Characterizing Exposure Trends from NHANES Urinary Biomonitoring Data

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ABSTRACT

- Knowing which environmental chemicals contribute to metabolites observed in humans is necessary for meaningful estimates of exposure and risk from biomonitoring data. It is also important to understand how these exposures might be changing over time.
- We employed a recently developed approach (a publicly available R package called "bayesmarker") using Bayesian methodology to infer ranges of exposure to parent compounds consistent with urinary biomarker levels reported in the National Health and Nutrition and Examination Survey (NHANES), which is representative of the U.S. population.
- Metabolites were linked to their parent chemicals using information from the NHANES reports and text mining of PubMed abstracts for metabolite names and synonyms.
- Chemical exposures were inferred for each NHANES cohort individually to identify temporal exposure trends for 179 unique parent chemicals of 151 NHANES metabolites.
- Exposure differences in population groups were also examined for unique patterns.

METHODS

The R package "bayesmarker" (github.com/USEPA/CompTox-HumanExposure-bayesmarker) is made up of 5 functions that are called in succession. The needed input is a single Excel file that has 3 tables, which are created manually based on the metabolites/cohorts of interest and organization of the NHANES data. Exposures are inferred by running the full modeling pipeline on each NHANES cohort individually from 1999-2016 to observe temporal changes in exposure. The output are exposure distributions via Markov chains for 10 different population groups based on age, gender, and body mass index. The package also allows for combining data from multiple cohorts to improve statistical power and reduce the uncertainty in exposure inferences. This was demonstrated by comparing changes in exposure using all data from 2000-2010 with data from 2011-2016.

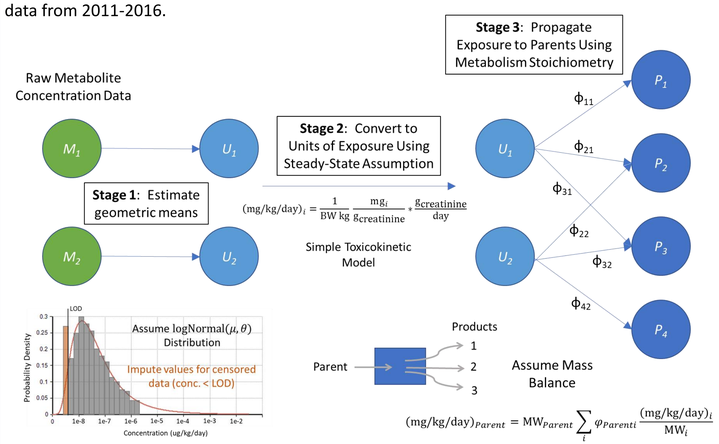

Figure 1. Depiction of the modeling pipeline used by bayesmarker. The statistical model has three stages: 1. Calculate distribution statistics (mean, standard deviation, etc.) for the population urine concentration measurements, 2. Convert to units of exposure via a simple toxicokinetic model assuming steady-state with creatinine correction, and 3. Propagate exposures from metabolites to parent chemicals using known metabolic links while assuming mass balance.

RESULTS

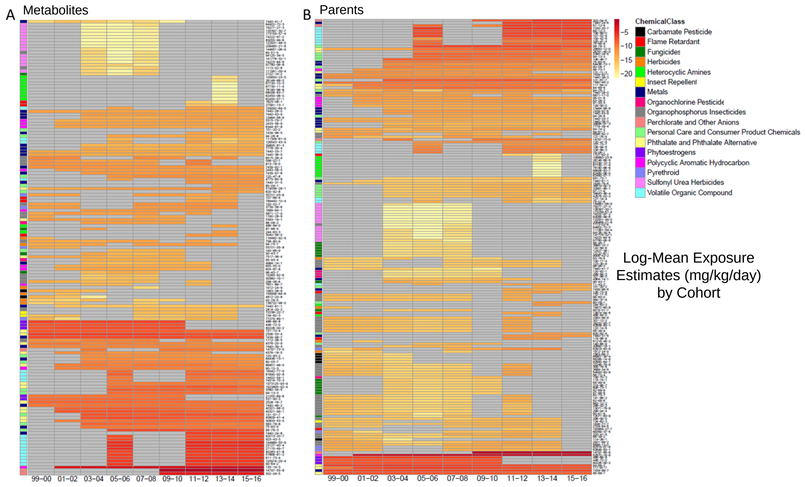

Figure 2. Estimated log-mean exposures in mg/kg bw/day of **A.** metabolites and **B.** parent chemicals from 1999 to 2016. The bayesmarker package was run for each NHANES cohort starting in 1999 to obtain geometric mean estimates in units of exposure for 151 metabolites and 179 parent chemicals. A grey cell indicates that metabolite was not measured in that cohort or none of a parent's metabolites were measured. Chemical class was obtained for metabolites from the NHANES report and propagated to the parent chemicals using a parent-metabolite map (the 3rd table of the package input file). Rows are clustered based on similarity in exposure profile.

