Using NHANES to Estimate Chemical Exposures and Inform High-Throughput Exposure Predictions

Zachary Stanfield, R. Woodrow Setzer, Victoria Hull, Risa R. Sayre, Kristin K. Isaacs, John F. Wambaugh

SOT RASS-ESS-ISES Combined Webinar

February 14, 2024

Conflict of Interest Statement and Disclaimer

- The authors have no conflict of interest to disclose
- The views expressed in this presentation are those of the authors, and do not necessarily reflect the views or policies of the U.S. EPA

Overview

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5. Summary

Journal of Exposure Science & Environmental Epidemiology www.nature.com/jes

ARTICLE

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Bayesian inference of chemical exposures from NHANES urine biomonitoring data

Zachary Stanfield[1], R. Woodrow Setzer[1], Victoria Hull[1,2], Risa R. Sayre[1], Kristin K. Isaacs[1] and John F. Wambaugh[1]

BACKGROUND: Knowing which environmental chemicals contribute to metabolites observed in humans is necessary for meaningful estimates of exposure and risk from biomonitoring data.
OBJECTIVE: Employ a modeling approach that combines biomonitoring data with chemical metabolism information to produce chemical exposure intake rate estimates with well-quantified uncertainty.
METHODS: Bayesian methodology was used to infer ranges of exposure for parent chemicals of biomarkers measured in urine samples from the U.S population by the National Health and Nutrition Examination Survey (NHANES). Metabolites were probabilistically linked to parent chemicals using the NHANES reports and text mining of PubMed abstracts.
RESULTS: Chemical exposures were estimated for various population groups and translated to risk-based prioritization using toxicokinetic (TK) modeling and experimental data. Exposure estimates were investigated more closely for children aged 3 to 5 years, a population group that debuted with the 2015–2016 NHANES cohort.
SIGNIFICANCE: The methods described here have been compiled into an R package, bayesmarker, and made publicly available on GitHub. These inferred exposures, when coupled with predicted toxic doses via high throughput TK, can help aid in the identification of public health priority chemicals via risk-based bioactivity-to-exposure ratios.

Keywords: Biomonitoring, Child Exposure/Health, Exposure Modeling, New Approach Methodologies (NAMs)

Journal of Exposure Science & Environmental Epidemiology; https://doi.org/10.1038/s41370-022-00459-0

Stanfield et al., 2022

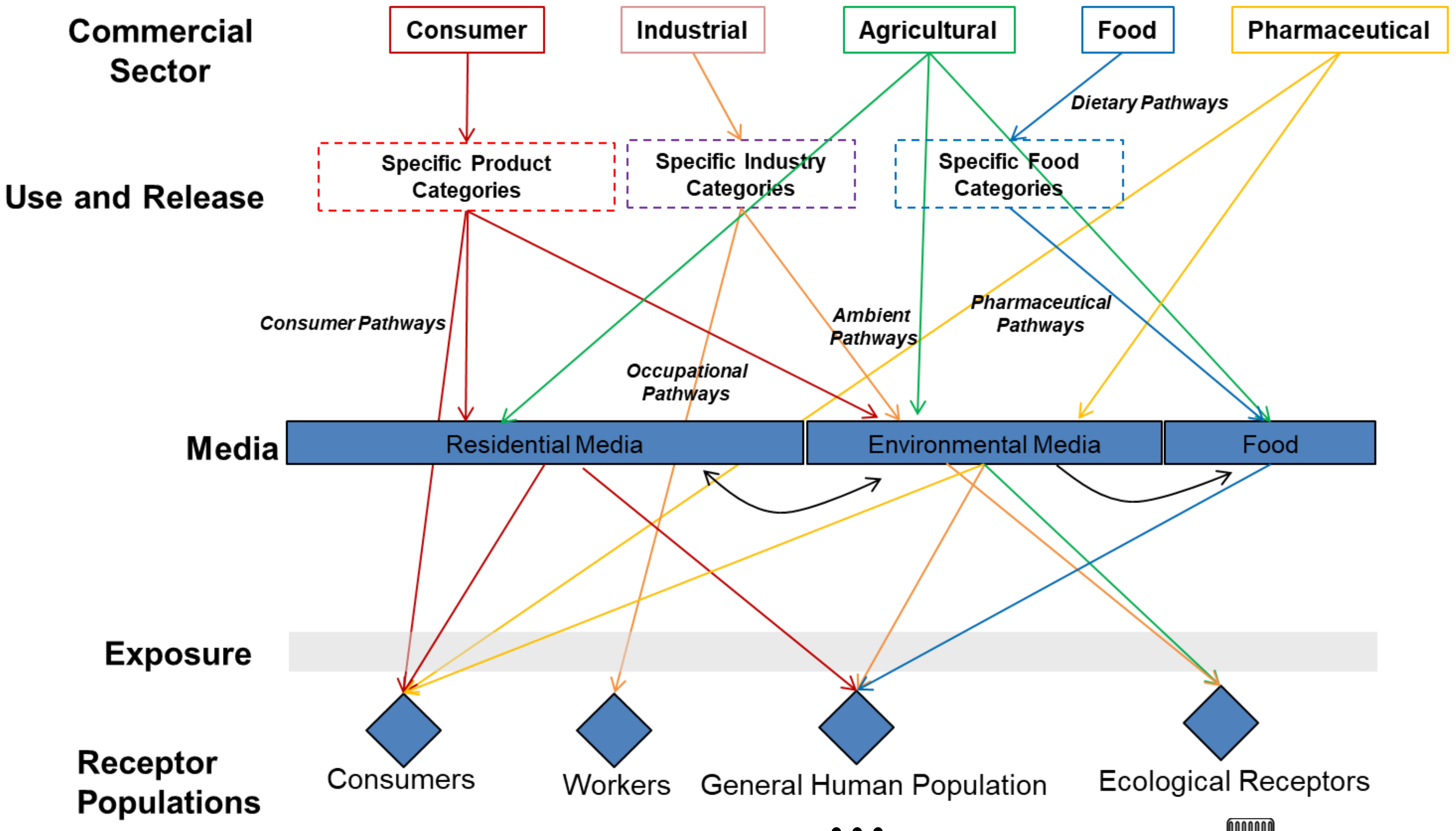
EPA's Exposure Forecasting Project

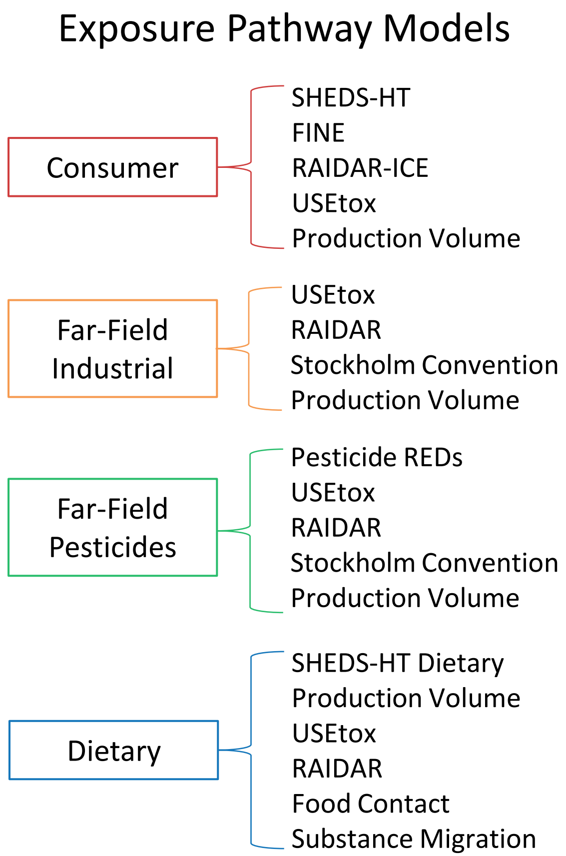
- EPA Office of Research and Development Exposure Forecasting (ExpoCast) project was established in 2009 as a partner project to EPA's Toxicity Forecasting (ToxCast) project
- ExpoCast seeks to develop the data, tools, and evaluation approaches required to generate rapid and scientifically-defensible exposure predictions for the full universe of existing and proposed commercial chemicals
- 380+ peer-reviewed publications since 2010
- ExpoCast scientists and trainees develop New Approach Methodologies (NAMs) for exposure

EPA Office of Research and Development Facility in Research Triangle Park, NC

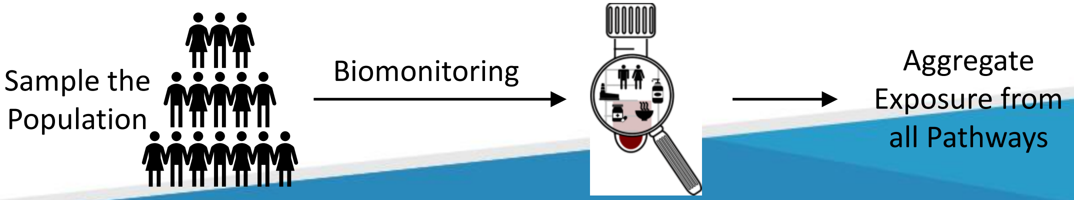
Slide adapted from Kristin Isaacs

Pathways of Chemical Exposure





Ring et al., 2019



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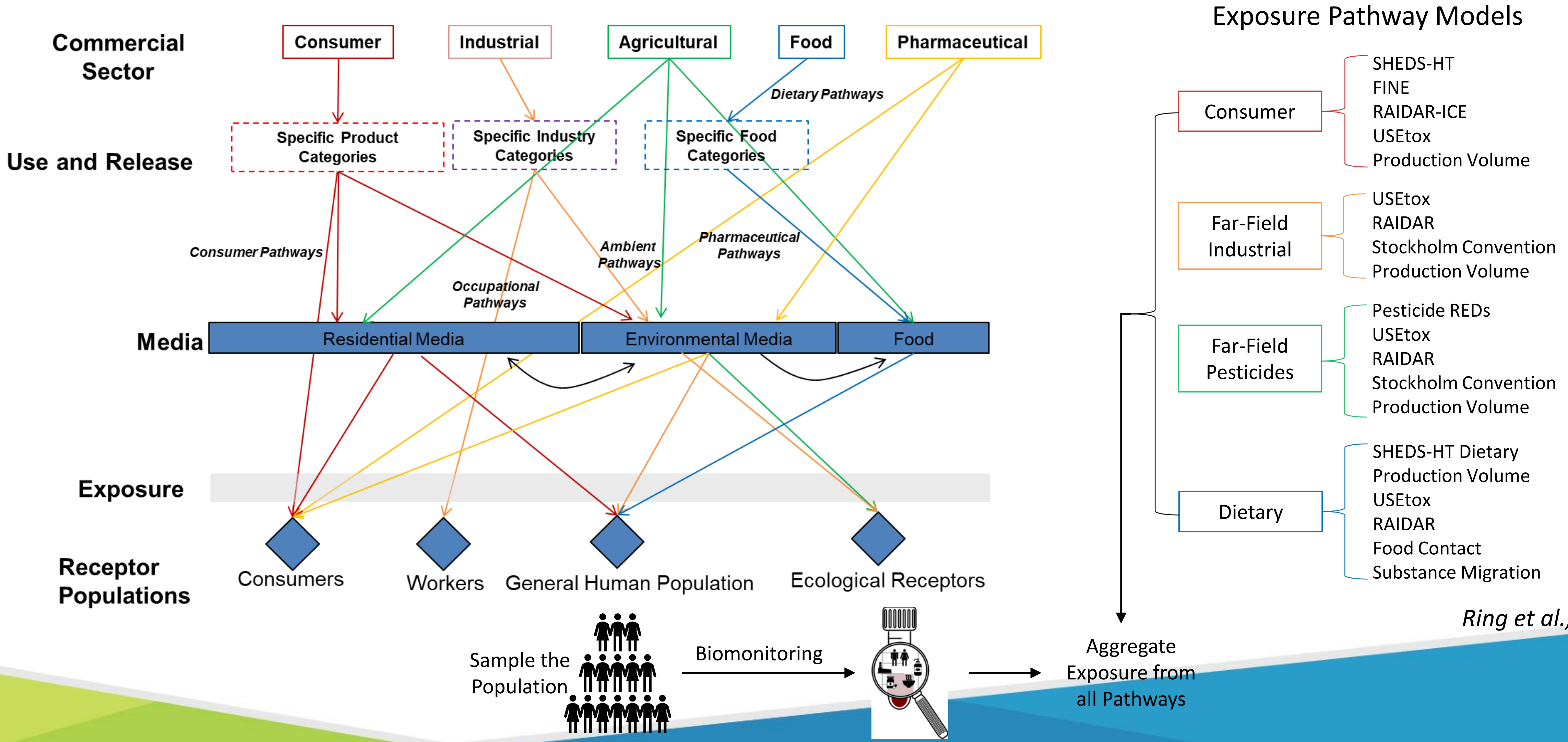

Ring et al., 2019

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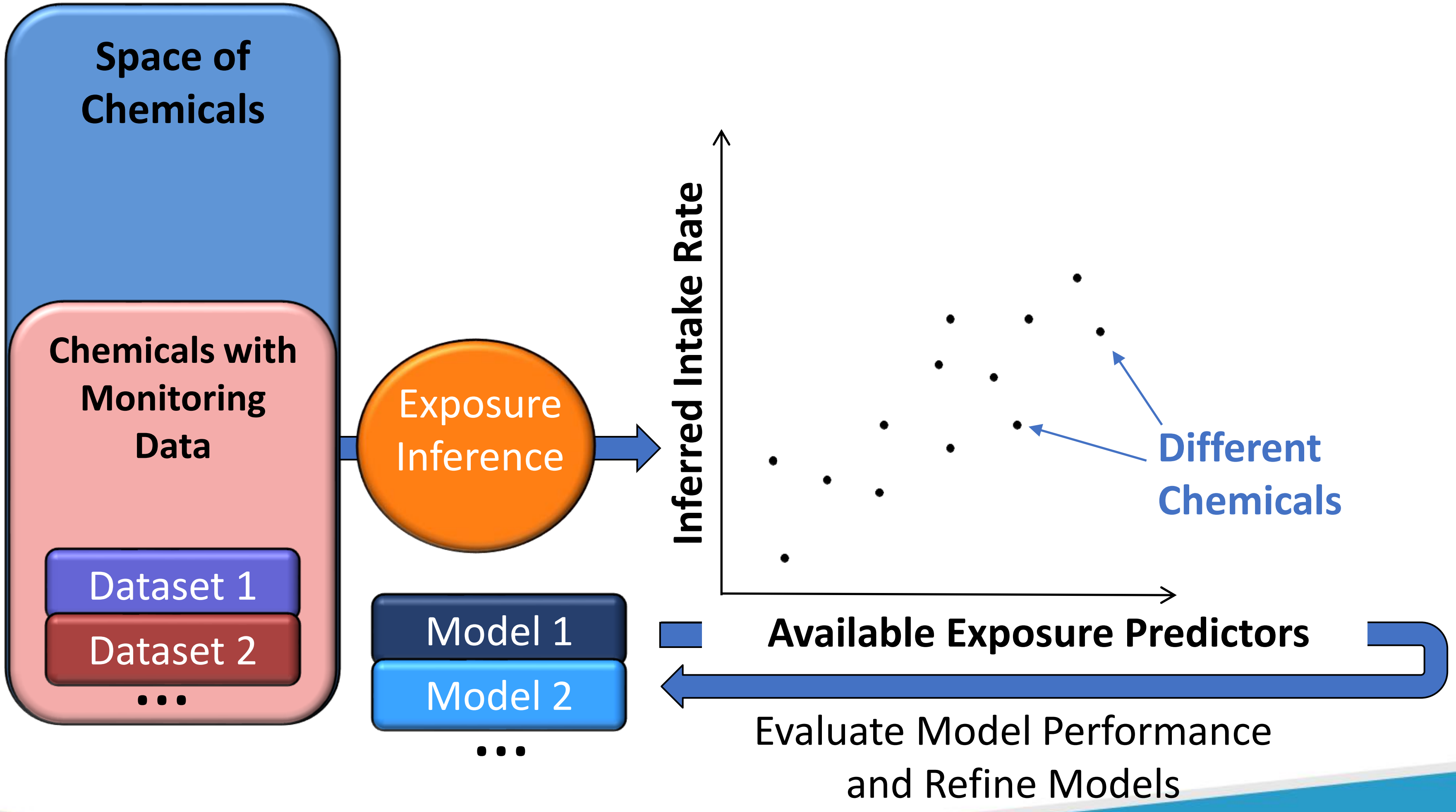
Systematic Empirical Evaluation of Models (SEEM)



