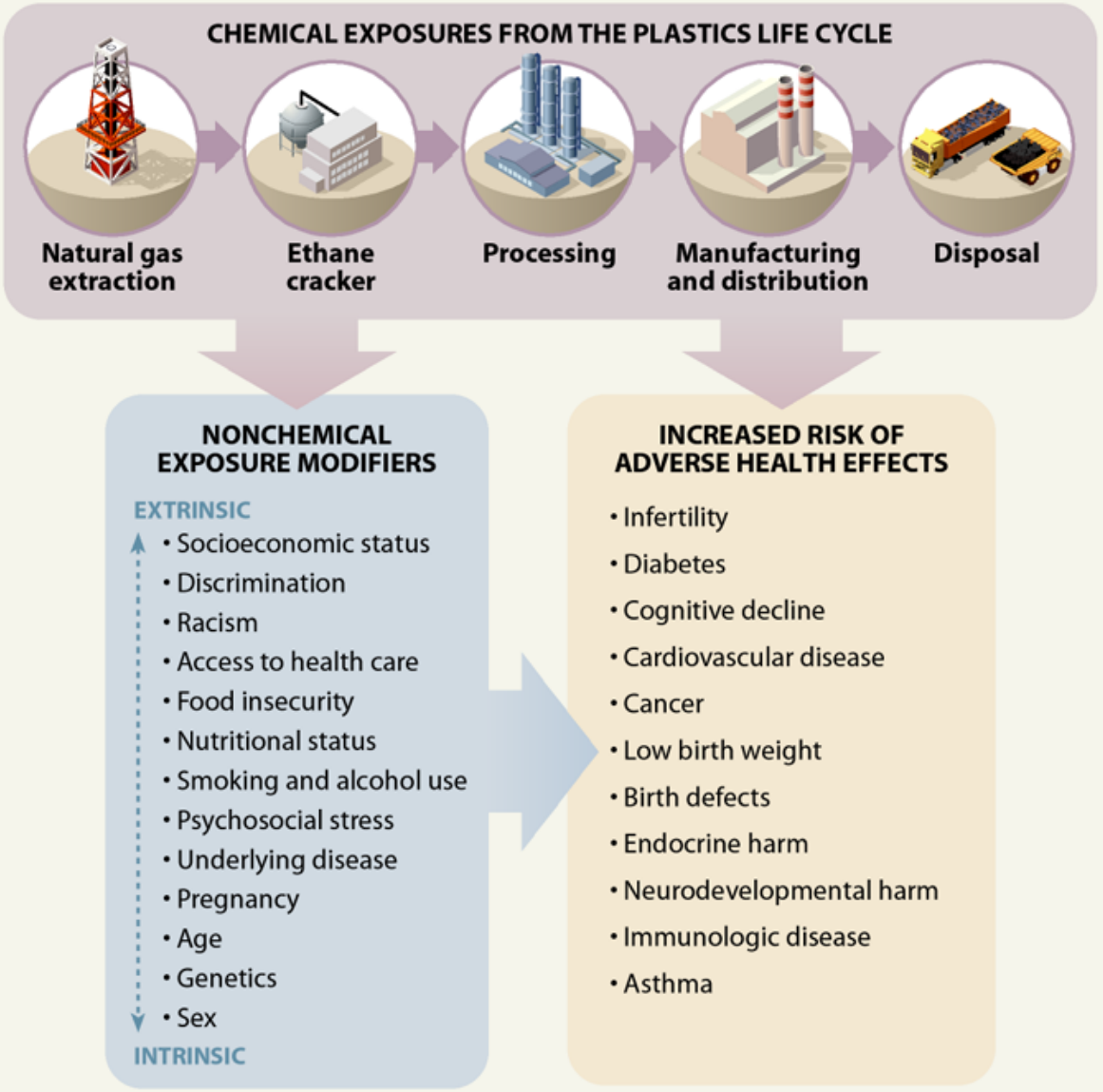
Psychosocial

Food Insecurity

Chemical Stressors

Health Effects of Petrochemicals

Fossil fuels provide the feedstock (ethane) for the chemicals and plastics that permeate daily life. Exposures from extraction through disposal of petrochemicals interact with a person's social and biological vulnerabilities to increase the risk of numerous diseases and health conditions, some of which are shown here.



SOURCE: The New England Journal of Medicine

PAUL HORN / Inside Climate News

Woodruff NEJM 2024

Goal: Research to inform systemic solutions to reduce harmful exposures and improve health and health equity

- Prioritize chemical exposures
  - Multiple chemicals
  - Susceptible period of development
  - Demographic differences
- Identify overlap with social stressors
- Evaluate key health effects
  - Evaluate upstream indicators of harm for earlier intervention

How many chemicals are we exposed to?

EPA United States Environmental Protection Agency

Environmental Topics | Laws & Regulations | About EPA

TSCA Chemical Substance Inventory

~80,000 chemical substances in total

~40,000 chemical substances actively used in the US

The inventory does not include
- Pesticides
- Food additives
- Drugs
- Cosmetics
- Tobacco products
- Nuclear materials
- Munitions

Critical period of development with unique susceptibility to biological/chemical perturbations

CompTox Chemicals Dashboard

883 Thousand Chemicals

Chemicals | Product/Use Categories | Assay/Gene

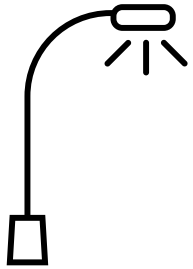
Search for chemical by systematic name, synonym, CAS number, DTXSID or InChIKey

Identifier substring search

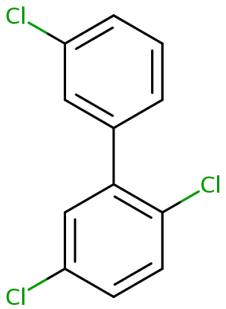
Chemical manufacturers in the united states are allowed to self-regulate

Chemical analysis

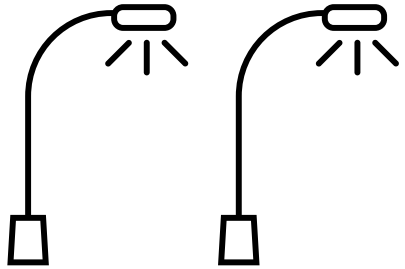
Targeted analysis



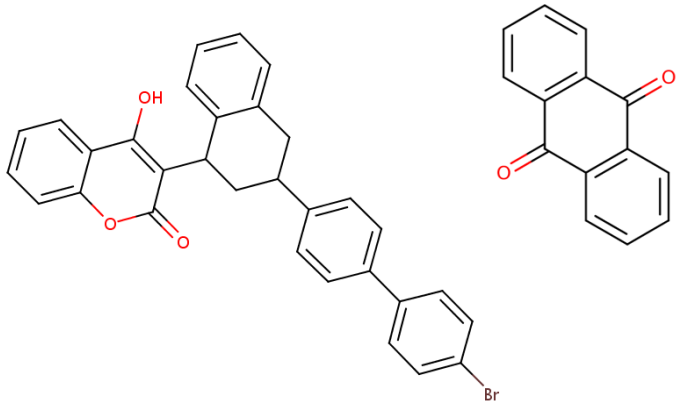
e.g., a list of 10 PCBs



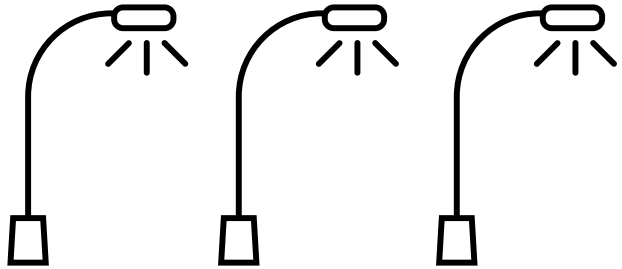
Suspect screening



e.g., a list of 1000 pesticides

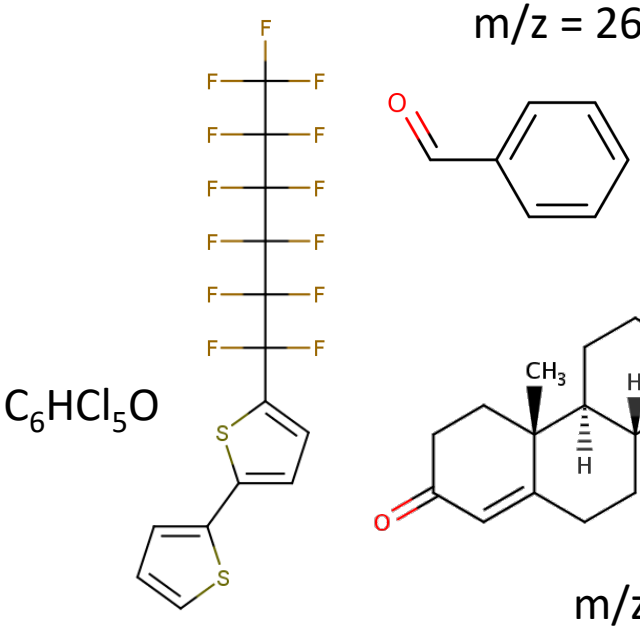


Non-targeted analysis



e.g., all detectable masses in an LC/QTOF system

m/z = 263.847003



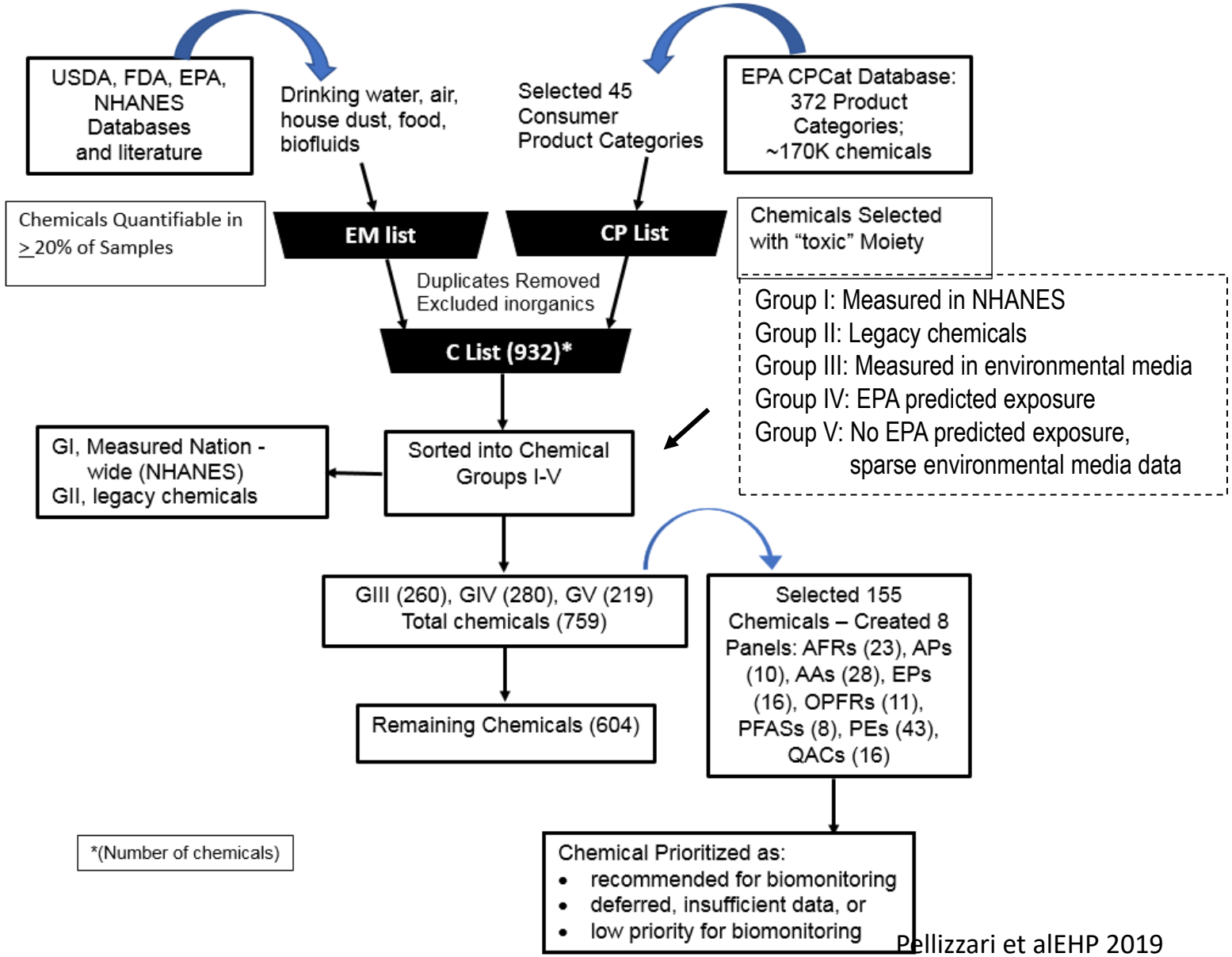
C_6HCl_5O

$C_{21}H_{30}O_5$

m/z = 362.209324

Rigorous review of *extant* data to prioritize 155 chemicals in 8 classes for biomonitoring in pregnant women – NIH ECHO

Chemical Classes
Alternate flame retardants
Alternative plasticizers
Aromatic amines
Environmental phenols
Organophosphorus flame retardants
Perfluoroalkyl substances
Pesticides
Quaternary ammonium compounds



3 multipollutant panels
89 urinary biomarkers for 9 groups
4 Melamine/derivatives
41 Aromatic amines

Pellizzari et alEHP 2019

Policy Failure: Dozens of chemicals detected in pregnancy samples

Melamine and analogues (2)

Aromatic Amines (9)

Benzophenones & Parabens (6)

Bisphenols (2)

Phthalates, Terephthalates, and phthalate alternatives (16)

Fungicides and Herbicides (4)

Neonicotinoid insecticides (2)
Organophosphate insecticide (1)

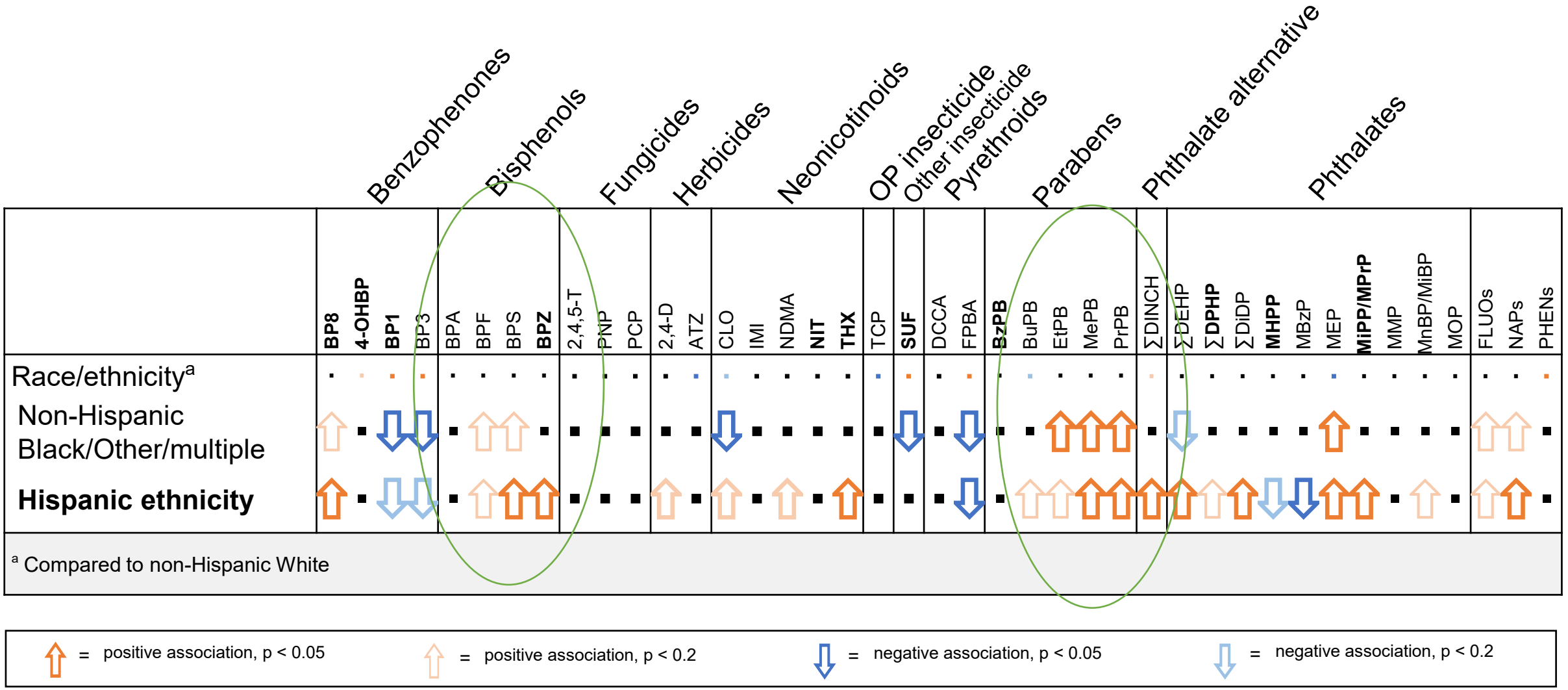
Newer Flame Retardants (2)

Polycyclic aromatic hydrocarbons (4)

Buckley JP, … Woodruff TJ.. Environ Sci Technol. 2022 May 17
Choi et al. Chemosphere Nov 2022

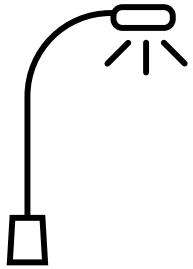
ECHO
Environmental influences on Child Health Outcomes
A program supported by the NIH

