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

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CHE Cancer Series Webinar

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Air pollution: a ubiquitous and heterogenous mixture

~7 million deaths worldwide



Air pollution as a breast carcinogen

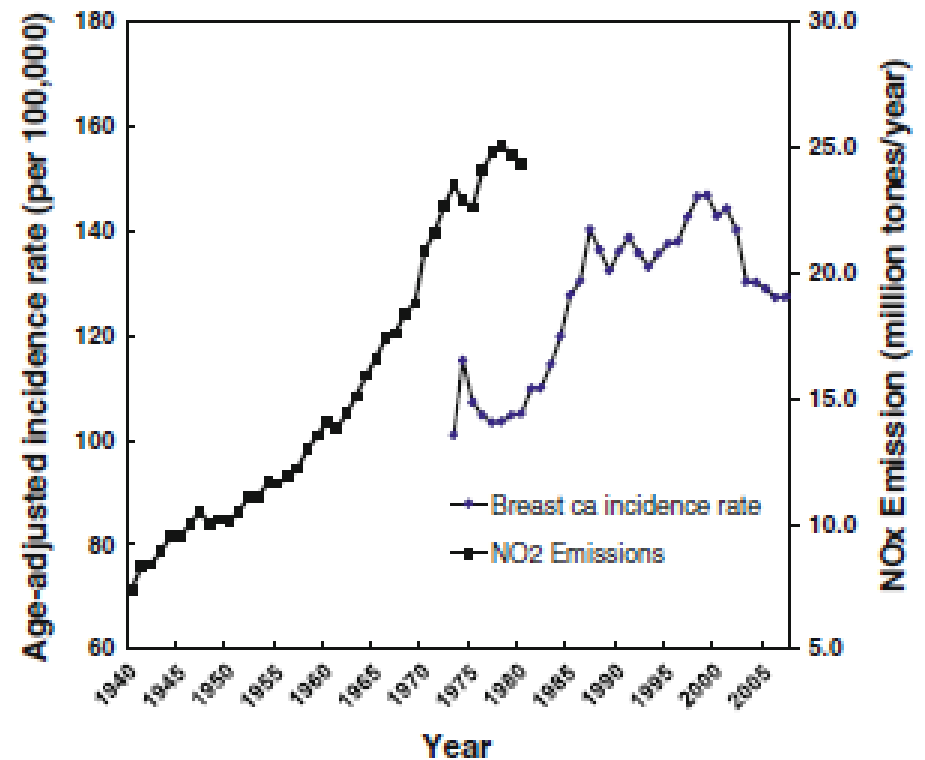
IARC classified outdoor air pollution as Group 1 carcinogen

- 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



NO_x emissions and breast cancer incidence

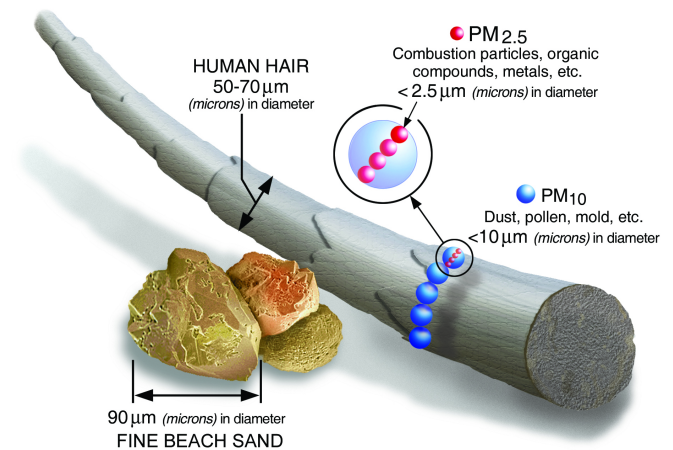
Air pollution may be related to breast cancer risk