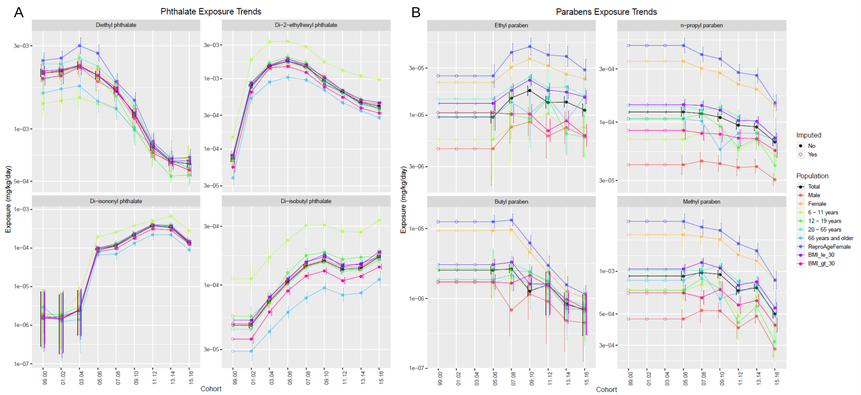

Figure 3. Exposure trends by population group for select **A.** phthalates and **B.** parabens. Geometric mean exposure estimates (mg/kg/day) with 95% confidence intervals shown as error bars. Missing data for cohorts were imputed based on surrounding non-missing data (propagation of oldest existing value backwards, newest existing value forwards, and average between two surrounding existing values.

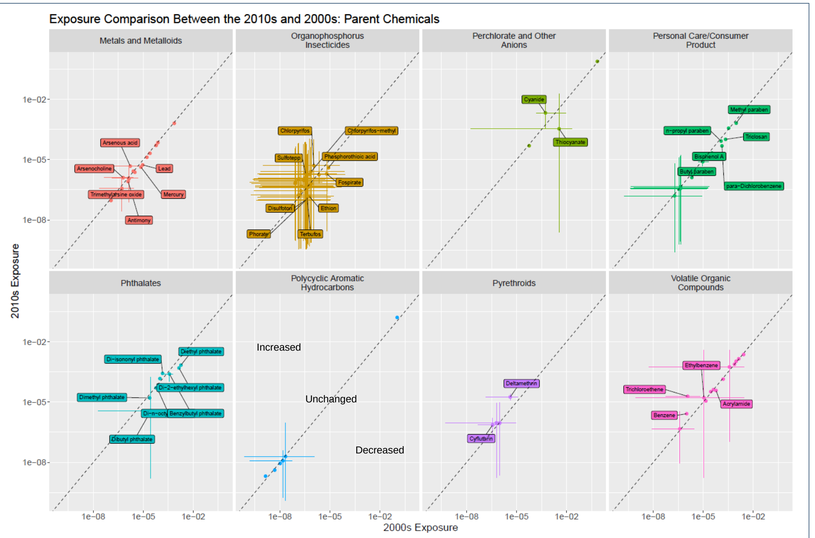

Figure 4. Decade comparison, 2000s versus 2010s, for estimated exposure means of parent chemicals. NHANES cohorts were combined by decade (for example, 11-12, 13-14, and 15-16 for 2010s) using the 2-year survey weights. Error bars indicate 95% confidence intervals. Chemicals on the dotted line indicate no change in exposure across decades, above the dotted line indicates higher exposure in the 2010s (increase), and below indicates higher exposure in the 2000s (decrease).

CONCLUSIONS AND FUTURE WORK

Conclusions

- Fully utilized the continuous NHANES survey resulting in an exposure landscape spanning the past decade and a half
- Observed a number of expected outcomes from these exposure trends:
  - Decreases in chemicals like triclosan, bisphenol A, and a number of metals
  - Decreases in a banned phthalates in the cohort after the regulation was made along with and increase in phthalates that were then used as alternatives
- Identified population-specific exposures for certain chemicals:
  - Parabens (used in cosmetics and consumer products) showed higher exposure to females and lower exposure to males
  - Higher exposure to chemicals used in production processes (e.g., N,N-Dimethyl-formamide and acrylonitrile) for working age individuals/males and lower for children
- Clustered chemicals by exposure patterns and prioritized chemicals by exposure trajectory

Future Work

- Update these exposure inferences over time by:
  - Incorporating new NHANES data that has been recently released (2017-2020)
  - Collecting more parent-metabolite links from the literature or metabolic modelling
- Expand the generality of bayesmarker to work with biomonitoring studies beyond NHANES
- Consider emerging technologies like non-targeted analysis (NTA) to move from a panel of biomarkers to a more complete view of aggregated exposure

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