Air Pollution, Clustering of Particulate Matter Components, and Breast Cancer in the Sister Study: A U.S.-Wide Cohort

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Air pollution: a ubiquitous and heterogenous mixture

~7 million deaths worldwide

WHO, 2016
Air pollution as a breast carcinogen

IARC classified outdoor air pollution as Group 1 carcinogen
• Particulate matter (PM), nitrogen oxides, volatile organic compounds, metals, hydrocarbons

Airborne pollutants reach breast tissue
• Inhaled toxicants have been measured in breast fluid

Breast cancer incidence increases with traffic emissions

NOx emissions and breast cancer incidence

Chen and Bina 2012; Hill et al., 1979; Brody et al., 2007; Huff et al., 1989; Chen at al., 2013
Air pollution may be related to breast cancer risk

Evidence from population-based studies has been inconclusive

- Markers of traffic-related pollution (NO₂, PAHs) tend to be positively related to breast cancer risk
- Largely null associations observed for particulate matter

PM is a complex mixture

- PM aggregate measure based on size
- Geographical variability in composition
Study Aims

Estimate the association between air pollutants (PM$_{2.5}$, PM$_{10}$, NO$_2$) and breast cancer risk

• Evaluate whether these associations vary by geographic region
Study Population: Sister Study

Prospective cohort study (n=50,884)
• Recruitment from 2003-2009
• Eligibility criteria:
  • Breast cancer-free women
  • Ages 35-74
  • Residents of the U.S. and Puerto Rico
  • Sister diagnosed with breast cancer
• Completed extensive questionnaire at baseline

Follow-up
• Annual health updates and biennial surveys
  • Response rates ≥90% over follow-up
• Diagnoses confirmed by medical record and pathology reports

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<td><strong>Total Cases</strong></td>
<td>3,002</td>
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<td><strong>Invasive cases</strong></td>
<td>2,345</td>
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<td><strong>ER+PR+</strong></td>
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Air pollution exposure assessment: PM$_{2.5}$, PM$_{10}$ and NO$_2$

Limited to women living in the contiguous US (n=49,771)

Sampson et al., 2013
Statistical analysis

Cox proportional hazards models estimate HRs and 95% CIs for an interquartile range (IQR) increase in air pollutants in breast cancer risk
  • Age at baseline to age at breast cancer diagnosis or censoring

Stratified and tested for modification
census geographic region

Adjusting for age, race, education,
smoking status, menopausal hormone therapy
Sister Study baseline characteristics

Median age was 55.6 years
84% Non-Hispanic white
51% bachelor’s degree or higher
33% annual household income >$100,000
54% never smokers

Average of 8.4 years of follow-up
Air pollution and breast cancer risk

White et al., 2019 Environmental Health Perspectives
Air pollution and breast cancer risk, by region

PM$_{2.5}$
- Northeast
- Midwest
- South
- West

PM$_{10}$
- Northeast
- Midwest
- South
- West

NO$_2$
- Northeast
- Midwest
- South
- West

HRs and 95% CIs

* heterogeneity p values

Invasive breast cancer

White et al., 2019 Environmental Health Perspectives
Study Aims

Estimate the association between air pollutants (PM$_{2.5}$, PM$_{10}$, NO$_2$) and breast cancer risk

- Evaluate whether these associations vary by geographic region

Evaluate whether the associations for PM$_{2.5}$ and breast cancer risk vary by PM$_{2.5}$ component profiles using predictive k-means clustering
K-means covariate adaptive clustering

PM$_{2.5}$ components

- 130 US EPA Air Quality System monitoring locations that measured mass concentrations for 22 PM$_{2.5}$ component species in 2010
  - Elemental carbon (EC), organic carbon (OC), NO$_3^-$, SO$_4^{2-}$, Al, As, Br, Cd, Ca, Co, Cr, Cu, Fe, K, Mn, Na, S, Si, Se, Ni, V and Zn
  - Mass concentrations were converted to relative composition

Dimension reduction technique to partition multi-pollutant observations into clusters

- Clusters locations using both PM component observations and geographic covariates
- Cluster membership was predicted for each study participant based on residential location

Keller et al., 2017; Brook et al., 2010; Franklin et al., 2008
PM$_{2.5}$ and breast cancer, by PM$_{2.5}$ cluster

Results for DCIS were less precise, but similar to geographic regions

White et al., 2019 Environmental Health Perspectives

Invasive breast cancer
**Cluster 4:** Low sulfur fractions and high fractions of sodium and nitrate
  - indicative of marine aerosols and agricultural emissions

**Cluster 7:** High fractions of Si, Ca, K and Al
  - indicative of the surface soil in the Western US
Summary of findings and considerations

Air pollution was associated with both DCIS and invasive breast cancer
  • Associations varied notably by geographic region and component clusters

Differences by invasive and DCIS were unexpected
  • Adjustment for additional SES variables and screening practices did not change these results
  • Air pollutant mixtures may contribute differently to breast cancer risk by stage of disease, possibly by influencing tumor growth rates
    • LIBCSP observed stronger association for PAH-based traffic model for DCIS than invasive
    • Similar geographic region to where we observed a positive association for DCIS

Generalizability
  • Predominately a population of white women, all with a family history of breast cancer

Mordukovich et al., 2015
Study innovations

First study to consider PM$_{2.5}$ components using a mixtures approach

- Air pollution is a complex mixture – important to address heterogeneity
- K-means clustering allows for consideration of correlated components
- Unsupervised approach, may be other groups or combinations of pollutants that are more strongly related to breast cancer risk

Prior studies that observed a null association for overall PM and breast cancer may have been masking over the heterogeneity in exposure
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Thank you!

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P.S. I’m hiring! Looking for a post-doc? Email me!
PM2.5 exposure levels by cluster