PLEASE READ THIS DOCUMENT PRIOR TO THE WORKSHOP BREAKOUT SESSION

Use-Case 2: Combine individual level data from multiple independent studies to understand (with increased statistical power) how exposures X+Y impact health outcome Z

We will work through 1-2 mock harmonizations. For each mock harmonization, we have multiple studies that are eligible for data harmonization and subsequent pooling to conduct an analysis. We will not use all variables but all are provided in datasets to facilitate discussion. During the harmonization process, we will:

1. Review existing metadata including text descriptions and data dictionaries to assess completeness of what is currently reported by studies. This includes both variable and study information.
2. Identify minimum amount of metadata needed to harmonize data with focus on descriptors of study design and potential differences across demographic and biomarker-based exposures.
3. Discuss sources of data standards that could be used within metadata templates to facilitate harmonization, sharing and application of semantic-enabled technologies such as ontologies
4. Develop strategies to increase the adoption of metadata and data standards when describing existing datasets to facilitate harmonization and sharing

For each study, we have a short, free-text description of the individual study, data dictionaries and abridged datasets. File names for data dictionaries and datasets are listed under each study. Each dataset, limited to 20 observations, is provided to illustrate the structure of the data for that particular study. Changes have been made to these study materials to aid in the development of this use-case. Thus, these documents will not match what is publicly available on the HHEAR Data Repository.

Harmonization Example #1: Metals Exposure in Pregnancy and Birth Outcomes in Offspring

In this example, our goal is to determine if we can pool data to investigate whether metals exposure assessed in pregnancy is associated with greater risk of adverse birth outcomes in offspring. We have three potential studies to include and we will assess whether data can be harmonized and pooled.

Variables to consider for harmonization:

Metals exposure (multiple elements) measured in pregnancy
Birth weight
Gestational age
Maternal covariates that may induce confounding or be modifiers of interest

Harmonization Example #2: Childhood Phthalate Exposure and Childhood Asthma

In this example, our goal is to determine if we can pool data to investigate whether phthalate exposure in childhood is associated with increased incidence of asthma and/or asthma exacerbations. Here, we have two potential studies to include and we will assess whether data can be harmonized and pooled.

Variables to consider for harmonization:

Phthalates Exposure (multiple metabolites) measured in childhood
Measures of childhood asthma status
Measures of childhood asthma exacerbations
Measures of childhood asthma severity
Child covariates that may induce confounding or be modifiers of interest

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Harmonization Example #1: Metals Exposure in Pregnancy and Birth Outcomes in Offspring

Study 1

2016-34: Relating metals exposure to birth and early childhood outcomes via the metabotype of cord blood.

The study will study metals exposure in pregnant mothers to birth and early childhood outcomes in a Bangladeshi birth cohort. We will assess differences in anthropomorphic birth outcomes based on cord blood metabolite profiles acquired using a targeted 1H NMR-based platform. We will utilize established as well as novel analytic approaches in the field of metabolomics.

Files:

Data Dictionaries: 2016-34-DD-DemoHealth and 2016-34-DD-Metals
Datasets: 2016-34-DemoHealth and 2016-34-Metals

Study 2

2016-1740: Mitochondrial DNA biomarkers of prenatal metal mixture exposure: intergenerational inheritance and infant growth

Project Viva is a prospective pre-birth cohort of mother-infant pairs, recruited in Eastern Massachusetts between 1999 and 2002 during the first prenatal visit at Atrius Harvard Vanguard Medical Associates. In-person visits with mothers were completed during the first (median 9.9 weeks of gestation) and second trimesters (median 27.9 weeks). We saw mothers and children in the hospital during the delivery admission and during infancy (median age 6.3 months). Follow-up visits have been completed in early childhood (median 3.2 years), mid-childhood (median 7.7 years), early adolescence (median 12.9 years) and currently a teenage follow-up visit is underway. Information was collected from mothers via interviews and questionnaires, performed anthropometric and neurodevelopmental assessments in children and collected bio-specimens in pregnancy and at each study visit. Our objective for this project is to evaluate whether maternal prenatal exposure to metal mixtures in early pregnancy can disrupt molecular markers of mitochondrial DNA damage and abundance in mothers and children as a key mediator of metabolism and infant growth. Project Viva website: https://www.hms.harvard.edu/viva