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

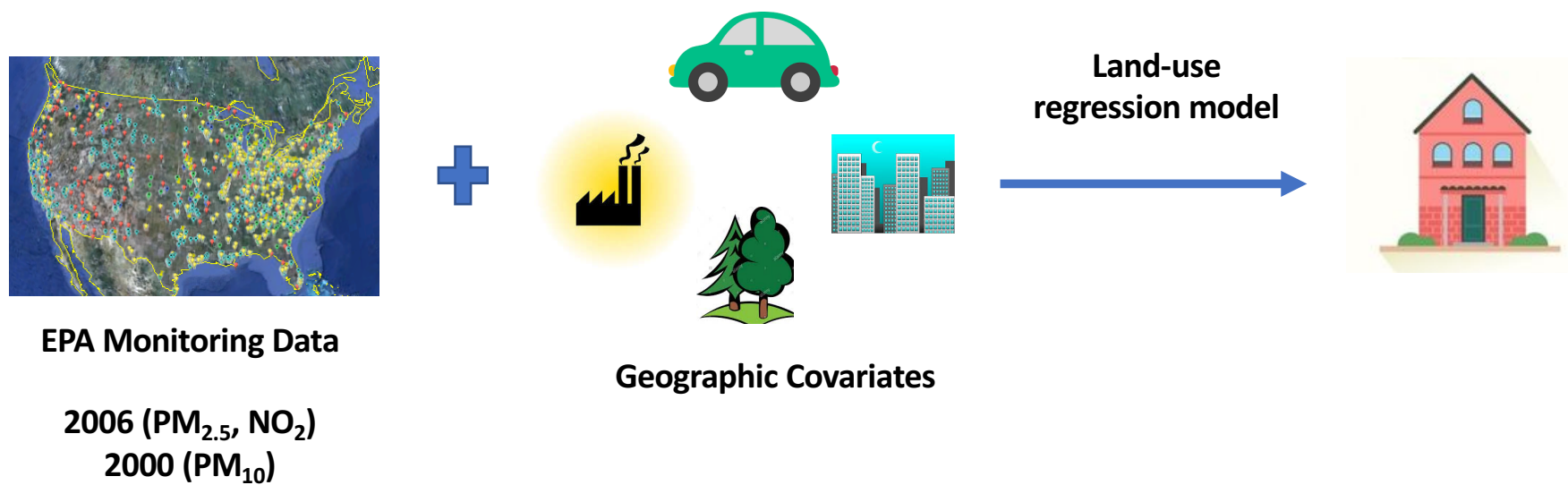
Follow-up

- Annual health updates and biennial surveys
 - Response rates $\geq 90\%$ over follow-up
- Diagnoses confirmed by medical record and pathology reports



