Bayesian Inference of Chemical Exposures from NHANES Biomonitoring Data

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ABSTRACT

- Biomonitoring data provides insight into the chemicals, and their concentrations, commonly present in humans, but it is also important to know which chemicals in the environment contribute to the observed metabolites for the sake of estimating exposure and risk.
- Here we used Bayesian methodology to infer ranges of exposure for parent chemicals consistent with biomarkers identified in urine samples from the U.S population by the National Health and Nutrition Examination Survey (NHANES).
- Metabolites were linked to their parent chemicals using information from the NHANES reports and text mining of PubMed abstracts for metabolite names and synonyms.
- We calculated chemical exposure and risk estimates for various population groups.
- We investigated exposure to children between the ages of 0 and 5, a population group that was debuted in the 2015-2016 NHANES cohort (measurement data for 50 metabolites).

METHODS

This work is an update to the method presented in Wambaugh et al 2014. Briefly, metabolite urine concentration measurements from NHANES (CDC 2016) are used in a Bayesian inference model to estimate mean parent chemical exposures across various population groups. NHANES data from 2011-2016 were added and the code has been converted into an R package that will be made public. Results were generated using data available from the most recent cohort to obtain the current exposure estimates. The functions calc_tkstats() and calc_mc_css() from the HTTK package (Pearce et al 2017) were used to obtain bioactivity:exposure (BER) ratios.

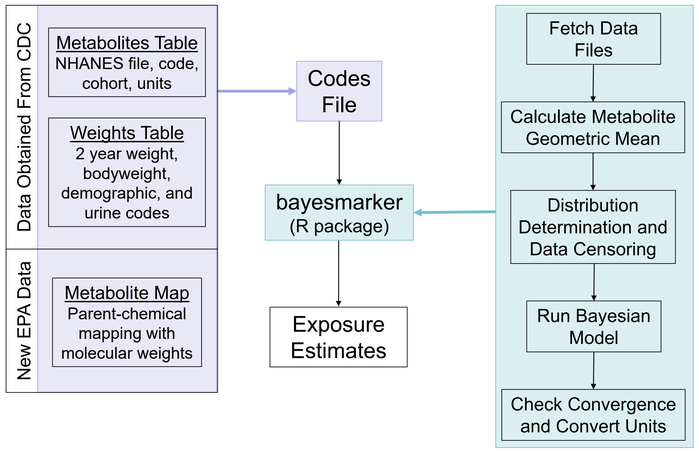

Figure 1. Depiction of general workflow for the bayesmarker R package (in production). The input dataset is a single Excel file that has 3 sheets (tables; described in the purple box). These tables are created manually based on which metabolites/cohorts are of interest and how the NHANES data is organized. The NHANES survey weights are needed to translate from their oversampling procedure to represent the modern U.S. population. The package has 5 major functions (descriptions in green box). The number of metabolites was increased from 68 (Wambaugh et al 2014) to 151 (measured in at least one cohort) and the number of parent chemicals increased from 106 to 179 via 270 links to metabolites.

RESULTS

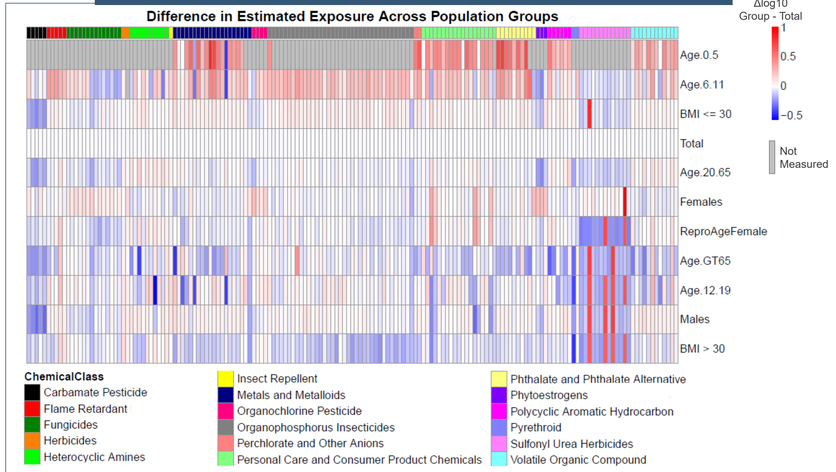

Figure 2. Difference in inferred chemical exposure between each population group and the total population. Chemicals are arranged by class (indicated on the top of the heatmap). Estimates were calculated using the most recent NHANES cohort for each metabolite. The log10 difference in exposure from a population group and all individuals is shown. Red indicates higher exposure, blue lower exposure. Chemicals with an insufficient number of observations above the limit of detection (LOD) and were removed.