Wambaugh et al., 2019

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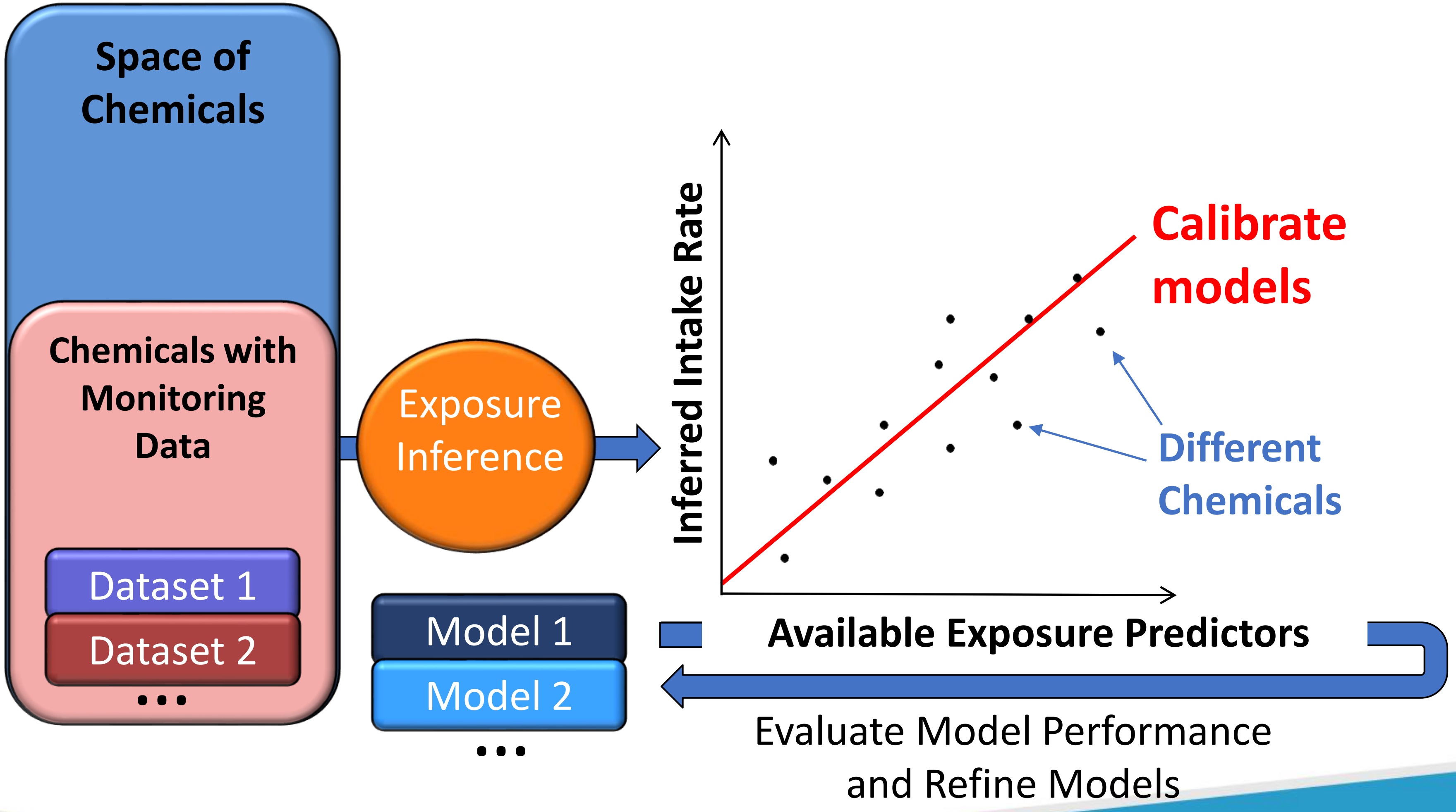

Wambaugh et al., 2019

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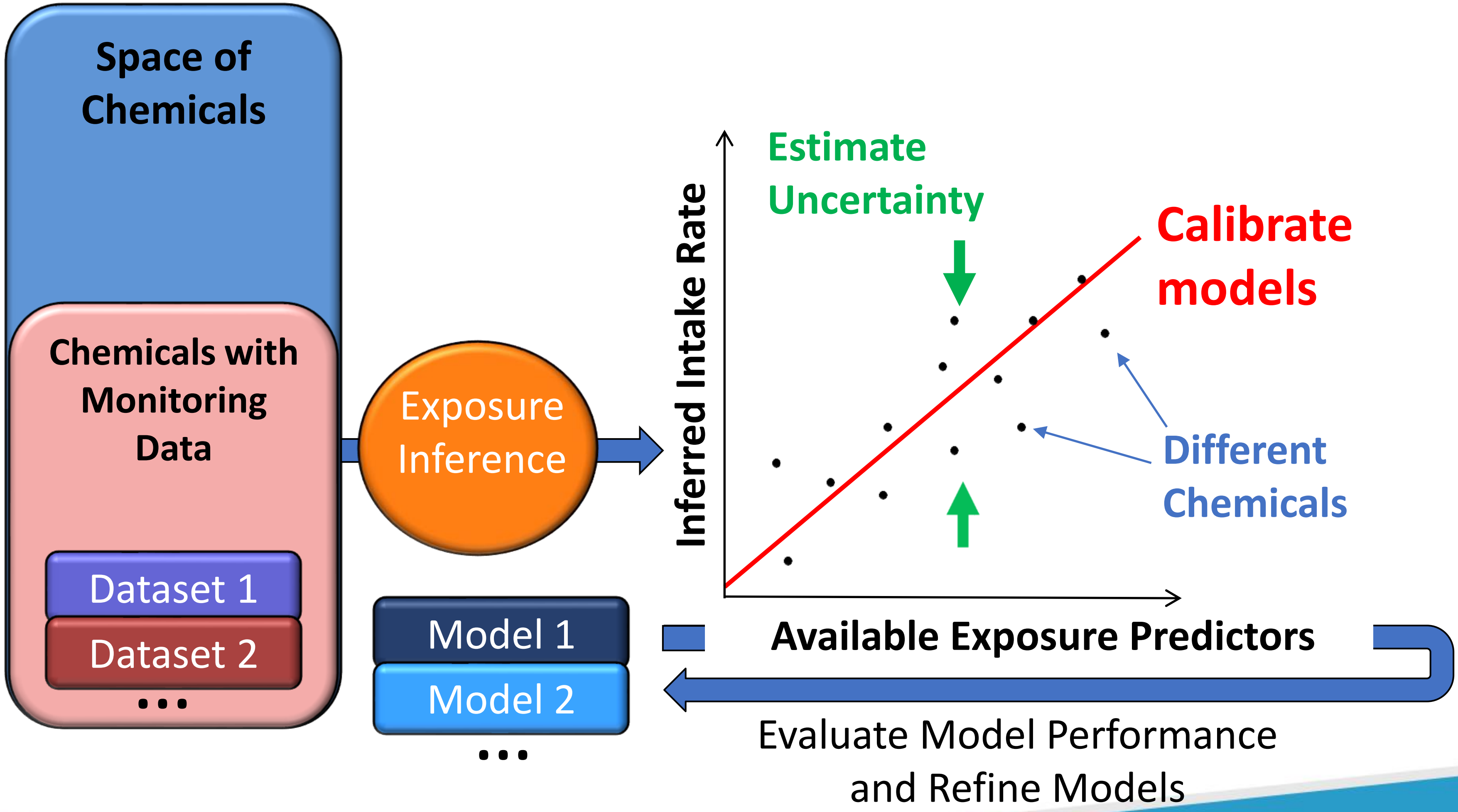

Wambaugh et al., 2019

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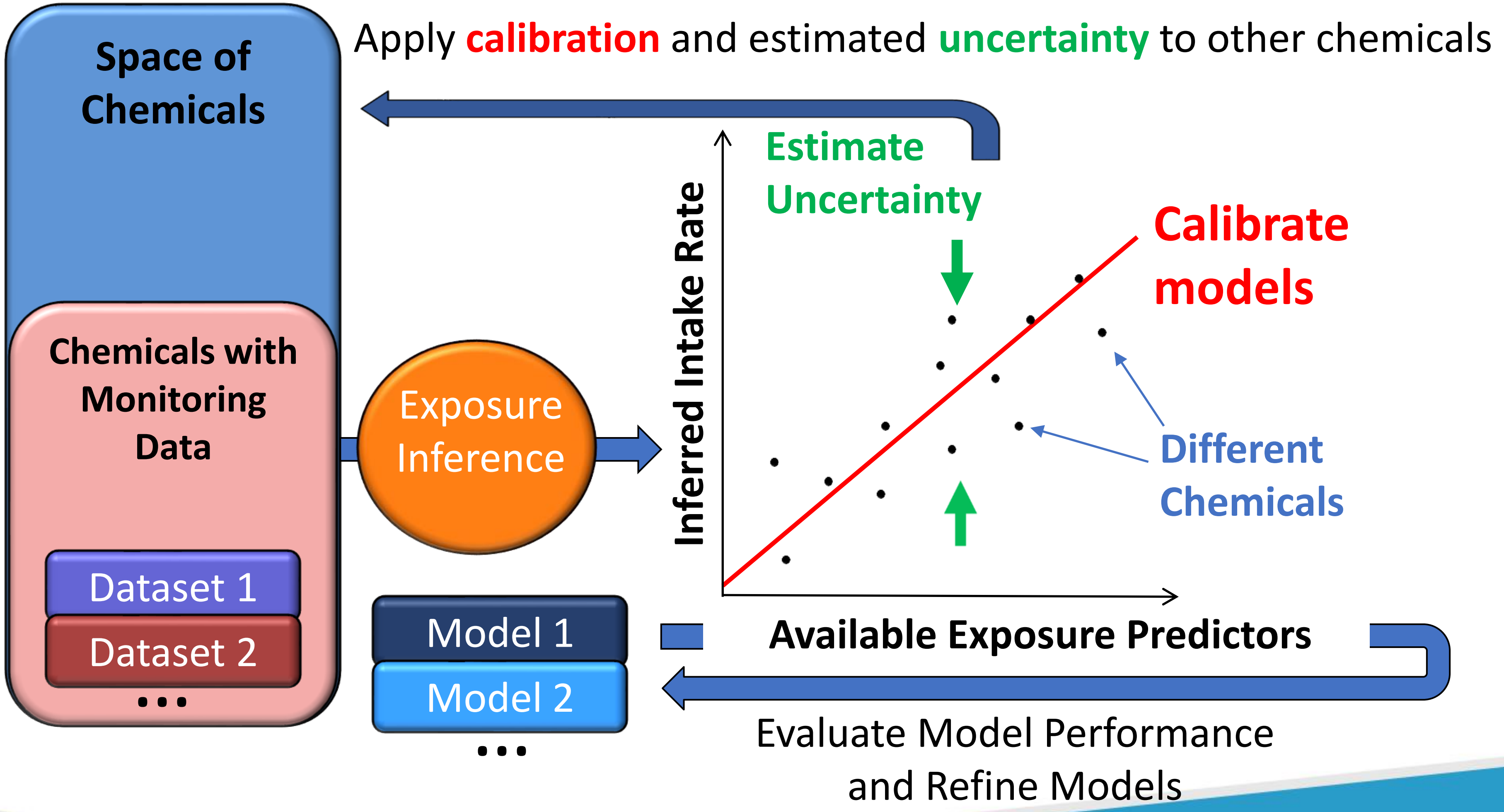


Wambaugh et al., 2019

How do we use biomonitoring data to evaluate high-throughput exposure models?

Exposure Models

Daily Intake Rate (mg/kg/day)

Biomonitoring Data

Biomarker Concentrations (ug/L)

Reverse Dosimetry/Exposure Inference

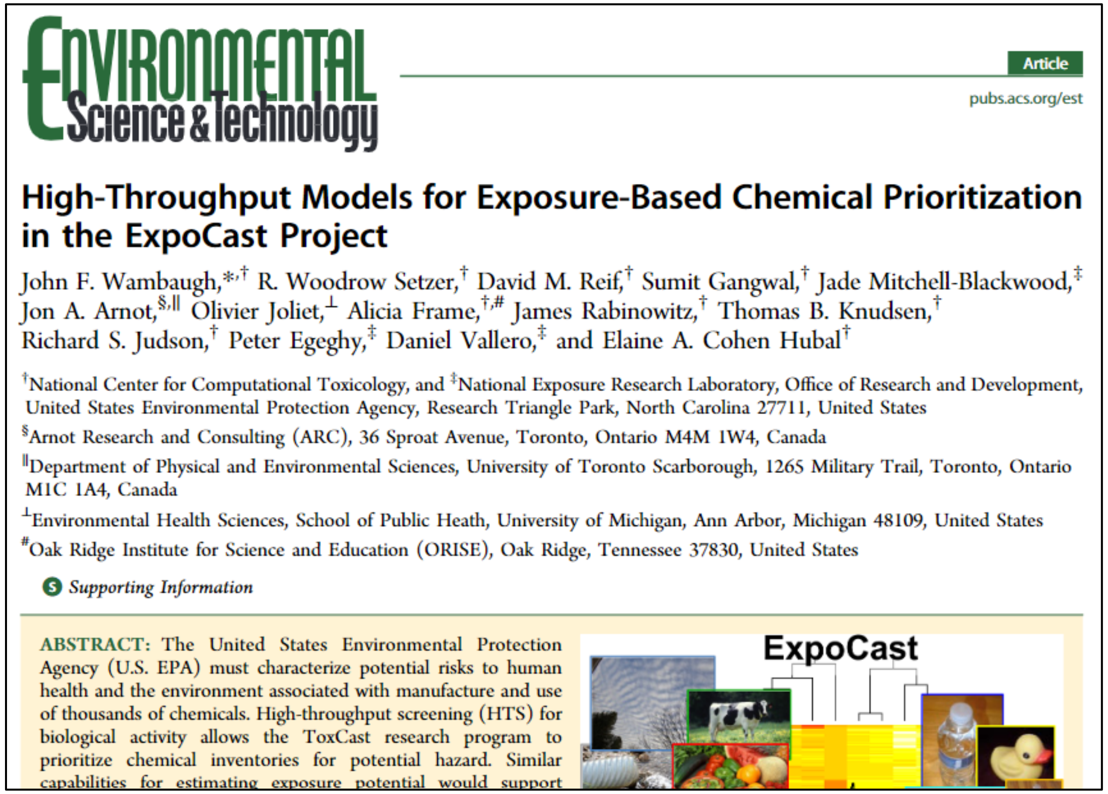
How do we use biomonitoring data to evaluate high-throughput exposure models?