Total Cases	3,002
Invasive cases	2,345
ER+PR+	1,415

Air pollution exposure assessment: PM_{2.5}, PM₁₀ and NO₂



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

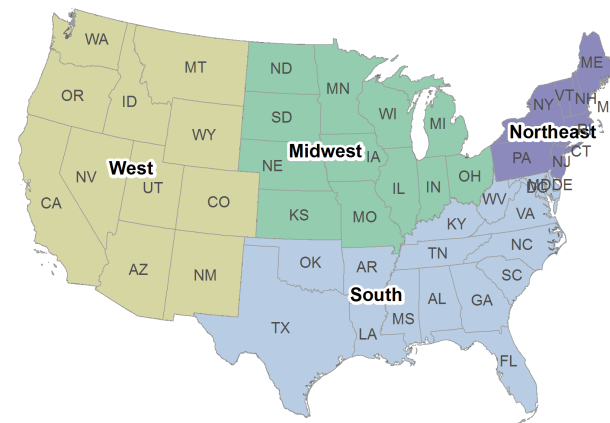
Statistical analysis

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

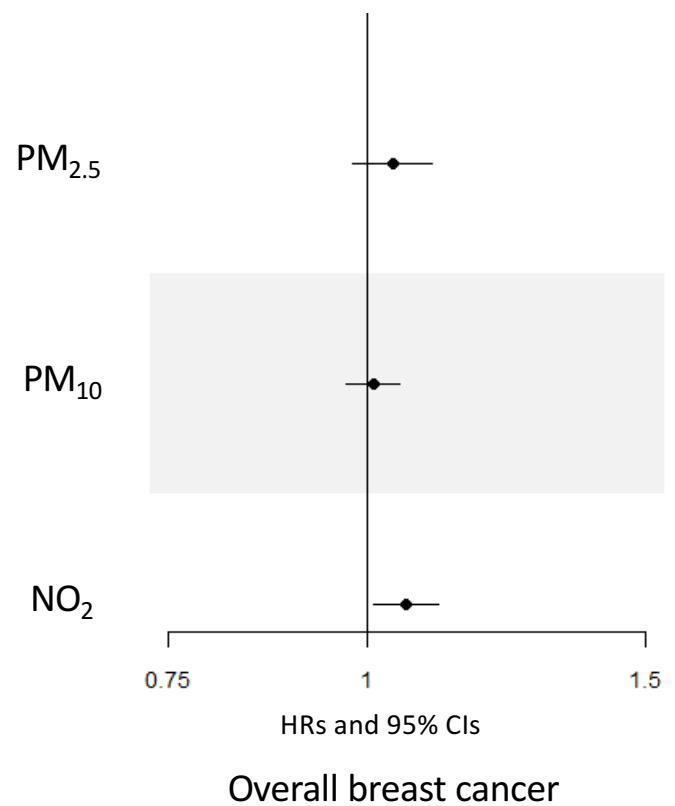
33% annual household income >\$100,000

54% never smokers

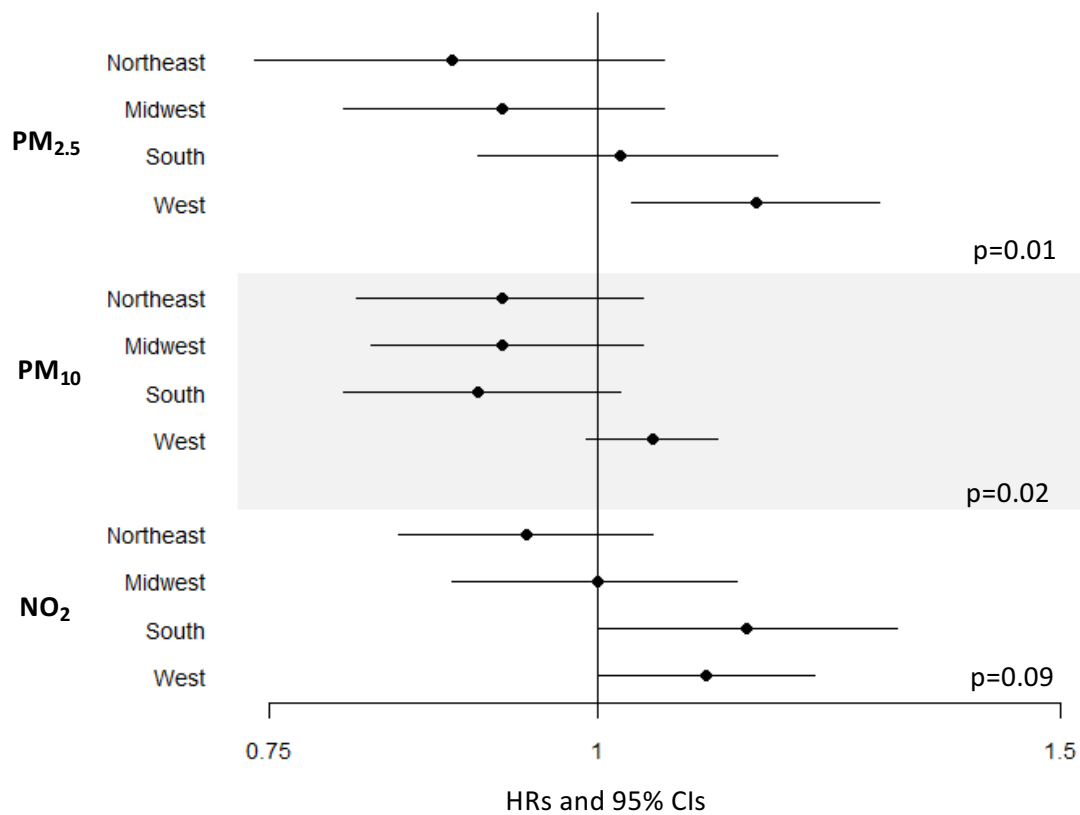
Average of 8.4 years of follow-up



Air pollution and breast cancer risk



Air pollution and breast cancer risk, by region



*heterogeneity p values

Invasive breast cancer

Study Aims

Estimate the association between air pollutants ($PM_{2.5}$, PM_{10} , NO_2) and breast cancer risk

