# The Use of Risk-Screening Environmental Indicators (RSEI) in Health Research

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# Outline

- ☑ Background
  - ☑ Terminology
  - ☑ HDP Overview
  - ☑ Geospatial trends of HDP
- ☑ Methods

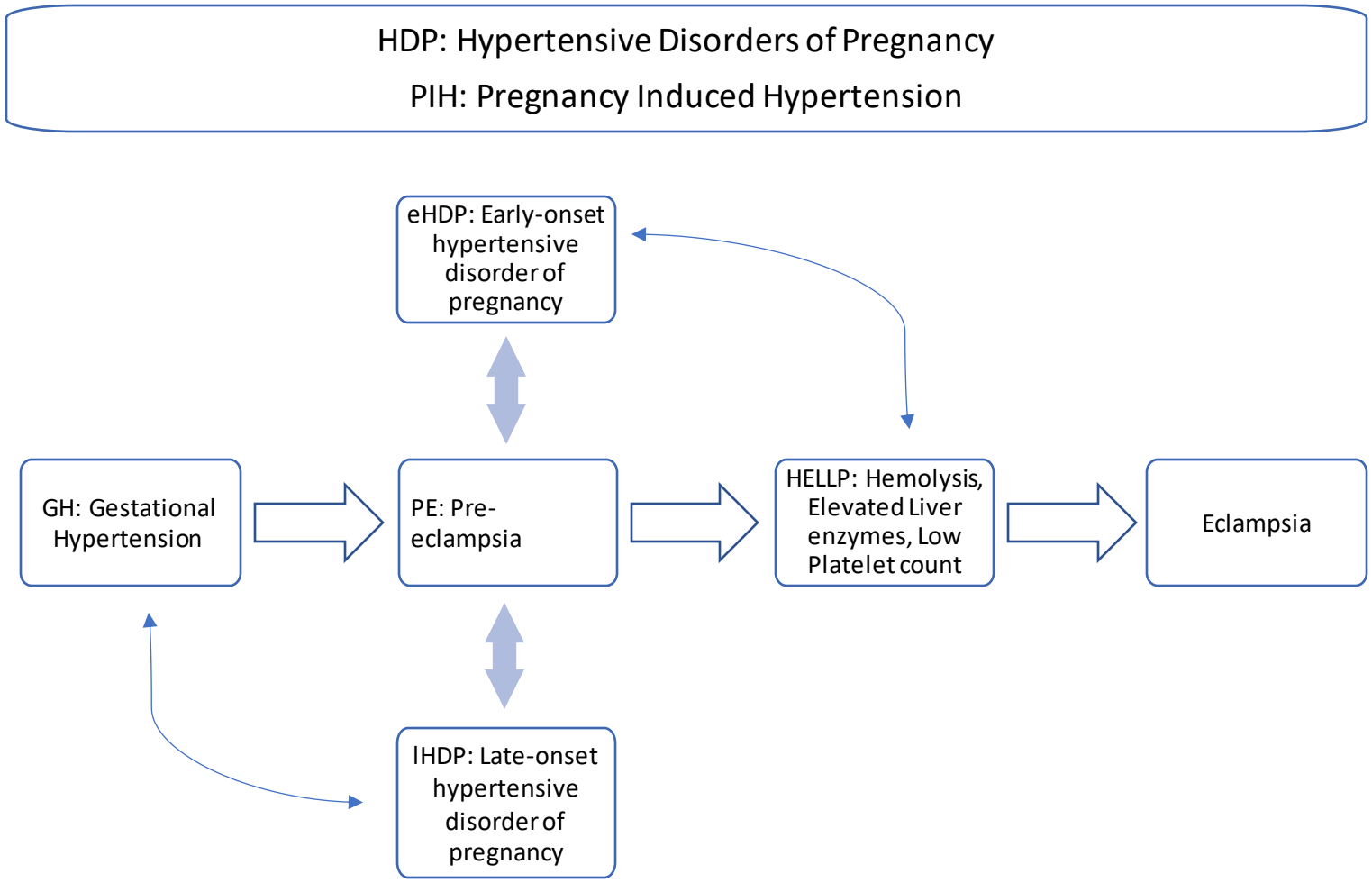
- ☑ Findings
- ☑ Conclusions
- ☑ Future directions

# HDP Overview

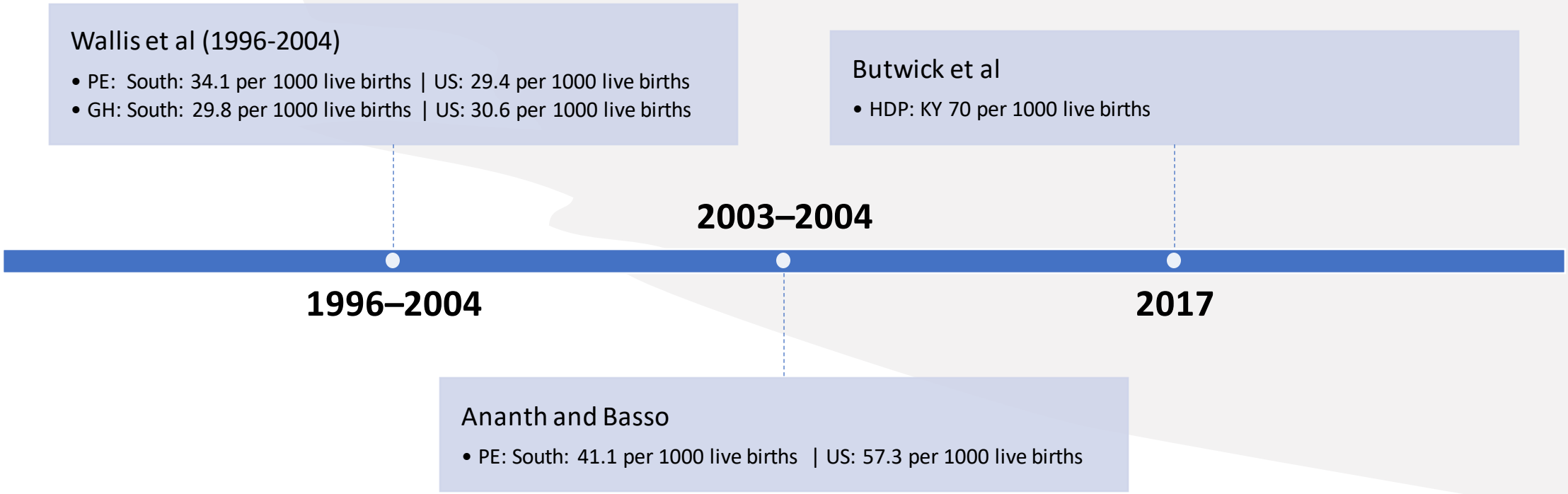
- Hypertension during pregnancy is one of the most common causes of both maternal and perinatal morbidity and mortality
  - Impacts 8-10% of pregnancies in the US each year
  - Associated with 6.6% of maternal deaths in the US, 2014-2017
- Preliminary evidence suggests that gestational age of onset may indicate distinctive diseases.
- Treatment options are limited
  - Untreated can lead to maternal organ failure, seizure, stroke, or death
  - Drug regimens are limited and often **ineffective**
  - Current treatment can lead to the birth of a premature infant