Multiple chemical exposures higher in Hispanic and Black women

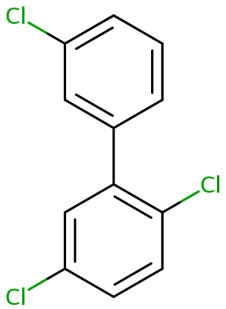


Chemical analysis

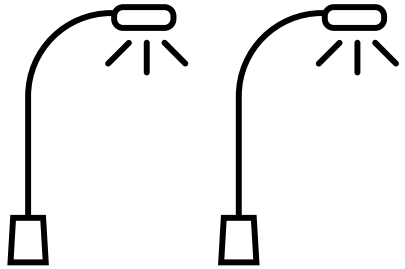
Targeted analysis



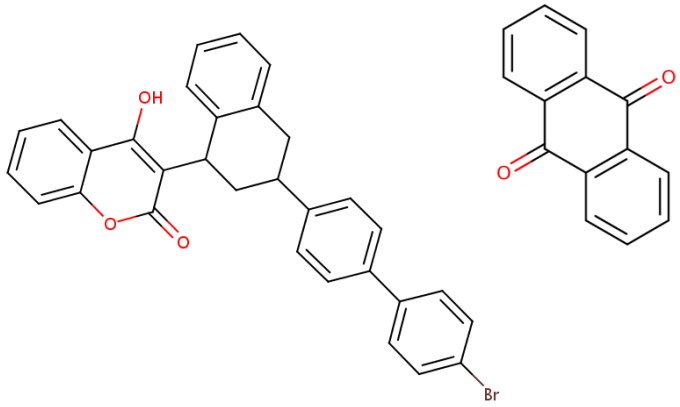
e.g., a list of 10 PCBs



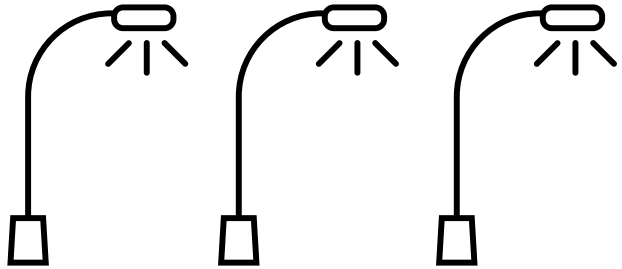
Suspect screening



e.g., a list of 1000 pesticides

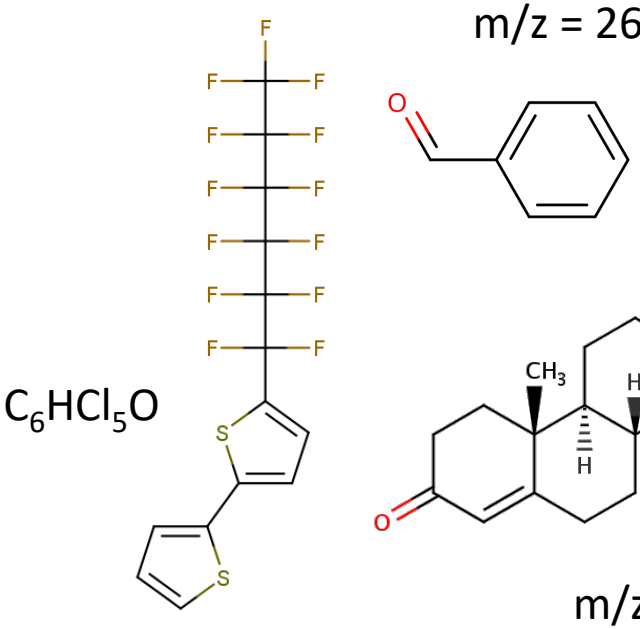


Non-targeted analysis



e.g., all detectable masses in an LC/QTOF system

m/z = 263.847003



C_6HCl_5O

$C_{21}H_{30}O_5$

m/z = 362.209324

300 maternal blood samples

+

300 cord blood samples

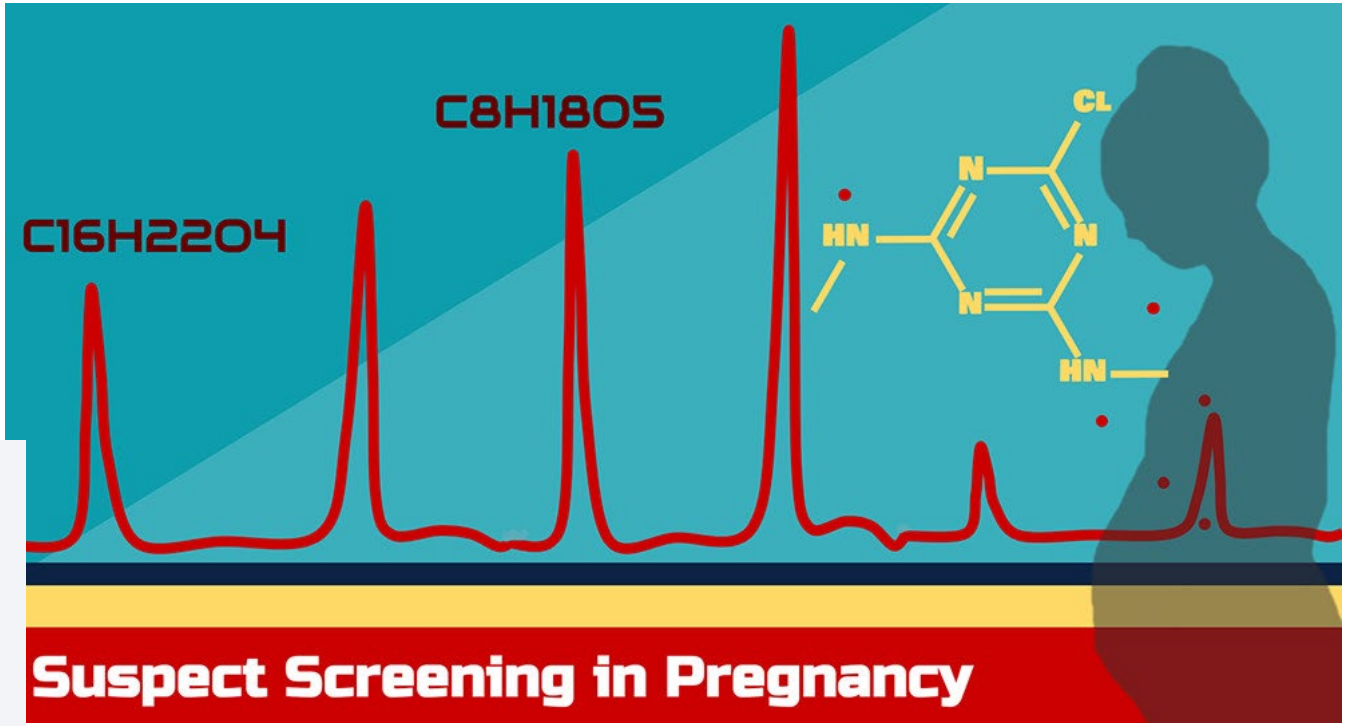
Chemical analysis with high resolution mass spectrometry (HRMS)

Blood samples extraction and clean-up → Analysis with LC – QTOF/MS in ESI+/- modes → Feature extraction and alignment - Profinder → Formula assignment – MPP

MPP → MS/MS in ESI+/- for selected features → Confirmation with analytical standards

Using Nontargeted High Resolution Mass Spectrometry to Scan for the Chemisome

109 chemicals in pregnant women, 55 chemicals never before reported in people



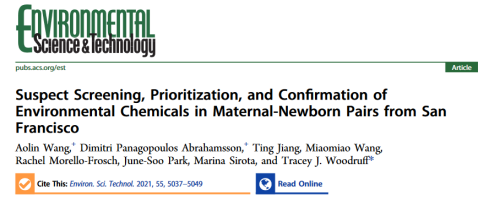
Research • March 16, 2021

UCSF Study Finds Evidence of 55 Chemicals Never Before Reported in People

By Laura Kurtzman

Scientists at UC San Francisco have detected 109 chemicals in a study of pregnant women, including 55 chemicals never before reported in people and 42 “mystery chemicals,” whose sources and uses are unknown.

The chemicals most likely come from consumer products or other industrial sources. They were found both in the blood of pregnant women, as well as their newborn children, suggesting they are traveling through the mother’s placenta.


Environmental Science & Technology

pubs.acs.org/est Article

Suspect Screening, Prioritization, and Confirmation of Environmental Chemicals in Maternal-Newborn Pairs from San Francisco

Aolin Wang,† Dimitri Panagopoulos Abrahamsson,† Ting Jiang, Miaomiao Wang, Rachel Morello-Frosch, June-Soo Park, Marina Sirota, and Tracey J. Woodruff*

Cite This: Environ. Sci. Technol. 2021, 55, 5037−5049 Read Online

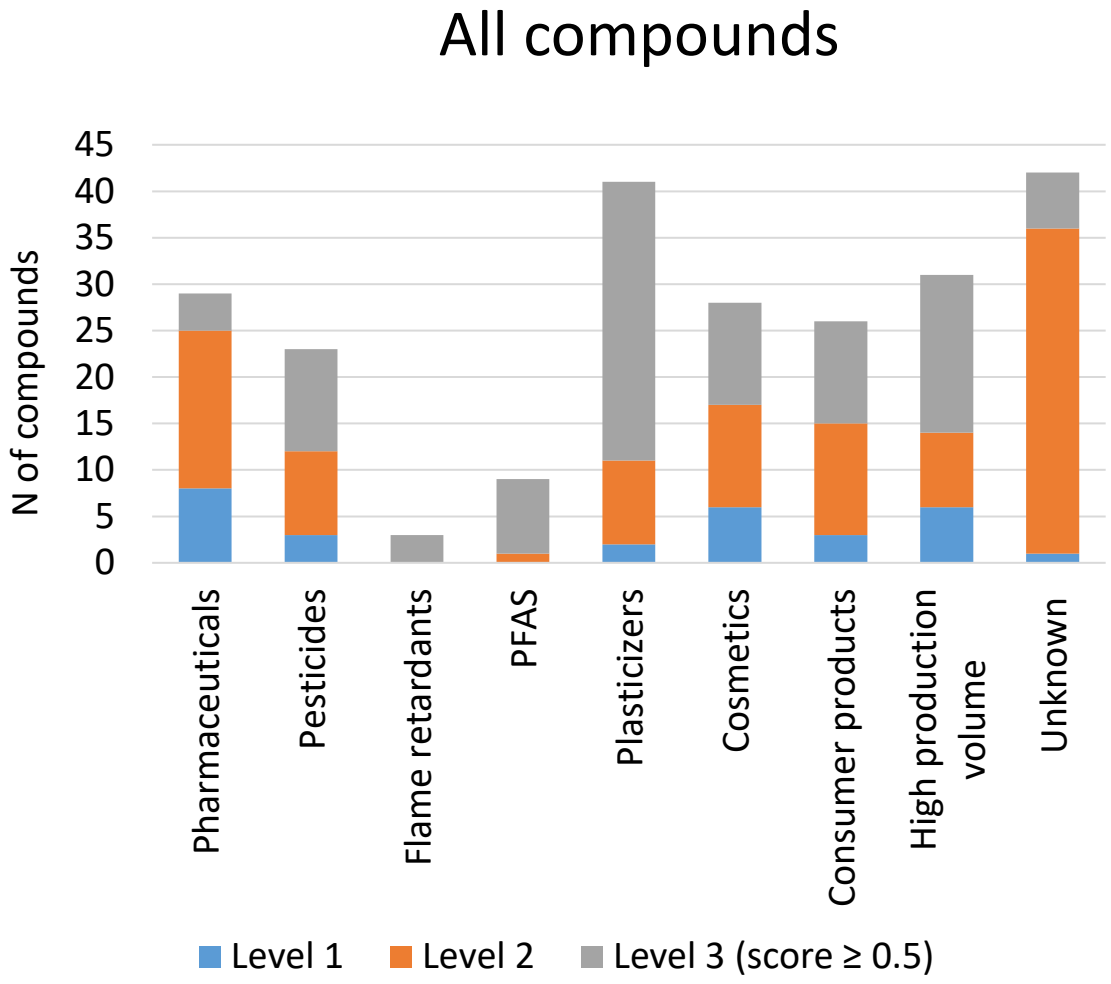

Environmental Science & Technology

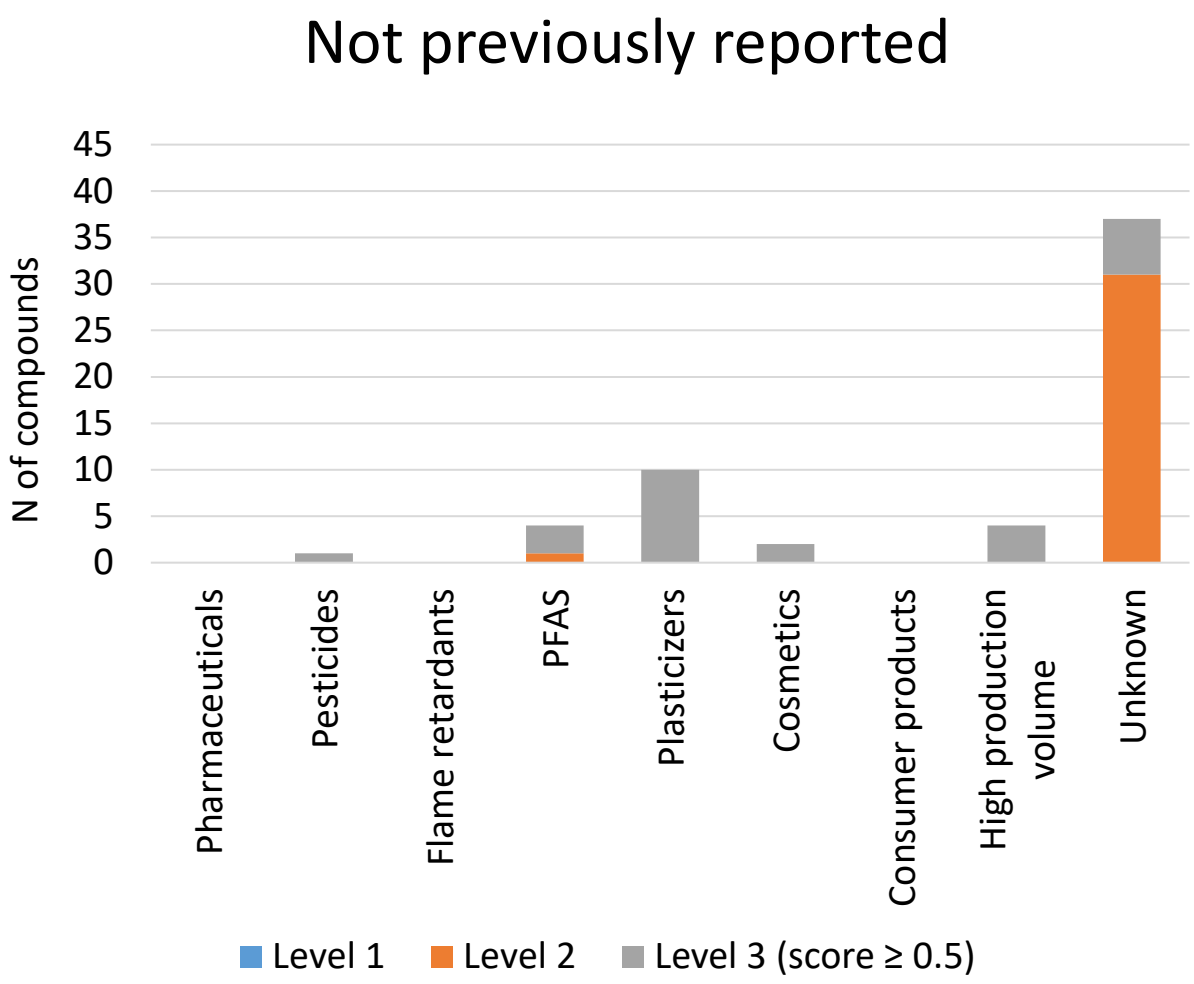
pubs.acs.org/est Article

Comprehensive Non-targeted Analysis Study of the Prenatal Exposome

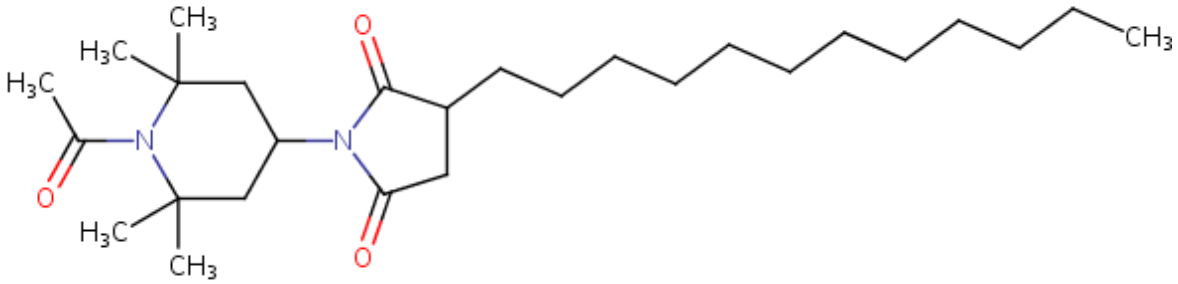
Dimitri Panagopoulos Abrahamsson, Aolin Wang, Ting Jiang, Miaomiao Wang, Adi Siddharth, Rachel Morello-Frosch, June-Soo Park, Marina Sirota,* and Tracey J. Woodruff*

Cite This: https://doi.org/10.1021/acs.est.1c01010 Read Online


All compounds
N of compounds
45
40
35
30
25
20
15
10
5
0
Pharmaceuticals
Pesticides
Flame retardants
PFAS
Plasticizers
Cosmetics
Consumer products
High production volume
Unknown
Level 1
Level 2
Level 3 (score ≥ 0.5)