Exposure Models → Daily Intake Rate (mg/kg/day)

Biomonitoring Data → Biomarker Concentrations (ug/L)

Biomarker Concentrations (ug/L) → Daily Intake Rate (mg/kg/day)

Reverse Dosimetry/Exposure Inference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High-Throughput Models for Exposure-Based Chemical Prioritization in the ExpoCast Project

John F. Wambaugh,*,† R. Woodrow Setzer,† David M. Reif,† Sumit Gangwal,† Jade Mitchell-Blackwood,‡ Jon A. Arnot,§,∥ Olivier Joliet,⊥ Alicia Frame,†,# James Rabinowitz,† Thomas B. Knudsen,† Richard S. Judson,† Peter Egeghy,‡ Daniel Vallero,‡ and Elaine A. Cohen Hubal†

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⊥Environmental Health Sciences, School of Public Heath, University of Michigan, Ann Arbor, Michigan 48109, United States

#Oak Ridge Institute for Science and Education (ORISE), Oak Ridge, Tennessee 37830, United States

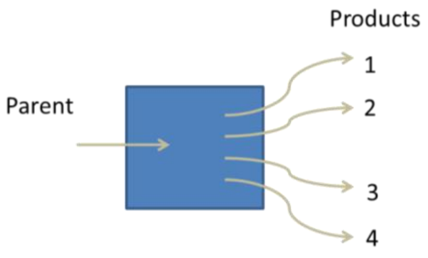
Supporting Information

ABSTRACT: The United States Environmental Protection Agency (U.S. EPA) must characterize potential risks to human health and the environment associated with manufacture and use of thousands of chemicals. High-throughput screening (HTS) for biological activity allows the ToxCast research program to prioritize chemical inventories for potential hazard. Similar capabilities for estimating exposure potential would support

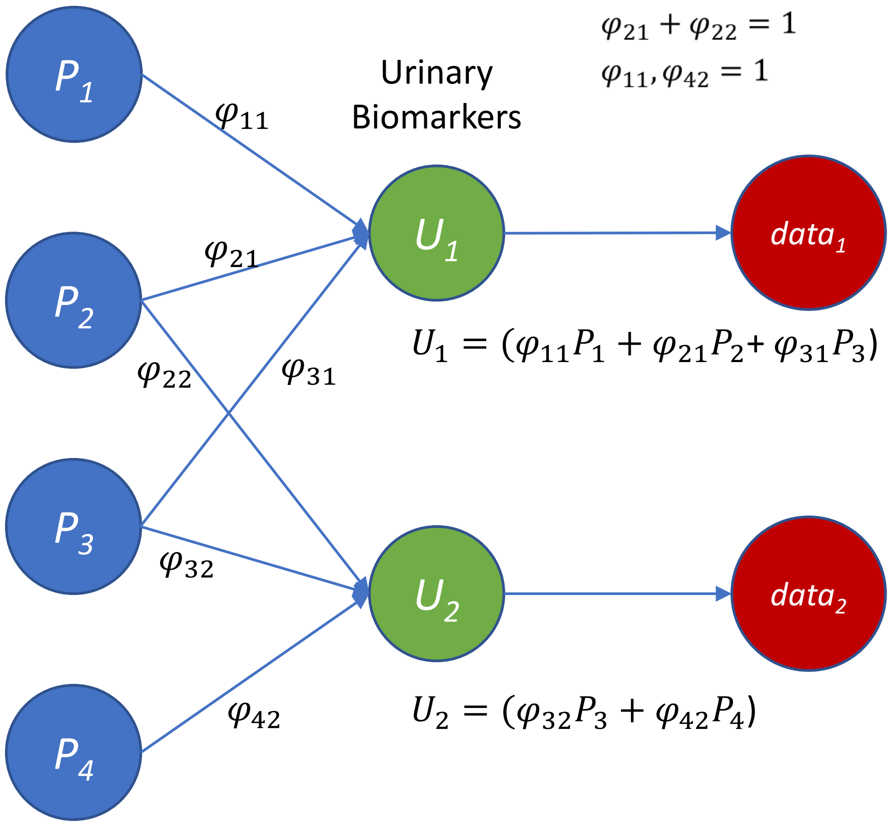
ExpoCast

Wambaugh et al., 2013

Problem Description



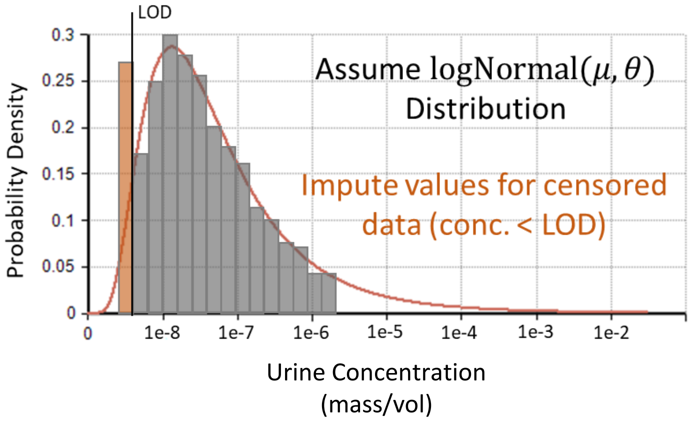
$$(\mathrm{mg/kg/day})_0 = \mathrm{MW}_0 \sum_i \phi_{0i} \frac{(\mathrm{mg/kg/day})_i}{\mathrm{MW}_i}$$



$0 \leq \varphi_{ij} \leq 1$
$\varphi_{31} + \varphi_{32} = 1$
$\varphi_{21} + \varphi_{22} = 1$
$\varphi_{11}, \varphi_{42} = 1$

$U_1 = (\varphi_{11}P_1 + \varphi_{21}P_2 + \varphi_{31}P_3)$

$U_2 = (\varphi_{32}P_3 + \varphi_{42}P_4)$



Slide adapted from R. Woodrow Setzer

Problem Description

Reverse toxicokinetics (tk) approach

- Assume individuals are at steady-state equilibrium due to a constant rate of exposure to one or more parent compounds *(Lakind & Naiman, 2008; Mage et al., 2004; Tan et al., 2007)*
- Estimate the rate at which chemicals are filtered into urine by the kidneys
  - Chemicals are assumed to be (mainly) cleared by the kidneys via glomerular filtration, which can be estimated by creatinine excretion rates (CER)
  - Creatinine correction

$$(\text{mg/kg/day})_i = \frac{1}{\text{BW kg}} \frac{\text{mg}_i}{\text{g}_{\text{creatinine}}} * \frac{\text{g}_{\text{creatinine}}}{\text{day}}$$

  - When available, use urine flow data
    - CER ($g_{creatinine}$/day) = creatinine conc. (g/mL) * urine flow rate (mL/min) * 24*60 (min/day)
  - When not available, model daily excretion
    - Is a function of muscle mass, which is influenced by sex, race, age, and bodyweight

How do we model this problem?

Model Needs

- Handle censored data
- Determine optimal parent-metabolite fractions (φ's)
- Incorporate distribution information for urine concentrations
- Include confidence assessment
    - How certain are we of our results?

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Model Needs

- Handle censored data
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- Incorporate distribution information for urine concentrations
- Include confidence assessment
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Bayesian Inference

- Allows easy incorporation of censored data
- Can integrate prior information about the system
  - Considers what we already know and extrapolates the rest from the accompanying data
- Returns a distribution of parameter values that aids in downstream statistical analyses

Bayesian Inference

- A method of statistical inference using Bayes' theorem

$$P(H \mid E) = \frac{P(E \mid H) \cdot P(H)}{P(E)}$$

H = hypothesis, P(H) = prior probability, E = evidence, P(H|E) = posterior probability, P(E|H) = likelihood, P(E) = model evidence

- Uses prior knowledge (prior distribution) in order to estimate posterior probabilities
- Models describe the problem as a directed graph where nodes are parameters and data, and edges denote dependencies between parameters and data
- Employs Markov Chain Monte Carlo (MCMC)
  - A method for integrating over probability space to perform a Bayesian analysis (Gelman et al., 2013)
  - Converges on the "posterior" space where all iterations are equally likely and Markov chain iterations represent samples from the posterior distribution
- Can be implemented in R using JAGS (http://mcmc-jags.sourceforge.net/) and Stan (https://mc-stan.org/) programming via the packages rjags and rstan

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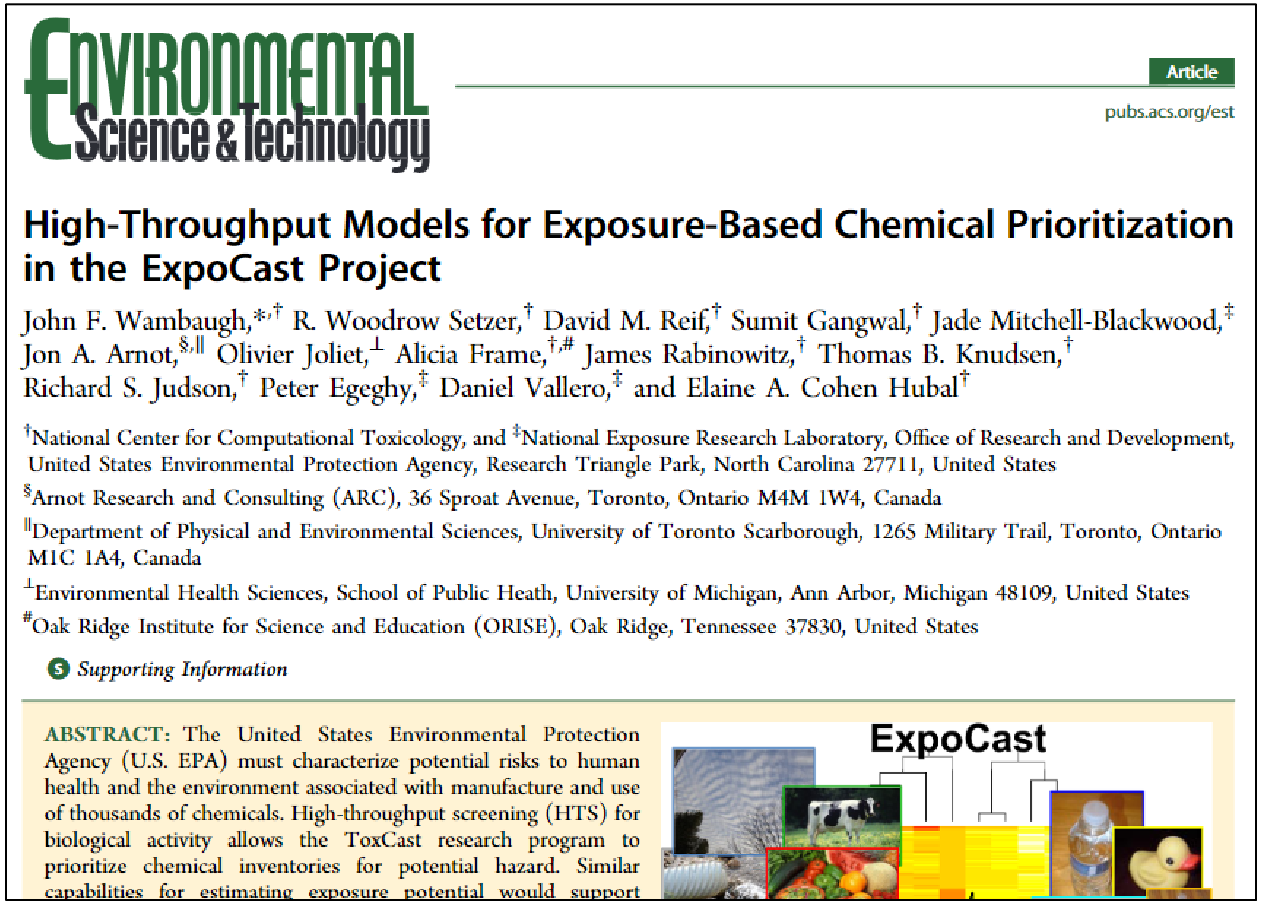
```
model{
 ## Model the parent exposures
 for (i in 1:N) {
  lP[i] ~ dnorm(lPmu, tau.V)
  P[i]<- exp(lP[i])
 }
 lPmu ~ dnorm(0, 0.001)

 ## code so that prior for sd(log(P[i])) is half-Cauchy(25)
 sd.dum ~ dt(0,1/625,1)
 sd.V <- abs(sd.dum)
 tau.V <- 1/pow(sd.V,2)

 ## Link the unobserved parent exposure to the observed (but censored) metabolites.
 lU <- log(t(Phi) %*% P)
 ## tau.se <- 1/(se * se)
 for (j in 1:Mn) {
  ly[j] ~ dnorm(lU[j],tau.se[j])
 }
 for (j in (Mn+1):M) {
  Pralod[j - Mn] <- 1 - pnorm(lod[j - Mn], lU[j], tau[j - Mn])
  ly[j] ~ dbin(Pralod[j - Mn], SS[j - Mn])
 }
 ## Estimate mixmu, mixtau, mixpi externally, and input as data.
 for (j in 1:(M - Mn)) {
  lsd[j] ~ dnormmix(mixmu, mixtau, mixpi)
  tau[j]  <- exp(-2*lsd[j])
 }

 for (i in 1:NBranches)
 {
  phi[Bstart[i]:Bstop[i]] ~ ddirch(Alpha[Bstart[i]:Bstop[i]])
 }

 for (i in 1:Ndelta) {
  Phi[indx[i,1],indx[i,2]] <- phi[i]
 }
}
```

Inferring Exposure from NHANES Data



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Environmental Science & Technology

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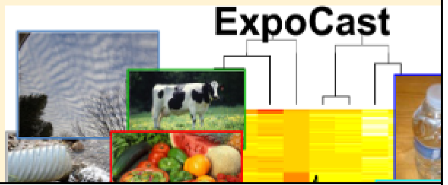

Wambaugh et al., 2013

Journal of Exposure Science & Environmental Epidemiology www.nature.com/jes

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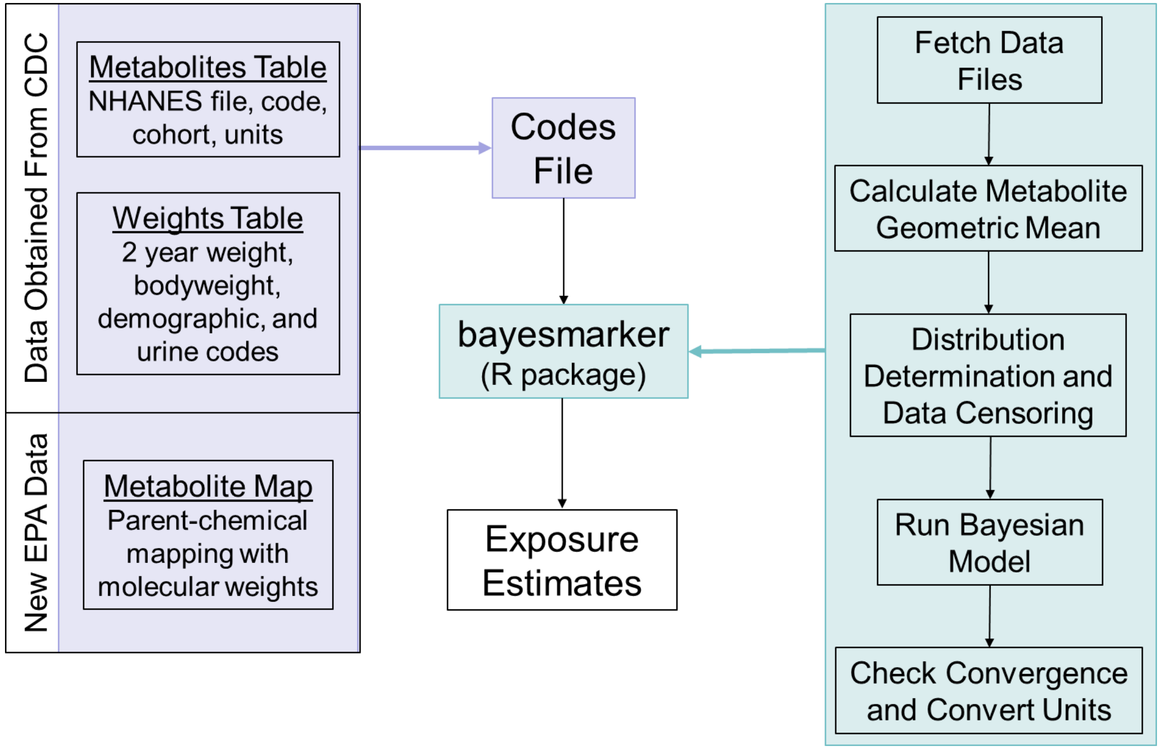
Stanfield et al., 2022