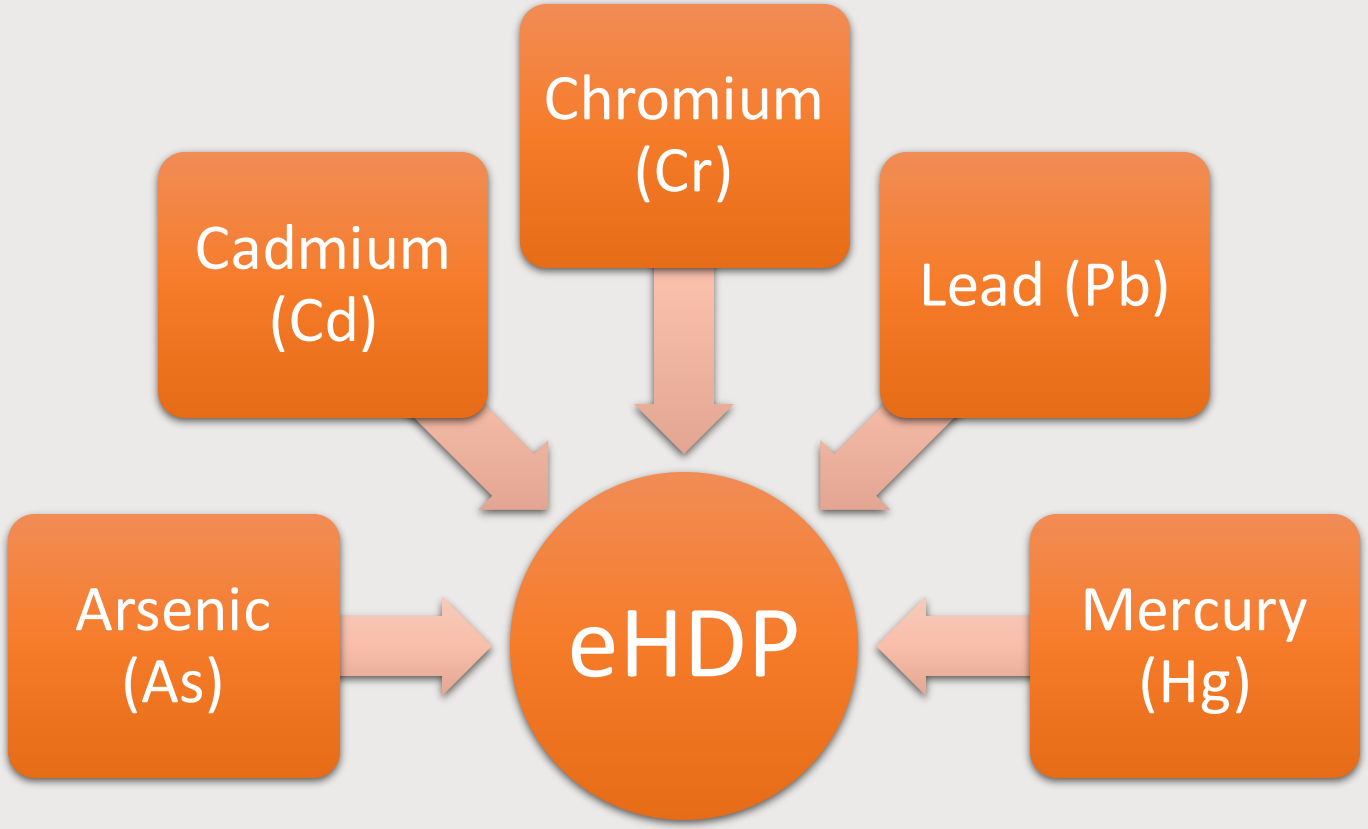
| Established maternal risk factor for HDP | | |
|---|---|---|
| **Demographic Characteristics** | - | **Obesity**<br>- **Maternal Age** |
| **Pre-existing health conditions** | - | **Chronic hypertension**<br>- Renal Disease<br>- Family history of PE<br>- Type I and Type II **diabetes**<br>- Lupus |
| **Pregnancy factors** | - | **Primiparity**<br>- Previous HDP pregnancy<br>- **Multifetal pregnancy**<br>- **Infertility treatment** |
| **Partner characteristics** | - | Fathered a previous preeclamptic pregnancy<br>- Length of sexual relationship |

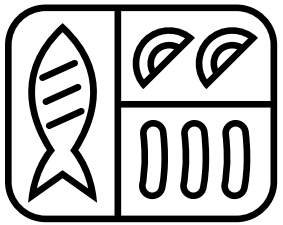
# Terminology

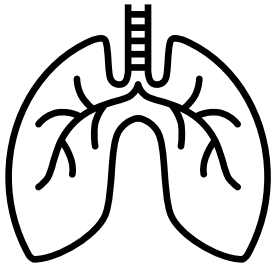


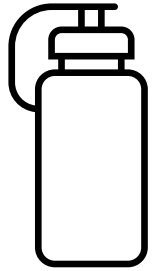
# Geospatial Trends of HDP




Chromium (Cr)
Cadmium (Cd)
Lead (Pb)
Arsenic (As)
eHDP
Mercury (Hg)







# Specific Aims

01

Examine the distribution of emissions of COCs and potential overlaps with eHDP clusters using an LCA.