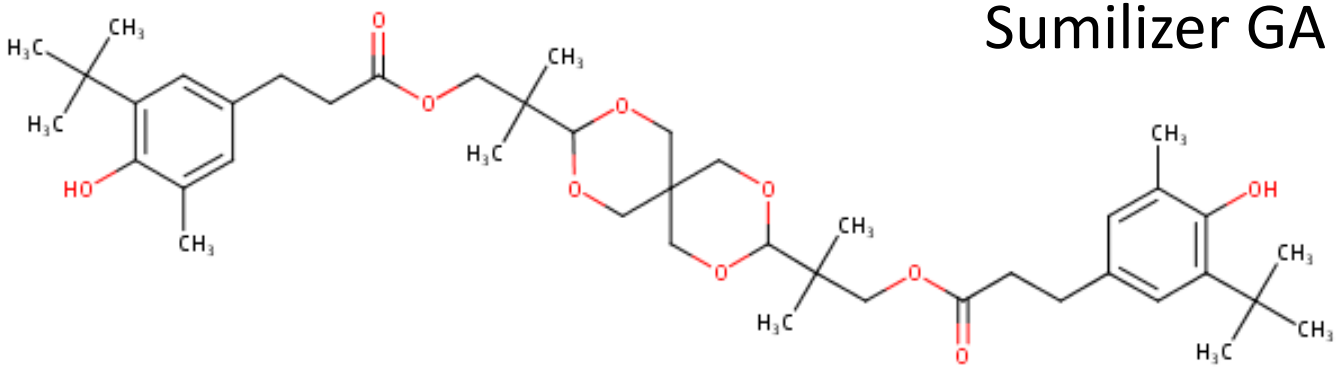

Not previously reported
N of compounds
45
40
35
30
25
20
15
10
5
0
Pharmaceuticals
Pesticides
Flame retardants
PFAS
Plasticizers
Cosmetics
Consumer products
High production volume
Unknown
Level 1
Level 2
Level 3 (score ≥ 0.5)

1-(1-Acetyl-2,2,6,6-tetramethylpiperidin-4-yl)-3-dodecylpyrrolidine-2,5-dione

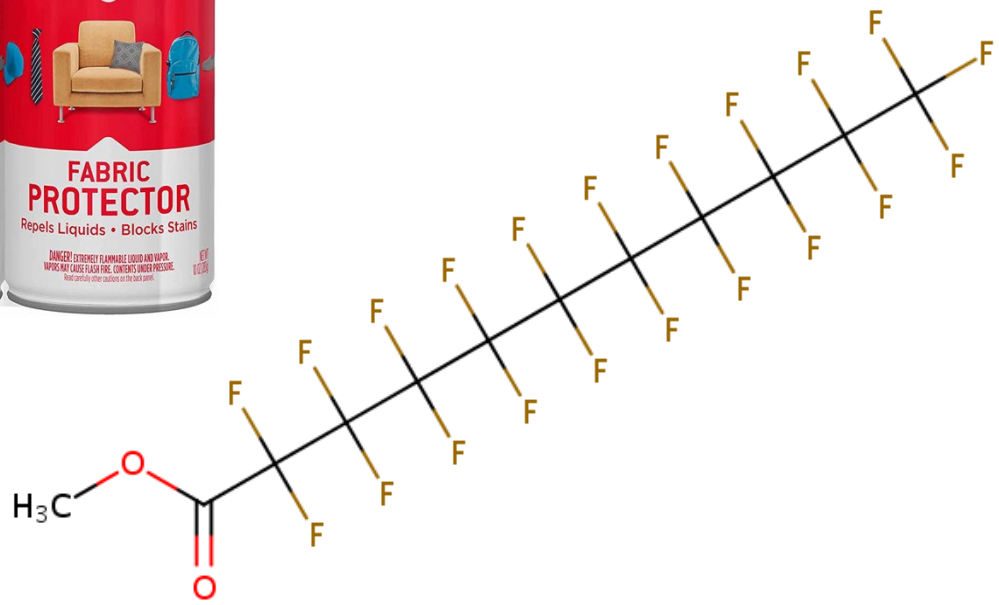


Consumer products, personal care, fragrances

Sumilizer GA 80

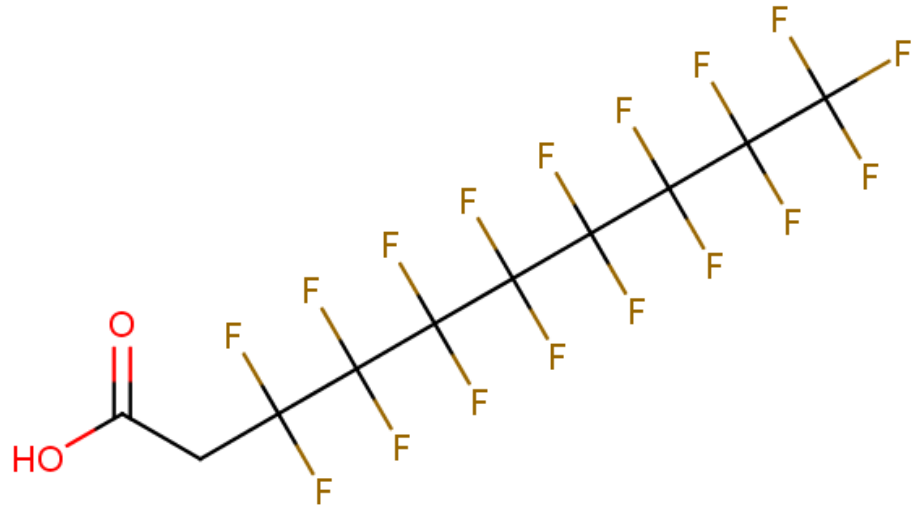


Plasticizer, used in the production of plastic polymers



methyl perfluoroundecanoate

Impurity of PFNA (used in fluoropolymer manufacture) and a break down product of long-chain fluorotelomer-based products

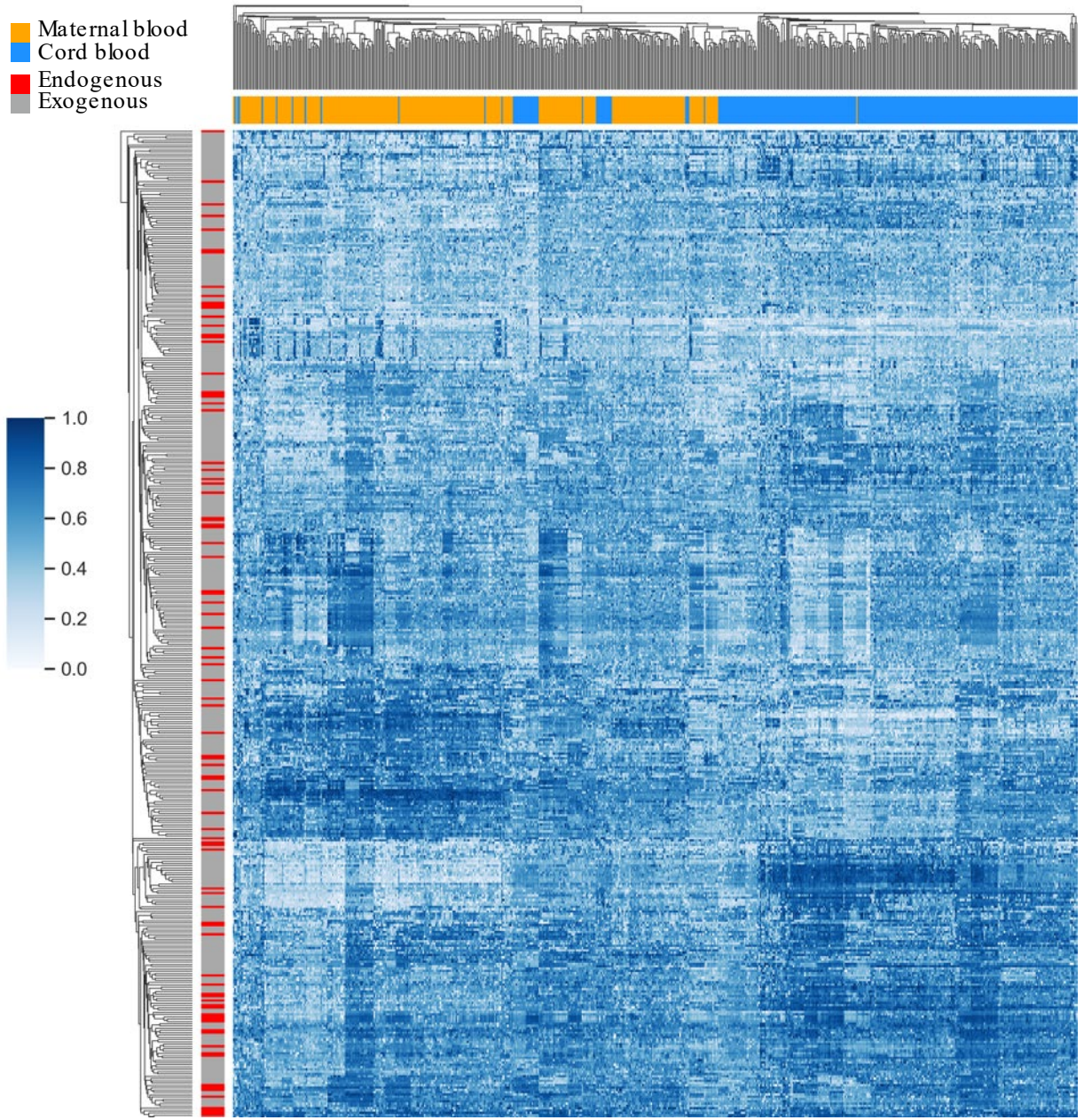


2-perfluorooctyl ethanoic acid

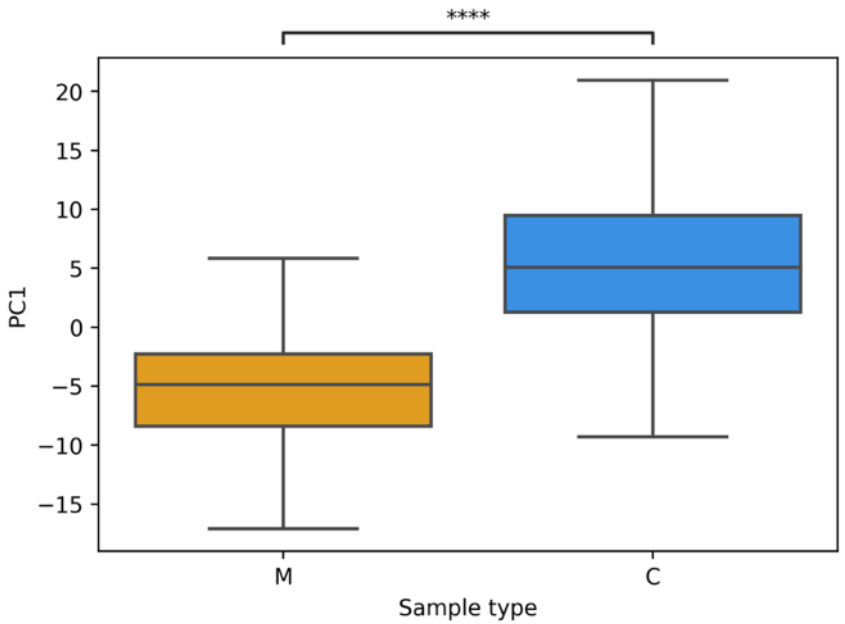
Most probably derived from long-chain fluorotelomer products used as surface protectors in textiles, food contact materials, carpets, etc. (i.e. fluorotelomer-based side-chain fluorinated polymers that were typically acrylates)

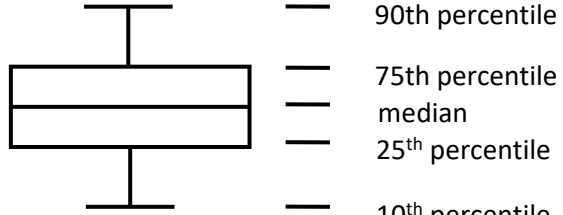
Differentially enriched in M and C

Significant after BH correction FDR 5% n = 450 (total n = 685)



p <= 1.00e-04





Can use nontargeted analysis to link exogenous/endogenous chemicals – biomarkers of disease

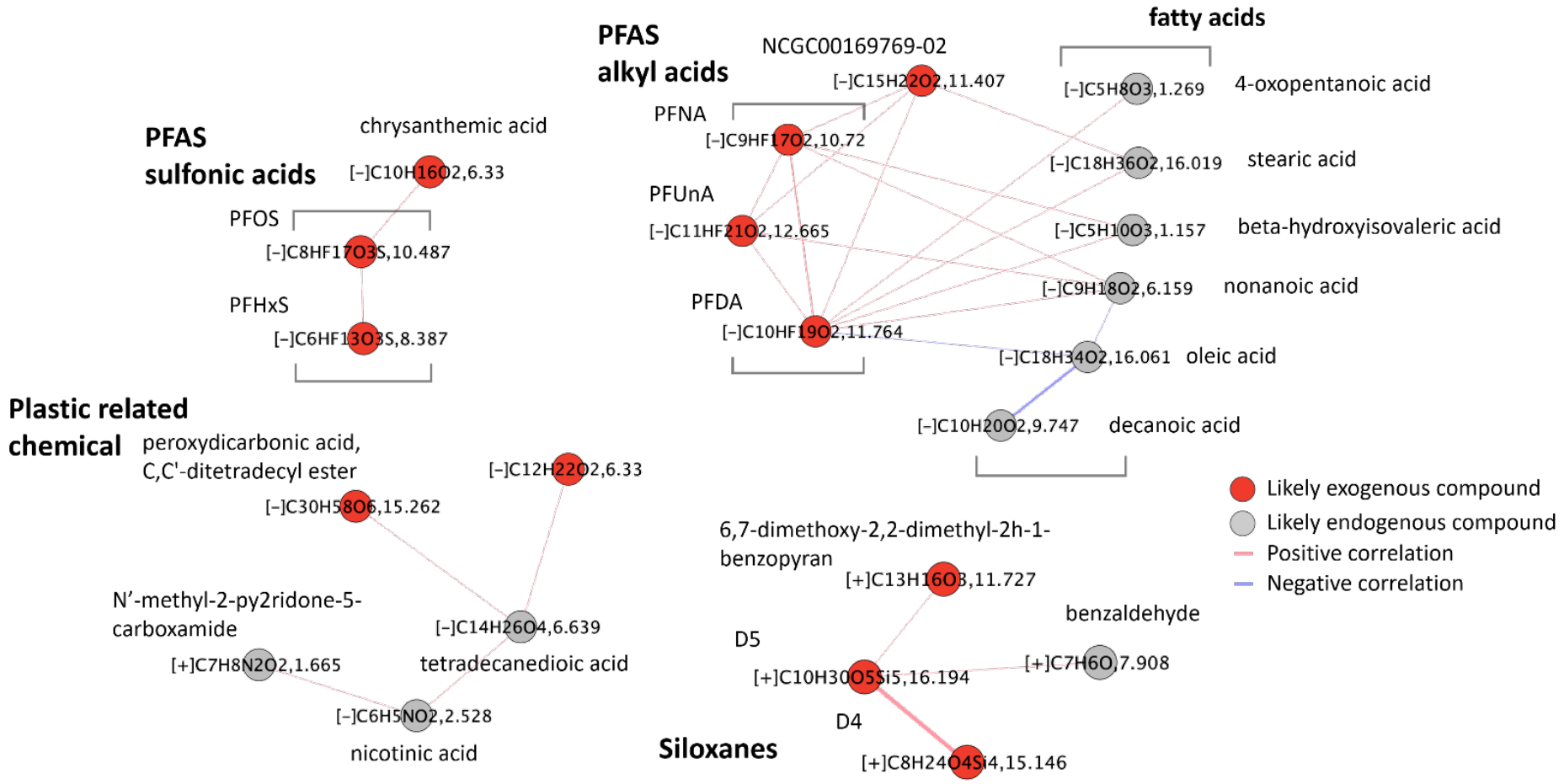
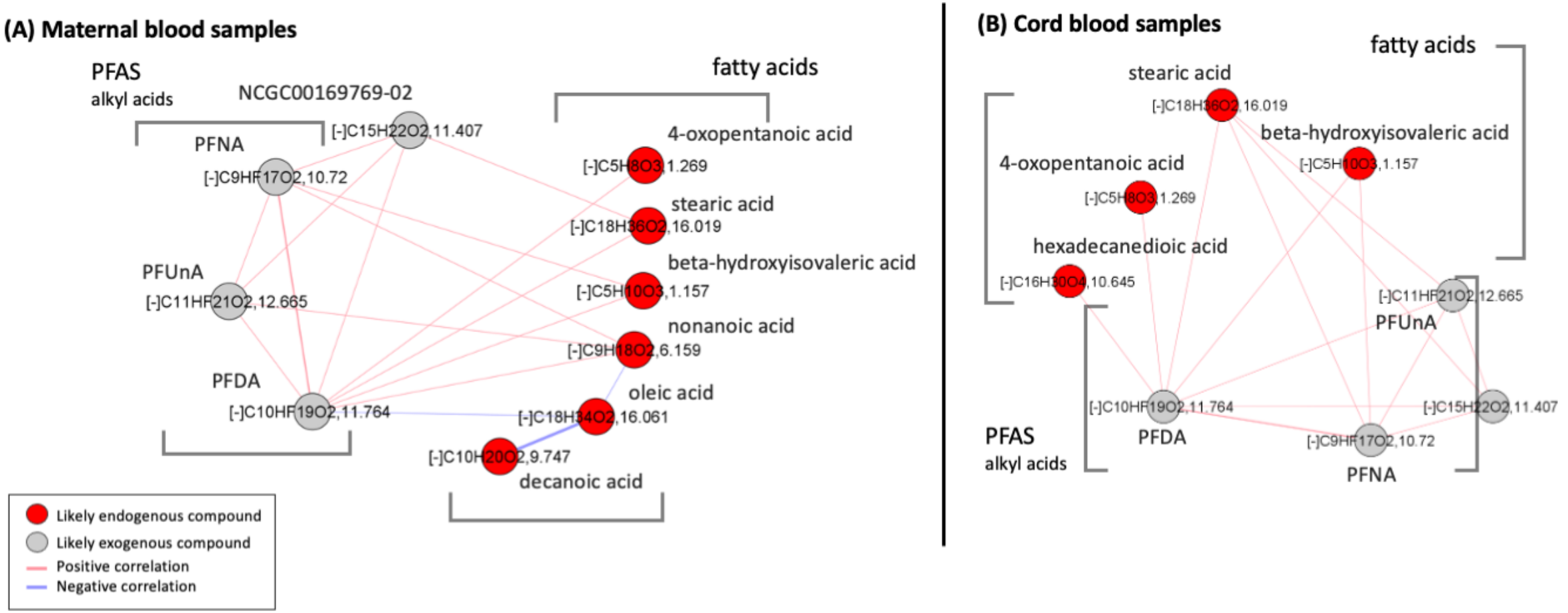


Figure 2. Molecular interaction networks for endogenous (red) and exogenous (gray) chemical features in maternal blood samples (n=295). Network shows features with annotation scores >0.3 or identified with MS/MS or with analytical standards. Lines represent correlations with |r|>0.4 (red lines positive and blue lines negative) and thickness indicates strength of correlation (|r|=0.4–1).