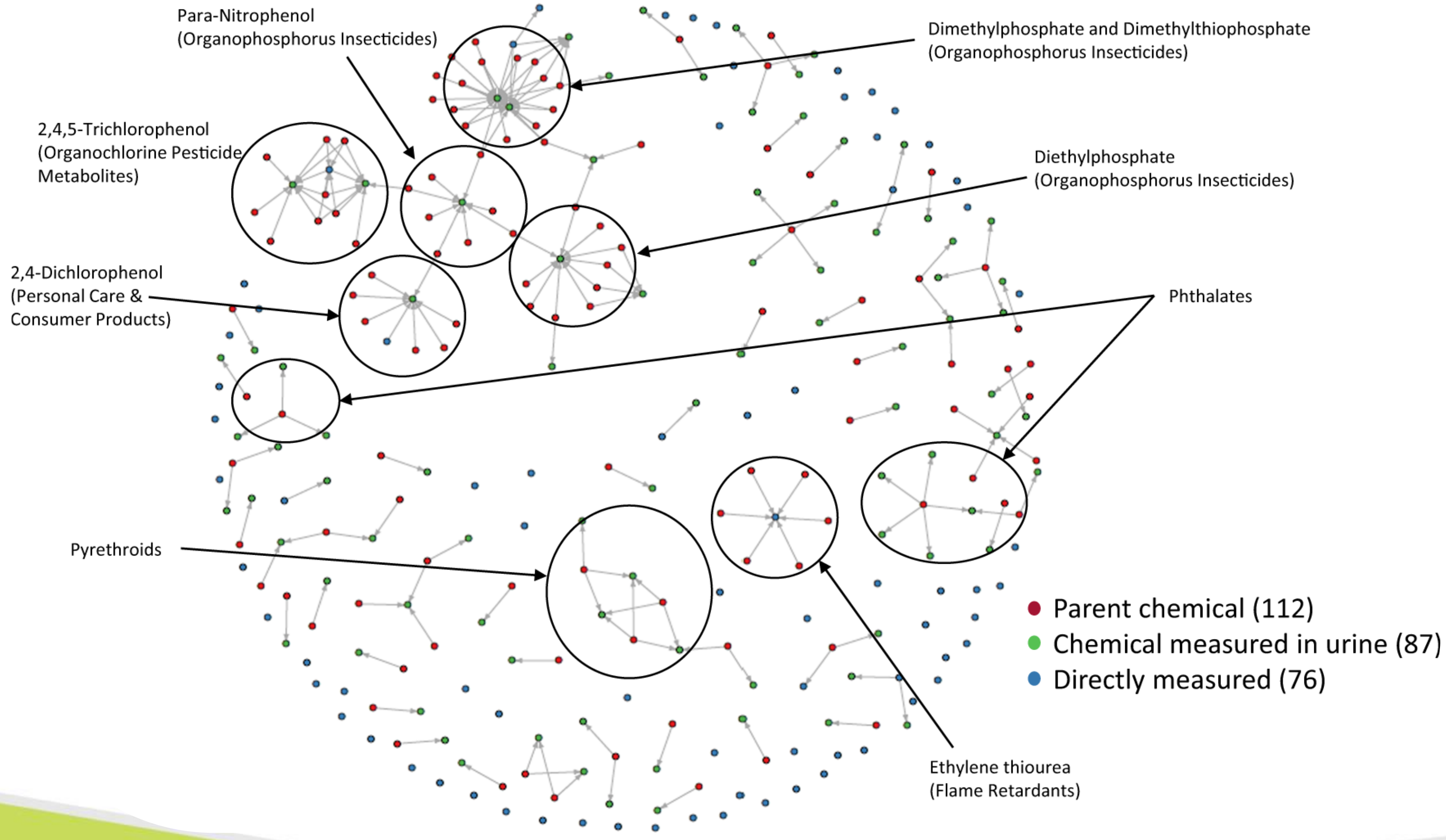
The bayesmarker R Package



https://github.com/USEPA/CompTox-HumanExposure-bayesmarker

Stanfield et al., 2022

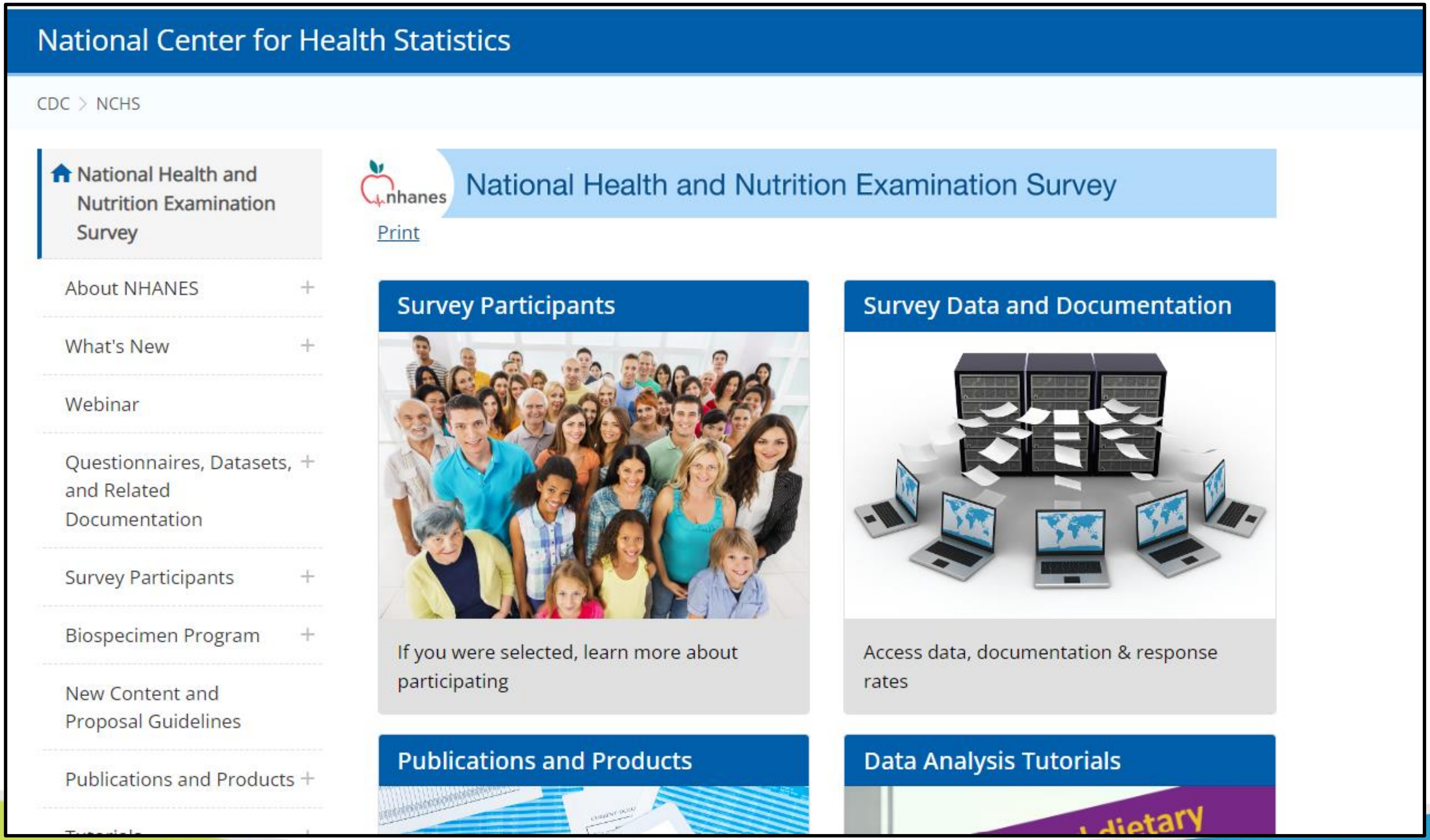
Parent-Metabolite Network



- Wambaugh et al., 2013
  - 68 metabolites linked to 109 parent chemicals
- Stanfield et al., 2022
  - 151 metabolites linked to 179 parent chemicals (270 edges)
    - New metabolites curated by Victoria Hull
  - Evidence added from:
    - NHANES reports
    - Text mining of PubMed abstracts using chemical synonyms and metabolism keywords (Risa Sayre)

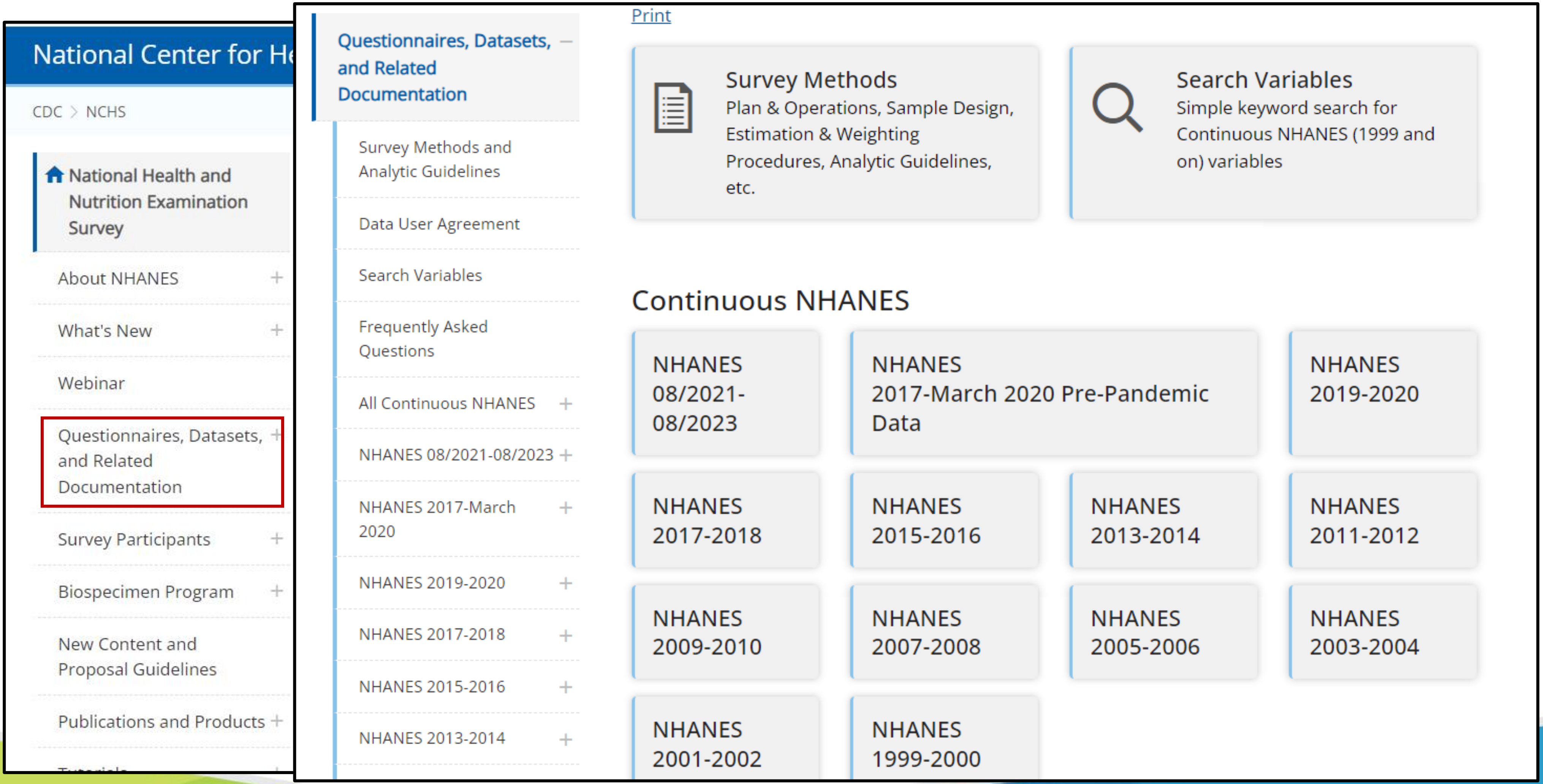
Stanfield et al., 2022

NHANES Overview



https://www.cdc.gov/nchs/nhanes/index.htm

NHANES Overview



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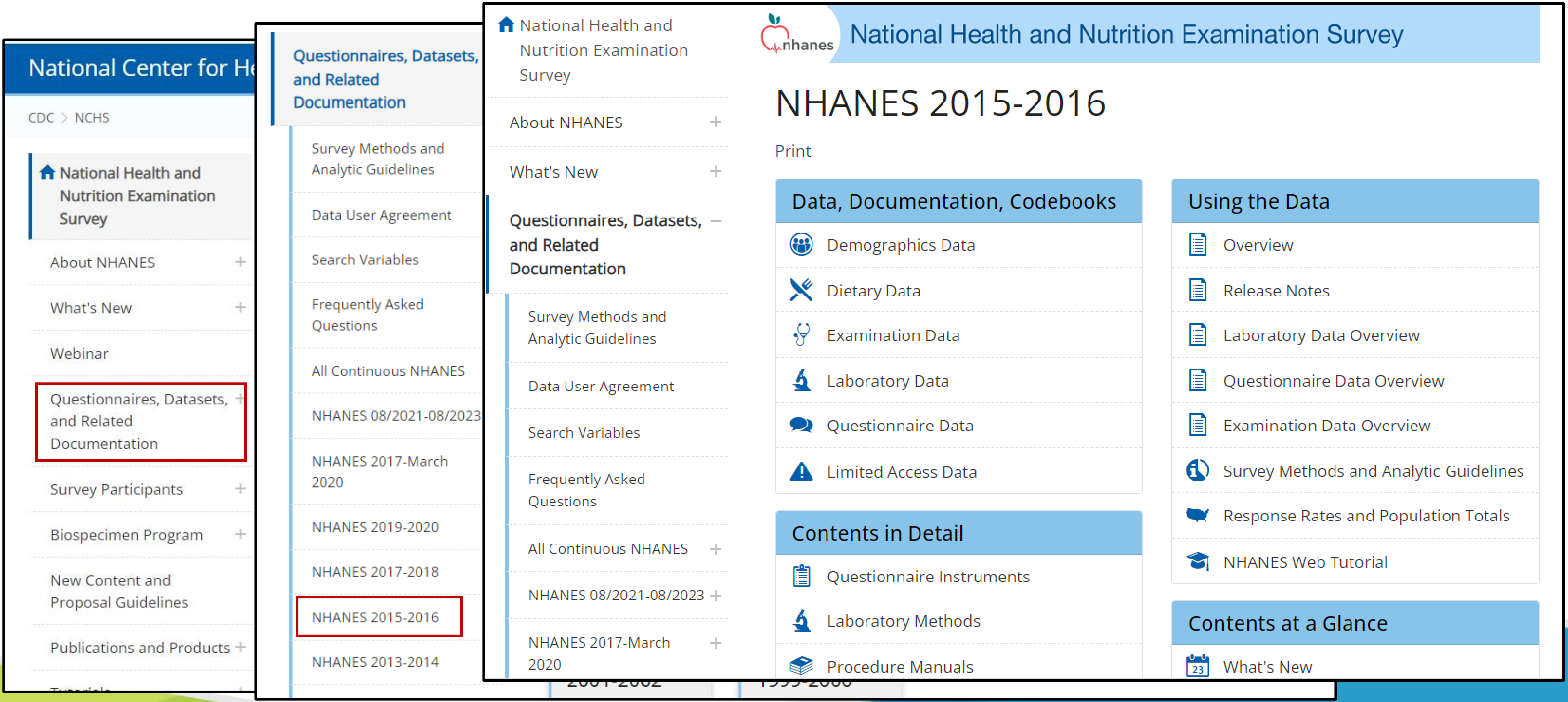
NHANES Overview



https://www.cdc.gov/nchs/nhanes/index.htm

NHANES Overview

Demographic Data

National Health and Nutrition Examination Survey

2015-2016 Data Documentation, Codebook, and Frequencies

Demographic Variables and Sample Weights (DEMO_I)

Data File: DEMO_I.xpt

First Published: September 2017

Last Revised: NA

Component Description

The demographics file provides individual, family, and household-level information on the following topics:

- Survey participant's household interview and examination status;
- Interview and examination sample weights;
- Masked variance units;
- Language of questionnaires used for the interviews conducted in the household and in the mobile examination center;
- Use of proxy or interpreter during the interviews;
- The six-month time period when the examination was performed;
- Pregnancy status;
- Household and family income;
- Household and family sizes;
- Household composition: the number of children (aged 5 years or younger and 6-17 years old), and adults aged 60 years or older, in the household;
- Demographic information about the household reference person; and
- Other selected demographic information, such as gender, age, race/Hispanic origin, education, marital status, military service status, country of birth, citizenship, and years of U.S. residence.

The format and coding for all the variables included in the 2015-2016 NHANES demographics file are identical to those released for the 2013-2014 survey cycle.