02

Describe demographic characteristics of the exposed & eHDP cases

03

Identify demographic / environmental covariates associated with eHDP

04

Assess individual level geospatial trends of disease

# Methods: Data Sources

UK Medical IRB and Ky CHFS IRB approved research

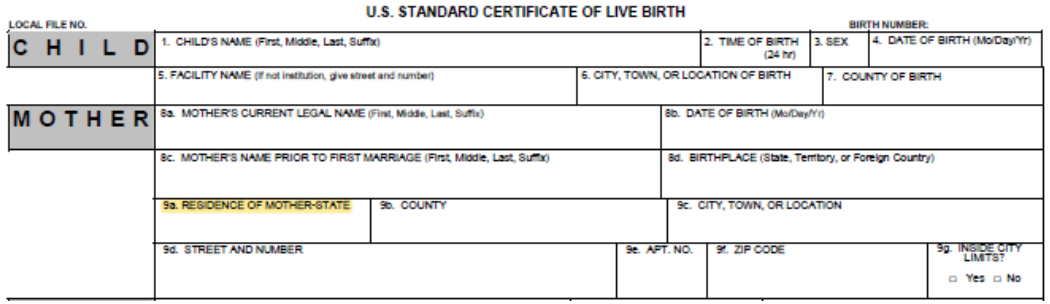
RUCC:  US DEPT OF AGRICULTURE

CARTOGRAPHIC BOUNDARY FILES: UNITED STATES CENSUS BUREAU

2003 US STANDARD CERTIFICATE OF LIVE & STILLBIRTH, 2008-2017

RISK SCREENING ENVIRONMENTAL INDICATOR (RSEI MODEL) 2007-2017

# Methods: Data



U.S. STANDARD CERTIFICATE OF LIVE BIRTH

LOCAL FILE NO. BIRTH NUMBER:

**CHILD**

1. CHILD'S NAME (First, Middle, Last, Suffix) | 2. TIME OF BIRTH (24 hr) | 3. SEX | 4. DATE OF BIRTH (Mo/Day/Yr)

5. FACILITY NAME (If not institution, give street and number) | 6. CITY, TOWN, OR LOCATION OF BIRTH | 7. COUNTY OF BIRTH

**MOTHER**

8a. MOTHER'S CURRENT LEGAL NAME (First, Middle, Last, Suffix) | 8b. DATE OF BIRTH (Mo/Day/Yr)

8c. MOTHER'S NAME PRIOR TO FIRST MARRIAGE (First, Middle, Last, Suffix) | 8d. BIRTHPLACE (State, Territory, or Foreign Country)

9a. RESIDENCE OF MOTHER-STATE | 9b. COUNTY | 9c. CITY, TOWN, OR LOCATION

9d. STREET AND NUMBER | 9e. APT. NO. | 9f. ZIP CODE | 9g. INSIDE CITY LIMITS? ☐ Yes ☐ No

COMMONWEALTH OF KENTUCKY

REGISTRAR OF VITAL STATISTICS

CERTIFIED RECORD OF BIRTH

Kentucky

FILE NO. [redacted] COUNTY OF BIRTH: [redacted]

CHILD'S NAME: ELLIOT [redacted]

CHILD'S DATE OF BIRTH: APRIL 08, [redacted] SEX: MALE

MOTHER'S MAIDEN NAME: COURTNEY [redacted]

MOTHER'S AGE: [redacted]

FATHER'S NAME: TRAVIS [redacted]

FATHER'S AGE: [redacted]

DATE FILED BY REGISTRAR: [redacted]

This record certifies that the above birth occurred on the date and place shown. The original certificate of birth is registered at the Kentucky Office of Vital Statistics under the file number shown.

DATE ISSUED [redacted]

Christina S. Stewart

State Registrar

DOCUMENT CONTAINS A WATERMARK – HOLD UP TO LIGHT TO VIEW

Birth records to Kentucky residents were obtained from Kentucky Vital Statistics (2003 US Standard Certificate of Live & Stillbirth, 2008-2017)

(N=556,744)

Excluded (n=342,754)

- Chronic Hypertension (n=10,752)
- Non-primaparious records (n=327,759)
- Multifetal pregnancy (n=5,206)
- Extreme maternal ages (<11 and>50) (n=215)
- Extreme gestational ages at birth (<20 or >45) (n=565)
- Unknown child sex (n=20)
- Unknown geocode (n=3)
- Geocoded outside of the state (n=473)

Primiparous singleton live births that occurred between 20-42 weeks that occurred to women aged 11-50 (N=212,527)

# Methods: Overview

Cross sectional study

**Mapping**

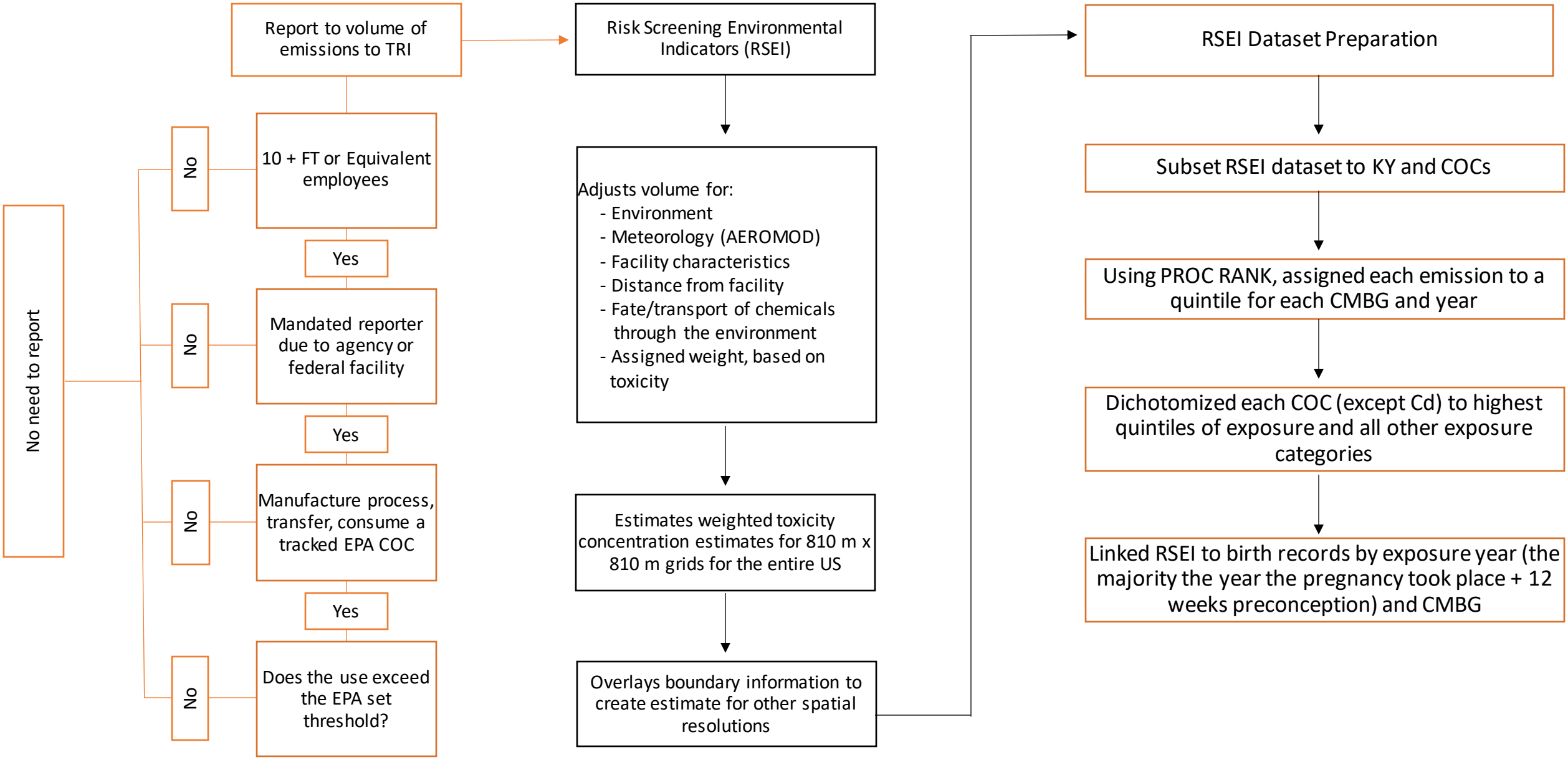
- Median toxicity concentrations of metals for each census micro-block group, Kentucky 2007-2017
- Spatial Analysis of eHDP (Bernoulli Model | Individual level Spatial Scan)