Abrahamsson et al. ES&T 2021

PFAS and lipid metabolism dysregulation



NAS 2022 Report on PFAS concluded sufficient evidence that PFASD causes dyslipidemia (in adults and children)

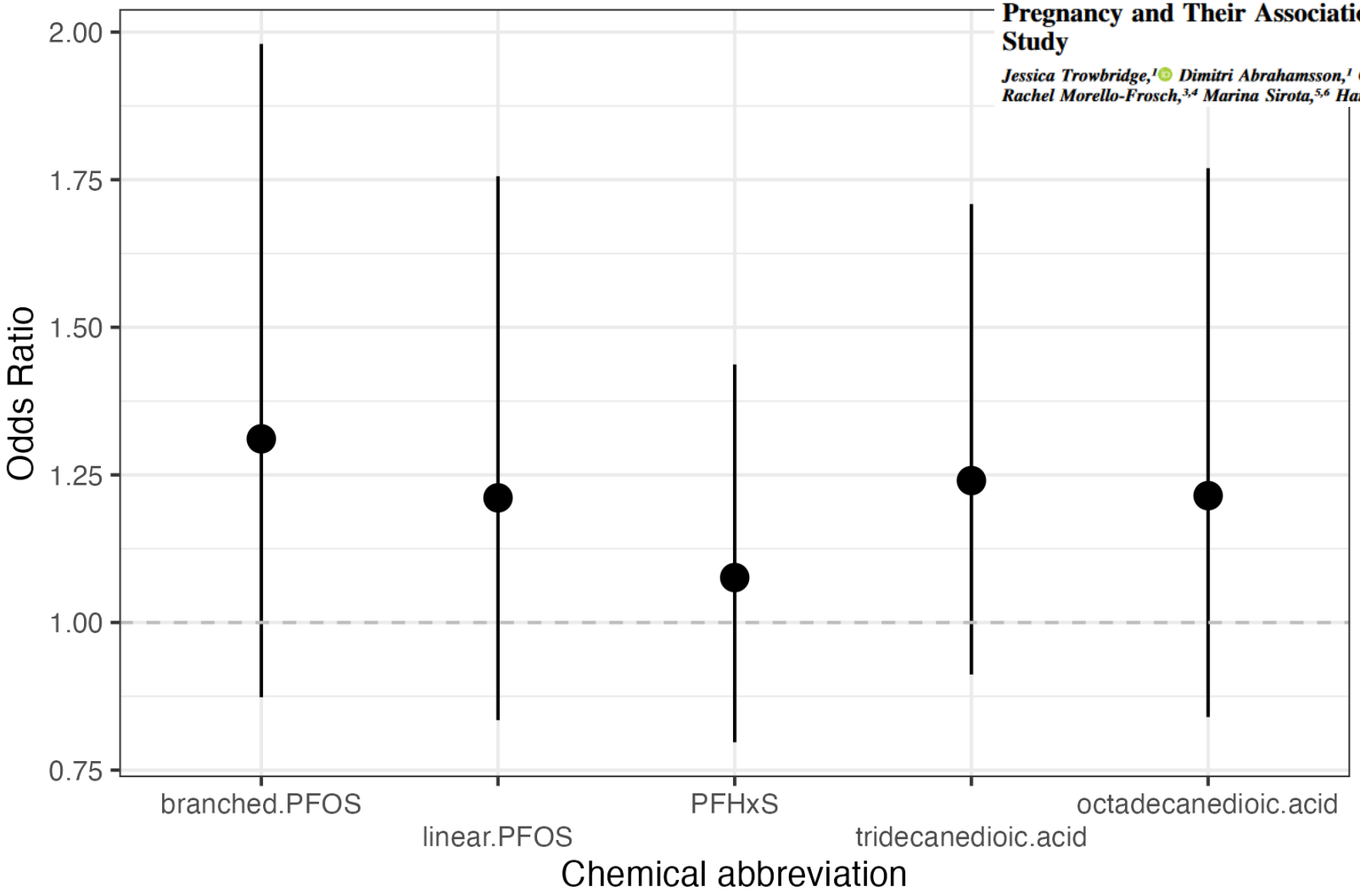
Increasing exposure associated with increased risk of gestational diabetes mellitus (GDM)

Research

A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP11546.

Extending Nontargeted Discovery of Environmental Chemical Exposures during Pregnancy and Their Association with Pregnancy Complications—A Cross-Sectional Study

Jessica Trowbridge,[1] Dimitri Abrahamsson,[1] Garret D. Bland,[1] Ting Jiang,[2] Miaomiao Wang,[2] June-Soo Park,[1,2] Rachel Morello-Frosch,[3,4] Marina Sirota,[5,6] Harim Lee,[1] Dana E. Goin,[1] Marya G. Zlatnik,[1] and Tracey J. Woodruff[1]

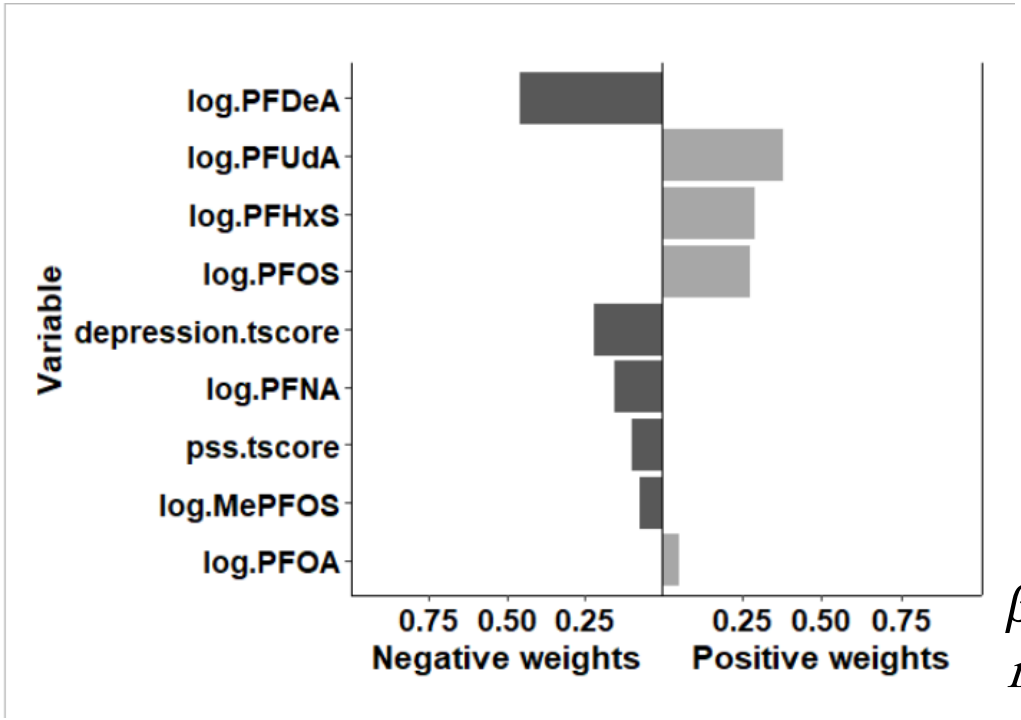


OR (95%CI) of an IQR increase in exposure

Goal: Research to inform systemic solutions to reduce harmful exposures and improve health and health equity

- Prioritize chemical exposures
  - Multiple chemicals
  - Susceptible period of development
  - Demographic differences
- Identify overlap with social stressors
- Evaluate key health effects
  - Evaluate upstream indicators of harm for earlier intervention

Joint effect of PFAS and stress on fetal growth is greater than effect of individual mixture groups



	β	(95% CI)
PFAS & Psychosocial Stress	-0.09	(-0.21, 0.03)
PFAS Alone	-0.03	(-0.13, 0.07)
Psychosocial Stress Alone	-0.06	(-0.13, 0.01)

(Perceived Stress, Depression)

β is interpreted as the effect on birthweight z-scores of increasing every exposure in the mixture by one quantile.

Models are adjusted for maternal education, age, race/ethnicity, pre-pregnancy BMI, parity, and cohort.

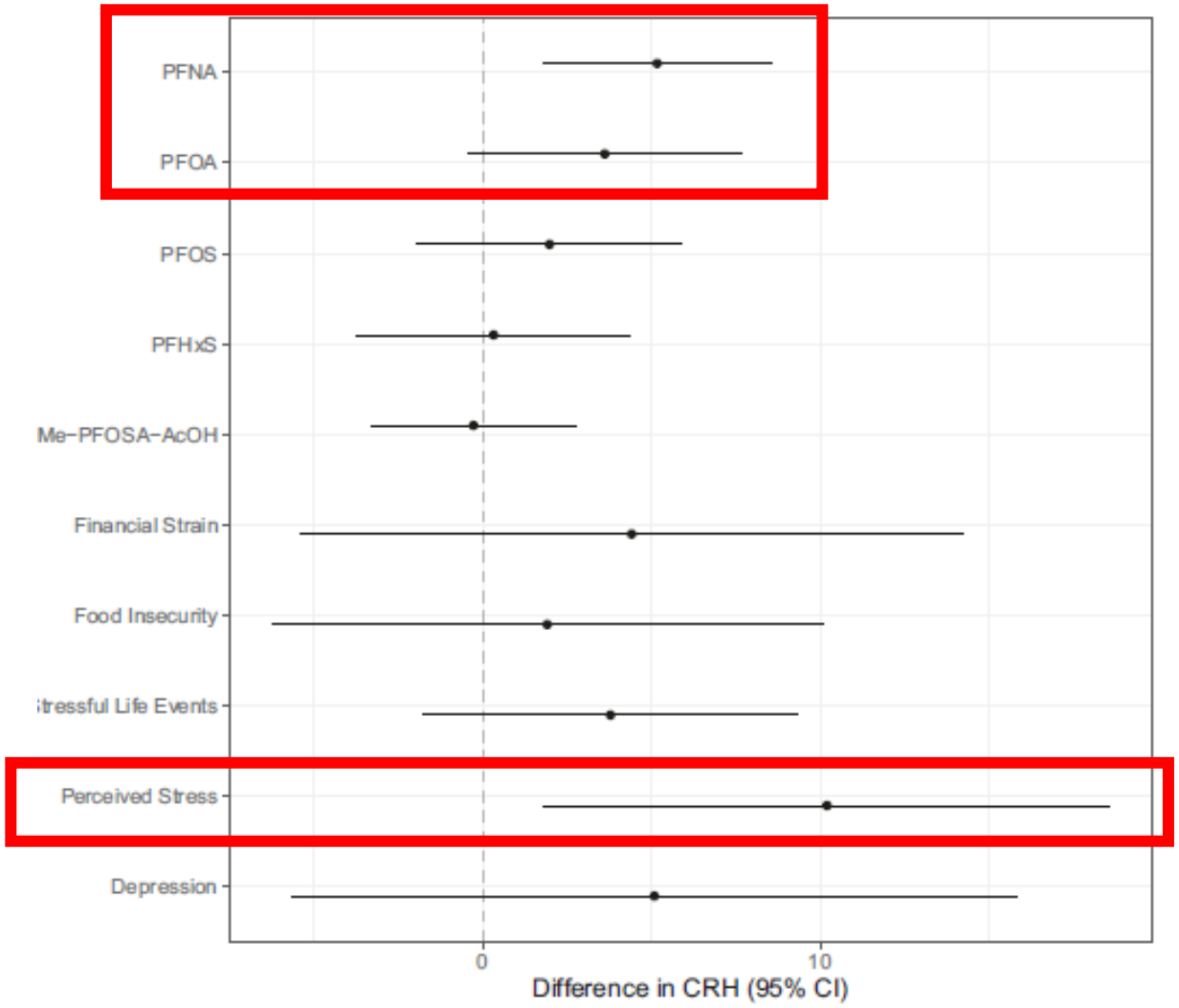
Eick et al, 2022, In Revision

Corticotropin releasing hormone or CRH as a mediating pathway?

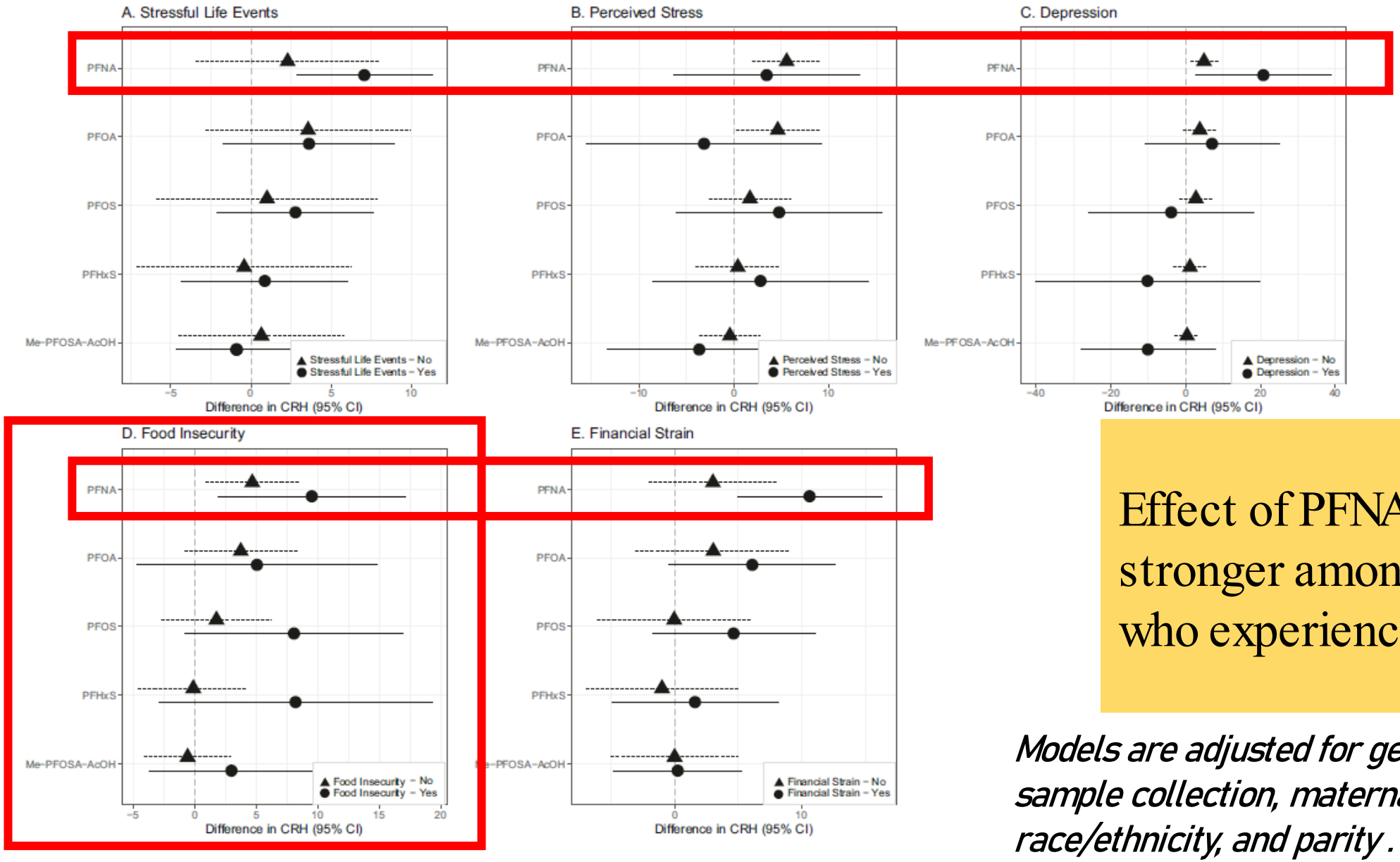
- Stress activates HPAaxis, increasing cortisol production and CRH
- Excess CRH → preterm birth
- CRHalso elevated in response to other classes of environmental chemicals

Models are adjusted for gestational age at sample collection, maternal age, race/ethnicity, and parity .

Eick et al, 2021, *JESEE*



Eick et al, 2021, *JESEE*



Effect of PFNAon CRH stronger among those who experienced stress

Models are adjusted for gestational age at sample collection, maternal age, race/ethnicity, and parity .