Similar to the 2011-2014 cycle, the sample design for NHANES 2015-2016 also includes an

TABLE OF CONTENTS

- Component Description
- Eligible Sample
- Interview Setting and Mode of Administration
- Quality Assurance & Quality Control
- Data Processing and Editing
- Analytic Notes
- References
- Codebook
  - SEQN - Respondent sequence number
  - SDDSRVYR - Data release cycle
  - RIDSTATR - Interview/Examination status
  - RIAGENDR - Gender
  - RIDAGEYR - Age in years at screening
  - RIDAGEMN - Age in months at screening - 0 to 24 mos
  - RIDRETH1 - Race/Hispanic origin
  - RIDRETH3 - Race/Hispanic origin w/ NH Asian
  - RIDEXMON - Six month time period
  - RIDEXAGM - Age in months at exam - 0 to 19 years
  - DMQMILIZ - Served active duty in US Armed Forces
  - DMQADFC - Served in a foreign country
  - DMDBORN4 - Country of birth
  - DMDCITZN - Citizenship status
  - DMDYRSUS - Length of time in US
  - DMDEDUC3 - Education level - Children/Youth 6-19
  - DMDEDUC2 - Education level - Adults 20+

NHANES Overview

National Health

2015-2016 Data Docu

Demographic Variable

Data File: DEMO_I.xpt

First Published: Septembe

Last Revised: NA

Component Descript

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National Health and Nutrition Examination Survey

2015-2016 Data Documentation, Codebook, and Frequencies

Body Measures (BMX_I)

Data File: BMX_I.xpt

First Published: September 2017

Last Revised: NA

Component Description

NHANES body measures data are used to monitor trends in infant and child growth, to estimate the prevalence of overweight and obesity in U.S. children, adolescents, and adults, and to examine the associations between body weight and the health and nutritional status of the U.S. population. The new collected Sagittal Abdominal Diameter (SAD) data will be used to establish population-based reference ranges, and to improve the health risk assessments associated with body weight and obesity.

The measurements and target age groups for the NHANES 2015–2016 body measures component are as follows:

- Weight: All ages
- Head circumference: birth through 6 months of age
- Recumbent length: birth through 47 months of age
- Standing height: 2 years and older
- Upper leg length: 8 years and older
- Upper arm length: 2 months of age and older
- Mid-upper arm circumference: 2 months of age and older
- Waist circumference: 2 years of age and older
- Sagittal abdominal diameter: 8 years of age and older

Eligible Sample

All survey participants were eligible for the body measures component. Pregnant women and

TABLE OF CONTENTS

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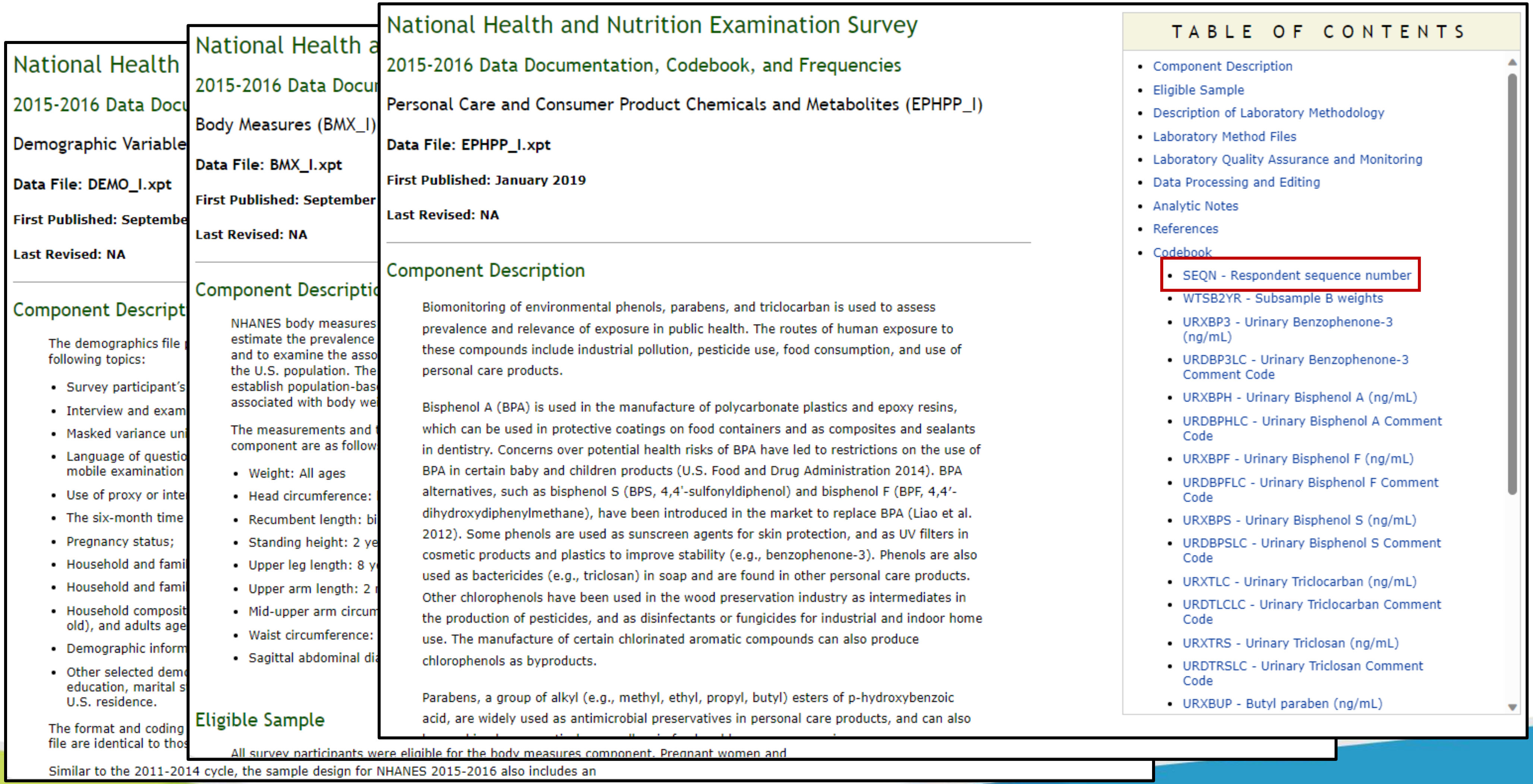
- Eligible Sample
- Protocol and Procedure
- Quality Assurance & Quality Control
- Data Processing and Editing
- Analytic Notes
- References
- Codebook
  - SEQN - Respondent sequence number
  - BMDSTATS - Body Measures Component Status Code
  - BMXWT - Weight (kg)
  - BMIWT - Weight Comment
  - BMXRECUM - Recumbent Length (cm)
  - BMIRECUM - Recumbent Length Comment
  - BMXHEAD - Head Circumference (cm)
  - BMIHEAD - Head Circumference Comment
  - BMXHT - Standing Height (cm)
  - BMIHT - Standing Height Comment
  - BMXBMI - Body Mass Index (kg/m**2)
  - BMDBMIC - BMI Category - Children/Youth
  - BMXLEG - Upper Leg Length (cm)
  - BMILEG - Upper Leg Length Comment
  - BMXARML - Upper Arm Length (cm)
  - BMIARML - Upper Arm Length Comment
  - BMXARMC - Arm Circumference (cm)
  - BMIARMC - Arm Circumference Comment
  - BMXWAIST - Waist Circumference (cm)
  - BMIWAIST - Waist Circumference Comment

Examination
Data

NHANES Overview



National Health and Nutrition Examination Survey

2015-2016 Data Documentation, Codebook, and Frequencies

Personal Care and Consumer Product Chemicals and Metabolites (EPHPP_I)

Data File: EPHPP_I.xpt

First Published: January 2019

Last Revised: NA

Component Description

Biomonitoring of environmental phenols, parabens, and triclocarban is used to assess prevalence and relevance of exposure in public health. The routes of human exposure to these compounds include industrial pollution, pesticide use, food consumption, and use of personal care products.

Bisphenol A (BPA) is used in the manufacture of polycarbonate plastics and epoxy resins, which can be used in protective coatings on food containers and as composites and sealants in dentistry. Concerns over potential health risks of BPA have led to restrictions on the use of BPA in certain baby and children products (U.S. Food and Drug Administration 2014). BPA alternatives, such as bisphenol S (BPS, 4,4'-sulfonyldiphenol) and bisphenol F (BPF, 4,4'-dihydroxydiphenylmethane), have been introduced in the market to replace BPA (Liao et al. 2012). Some phenols are used as sunscreen agents for skin protection, and as UV filters in cosmetic products and plastics to improve stability (e.g., benzophenone-3). Phenols are also used as bactericides (e.g., triclosan) in soap and are found in other personal care products. Other chlorophenols have been used in the wood preservation industry as intermediates in the production of pesticides, and as disinfectants or fungicides for industrial and indoor home use. The manufacture of certain chlorinated aromatic compounds can also produce chlorophenols as byproducts.

Parabens, a group of alkyl (e.g., methyl, ethyl, propyl, butyl) esters of p-hydroxybenzoic acid, are widely used as antimicrobial preservatives in personal care products, and can also

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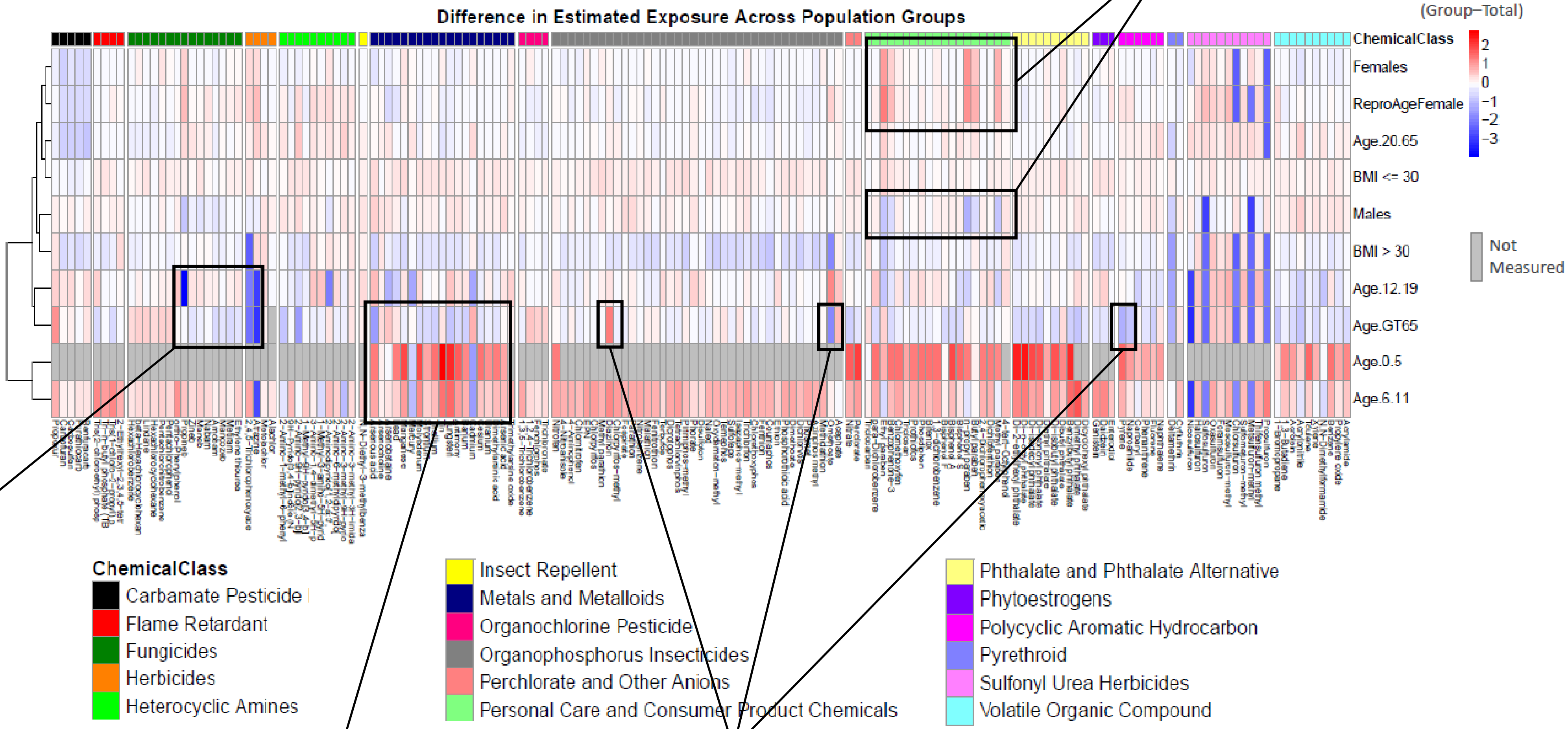
- Codebook
  - SEQN - Respondent sequence number
  - WTSB2YR - Subsample B weights
  - URXBP3 - Urinary Benzophenone-3 (ng/mL)
  - URDBP3LC - Urinary Benzophenone-3 Comment Code
  - URXBPH - Urinary Bisphenol A (ng/mL)
  - URDBPHLC - Urinary Bisphenol A Comment Code
  - URXBPF - Urinary Bisphenol F (ng/mL)
  - URDBPFLC - Urinary Bisphenol F Comment Code
  - URXBPS - Urinary Bisphenol S (ng/mL)
  - URDBPSLC - Urinary Bisphenol S Comment Code
  - URXTLC - Urinary Triclocarban (ng/mL)
  - URDTLCLC - Urinary Triclocarban Comment Code
  - URXTRS - Urinary Triclosan (ng/mL)
  - URDTRSLC - Urinary Triclosan Comment Code
  - URXBUP - Butyl paraben (ng/mL)

Laboratory Data

Results

Demographic-specific Exposures

Higher exposure to parabens for women, lower for men



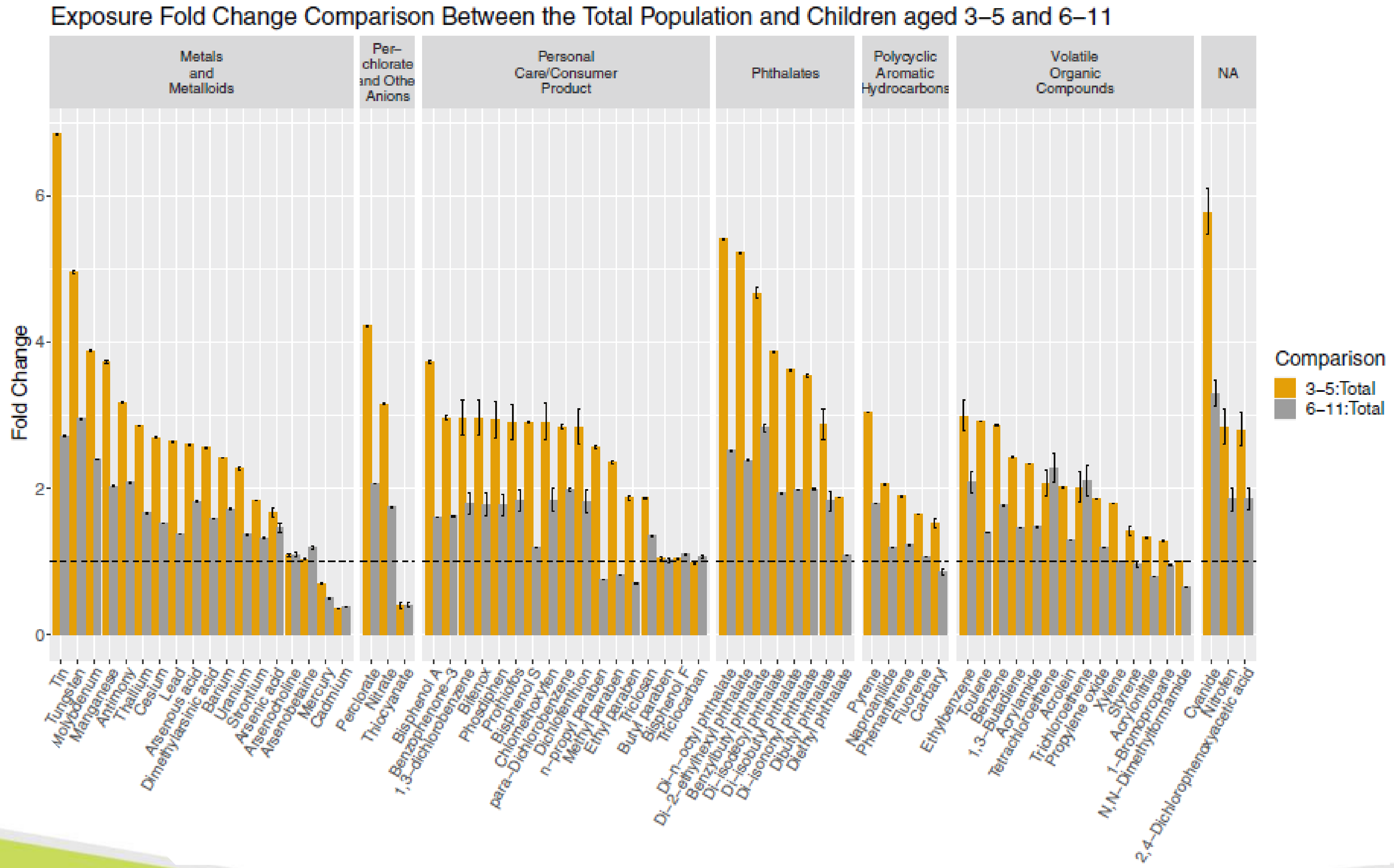
Lower exposure for teens and seniors for certain fungicides and herbicides