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Evaluate whether the associations for $PM_{2.5}$ and breast cancer risk vary by $PM_{2.5}$ component profiles using predictive k-means clustering

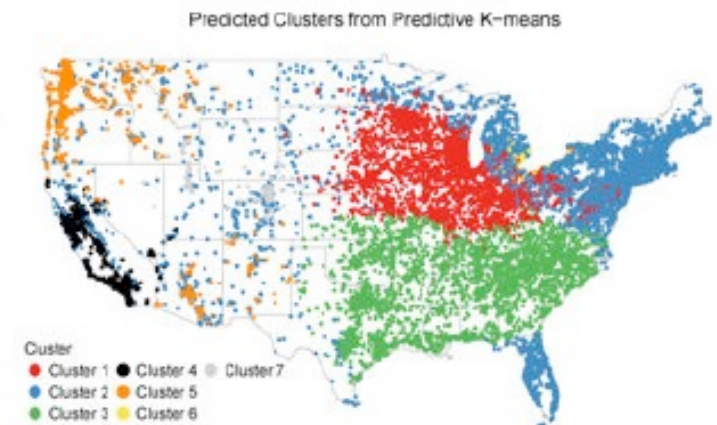
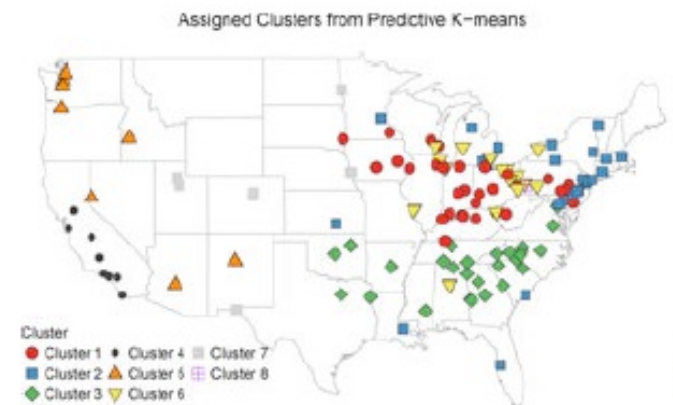
K-means covariate adaptive clustering

PM_{2.5} components

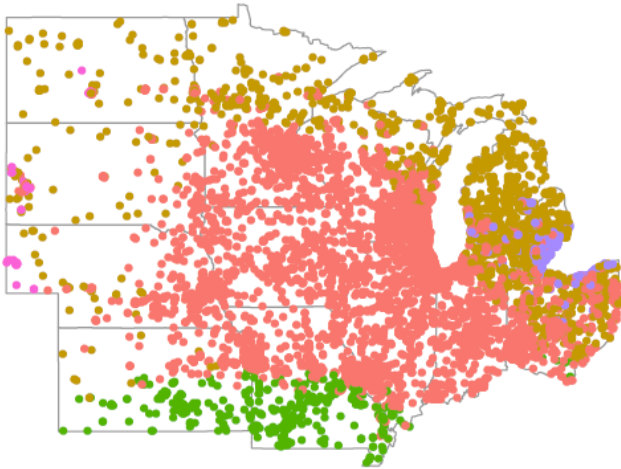
- 130 US EPA Air Quality System monitoring locations that measured mass concentrations for 22 PM_{2.5} component species in 2010
 - Elemental carbon (EC), organic carbon (OC), NO₃⁻, SO₄²⁻, Al, As, Br, Cd, Ca, Co, Cr, Cu, Fe, K, Mn, Na, S, Si, Se, Ni, V and Zn
- Mass concentrations were converted to relative composition