**Statistical analysis**

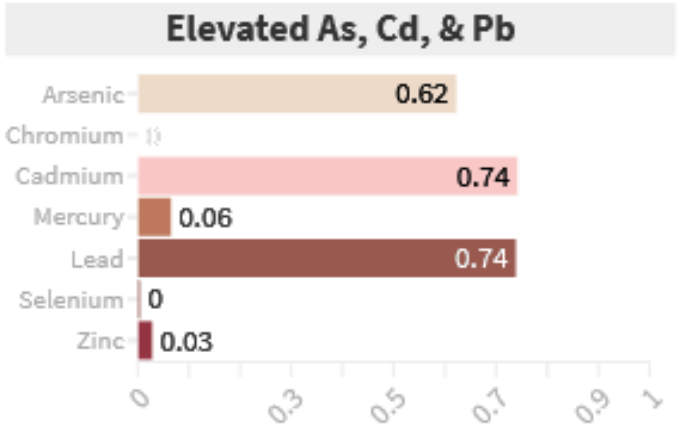
- Summarized demographic characteristics for the total population and by latent exposure class
- Logistic regression for both bivariable and multivariable relationships

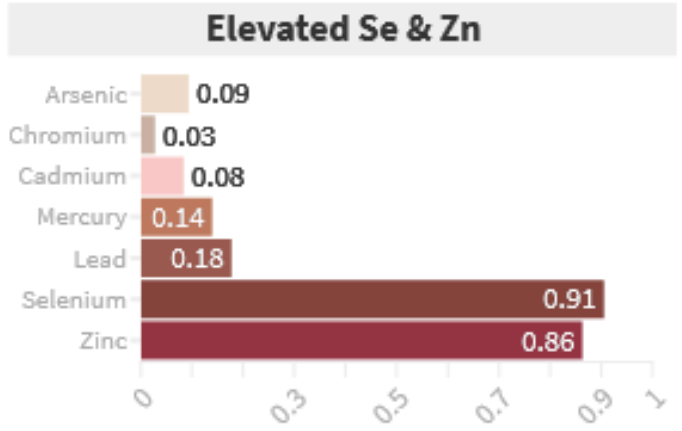
| Variable | Categories | Data source |
|---|---|---|
| Age, years | <20<br>21-24<br>25-28<br>>35 | Birth certificate |
| Maternal Body Mass Index, $kg/m^2$ | Underweight/Normal (<25.0)<br>Overweight (25-29.9)<br>Obese (≥30) | Calculated from Birth certificate |
| Geocoding Precision | Address point/Street segment<br>Midpoint of street/City/Zip/No Geocode | Generated from ESRI address coder |
| Area Deprivation Index ADI | Highest (8-10)<br>No/Lower deprivation (1-7) | Neighborhood Atlas |