Improving efficiency of identifying toxic chemicals

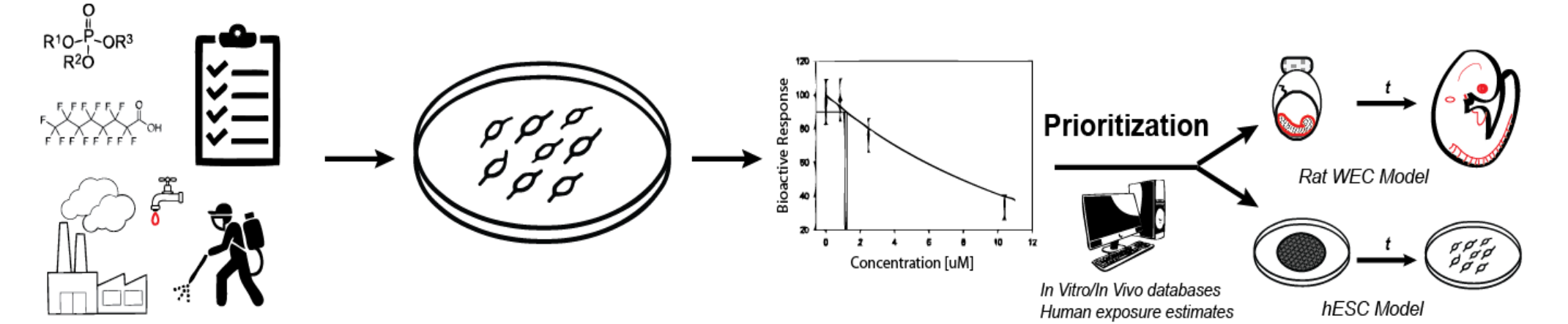
CATCHA
Center to Advance Toxicology and Chemical Hazard Assessment

Accelerating chemical hazard assessment for a safer tomorrow

- More rapidly generate data so decision-makers can act more quickly to prevent harmful chemical exposure and disease.

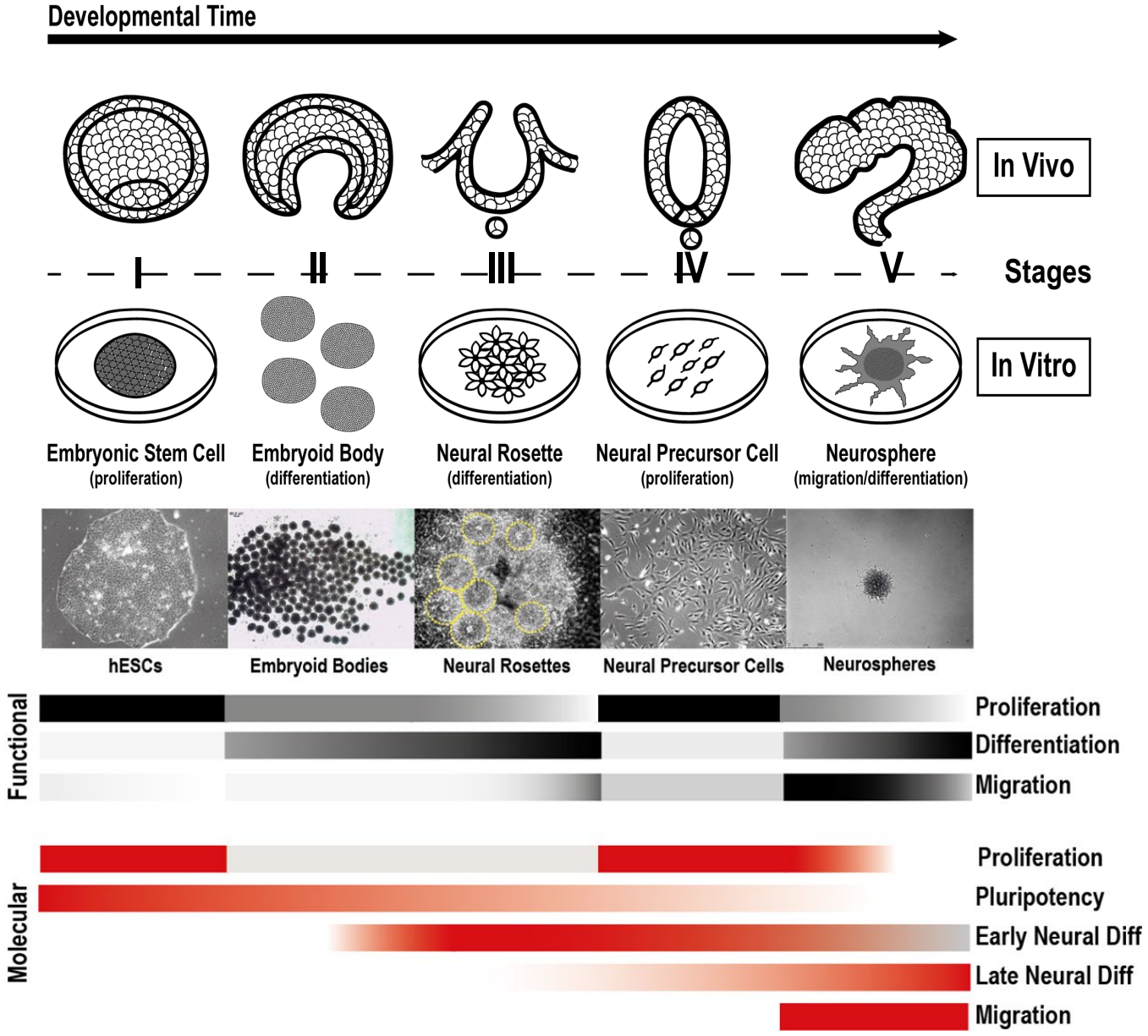
Dr. Joshua Robinson, UCS

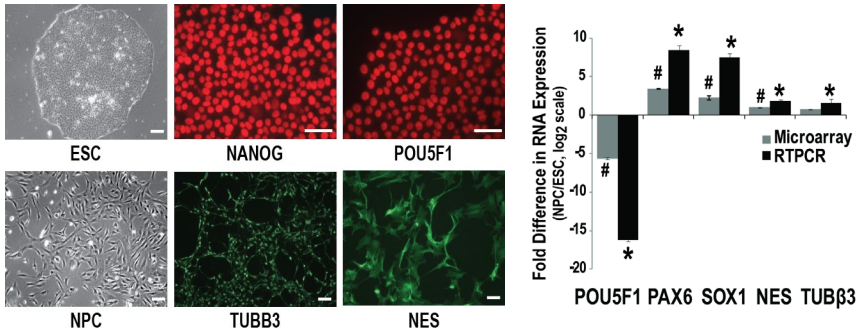
Multi-Level Strategy to Identify Harmful Chemicals
Example - Human Developmental Neurotoxicants



Chemical Testing Panel | Initial screen for DNT | Evalute Potency | Mechanistic investigations

A hESC Model to Assess for Developmental Neurotoxicity





Expression of pluripotent and neural markers

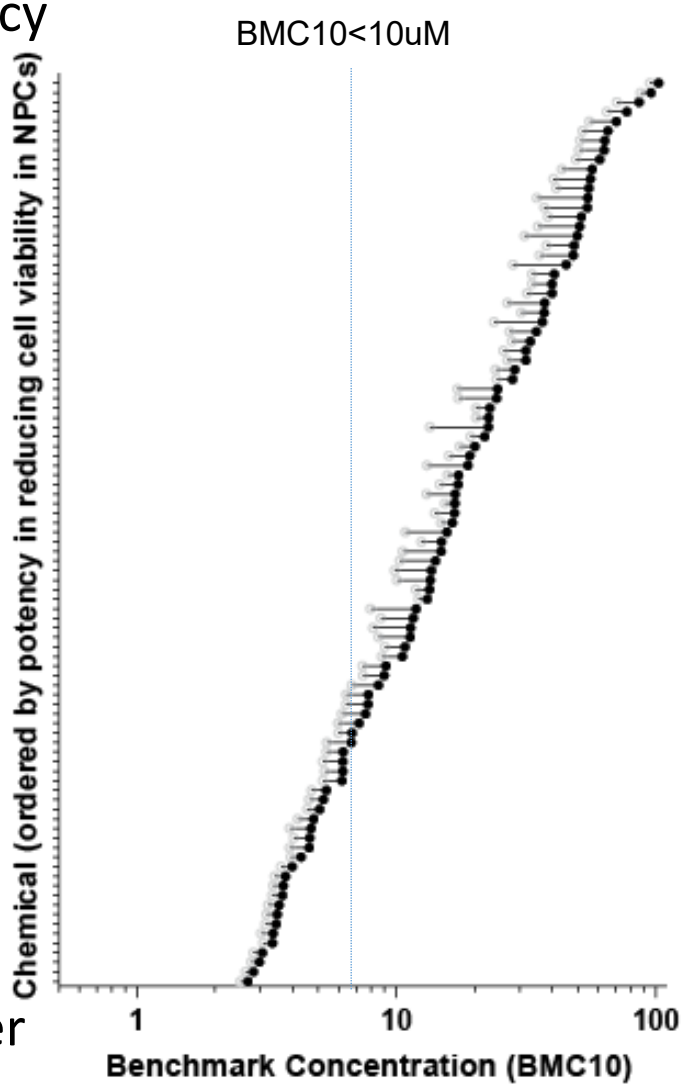
- Across five stages, pluripotent hESCs are differentiated towards a neuronal phenotype.
- Relevant cellular, molecular, and functional aspects of early neurodevelopment can be assessed in the context of chemical exposure.

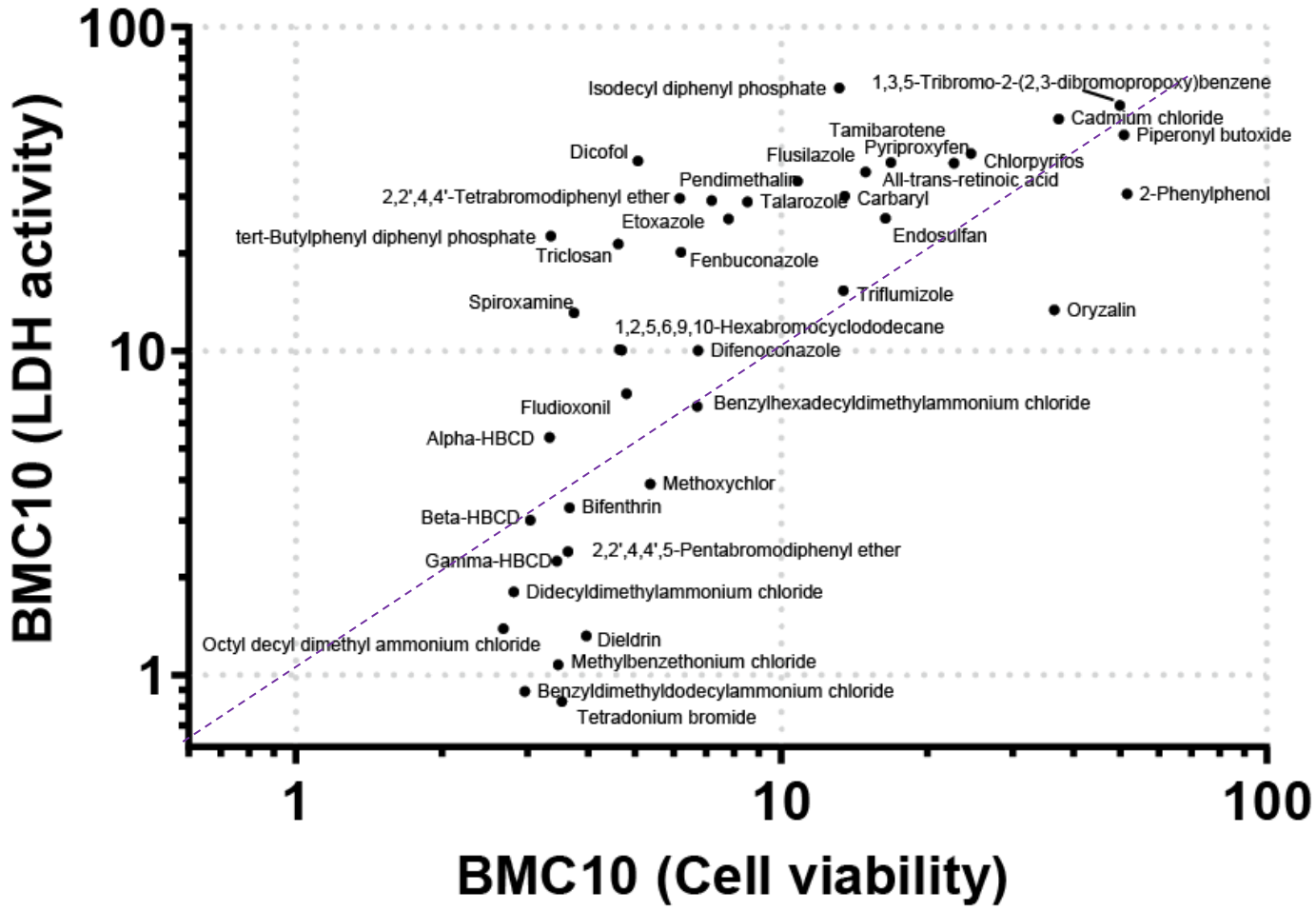
Chen *et al*., 2019; *Toxicological*

Screening Chemicals for Toxic Effects on NPC Viability and Death
Benchmark Concentrations of evaluated Chemicals by potency

Lower potency

Higher potency





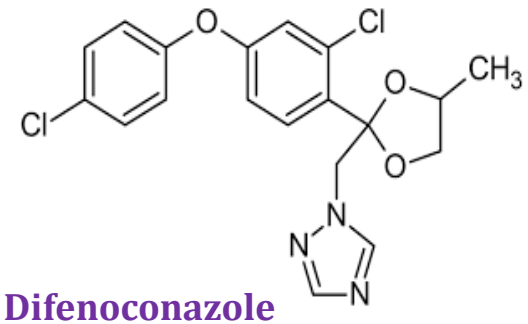
Credit – Josh Robinson

Compounds of concern: High Potencies, Human Exposure, Limited Information

Benzyldimethyldodecyl ammonium

- Common **Quaternary Ammonium Compound** (QAC) used as biocide

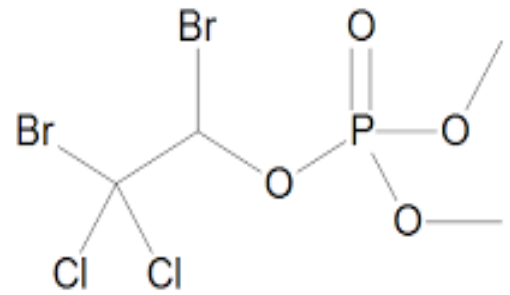
- Found in US women breast milk at 0.4 ng/mL (Zheng at al 2022)
- Impairs axonal projections (Sreevidya at al 2018)
- Alters oligodendrocyte development (Cohn et al 2023)
- Disrupts mitochondrial function (Osimitz & W. Droege 2022) and IL10 levels (Hrubec at al 2021)



Difenoconazole

- **Triazole** fungicide commonly applied in agriculture

- Detected in water, agricultural areas (Zhu at al., 2023)
- Alter cholesterol metabolism and retinoic acid signaling pathways (Mu et al., 2016); induce **apoptosis** and oxidative stress (Wang at al 2021)



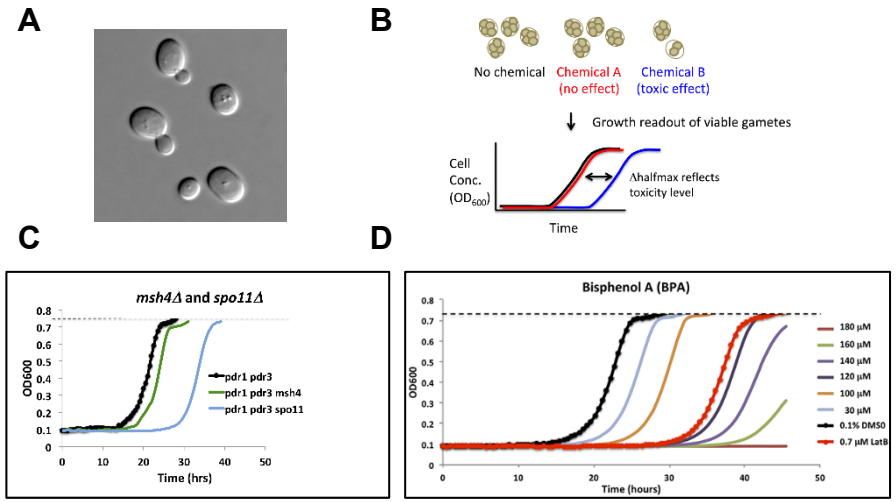
Naled (Dibrom)

- **Organophosphate** insecticide used in agriculture and mosquito control

- Detected in humans (umbilical cord blood;Silver at al., 2017)
- Acetylcholine esterase inhibitor; affect cholinergic synapse activity and disrupt Ca+ homeostasis (van Melis at al. 2023)