Opposite exposure of most metals for children and seniors

Higher exposure to diazinon, lower exposure to omethoate and pyrene

Stanfield et al., 2022

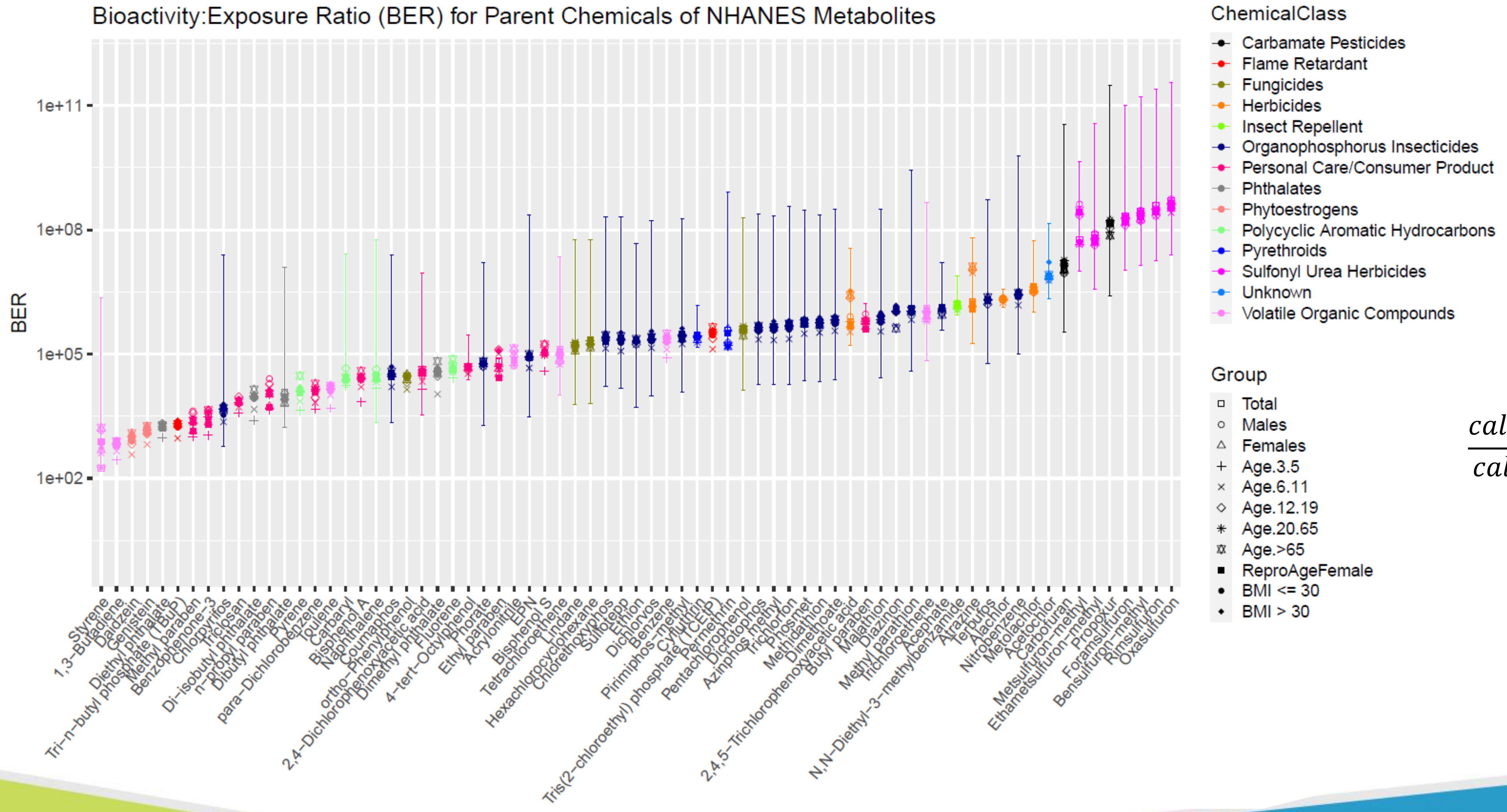
Examining Childhood Exposures (2015-2016)



- NHANES started monitoring urine metabolites in 3–5-year-olds in the 2015-2016 cohort
- Consistently higher exposure children aged 3-5, particularly for some metals and phthalates
- Noticeable difference for some personal care product chemicals between the two child populations compared to all individuals

Stanfield et al., 2022

Translating Exposure to Risk



$$\frac{Bioactivty}{Exposure} =$$

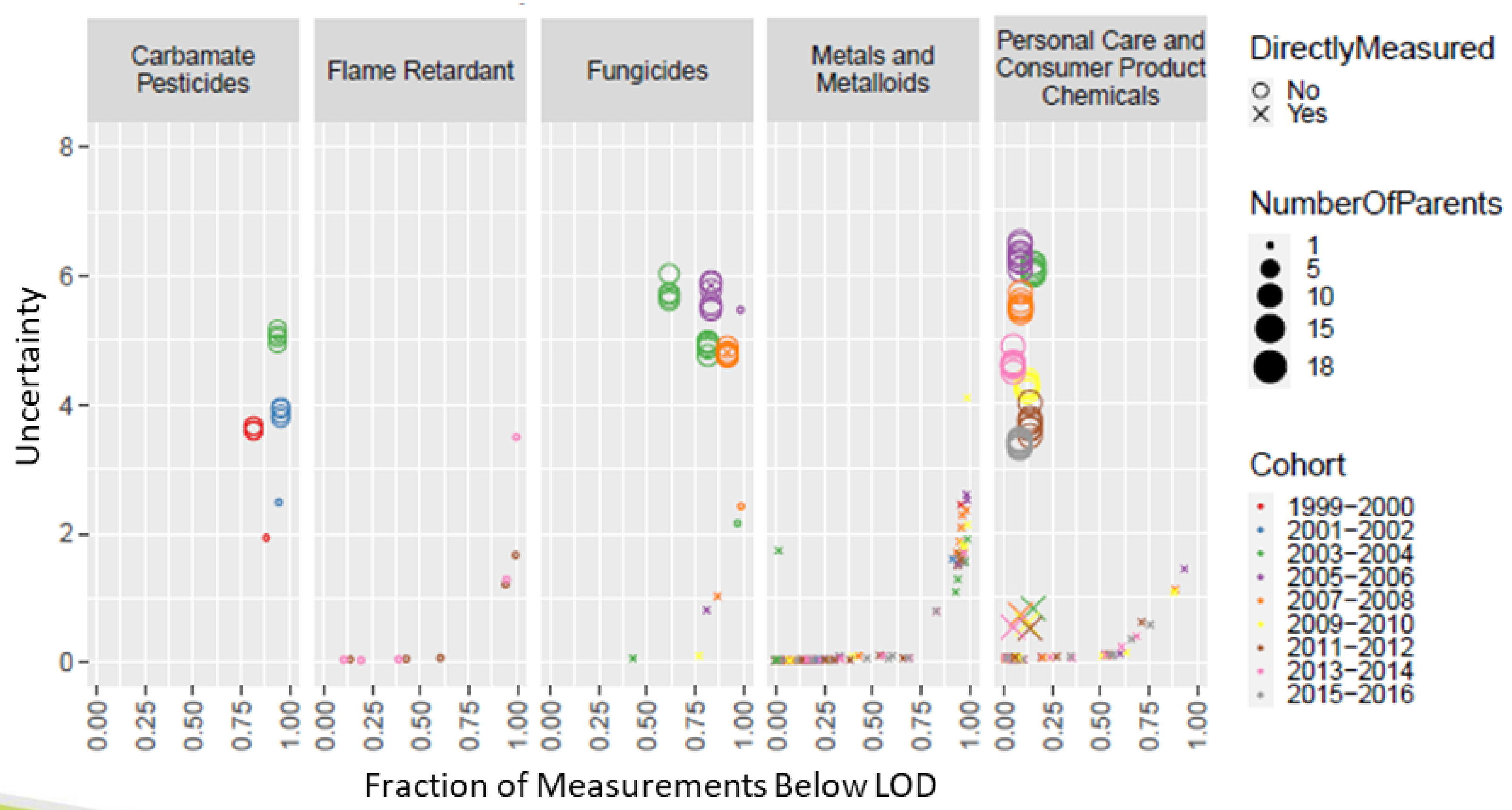
$$\frac{HED}{Plasma\ Conc.} =$$

$$\frac{calc\_tkstats(oral\ rat\ LD50\ *\ AF)}{calc\_mc\_css(inferred\ exposure)}$$

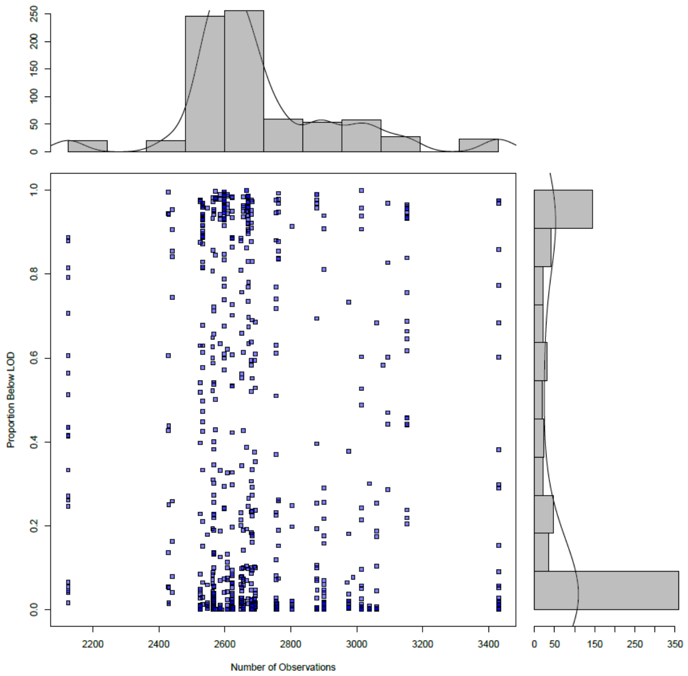
Mansouri et al., 2021
Venman and Flaga, 1985
Pearce et al., 2017

Stanfield et al., 2022

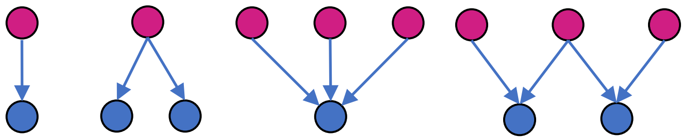
Contributors of Uncertainty



Censored Data



Metabolism



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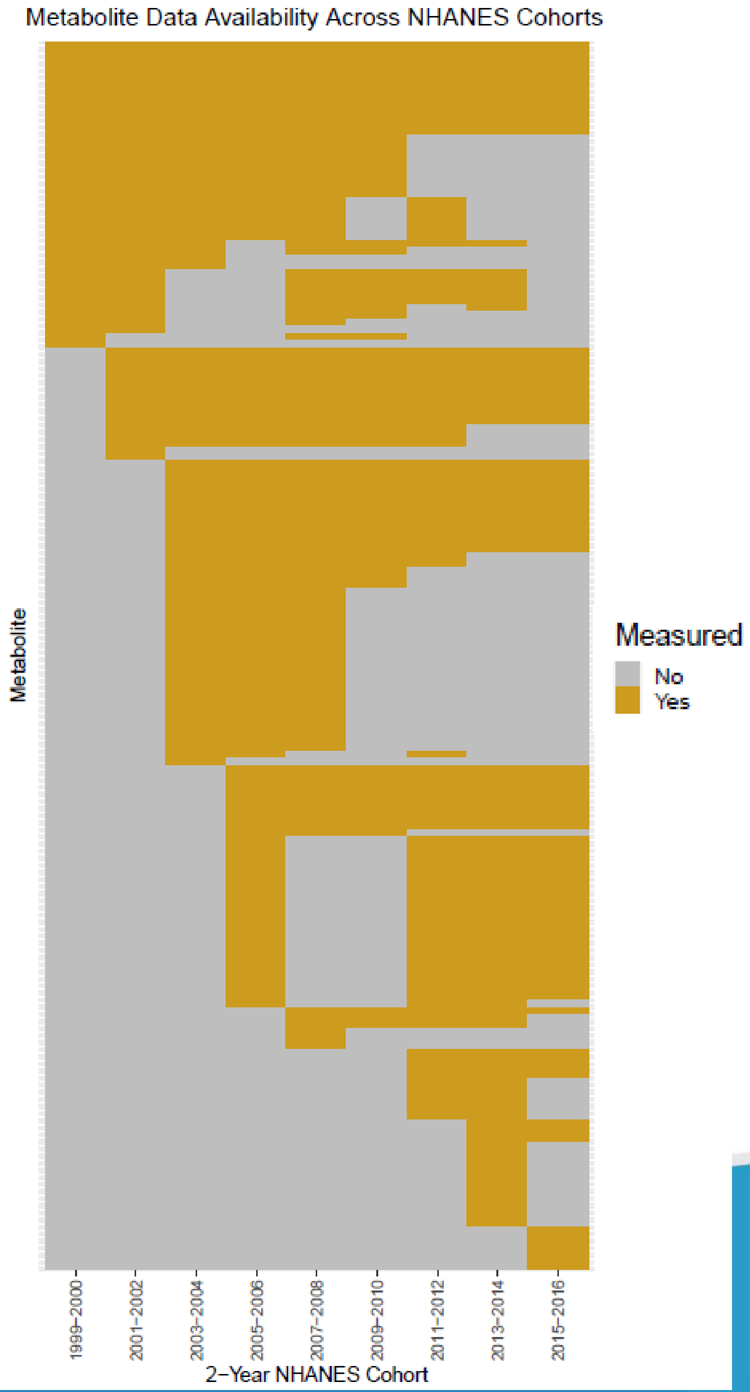
Making the Most of the NHAENES Data

- The NHANES continuous survey cohorts can be compared or combined
- We can generate exposure estimates for each cohort individually
- We can compare changes in exposure for biomarkers measured in multiple cohorts



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Research

A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP12188.

Characterizing Chemical Exposure Trends from NHANES Urinary Biomonitoring Data

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Background: Xenobiotic metabolites are widely present in human urine and can indicate recent exposure to environmental chemicals. Proper inference of which chemicals contribute to these metabolites can inform human exposure and risk. Furthermore, longitudinal biomonitoring studies provide insight into how chemical exposures change over time.

Objectives: We constructed an exposure landscape for as many human-exposure relevant chemicals over as large a time span as possible to characterize exposure trends across demographic groups and chemical types.

Methods: We analyzed urine data of nine 2-y cohorts (1999–2016) from the National Health and Nutrition Examination Survey (NHANES). Chemical daily intake rates (in milligrams per kilogram bodyweight per day) were inferred, using the R package bayesmarker, from metabolite concentrations in each cohort individually to identify exposure trends. Trends for metabolites and parents were clustered to find chemicals with similar exposure patterns. Exposure variation by age, gender, and body mass index were also assessed.