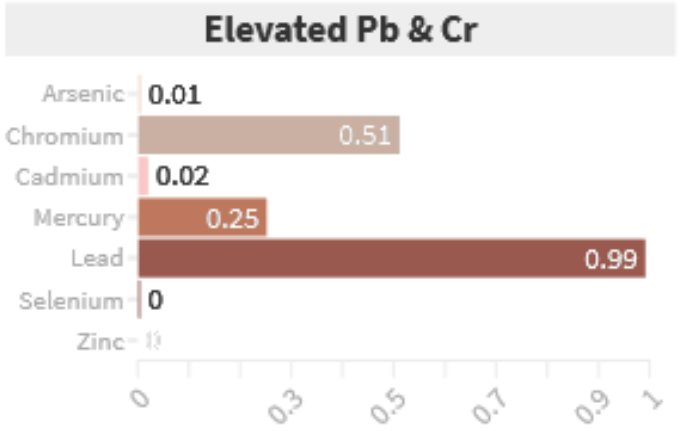
# Toxic Release Inventory(TRI) Program

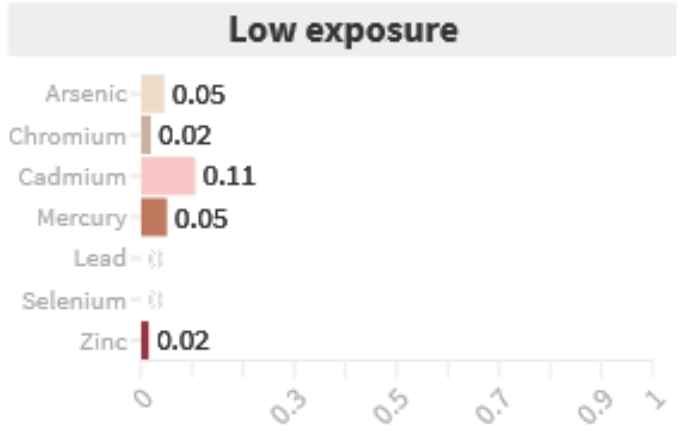


Class membership probabilities as a function of environmental metal exposure



# Results

- Geocoding precision of reduced dataset

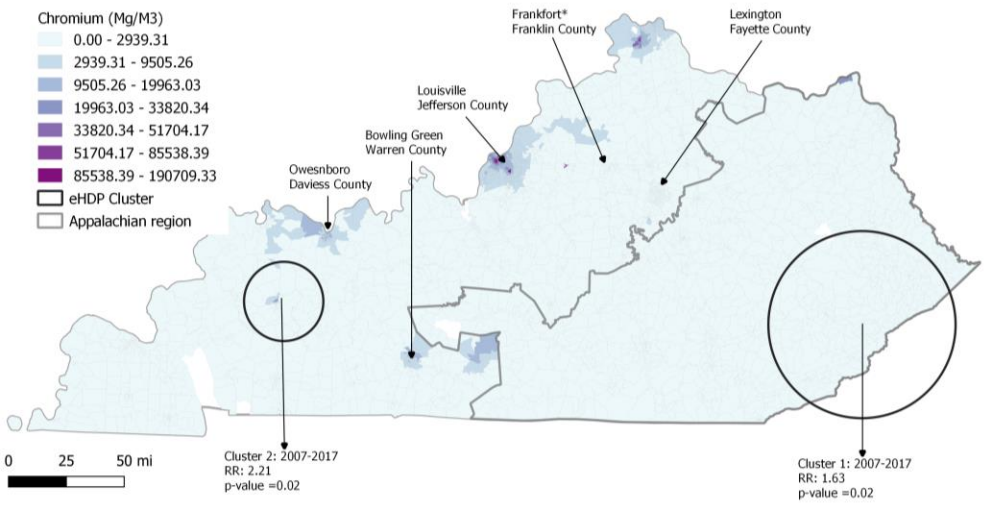
| | | | Total N (%) | Non-Appalachian N (%) | Appalachian N (%) |
|---|---|---|---|---|---|
| High Coordinate Precision |  | **Address Point**: An exact match of the address has been found | **127,165 (60.0)** | **105,681 (66.8)** | **21,484 (39.9)** |
| |  | **Street Segment:** The address has been narrowed down to a short segment of a street | **63,960 (30.2)** | **44,234 (28.0)** | **19,726 (36.6)** |
| Low Coordinate Precision |  | **Street:** Street has been identified, but house number may not be in the range of the street. | **3,879 (1.8)** | **1,608 (1.0)** | **2,271 (4.2)** |
| |  | **ZIP/City** | **17047 (8.0)** | **6,624 (4.2)** | **10,423 (19.3)** |
| |  | **Total records** | **N = 212,527** | **N = 158,147** | **N = 53,904** |

| | Total | Elevated As, Cd & Pb | Elevated Se & Zn | Elevated Pb & Cr | Low Exposure |
|---|---|---|---|---|---|
| | 205836 (100%) | 25596 (12.4%) | 43978 (21.4%) | 16575 (8.1%) | 119687 (58.2%)) |
| | N (%) | % | % | % | % |
| **Mother's age (years) †** | | | | | |
| >35 | 10054 (4.7) | 13.9 | 22.1 | 7.4 | 56.7 |
| 29-34 | 27686 (13.1) | 13.8 | 22.6 | 7.5 | 56.2 |
| 25-28 | 55338 (26.1) | 12.5 | 23.1 | 8.2 | 56.3 |
| 21-24 | 73473 (34.7) | 11.9 | 20.6 | 8.4 | 59.0 |
| <20 | 45500 (21.5) | 13.0 | 19.8 | 7.7 | 59.5 |
| **Mothers race†** | | | | | |
| Black | 17512 (8.3) | 31.4 | 14.8 | 10.1 | 43.7 |
| White | 180317 (85.0) | 10.3 | 22.1 | 7.8 | 59.8 |
| **Mother's BMI (kg/m$^2$) †** | | | | | |
| Obese | 49608 (24.1) | 11.6 | 20.9 | 7.4 | 60.1 |
| **Pre-existing diabetes †** | | | | | |
| Yes | 1608 (0.8) | 10.8 | 21.3 | 7.2 | 60.8 |
| **Smoking throughout pregnancy†** | | | | | |
| Yes | 30030 (14.2) | 10.5 | 19.6 | 7.8 | 62.2 |
| **Appalachian†** | | | | | |
| Appalachian | 53904 (25.4) | 0.3 | 8.1 | 10.1 | 81.4 |
| Not Appalachian | 158147 (74.6) | 16.8 | 25.9 | 7.3 | 49.9 |
| **RUCC Status†** | | | | | |
| Rural | 17261 (8.1) | 0 | 5.9 | 2.9 | 91.2 |
| Non-urban | 66531 (31.4) | 0.5 | 15.8 | 4.4 | 79.3 |
| Urban | 128259 (60.5) | 20.6 | 26.4 | 10.6 | 42.4 |

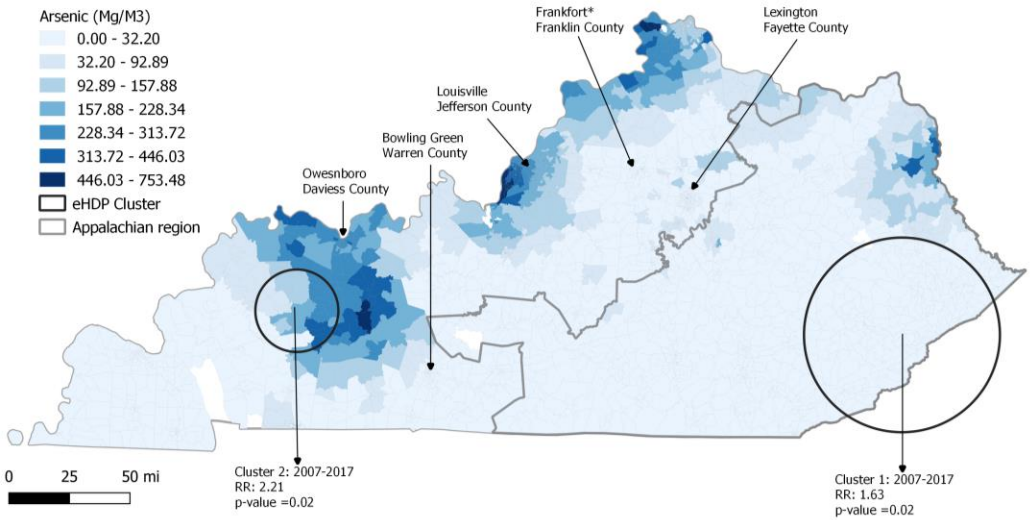
eHDP: early-onset hypertensive disorder of pregnancy, where hypertensive symptoms present before 35 weeks;
BMI: Body Mass Index; RUCC rural-urban continuum codes,
† Chi-square test statistics <0.05,
Metal Abbreviations: As: Arsenic, Cd: Cadmium, Cr: Chromium, Hg: Mercury, Pb: Lead, Se: Selenium, Zn: Zinc