Dimension reduction technique to partition multi-pollutant observations into clusters

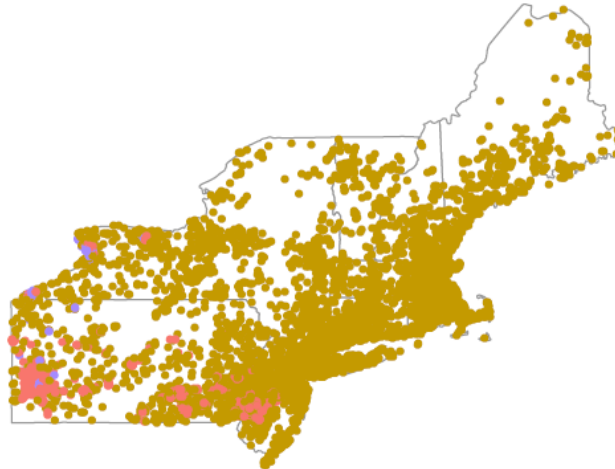
- Clusters locations using both PM component observations and geographic covariates
- Cluster membership was predicted for each study participant based on residential location



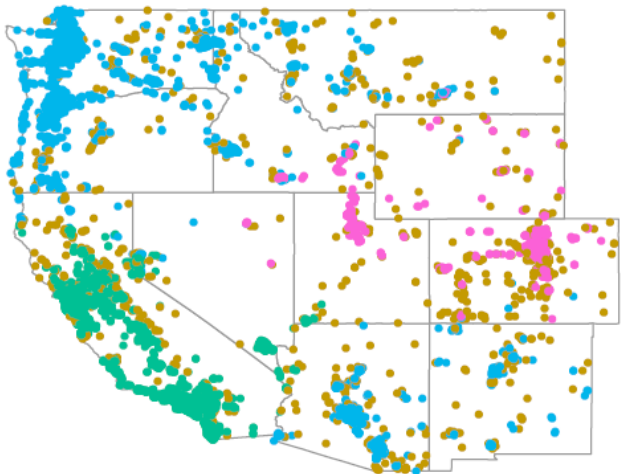
Midwest



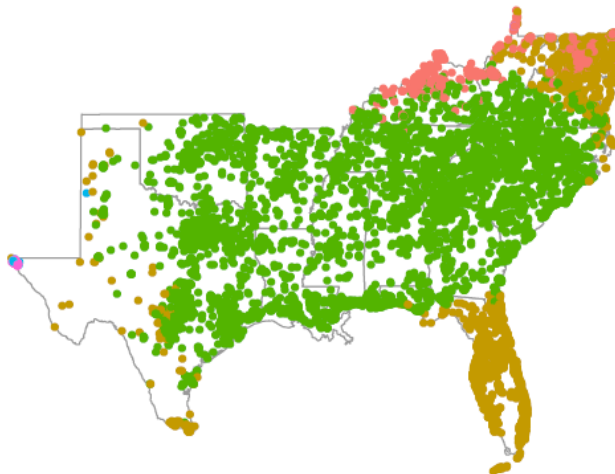
Northeast



West



South



Cluster

- Cluster 1
- Cluster 2
- Cluster 3
- Cluster 4
- Cluster 5
- Cluster 6
- Cluster 7