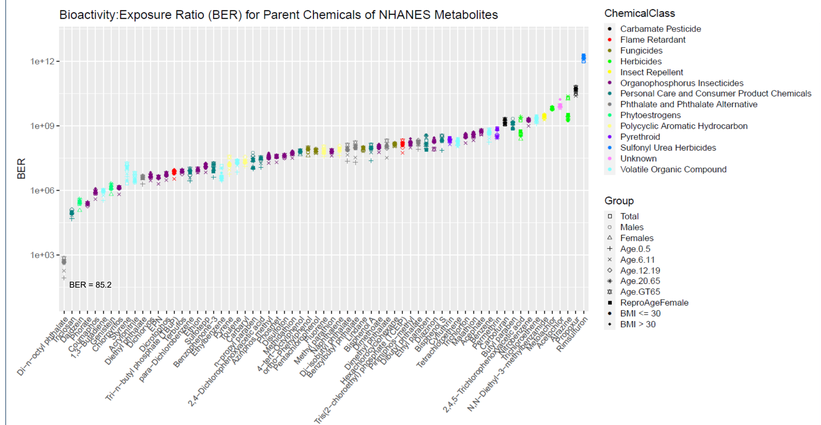

Figure 3. Inferred bioactivity:exposure ratios (BERs) for parent chemicals of NHANES metabolites. BER = human equivalent dose (HED)/exposure. HED is the human dose of a chemical that is expected to induce the same magnitude of toxic effect as the experimental animal dose, calculated here using rat oral LD50 values (LD50 is the concentration which causes the death of 50% of a group of test animals). The exposure value was obtained by scaling our exposure estimates by each chemical's predicted steady state concentration. Chemicals with smaller BERs are of more interest as the inferred exposure is closer to the concentration at which bioactivity occurs. Points indicate population group by shape and chemical class by color.

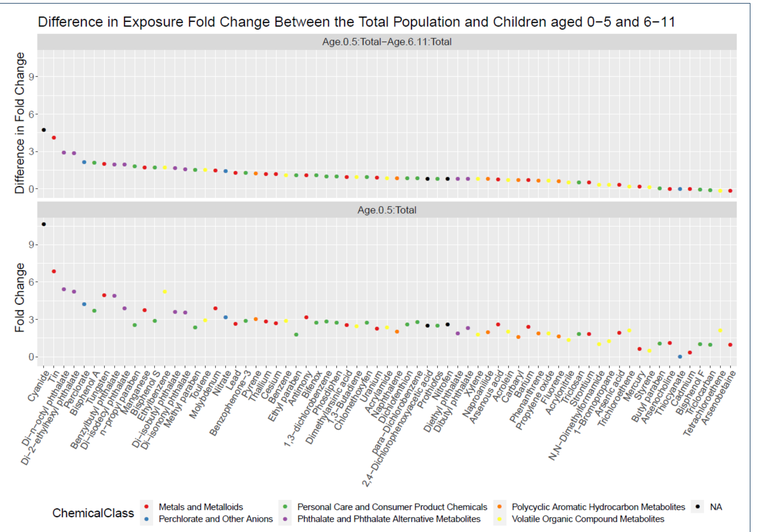

Figure 4. Examination of the new population group, 0 – 5-year-olds, introduced in the 2015-2016 NHANES cohort. The top plot shows the difference in two exposure comparisons (fold change): 1. 0-5 vs. Total and 2. 6-11 vs. Total, where chemicals are sorted from left to right by greatest difference. The bottom plot shows the fold change between 0 – 5-year-olds and all individuals. Chemicals are colored by the class of their metabolites (NA if from more than one class).

CONCLUSIONS AND FUTURE WORK

Conclusions

- Our updates resulted in 83 additional metabolites and 73 new parent chemical estimates.
- Certain population groups have higher or lower estimated exposure for various chemicals (e.g., higher exposure to Phytoestrogens for females).
- Bioactivity:exposure ratios ranged from 85.2 (Di-n-octyl phthalate) to about 1e+12 and helps us prioritize exposure to chemicals whose metabolites appear in urine.
- Exposure to children is typically higher than the rest of the population, and this trend was confirmed using the new 0 – 5 years population group in the 15-16 NHANES cohort. We identified chemicals that were most important for this group by comparing to 0 – 6-year-olds.

Future Work

- Publicly release bayesmarker package on GitHub (then possibly CRAN)
- Add additional analysis options (vignettes) to the package
- Run analysis for all NHANES cohorts to observe exposure changes of parents and metabolites over time as well as perform exposure forecasting and data combination across cohorts.

References

1. Wambaugh, J. F., Wang, A., Dionisio, K. L., Frame, A., Egeghy, P., Judson, R., & Setzer, R. W. (2014). High throughput heuristics for prioritizing human exposure to environmental chemicals. Environmental science & technology, 48(21), 12760-12767.
2. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2016, https://www.cdc.gov/nchs/nhanes/index.htm.
3. Pearce RG, Setzer RW, Strope CL, Sipes NS, Wambaugh JF (2017). "httk: R Package for High-Throughput Toxicokinetics." Journal of Statistical Software, 79(4), 1–25. doi: 10.18637/jss.v079.i04.

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