Demographic characteristics summary by latent metal class and the total population of primiparious mothers 2008-2017

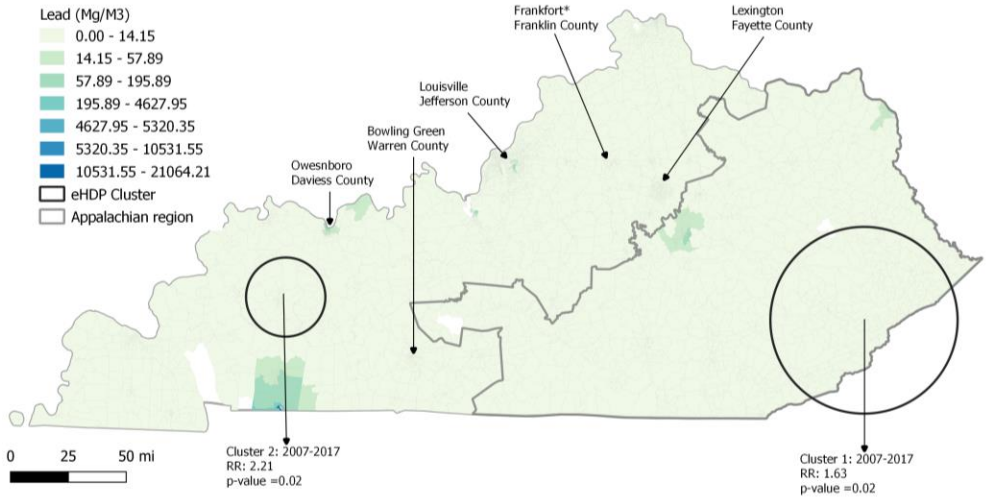
## Median concentrations of Chromium (Mg/m$^3$)