Files:

Data Dictionaries: 2016-1740-DD-DemoHealth and 2016-1740-DD-Metals
Datasets: 2016-1740-DemoHealth and 2016-1740-Metals

Study 3

2017-1945: Maternal and developmental risks from environmental and social stressors (MADRES)

The approved CHEAR project focuses on 250 participants from the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) study, which is a low-income predominately Hispanic pregnancy cohort in Los Angeles that was designed to evaluate the impacts of early life exposures to stress and environmental contaminants on obesity risk. The MADRES study began in 2015. Women and their infants are followed from early pregnancy through the first year of life. The objective of the project is to investigate the impacts of prenatal metal mixture exposures on newborn methylation patterns and birth weight, an important risk factor for long-term health. We will measure a panel of 21 metals in 1st and 3rd trimester urine samples and will additionally measure the cord blood CD4+ methylome, using whole genome bisulfite sequencing, in a smaller subset of participants (N = 30).

Files:

Data Dictionaries: 2017-1945-DD-DemoHealth and 2017-1945-DD-Metals
Datasets: 2017-1945-DemoHealth and 2017-1945-Metals

Harmonization Example #2: Childhood Phthalate Exposure and Childhood Asthma

Study Descriptions

Study 4

2016-1407: Pediatric Inner-City Environmental Exposures at school and home and asthma study

Asthma affects 25 million Americans, particularly urban minority children. Children spend nearly all day in school, yet little is known about the role of a child's exposure to widely disseminated industrial chemicals on asthma morbidity. Early animal models and population studies have begun to identify an association between phenolic chemical exposure and asthma development through proposed increased regulation of an individual's allergic immune response. The study population consists of urban school children with physician diagnosis of asthma ages 4 through 13 from the Northeastern United States. In a cross sectional study, we hypothesize that exposure to environmental exposures (e.g. phenols, phthalates, and environmental tobacco smoke) in urban school children and higher urinary biomarkers will preliminarily be associated with higher asthma morbidity. This study, nested within a school-based environmental intervention trial, (School Inner-City Asthma Intervention Study, SICAS2 U01 AI 110397), will evaluate the impact of environmental and personal care product use exposures on these biomarker levels and the impact that these exposures have on asthma morbidity, controlling comprehensively for other personal, home, and school environmental factors associated with asthma outcomes.

Files:

Data Dictionaries: 2016-1407-DD-DemoHealth and 2016-1407-DD-Phthalates
Datasets: 2016-1407-DemoHealth and 2016-1407-Phthalates

Study 5

2016-1450: Denver Asthma Panel Study

Urban environments are a poorly understood toxic environment for children with asthma. In order to develop effective therapies and interventions, improved characterization of exposures and exposure-health outcome relationships is needed. The Denver Asthma Panel Study (DAPS), which began in 2014, is the parent study for this project. The goal of DAPS was to investigate the relationships between asthma-relevant environmental exposures and asthma severity in an urban cohort of children, ages 8-16 years, with exacerbation-prone asthma. Personal and bedroom environmental exposures (particulate matter < 10 µm in diameter, ozone, and nitrogen dioxide) and asthma severity outcomes (lung function, exacerbations, inflammation, and control) were measured seasonally over the course of one year in the Denver metro area. A total of 68 participants were enrolled: 56 exacerbation-prone asthmatics and 12 control participants without allergies or asthma. Combined, the participants were 35 female, 69 Latino/Hispanic, 10 American Indian/Alaskan Native, 1 Asian, 19 Black/African American, 46 white, and 13 more than one race. The median age and annual household income was 11 years and $20,000–$24,999, respectively. The goal of this study is to expand our investigation of how asthma-relevant exposures (tobacco smoke, polycyclic aromatic hydrocarbons, phthalates, volatile organic compounds, and other exposure-related metabolites) impact asthma severity and biological responses (oxidative stress, cytokines, inflammatory markers, and other related metabolites).

Files:

Data Dictionaries: 2016-1450-DD-DemoHealth
Datasets: 2016-1450-DemoHealth and 2016-1450-Phthalates