CATCHA and Screening for repro/developmental toxicants

Yeast screening assay for meiosis



Dr. Jennifer Fung, UCSF

C. Elegans Assay for repro/developmental tox

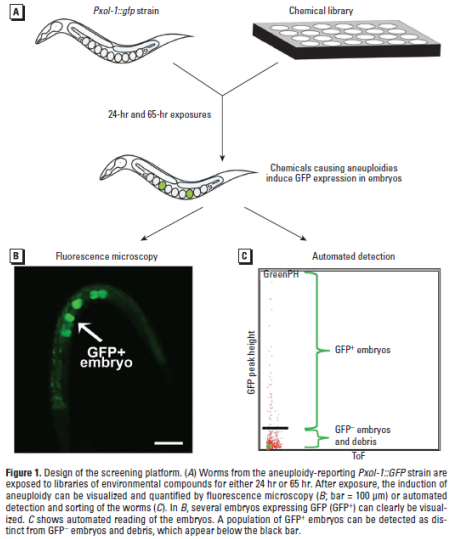
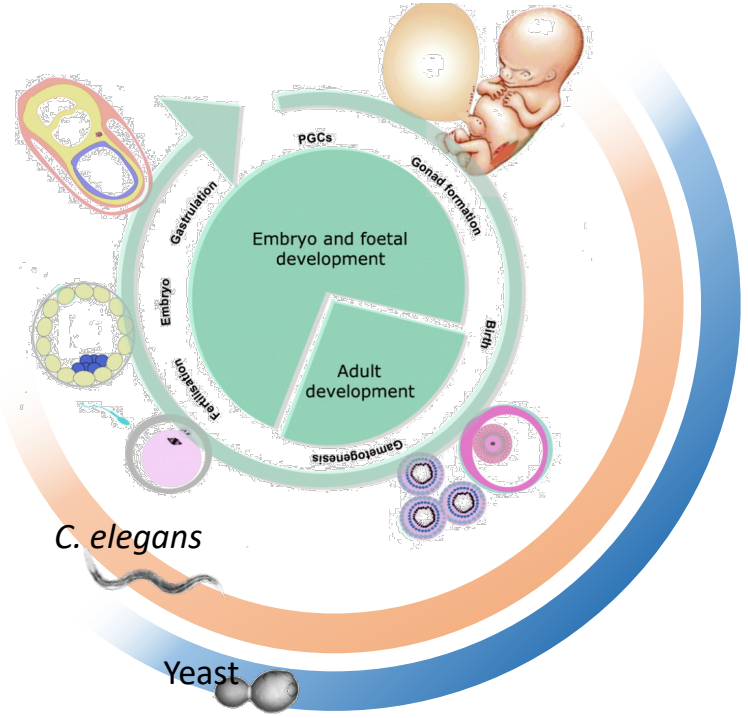
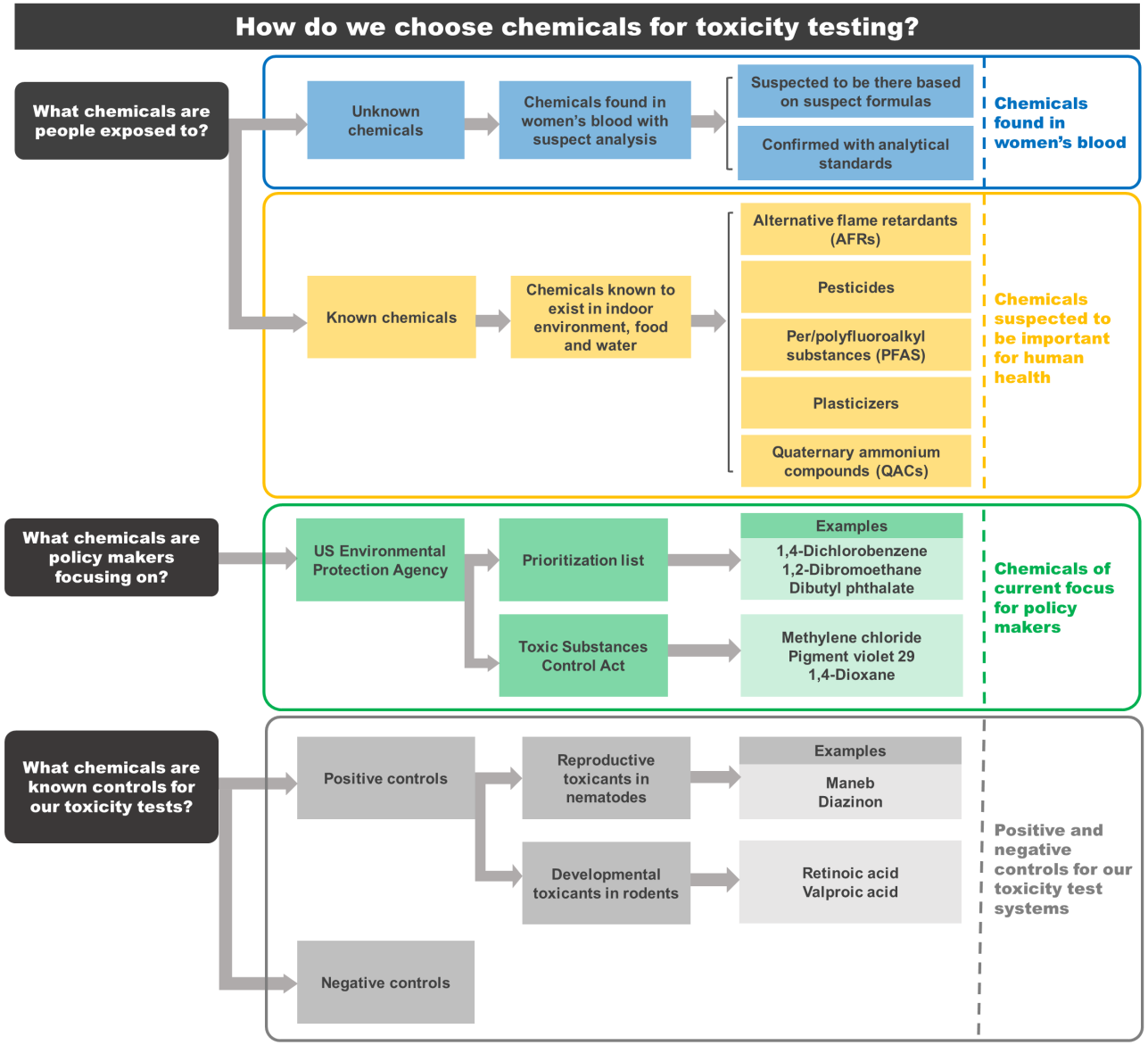


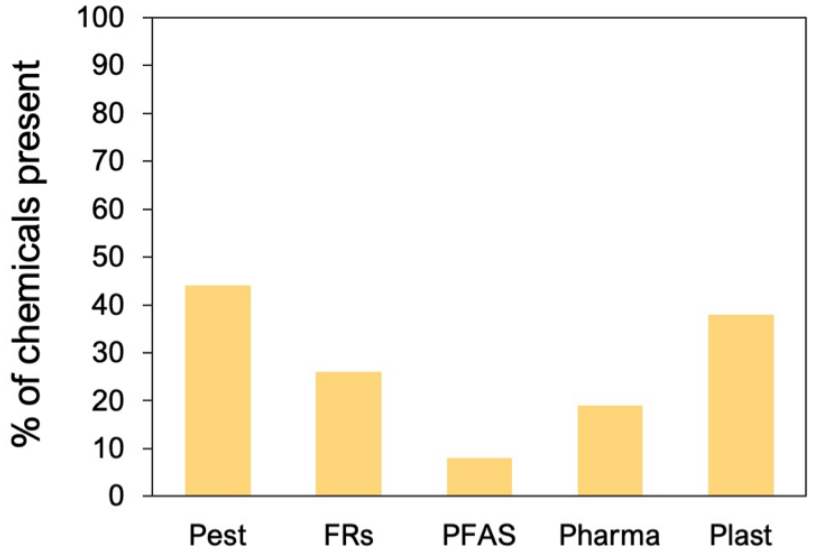
Figure 1. Design of the screening platform. (*A*) Worms from the aneuploidy-reporting *Pxol-1::GFP* strain are exposed to libraries of environmental compounds for either 24 hr or 65 hr. After exposure, the induction of aneuploidy can be visualized and quantified by fluorescence microscopy (*B*; bar = 100 µm) or automated detection and sorting of the worms (*C*). In *B*, several embryos expressing GFP (GFP$^+$) can clearly be visualized. *C* shows automated reading of the embryos. A population of GFP$^+$ embryos can be detected as distinct from GFP$^-$ embryos and debris, which appear below the black bar.

Dr. Patrick Allard, UCLA



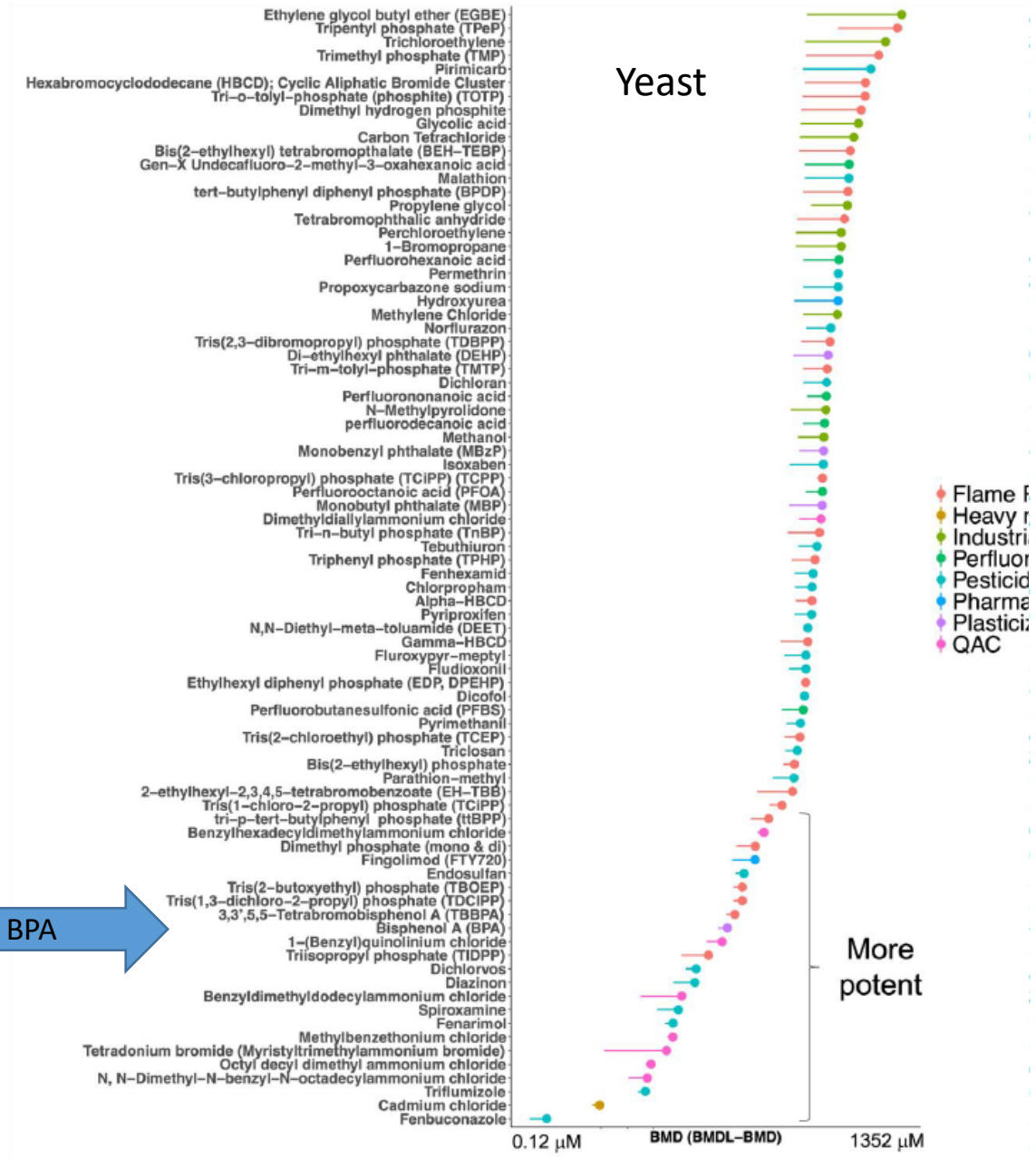
Using in vitro assays to screen chemicals for reproductive health effects





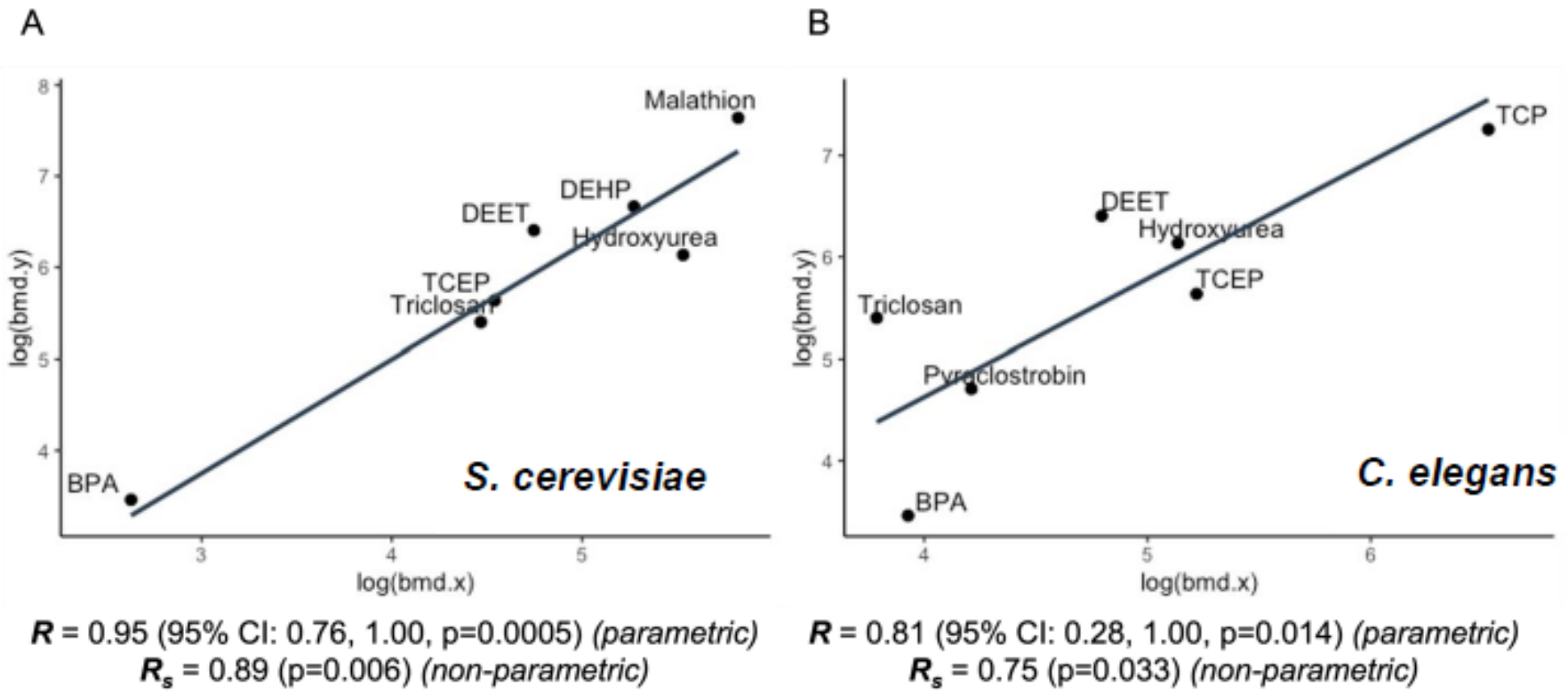
Abrahamsson et al. https://zenodo.org/record/5760170

Ranking potency (BMD10) from Yeast and c elegans Assay



Kumar et al and Ulaganathan et al 2024 Repro Tox

Potency is similar between reproductive effects in rodents and yeast/C. elegans assay.

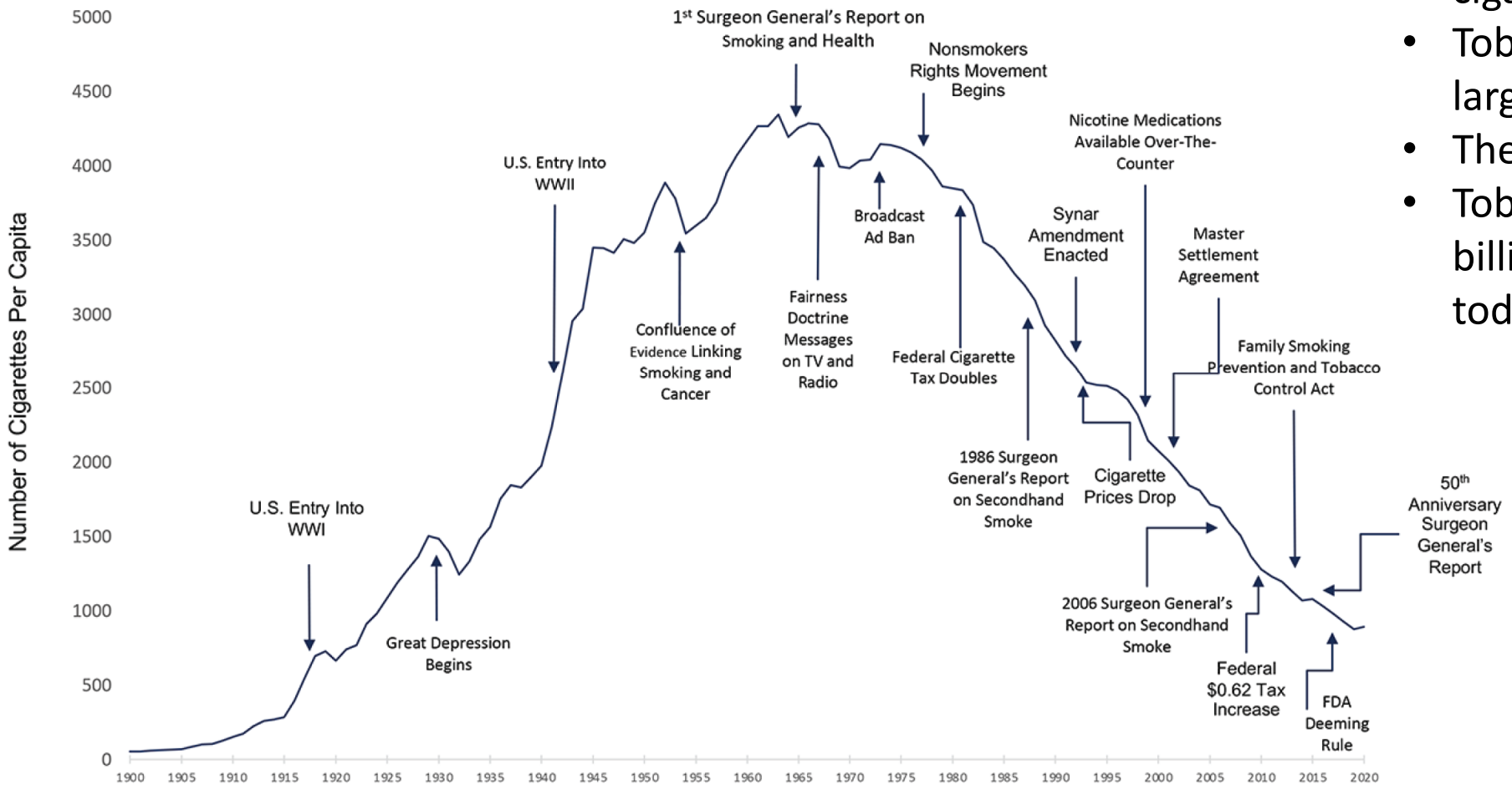


R = 0.95 (95% CI: 0.76, 1.00, p=0.0005) *(parametric)*
R_s = 0.89 (p=0.006) *(non-parametric)*