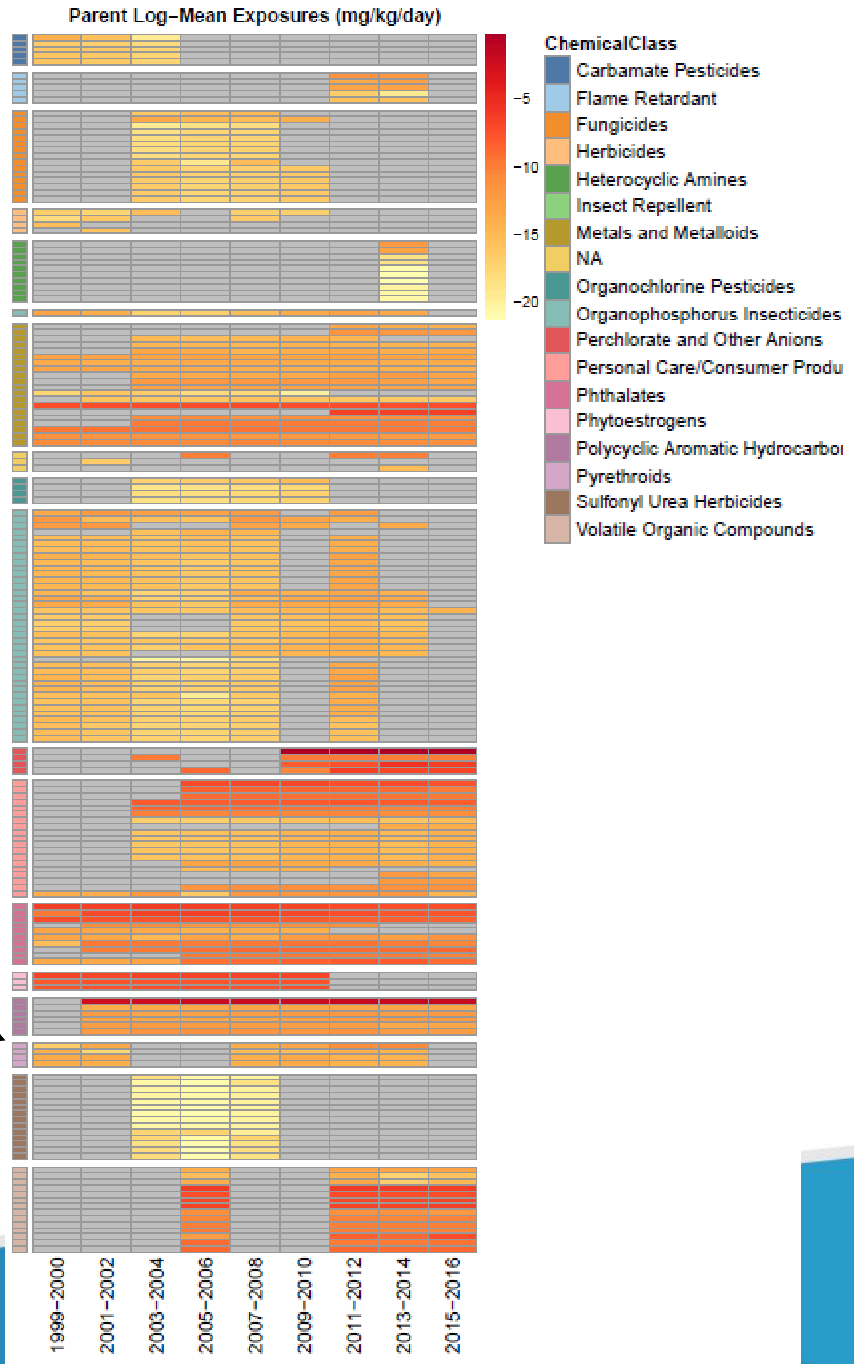
Results: Intake rates for 179 parent chemicals were inferred from 151 metabolites (96 measured in five or more cohorts). Seventeen metabolites and 44 parent chemicals exhibited fold-changes ≥ 10 between any two cohorts (deltamethrin, di-*n*-octyl phthalate, and di-isononyl phthalate had the greatest exposure increases). Di-2-ethylhexyl phthalate intake began decreasing in 2007, whereas both di-isobutyl and di-isononyl phthalate began increasing shortly before. Intake for four parabens was markedly higher in females, especially reproductive-age females, compared with males and children. Cadmium and arsenobetaine exhibited higher exposure for individuals >65 years of age and lower for individuals <20 years of age.

Discussion: With appropriate analysis, NHANES indicates trends in chemical exposures over the past two decades. Decreases in exposure are observable as the result of regulatory action, with some being accompanied by increases in replacement chemicals. Age- and gender-specific variations in exposure were observed for multiple chemicals. Continued estimation of demographic-specific exposures is needed to both monitor and identify potential vulnerable populations. https://doi.org/10.1289/EHP12188

Stanfield et al., 2024

Landscape of Chemical Exposure

- Exposure inference for 179 chemicals spanning 18 years
- Summary statistics
  - Median FC = 3.22
  - 44 with FC > 10
  - *Deltamethrin* had largest FC (increase; 369.91-fold or 2.57 orders of magnitude)



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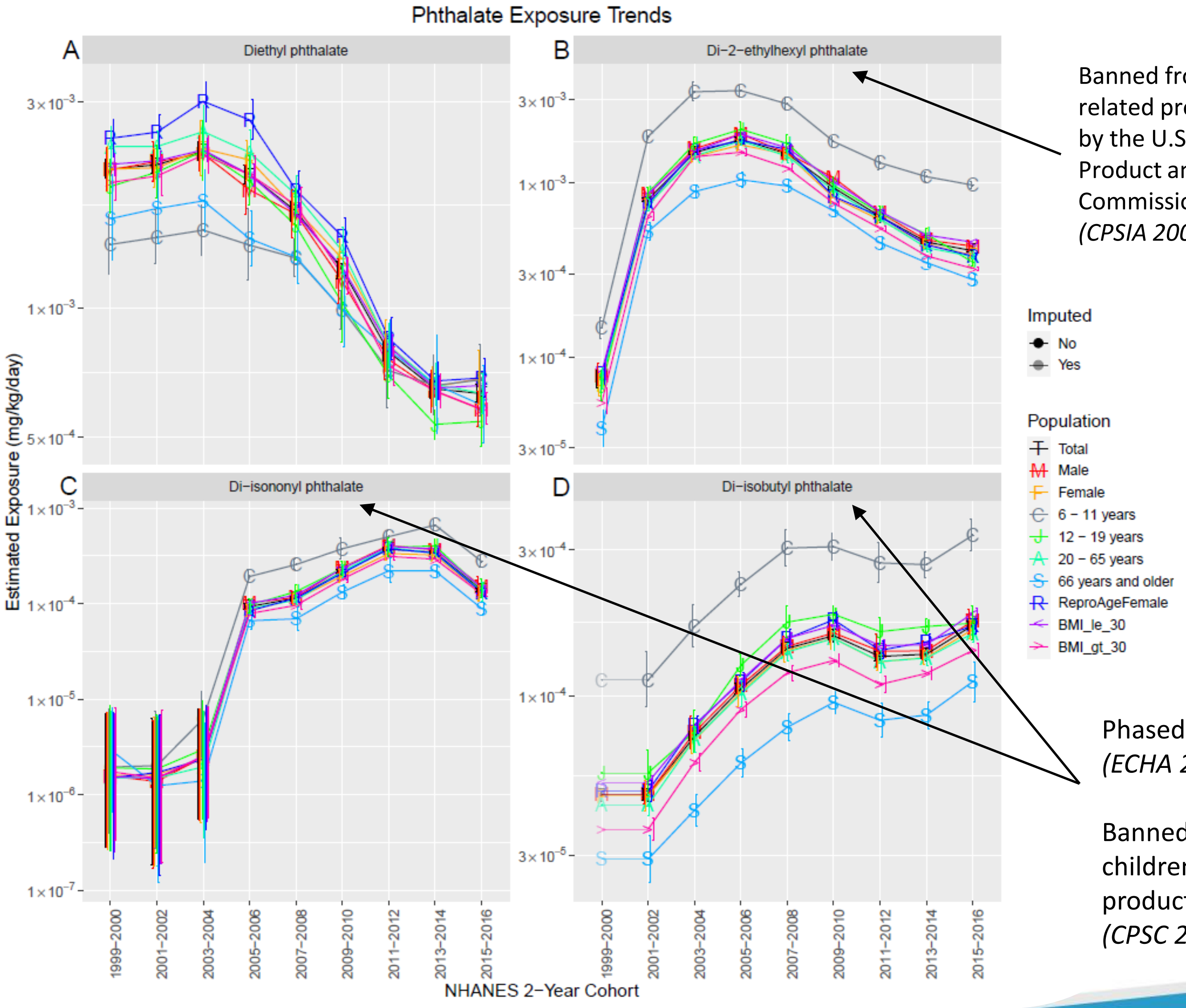
Phthalates

- Phthalates are used as plasticizers in a wide range of consumer goods such as
  - Food packaging
  - Vinyl flooring
  - Personal care products (soaps, shampoos, hair sprays, cosmetics)



Banned from children's related products in 2008 by the U.S. Consumer Product and Safety Commission (CPSC) *(CPSIA 2008)*

Phased into plastics *(ECHA 2010)*

Banned from children's related products in 2017 *(CPSC 2017)*

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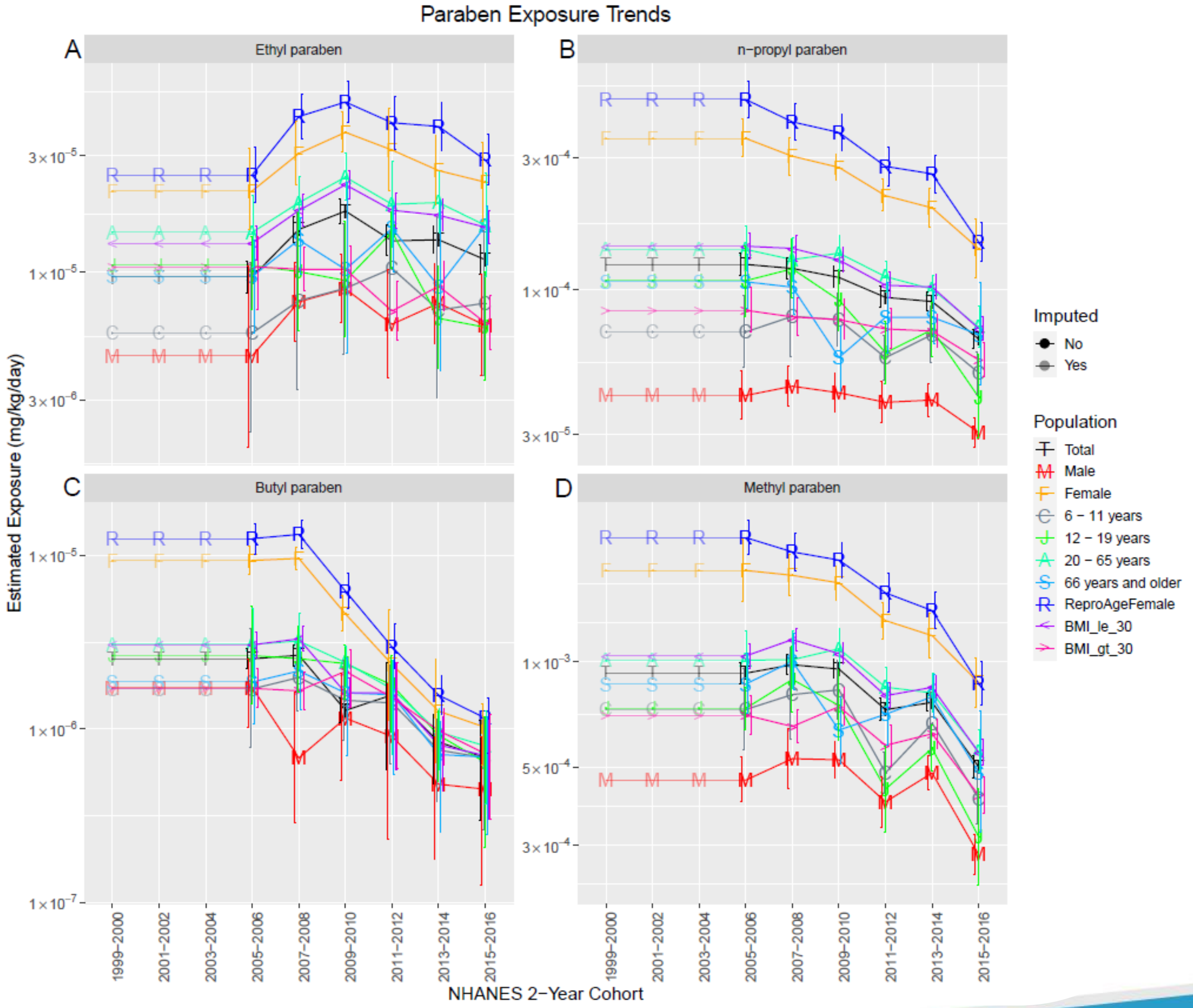
Parabens

- Parabens are primarily used as preservatives and antibacterial agents in cosmetics and other personal care products *(Shen et al., 2007)*
- Similar results seen for pregnant women in Puerto Rico *(Ashrap et al., 2018)*



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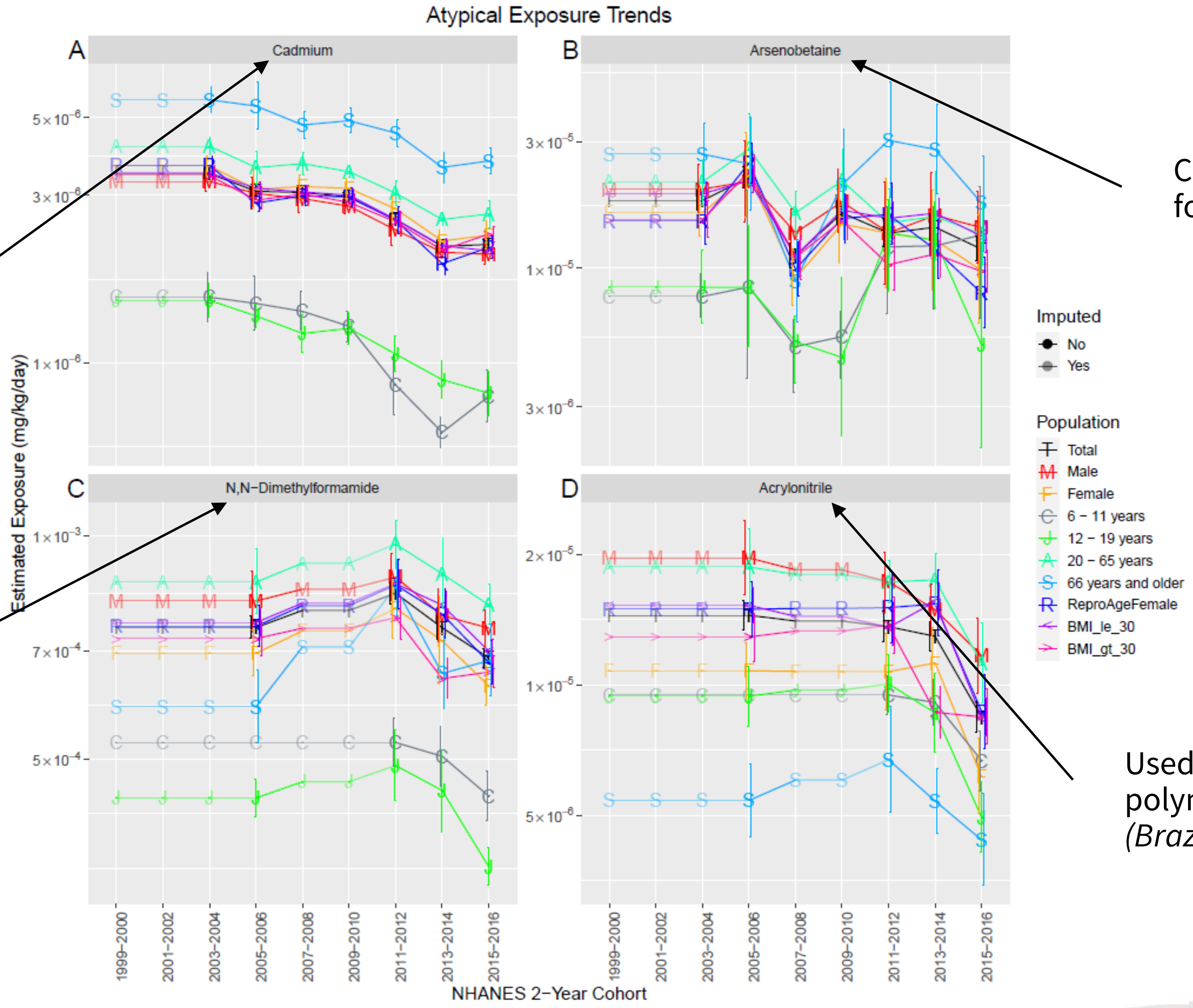
Age-Specific Exposures