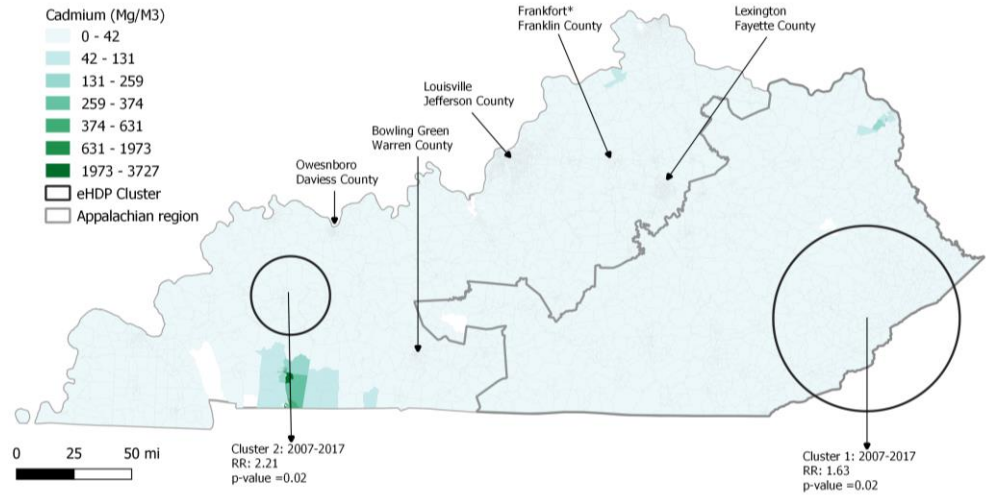

## Median concentrations of Arsenic (Mg/m$^3$)



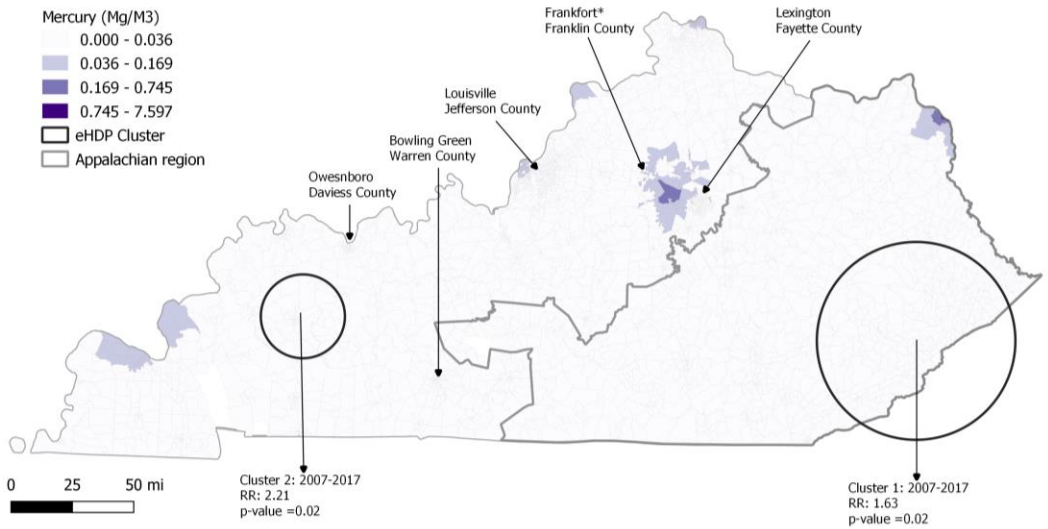

## Median concentrations of Lead (Mg/m$^3$)



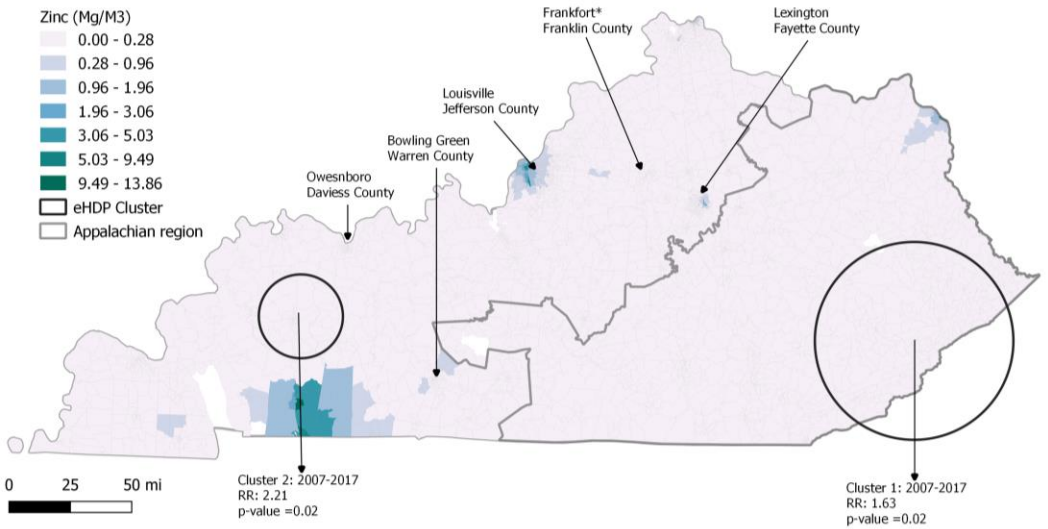

## Median concentrations of Cadmium (Mg/m$^3$)



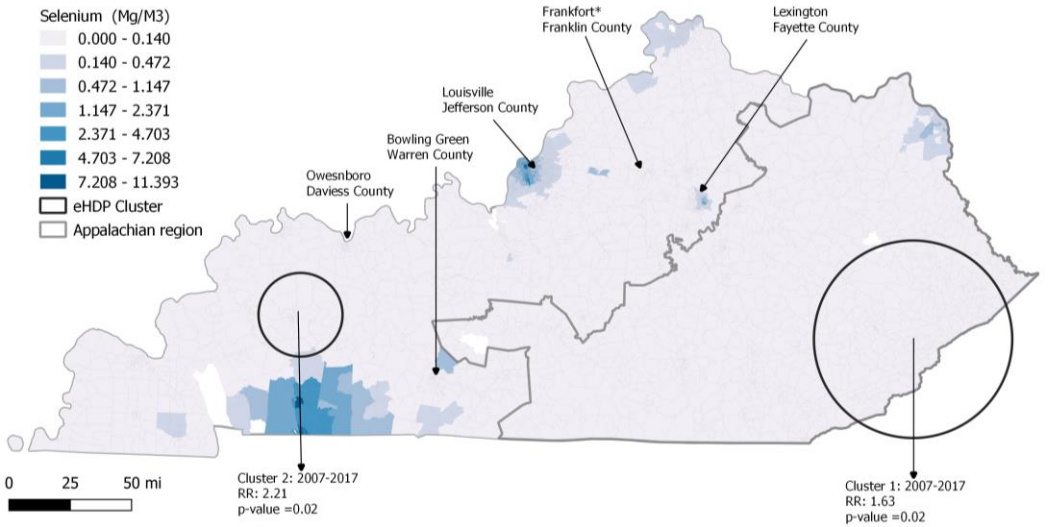
## Median concentrations of Mercury (Mg/m$^3$)