R = 0.81 (95% CI: 0.28, 1.00, p=0.014) *(parametric)*
R_s = 0.75 (p=0.033) *(non-parametric)*


Research
Clinical
Policy
Population Health

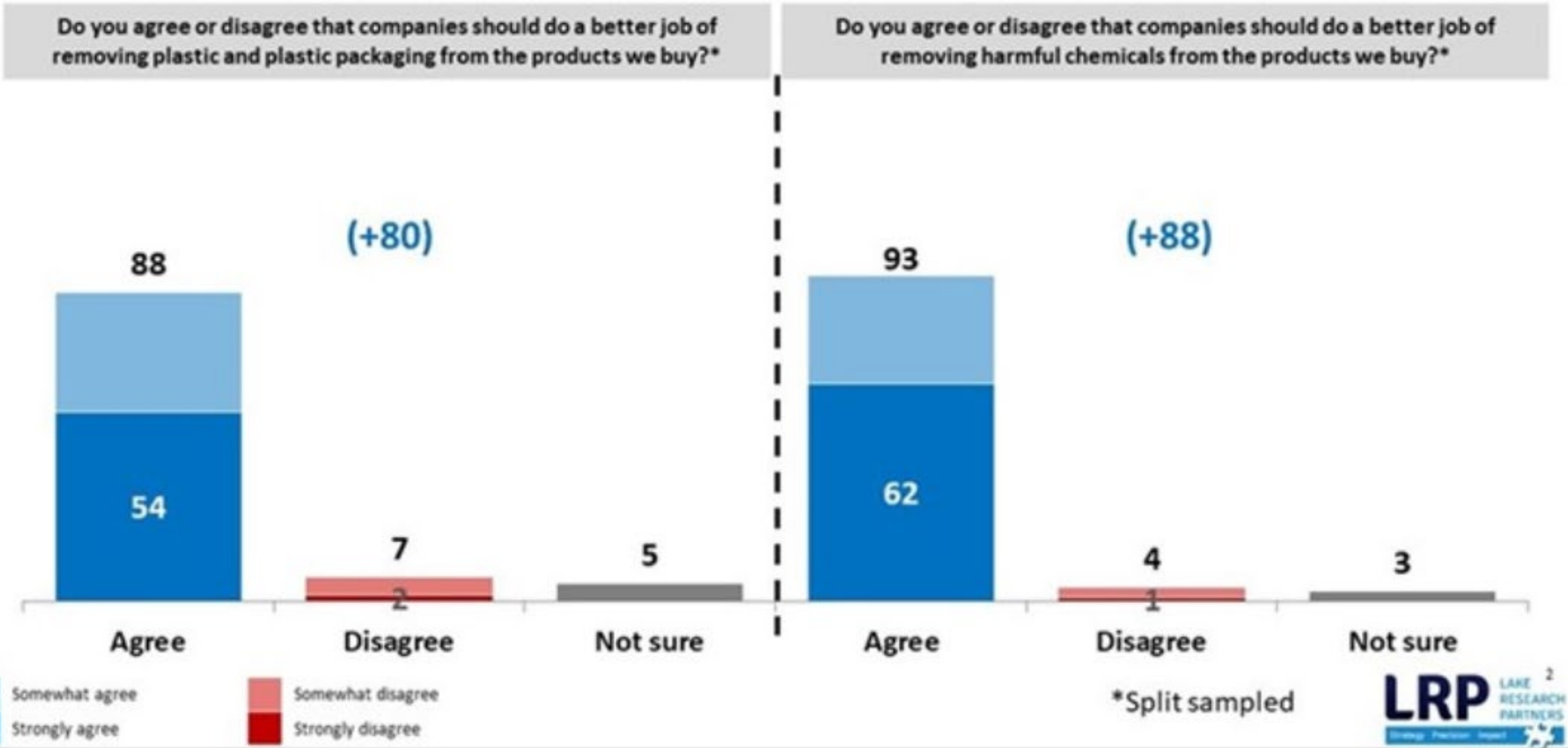
How science and action addressed smoking



- Adult per capita cigarette consumption peaked at 4,345 cigarettes
- Tobacco products were the third largest source of federal revenue
- The fifth leading US cash crop.
- Tobacco sales in 1962 totaled $8 billion (more than $80 billion in today's dollars)

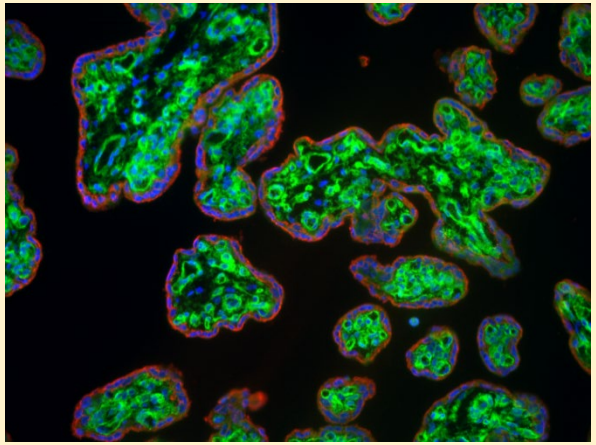
Clearing the Air, 1964 Surgeon General report https://escholarship.org/uc/item/1f84x7hv

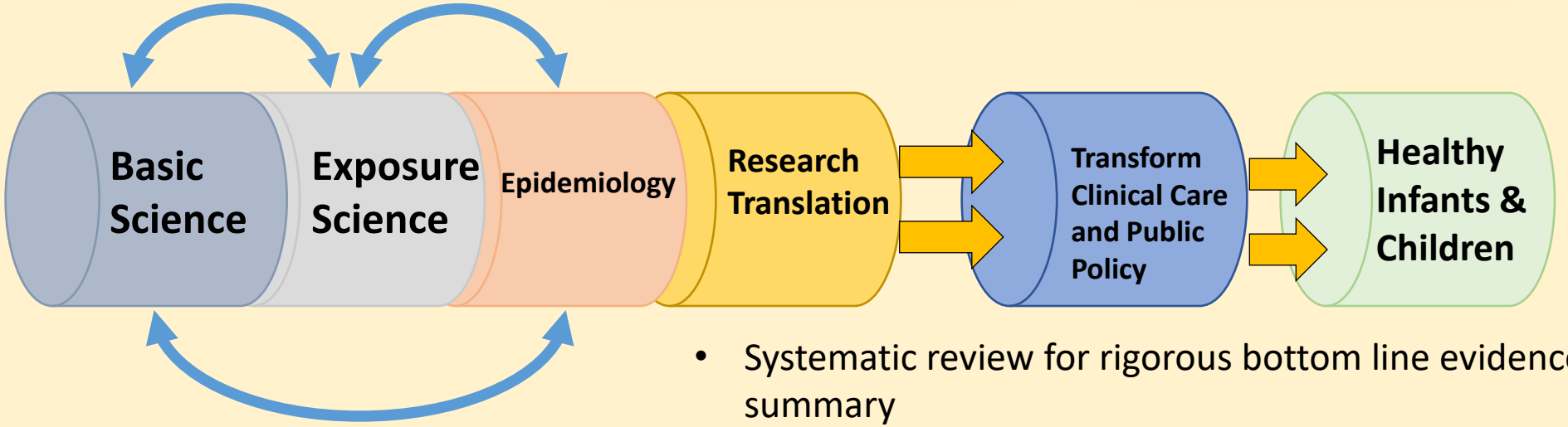
Voters agree that companies should do a better job safeguarding the products we buy, and with even more intensity in terms of harmful chemicals.



Policy Matters.

From Science to Action - Our Model



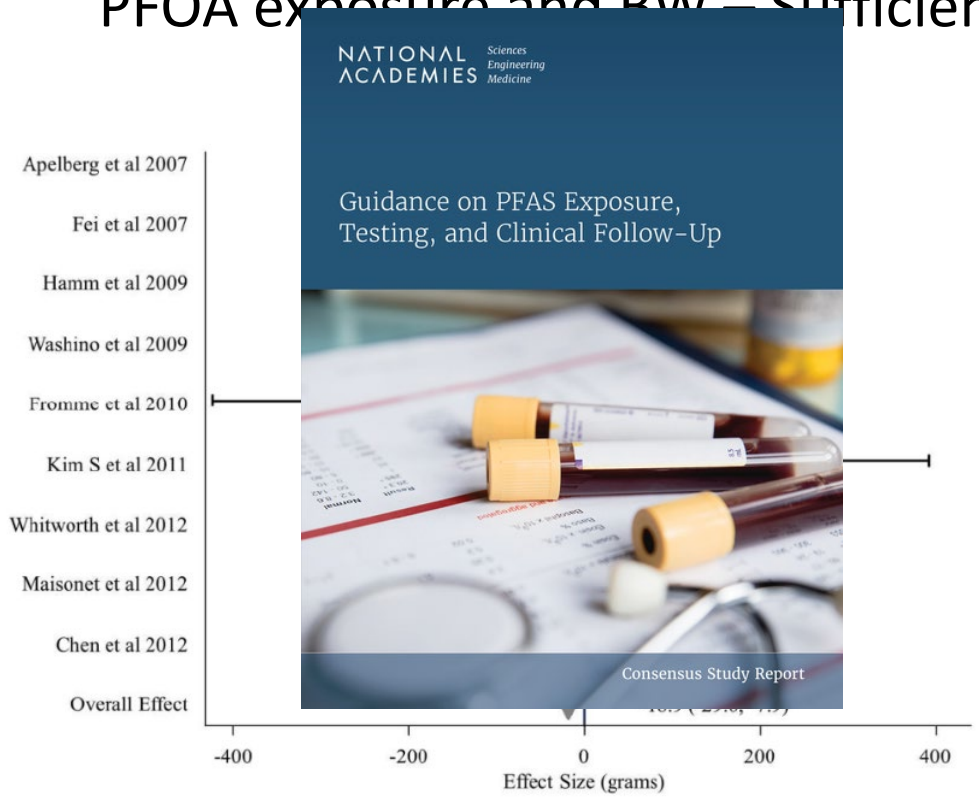


- Systematic review for rigorous bottom line evidence summary
- Improve hazard and risk assessment
- Engage clinical and public health partners

Systematic Review - UCSF Navigation Guide Epidemiology

A systematic and transparent method to evaluate the quality of evidence and to support evidence-based decision making, bridging the gap between clinical and environmental health

Systematic review and meta-analysis prena
PFOA exposure and BW – Sufficient

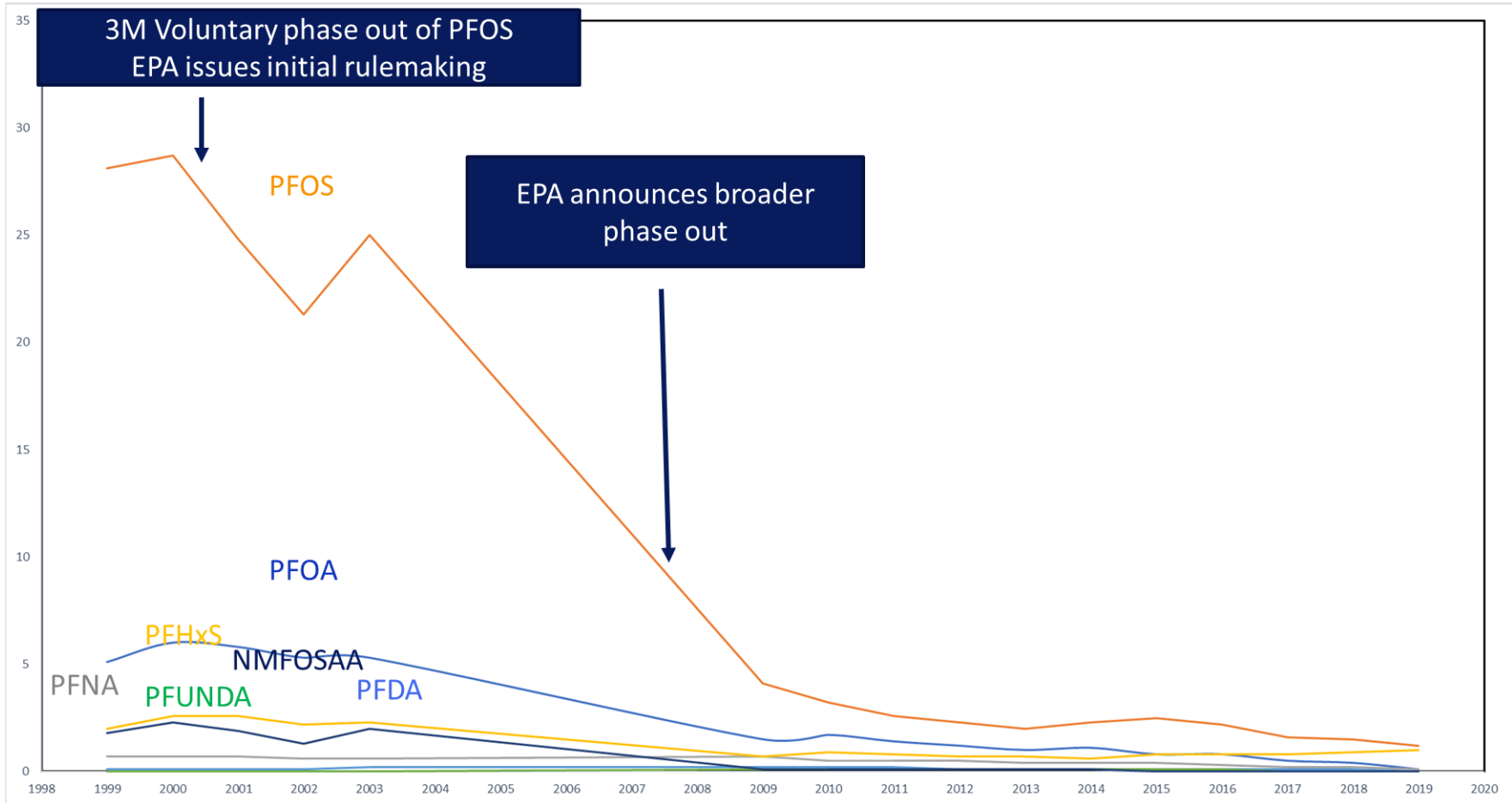


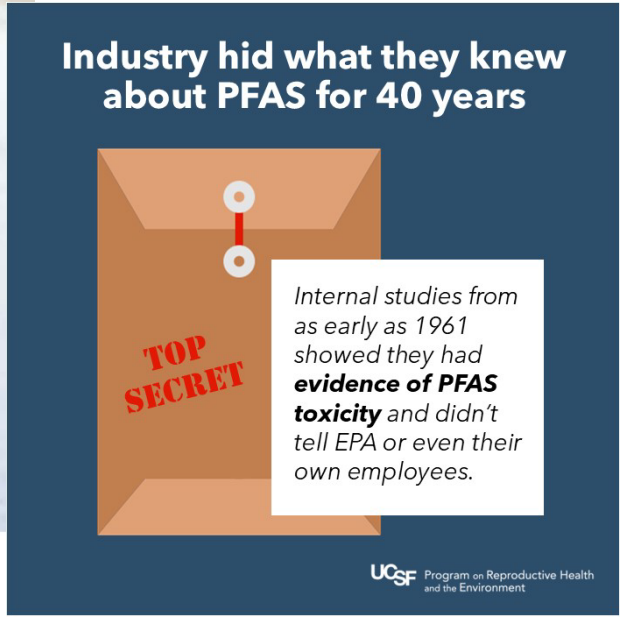
LBW

CATEGORY OF ASSOCIATION	HEALTH OUTCOMES WITH INCREASED RISK ASSOCIATE WITH PFAS EXPOSURE
Sufficient evidence of an association Based on strong evidence, there is high confidence that there is an association between exposure to PFAS and the health outcome. It is unlikely that the association is due to chance or bias.	• Decreased antibody response (in adults and children) • Dyslipidemia (in adults and children) • Decreased infant and fetal growth • Increased risk of kidney cancer (in adults)
Limited suggestive evidence of an association Based on limited evidence, there is moderate confidence that there is an association between exposure to PFAS and the health outcome. It is possible that the association is due to chance or bias.	• Increased risk of breast cancer (in adults) • Liver enzyme alterations (in adults and children) • Increased risk of pregnancy-induced hypertension (gestational hypertension and preeclampsia) • Increased risk of testicular cancer (in adults) • Thyroid disease and dysfunction (in adults) • Increased risk of ulcerative colitis (in adults)
Inadequate or Insufficient Evidence to Determine an Association Based on inconsistent evidence, a lack of evidence, or evidence of insufficient quality, there is moderate confidence that there is an association between exposure to PFAS and the health outcome. No conclusion can be made about a potential association.	• Immune effects other than reduced antibody response, and ulcerative colitis; Cardiovascular outcomes other than dyslipidemia; • Developmental outcomes other than small reductions in birthweight • Cancers other than kidney, breast, and testicular; Reproductive effects other than hypertensive disorders of pregnancy; Endocrine disorders other than thyroid hormone levels; Hepatic effects other than liver enzyme levels; Respiratory effects; Hematological effects • Musculoskeletal effects, such as effects on bone mineral density; Renal effects, such as renal disease; Neurological effects
Limited Suggestive Evidence of No Association Based on at least limited evidence, there is at least moderate confidence that there is NO association between PFAS and the health outcome.	• No outcomes were identified.