Previously used in plating and pigments in the 1990s

Then used in batteries

Recalls of children's jewelry in 2010 due to high levels of cadmium *(CPSC 2010a; CPSC 2010b)*

A solvent used in production processes for a wide variety of products and practices, including preparation of polyacrylonitrile *(Bipp 2011)*



Commonly found in fish

Used for chemical and polymer production *(Brazdil 2012)*

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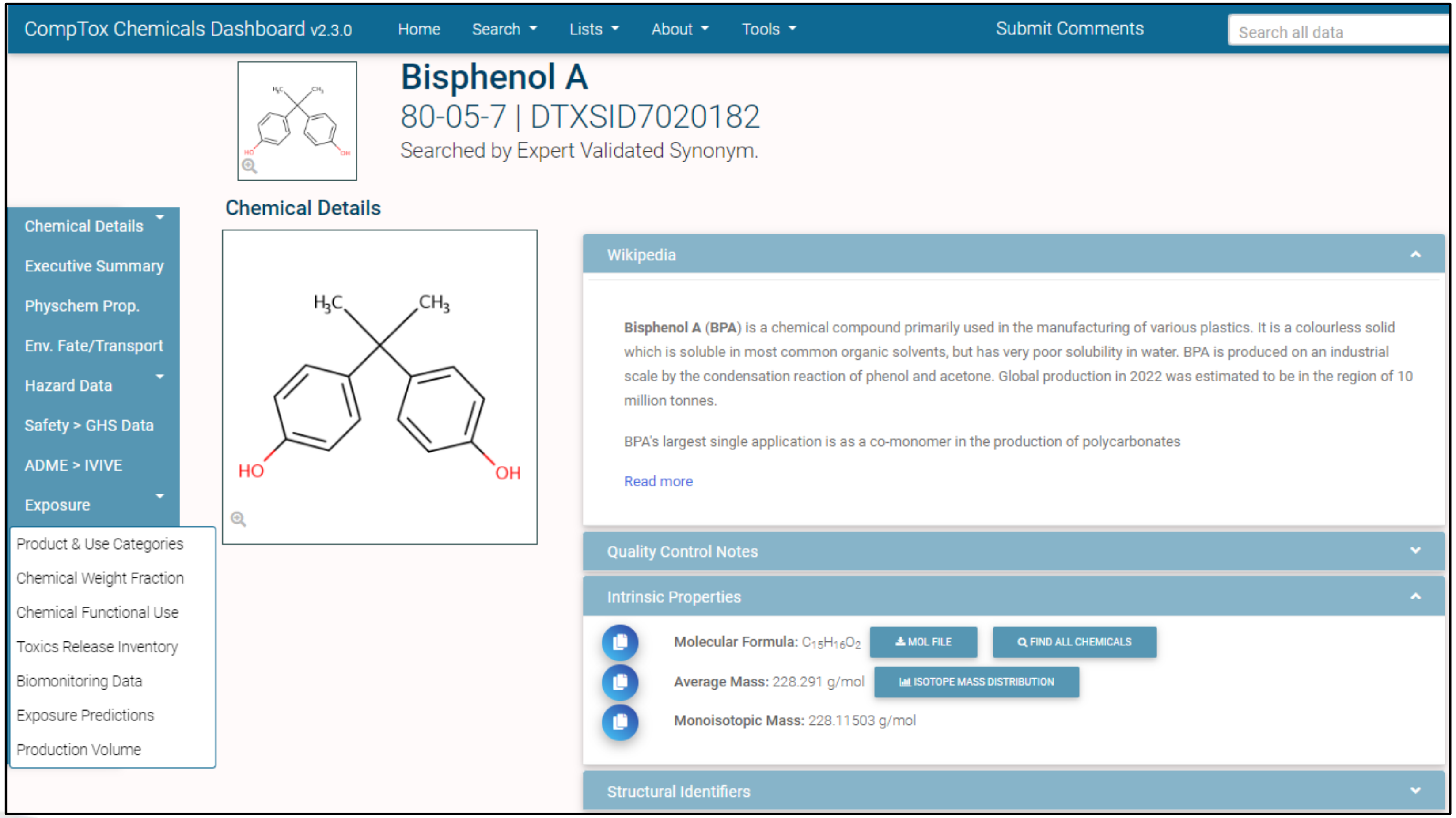
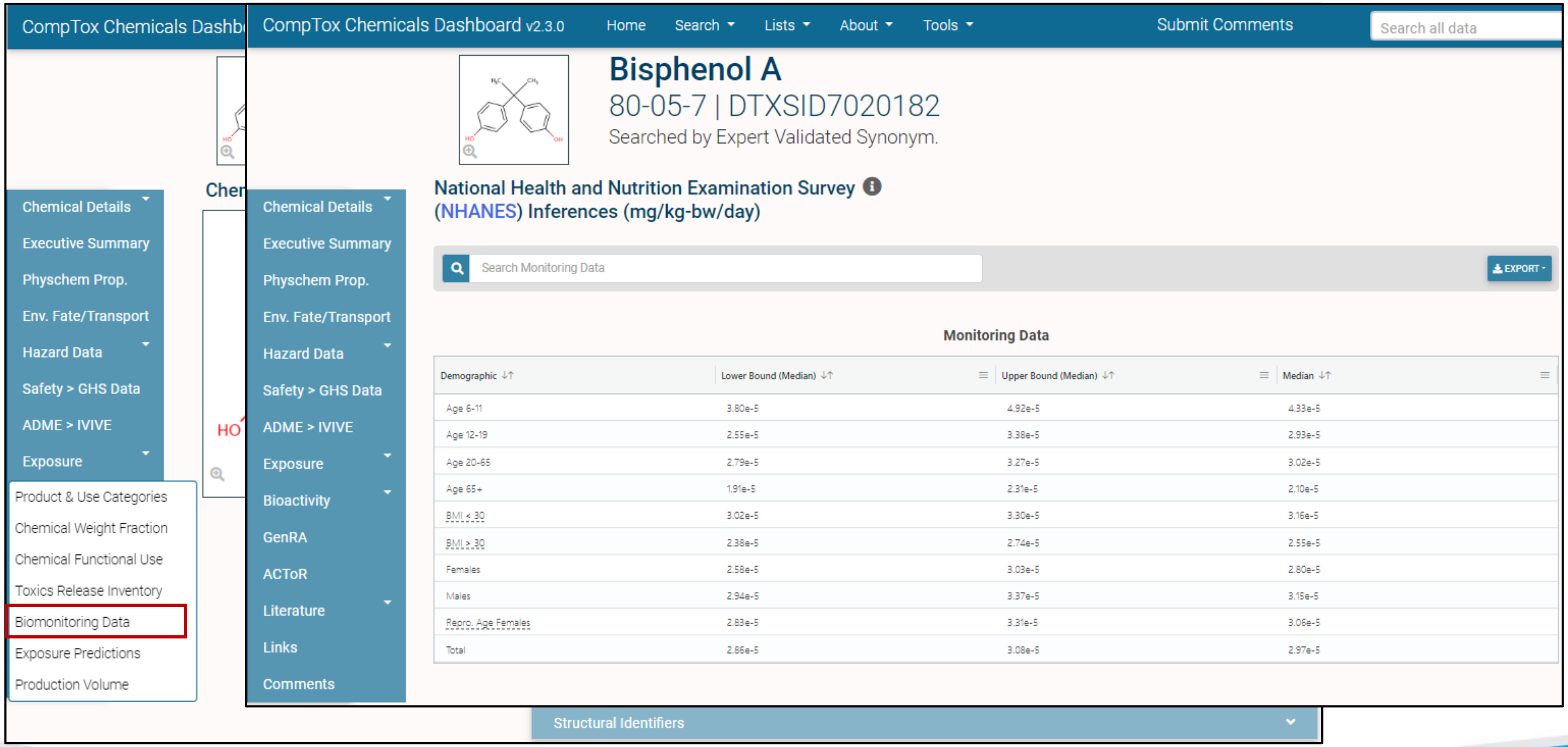
Where to Find Exposure Inferences



https://comptox.epa.gov/dashboard/

Where to Find Exposure Inferences



Demographic	Lower Bound (Median)	Upper Bound (Median)	Median
Age 6-11	3.80e-5	4.92e-5	4.33e-5
Age 12-19	2.55e-5	3.38e-5	2.93e-5
Age 20-65	2.79e-5	3.27e-5	3.02e-5
Age 65+	1.91e-5	2.31e-5	2.10e-5
BMI < 30	3.02e-5	3.30e-5	3.16e-5
BMI > 30	2.38e-5	2.74e-5	2.55e-5
Females	2.58e-5	3.03e-5	2.80e-5
Males	2.94e-5	3.37e-5	3.15e-5
Repro. Age Females	2.83e-5	3.31e-5	3.06e-5
Total	2.86e-5	3.08e-5	2.97e-5

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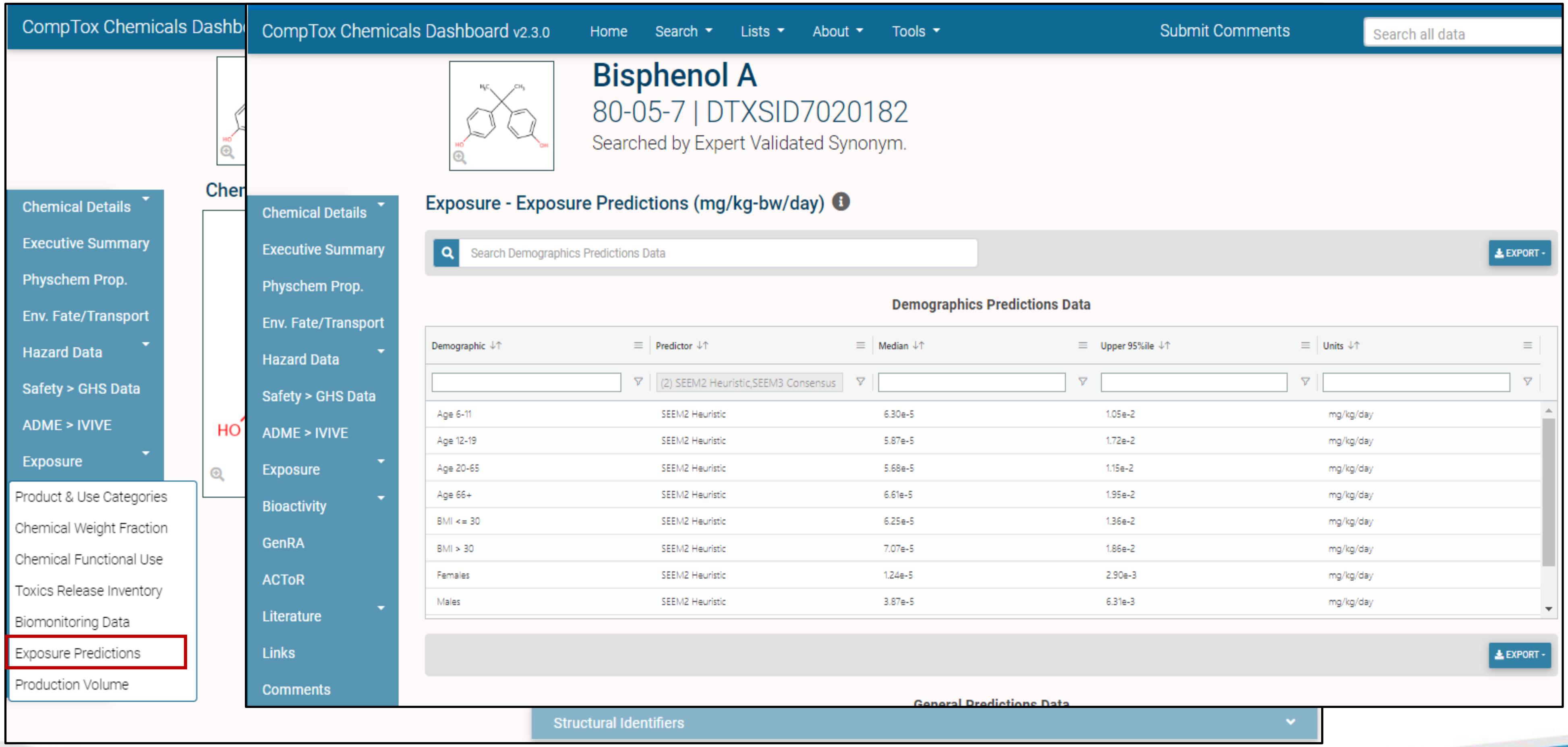

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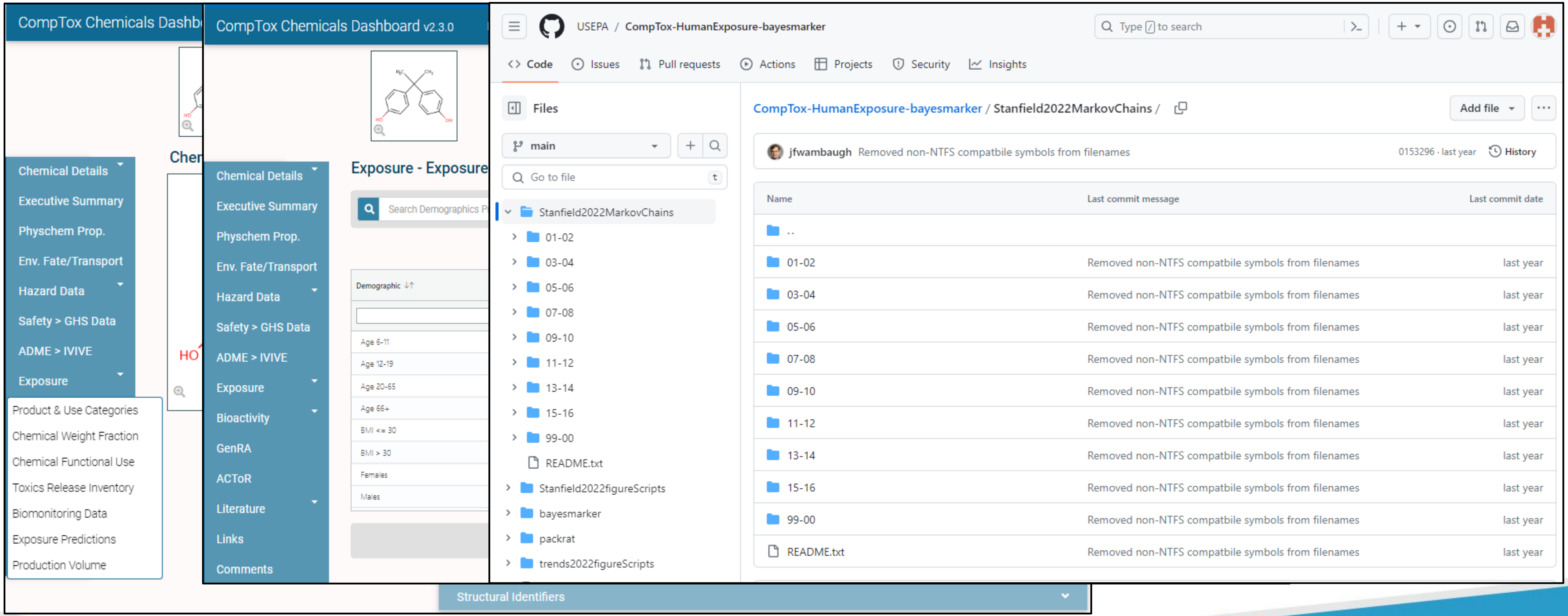

https://comptox.epa.gov/dashboard/

Summary

- A Bayesian inference approach was developed to provide higher-throughput exposure estimates based on measured data (for calibration of exposure models)
- Extended the data (cohorts, chemicals, metabolism links)
- Streamlined the pipeline in the form of the bayesmarker R package
- Extended analysis to examine trends of exposure based on the NHANES metabolite panel

Future Work

- Obtain exposure estimates using NHANES blood/serum concentrations (ongoing)
  - 76 chemicals (11 PFAS)
  - All cohorts (~5 per chemical on avg.) and same population groups
- Use new inferences in the development of SEEM4
  - Blood/serum and urine chemicals
  - Demographic-specific models

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Thank You!

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