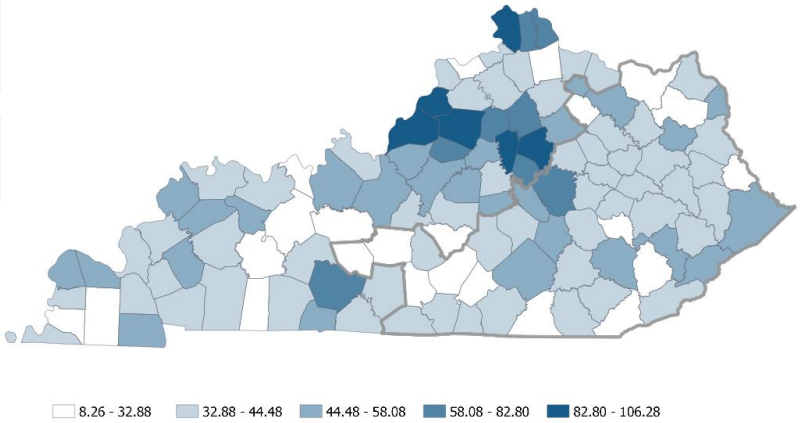

## Median concentrations of Zinc (Mg/m$^3$)



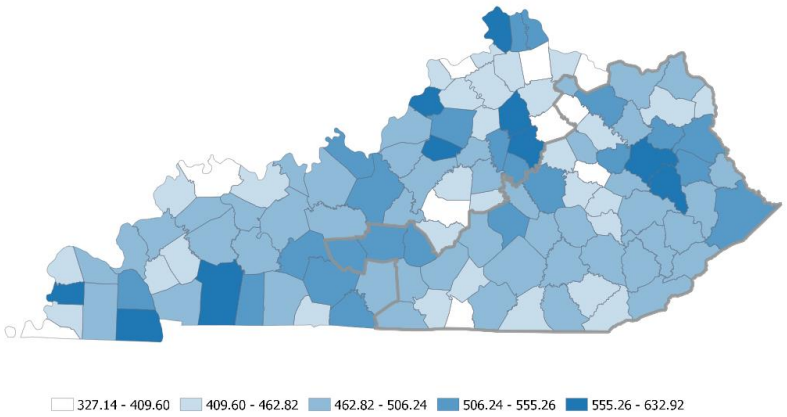

## Median concentrations of Selenium (Mg/m$^3$)



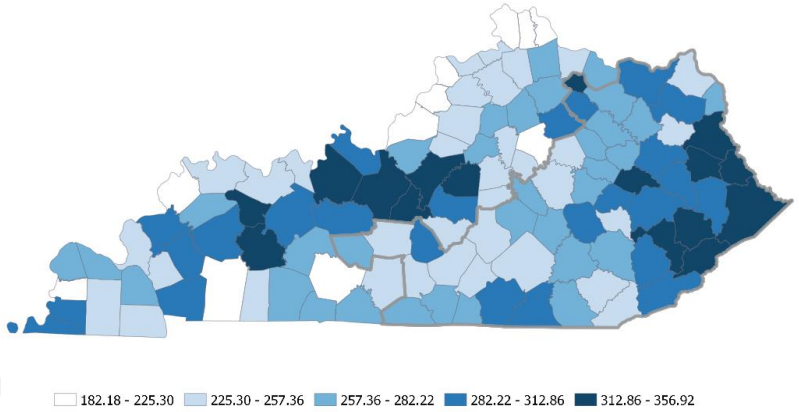
A. Maternal age ≥34



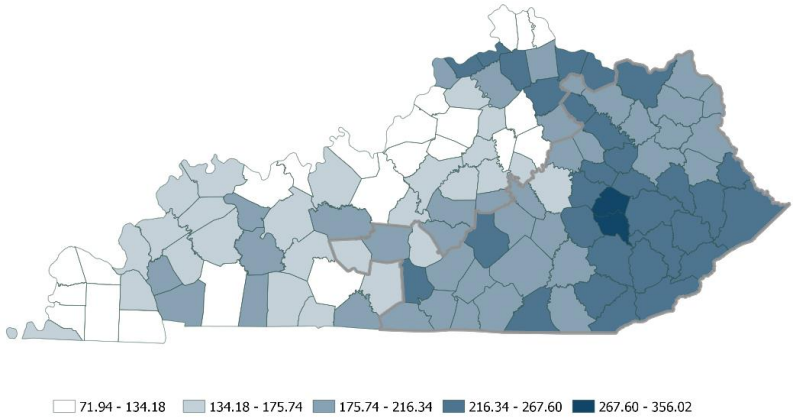

B. Married Mothers




c. Maternal Obesity




d. Maternal smoking throughout pregnancy




Choropleth maps of county-level prevalences of marriage, maternal obesity, and maternal smoking per 1000 births in Kentucky, 2008-2017

| | eHDP N (%) | PR (95% CI) | aPR (95% CI) | Sensitivity aPR (95% CI) |
|---|---|---|---|---|
| **Latent class metal exposure** | | | | |
| Elevated As, Cd & Pb | 166 (8.6) | 0.64 (0.56, 0.76) | 0.72 (0.60, 0.86) | 0.82 (0.20, 3.46) |
| Elevated Se & Zn | 418 (21.6) | 0.96 (0.86, 1.08) | 1.08 (0.96, 1.22) | 0.82 (0.50, 1.32) |
| Elevated Pb & Cr | 180 (9.3) | 1.12 (0.94, 1.30) | 1.22 (1.04, 1.44) | 1.58 (1.02, 2.46) |
| Low Exposure | 1168 (60.5) | Reference | Reference | Reference |
| **Mother's age** | | | | |
| >35 | 142 (7.3) | 2.06 (1.70, 2.52) | 1.96 (1.54, 2.50) | 2.68 (1.20, 5.98) |
| 29-34 | 289 (15.0) | 1.52 (1.30, 1.78) | 1.54 (1.26, 1.88) | 1.68 (0.82, 3.46) |
| 25-28 | 541 (28.0) | 1.42 (1.24, 1.64) | 1.38 (1.16, 1.66) | 1.26 (0.68, 2.36) |
| 21-24 | 647 (33.5) | 1.28 (1.12, 1.46) | 1.12 (0.96, 1.30) | 1.38 (0.82, 2.30) |
| <20 | 313 (16.2) | Reference | Reference | Reference |
| **Mother's race** | | | | |
| Black | 237 (12.3) | 1.52 (1.32, 1.74) | 1.60 (1.36, 1.88) | 2.08 (1.28, 3.34) |
| White | 1619 (83.8) | Reference | Reference | Reference |
| **Mother's BMI (kg/m$^2$)** | | | | |
| Obese | 766 (42.4) | 2.80 (2.50, 3.12) | 2.44 (2.18, 2.72) | 3.06 (2.06, 4.54) |
| **Pre-existing diabetes** | | | | |
| Yes | 87 (4.5) | 6.46 (5.18, 8.06) | 4.62 (3.64, 5.84) | 3.64 (1.40, 9.50) |
| **Smoking throughout pregnancy** | | | | |
| Yes | 232 (12.0) | Reference | Reference | Reference |
| **Appalachian** | | | | |
| Appalachian | 599 (31.0) | 1.32 (1.20, 1.46) | 1.20 (1.04, 1.36) | 0.66 (0.38, 1.16) |
| Not Appalachian | 1333 (69.0) | Reference | Reference | Reference |
| **RUCC Status** | | | | |
| Rural | 169 (8.7) | 1.20 (1.02, 1.42) | 1.06 (0.86, 1.28) | 2.60 (0.78, 8.70) |
| Non-Metro | 720 (37.3) | 1.34 (1.22, 1.46) | 1.20 (1.04, 1.36) | 1.60 (1.06, 2.44) |
| Urban | 1043 (54.0) | Reference | Reference | Reference |

BMI: Body Mass Index, RUCC: Rural-Urban Continuum Codes,
PR: Prevalence Ratio
aPR: adjusted Prevalence Ratio

Bivariate and multivariable associations between demographic characteristics, environmental exposures, and class membership

# Conclusions

**Supports existing literature**

1. Extreme maternal ages associated with increased prevalence eHDP
2. 60% increase in eHDP for Black women
3. eHDP 2.5 higher for women who are obese
4. eHDP 4.5 higher for women with pre-existing diabetes
5. Non-smoking showed a 30% increased prevalence of eHDP
6. Probable exposure to both Pb & Cr associated with a 22% increase in eHDP prevalence

**Findings (further exploration needed)**

1. As, Cd & Pb – no increased risk?
2. Concordance between RSEI scores and biological markers
3. Explore other health outcomes in association with industrial activity
4. Build a composite index to capture environmental exposure (Census of Ag, RSEI, USGS)

# Strengths and limitations

## Limitations

- Geocoding Precision
  - Rurality
- Birth certificates
  - eHDP definition
  - Self report bias
  - Hospital data collection variation
- Environmental exposure (RSEI)
  - Limited sources of exposure
  - Lots of estimations
  - Exposure assignment
  - Duration of residence
- Overall
  - Uncontrolled confounding of income

## Strengths

- Birth records
  - Able to detect rare effects
  - Demographic information (including maternal address)
- RSEI
  - Ability to assess multiple exposures estimated with similar methodologies
  - Precise spatial resolution of toxicity concentrations
- Methodologies
  - Ability to assess overlapping exposures (LCA)
  - Able to detect spatial clusters of disease
- Overall
  - Addresses gap in literature for eHDP

# Future directions

- Improve geocoding imprecision
- Individual risk assessment
- Case ascertainment

# Acknowledgements


| | |
|---|---|
| Funding | Central Appalachian Regional Education Research Center (CARERC)– Pilot Funding<br>Olive Ruth Russell Fellowship – Berea College |
| Ky Dept. for Public Health | Claudia Valdivieso<br>Jeffrey Sparks |
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