GUIDE

We can document prenatal PFAS exposures over time and influence of policies





Research · May 31, 2023

Makers of PFAS 'Forever Chemicals' Covered up the Dangers

Widely used in clothing, household products and food, they resist breaking down in the environment

By Susan Lamontagne

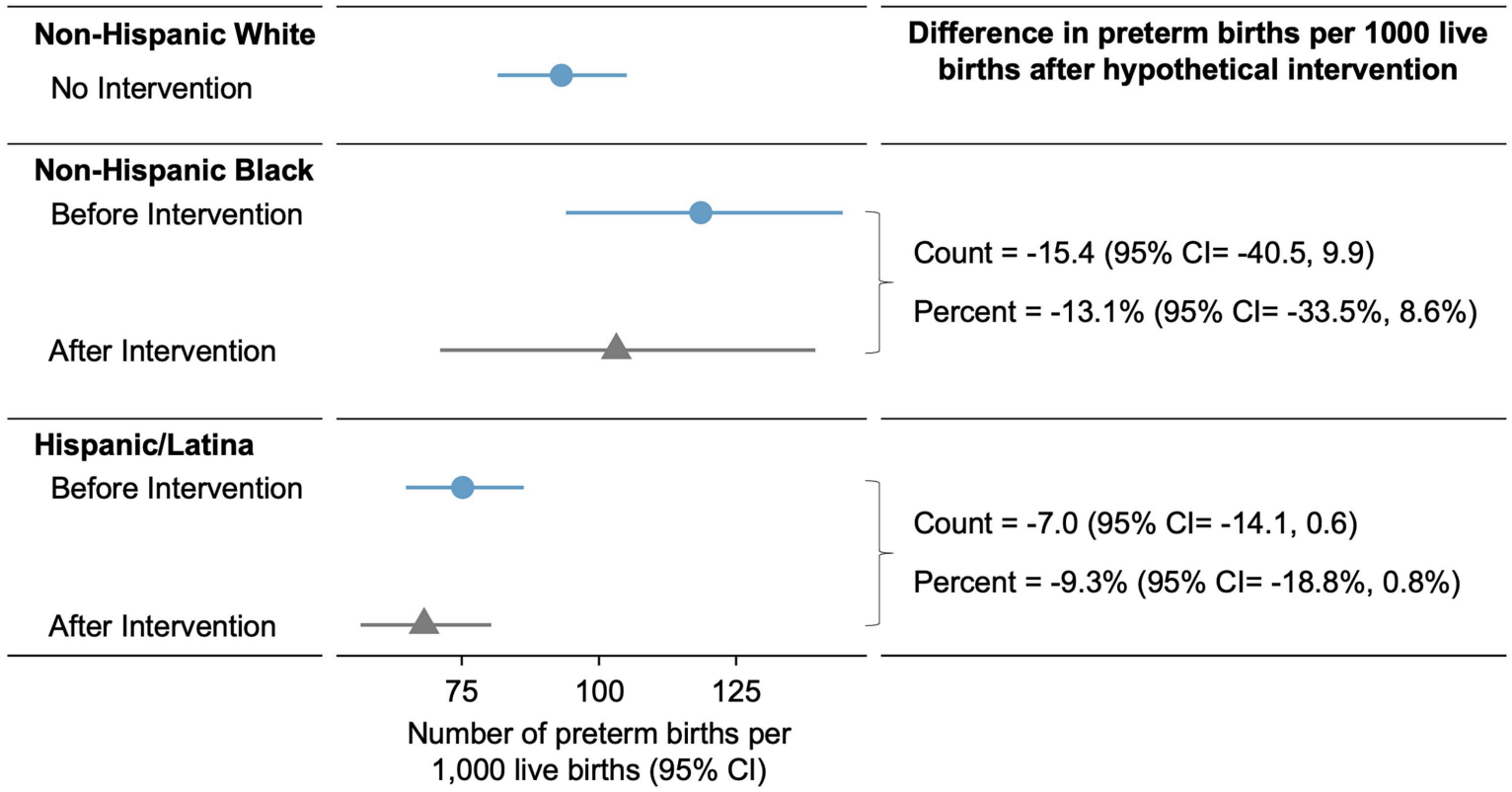
Intervening improves health – chemicals a win-win opportunity with excellent Return on Investment

Table 6-3: National Annualized Benefits, Option 1a (PFOA and PFOS MCLs of 4.0 ppt; Million $2021)

	3% Discount Rate			7% Discount Rate		
	5th Percentile[a]	Expected Value	95th Percentile[a]	5th Percentile[a]	Expected Value	95th Percentile[a]
Annualized CVD Benefits	$110.45	$525.05	$1,035.36	$86.32	$414.45	$817.79
Annualized Birth Weight Benefits	$95.73	$175.05	$276.44	$74.66	$136.97	$217.02
Annualized RCC Benefits	$52.92	$295.53	$744.64	$45.09	$213.78	$508.56
Annualized Bladder Cancer Benefits	$171.72	$220.48	$274.24	$101.34	$130.15	$161.56
Total Annualized Rule Benefits[b]	**$651.19**	**$1,216.08**	**$1,971.01**	**$471.53**	**$895.36**	**$1,456.23**

Abbreviations: CVD – cardiovascular disease; RCC – renal cell carcinoma.
Note: Detail may not add exactly to total due to independent rounding. Percentiles cannot be summed because health effects are not perfectly correlated.
[a]The 5th and 95th percentile range is based on modeled variability and uncertainty. This range does not include the uncertainty described in Table 6-48.
[b]See Table 7-6 for a list of the nonquantifiable benefits, and the potential direction of impact these benefits would have on the estimated monetized total annualized benefits in this table.

Reducing disparities in exposure to multiple phthalates would reduce preterm births among systematically marginalized racial and ethnic groups.
Result of hypothetical interventions that removes the disparity in phthalate exposure



www.figo.org

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

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

SPECIAL COMMUNICATION

International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals☆

Gian Carlo Di Renzo [a], Jeanne A. Conry [b], Jennifer Blake [c], Mark S. DeFrancesco [b], Nathaniel DeNicola [b], James N. Martin Jr. [b], Kelly A. McCue [b], David Richmond [d], Abid Shah [d], Patrice Sutton [e], Tracey J. Woodruff [e,*], Sheryl Ziemin van der Poel [f], Linda C. Giudice [g]

[a] International Federation of Gynecology and Obstetrics, London, UK
[b] American College of Obstetricians and Gynecologists, Washington, DC, USA
[c] Society of Obstetricians and Gynaecologists of Canada, Ottawa, ON, Canada
[d] Royal College of Obstetricians and Gynaecologists, London, UK
[e] Program on Reproductive Health and the Environment, University of California, San Francisco, San Francisco, CA, USA
[f] World Health Organization, Geneva, Switzerland
[g] American Society for Reproductive Medicine, Birmingham, AL, USA

ARTICLE INFO

Keywords:
Developmental health
Environmental chemicals
Reproductive environmental health
Toxic chemicals
Women's health

ABSTRACT

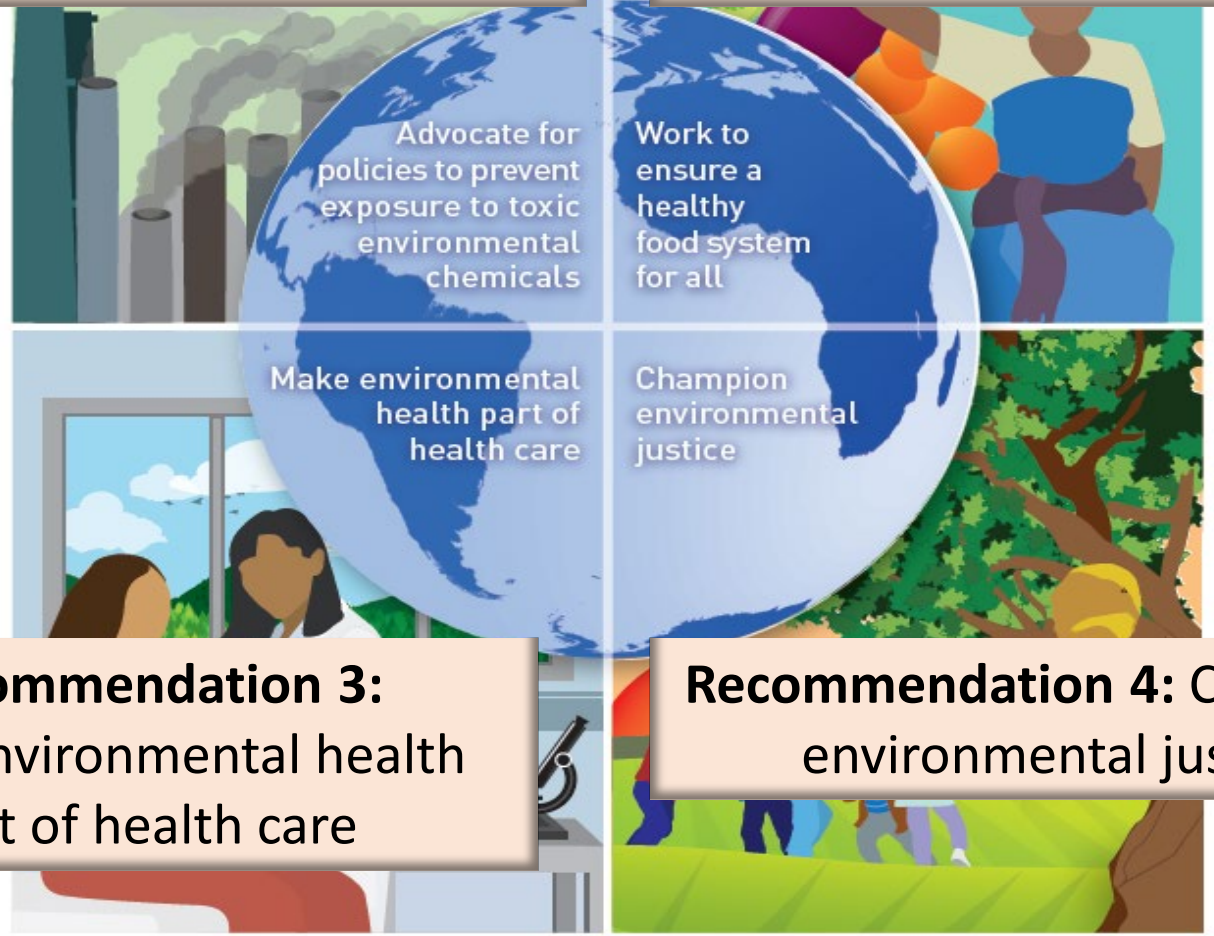
Exposure to toxic environmental chemicals during pregnancy and breastfeeding is ubiquitous and is a threat to healthy human reproduction. There are tens of thousands of chemicals in global commerce, and even small exposures to toxic chemicals during pregnancy can trigger adverse health consequences. Exposure to toxic environmental chemicals and related health outcomes are inequitably distributed within and between countries; universally, the consequences of exposure are disproportionately borne by people with low incomes. Discrimination, other social factors, economic factors, and occupation impact risk of exposure and harm. Documented links between prenatal exposure to environmental chemicals and adverse health outcomes span the life course and include impacts on fertility and pregnancy, neurodevelopment, and cancer. The global health and economic burden related to toxic environmental chemicals is in excess of millions of deaths and billions of dollars every year. On the basis of accumulating robust evidence of exposures and adverse health impacts related to toxic environmental chemicals, the International Federation of Gynecology and Obstetrics (FIGO) joins other leading reproductive health professional societies in calling for timely action to prevent harm. FIGO recommends that reproductive and other health professionals advocate for policies to prevent exposure to toxic environmental chemicals, work to ensure a healthy food system for all, make environmental health part of health care, and champion environmental justice.

INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS

Recommendations for Preventing Exposure to Toxic Chemicals

Recommendation 1: Advocate for policies to prevent exposure to toxic environmental chemicals

Recommendation 2: Work to ensure a healthy food system for all



Recommendation 3: Make environmental health part of health care

Recommendation 4: Champion environmental justice

TOXIC CHEMICALS & PREGNANCY

10 WAYS TO AVOID TOXICS DURING AND AFTER PREGNANCY

- PLASTICIZERS
- BISPHENOLS (BPA, BPB, BPF, BPS)
- PFAS (PFOA, Gen-X, PFBS)
- MERCURY
- PESTICIDES
- PHTHALATES
- PERC and TCE
- LEAD
- FLAME RETARDANTS (PBDEs, OPFRs)

1. Avoid eating, drinking or storing food in plastic
2. Don't microwave in plastic
3. Cook with cast iron or stainless steel rather than non-stick pans
4. Avoid eating fish high in mercury or PCBs like shark and swordfish
5. Eat fresh, organic foods whenever possible
6. Limit cosmetics use
7. Avoid dry cleaning or stain treating clothes
8. Use a wet mop when cleaning
9. Avoid consumer products with flame retardants
10. Remove shoes before entering your home

WHAT HEALTH PROFESSIONALS AND POLICYMAKERS CAN DO

- Advocate for policies to prevent exposure to toxic environmental chemicals
- Work to ensure a healthy food system for all
- Make environmental health part of health care
- Champion environmental justice

FIGO International Federation of Gynecology and Obstetrics

HEAL Health and Environment Alliance

UCSF Program on Reproductive Health and the Environment

For more information **FIGO.ORG**

PREGNANCY and CLIMATE CHANGE

The PROBLEM

Climate change worsens air pollution and extreme weather which can have severe impacts on health during and after pregnancy including:

- PRETERM BIRTH
- LOW BIRTHWEIGHT
- STILL BIRTH
- EFFECTS ON BRAIN DEVELOPMENT

What WE CAN DO

Advocate for public policies that lead to:

- GLOBAL REDUCTION IN AIR POLLUTION EMISSIONS
- STEADY DIVESTMENT FROM FOSSIL FUELS
- REDUCING TOXIC EXPOSURES

> *"The health impacts of our global climate crisis on maternal and child health can no longer be ignored."*
>
> *International Federation of Gynecology and Obstetrics (FIGO)*

FIGO International Federation of Gynecology and Obstetrics

HEAL Health and Environment Alliance

UCSF Program on Reproductive Health and the Environment

What's EPA missing?

EPA's risk evaluation methods are fundamentally behind the science

EPA assumes a "safe" level of chemical exposure.

BUT EPA'S EXPOSURE LEVELS AREN'T "SAFE"

For example, at the levels EPA calls "safe" for PCE, a solvent used in dry cleaning, **as many as 1 in 100** exposed people could experience memory loss.

That's not "safe."

The problem

EPA uses old methods to evaluate chemical risks that DO NOT properly capture health conditions that people may experience from low levels of exposure.

The solution

EPA needs to adopt the best available scientific methods to calculate chemical risks.

New scientific methods can help EPA to protect people better.

UCSF Program on Reproductive Health and the Environment

Science Action Network FOR HEALTH AND THE ENVIRONMENT

EPA needs a bigger umbrella

EPA's chemical risk evaluations leave many people unprotected by:

assuming everyday exposures do no harm

failing to account for underlying conditions like infertility and Parkinson's

failing to consider people exposed to multiple pollutants

The problem

EPA's approach to **risk evaluation** leaves many people unprotected from harmful chemicals

The solution

EPA can **protect more people** by using updated methods* that more realistically estimate real-world risk and harm.

*Probabilistic methods in chemical risk evaluations

EPA needs more inclusive methods to protect people better from harmful chemicals.

UCSF Program on Reproductive Health and the Environment

Science Action Network FOR HEALTH AND THE ENVIRONMENT

In Era of Sickness, Doctors Prescribe Unusual Cure: Voting

As the pandemic curbs in-person voter registration, a growing number of doctors and nurses are registering their patients to vote.

Conclusions

- Environmental chemical exposures are ubiquitous and are adversely impacting health and health equity
- Research can provide data to identify chemical and non-chemical stressors
  - Tools exist now to make a meaningful contribution
- Equitably and completely reducing the burden of toxic chemical exposures requires systemic changes



Thank you!

Thank you to our PRHE Faculty, Staff & Affiliates:

Aileen Andrade
Alana D'Aleo
Allison Landowski
Allison Rozema
Amy Padula
Anne Sausser
Annemarie Charlesworth
Cheryl Godwin de Medina
Courtney Cooper
Cynthia Melgoza Canchola
Dana Goin
Dimitri Abrahamsson
Erin DeMicco
Harim Lee
Jessica Trowbridge
Joshua Robinson
Kristin Shiplet
Laura Bettencourt
Lynn Harvey
Nadia Gaber
Nicholas Chartres
Maribel Juarez
Marya Zlatnick
Max Aung
Rachel Morello-Frosch
Stephanie Eick
Susan Lamontagne
Swati Rayasam
Tali Felson

Thank you to our funders:

The Tides Foundation
The Marisla Foundation
The California Environmental Protection Agency
The Passport Foundation
The JPB Foundation
The National Institutes of Health
The Clarence E. Heller Charitable Foundation
National Institute for Environmental Health Sciences

EaRTH Center

Peggy Reynolds
Diana Laird
Susan Fisher
Jennifer Fung

FOR MORE INFORMATION:
PRHE.UCSF.EDU
EARTH.UCSF.EDU

FOLLOW US

PRHEBlog

UCSF.PRHE

@UCSF_PRHE

YouTube

@UCSF_EaRTH

UCSF.EaRTH

UCSF EaRTH Center
Environmental Research and Translation for Health

UCSF Program on Reproductive Health and the Environment

Toxic Matters: New and Improved!

Prevent Toxic Chemical Exposures at Home

Leave your shoes at the door.

In addition to taking off your shoes, use a doormat to reduce dust. Shoes can carry toxic chemicals into your home.

Use non-toxic personal care products.

Many products have ingredients that can harm reproductive health. Avoid products with "fragrance," "parabens," and "oxybenzone."

Select products without flame retardants.

Select foam products, such as mattresses and upholstered furniture, that have a label that says "flame retardant free" or "compliant with TB-117-2013." Flame retardants can harm health and affect a child's brain.

Beware of lead paint.

Any home built before 1978 may have lead paint. Cover any lead paint with fresh paint, wallpaper or tiles. Keep children away from chipping paint and soil around your home. Never sand or remove lead paint yourself; hire a contractor who is certified in lead abatement.

Use the stove fan when cooking.

Cooking releases toxic chemicals into the air and the fan reduces exposures.

Avoid scented products.

Limit use of air fresheners, candles, oil lamps and wood fires unless they are necessary. Don't burn incense indoors.

https://prhe.ucsf.edu/toxic-matters