PM_{2.5} and breast cancer, by PM_{2.5} cluster

PM_{2.5} component clusters

Cases (N) Cluster

635 1

696 2

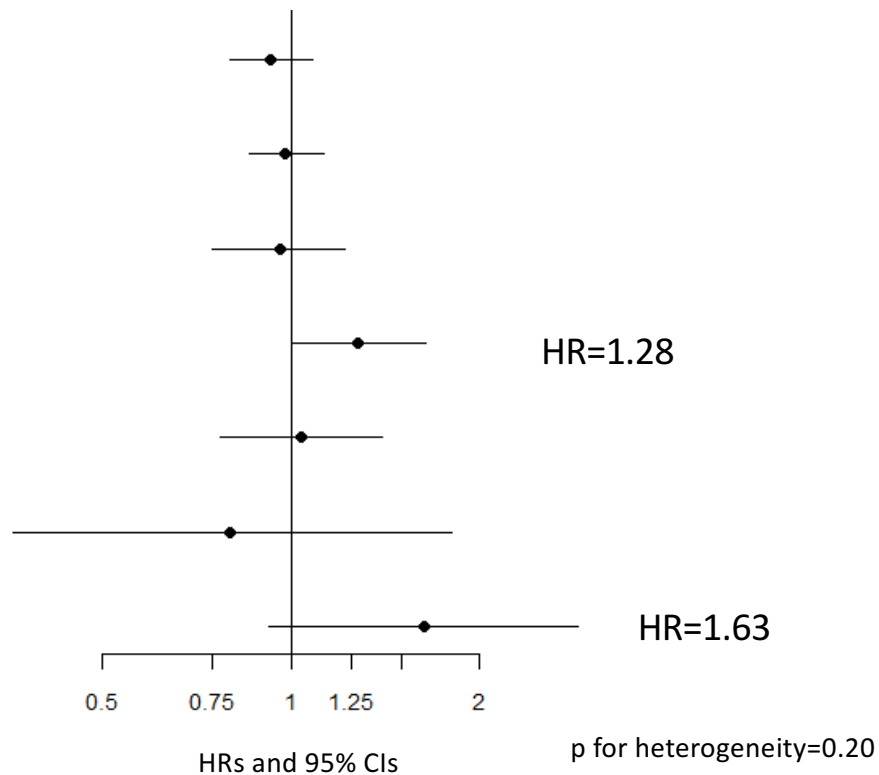
454 3

213 4

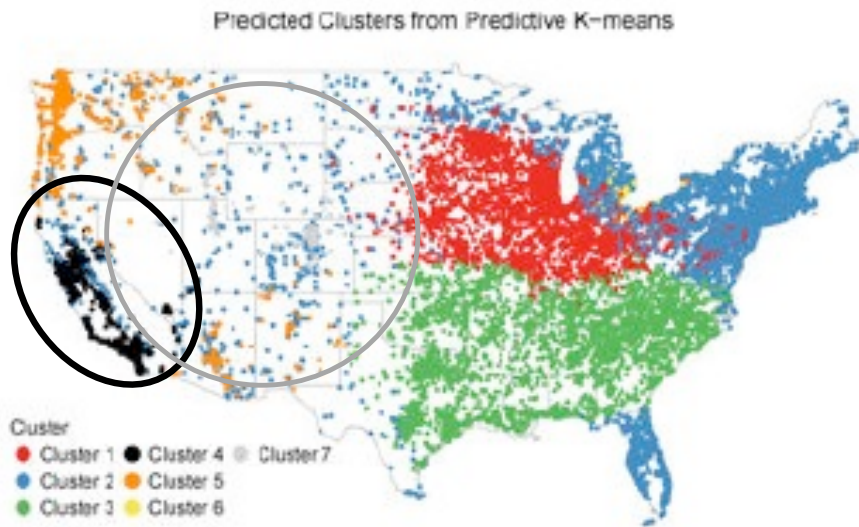
215 5

49 6

61 7



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

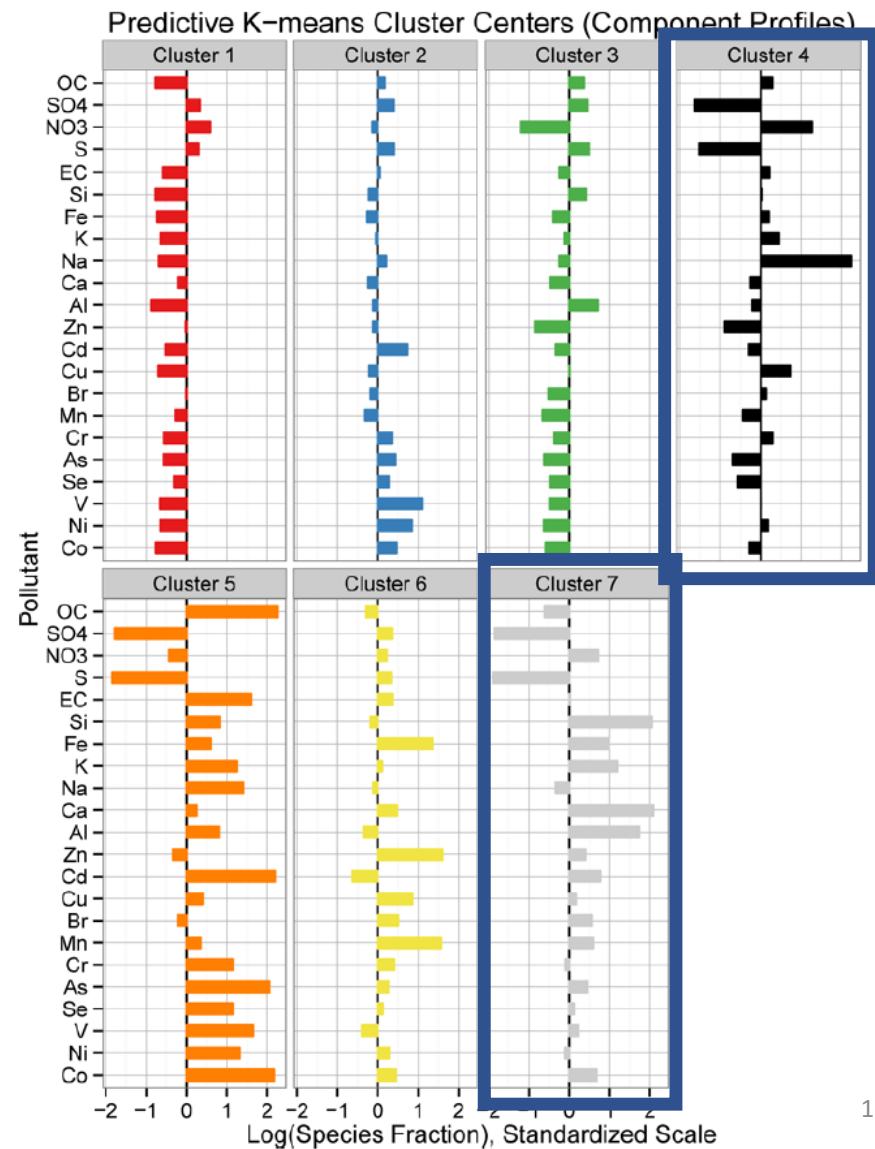


Cluster 4: Low sulfur fractions and high fractions of sodium and nitrate

- 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

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

Acknowledgements



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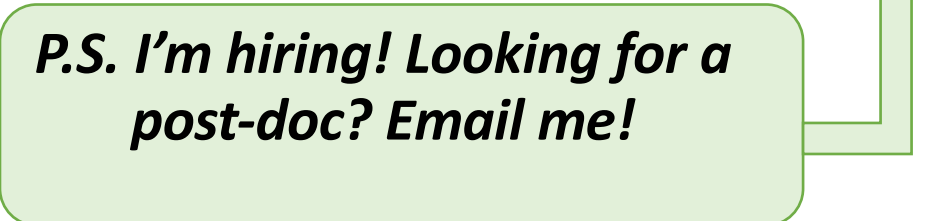
Joel D. Kaufman, University of Washington

White AJ, Keller JP, Zhao S, Carroll R, Kaufman JD, Sandler DP. Air pollution, clustering of particulate matter components and breast cancer in the Sister Study: A U.S.-wide cohort. Environ Health Perspect, 2019; 127(10):107002.

Thank you!

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***P.S. I'm hiring! Looking for a
post-doc? Email me!***



PM2.5 exposure levels by cluster

