Exposure to carcinogens and racial differences in leukocyte telomere length

Mediation analysis of race and environmental exposures on telomere length using data from the National Health and Nutrition Examination Survey (1999-2002)

Presented by Jonathan Boss and Emily Roberts

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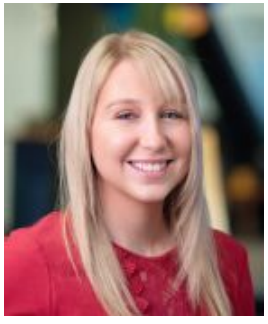
Department of Biostatistics, University of Michigan

Study Team



Advisor: Dr. Belinda Needham

Collaborators: Stephen Salerno, Dr. Ami Zota, Dr. Bhramar Mukherjee

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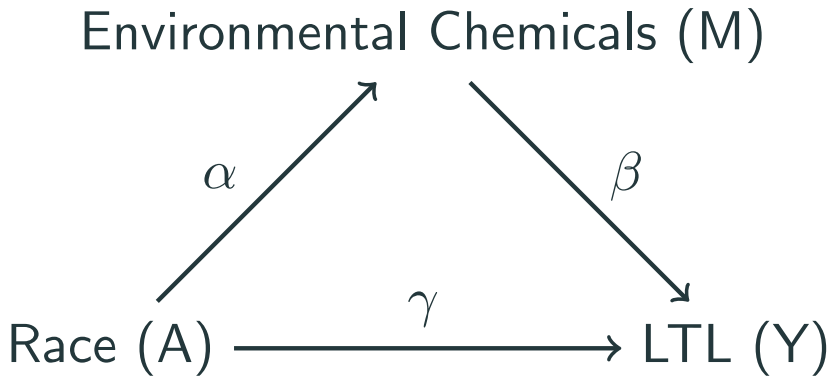
Study Background

- Many studies report that US Black adults have longer leukocyte telomere length (LTL) than US White adults.[1]
- This is surprising for two reasons:
  (i) Black adults are more likely to be exposed to risk factors for short LTL (e.g., low socioeconomic status[2], stressful life events[3]).
  (ii) Black adults are more likely to have health outcomes associated with short LTL (e.g., cardiovascular disease,[4,5] premature mortality[6]).
- Race differences in LTL are oftentimes attributed to genetics,[7,8] but recent studies have shown that exposure to carcinogens is associated with longer LTL.[9,10,11,12,13]
- We hypothesize that Black individuals have longer LTL than White individuals due to greater exposure to carcinogens resulting from residential[14] and occupational[15,16] segregation.

Objectives and Data Source

Conceptual Diagram

$$\text{Total Effect} = \text{Direct Effect} + \text{Indirect Effect} = \gamma + \alpha\beta$$



Do chemical exposures act as mediators between race and LTL?

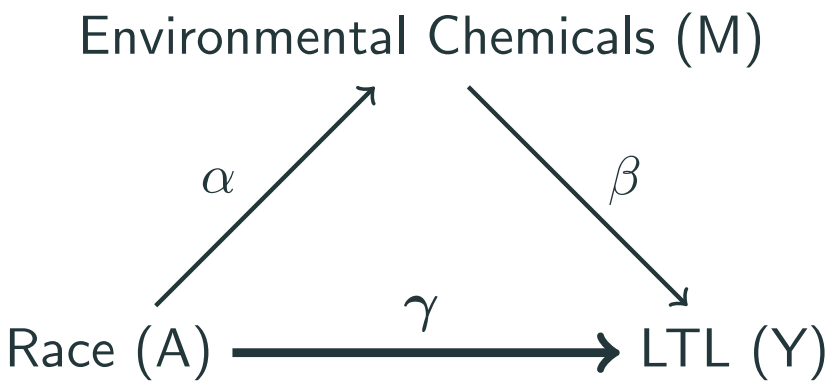
National Health and Nutrition Examination Survey (NHANES)

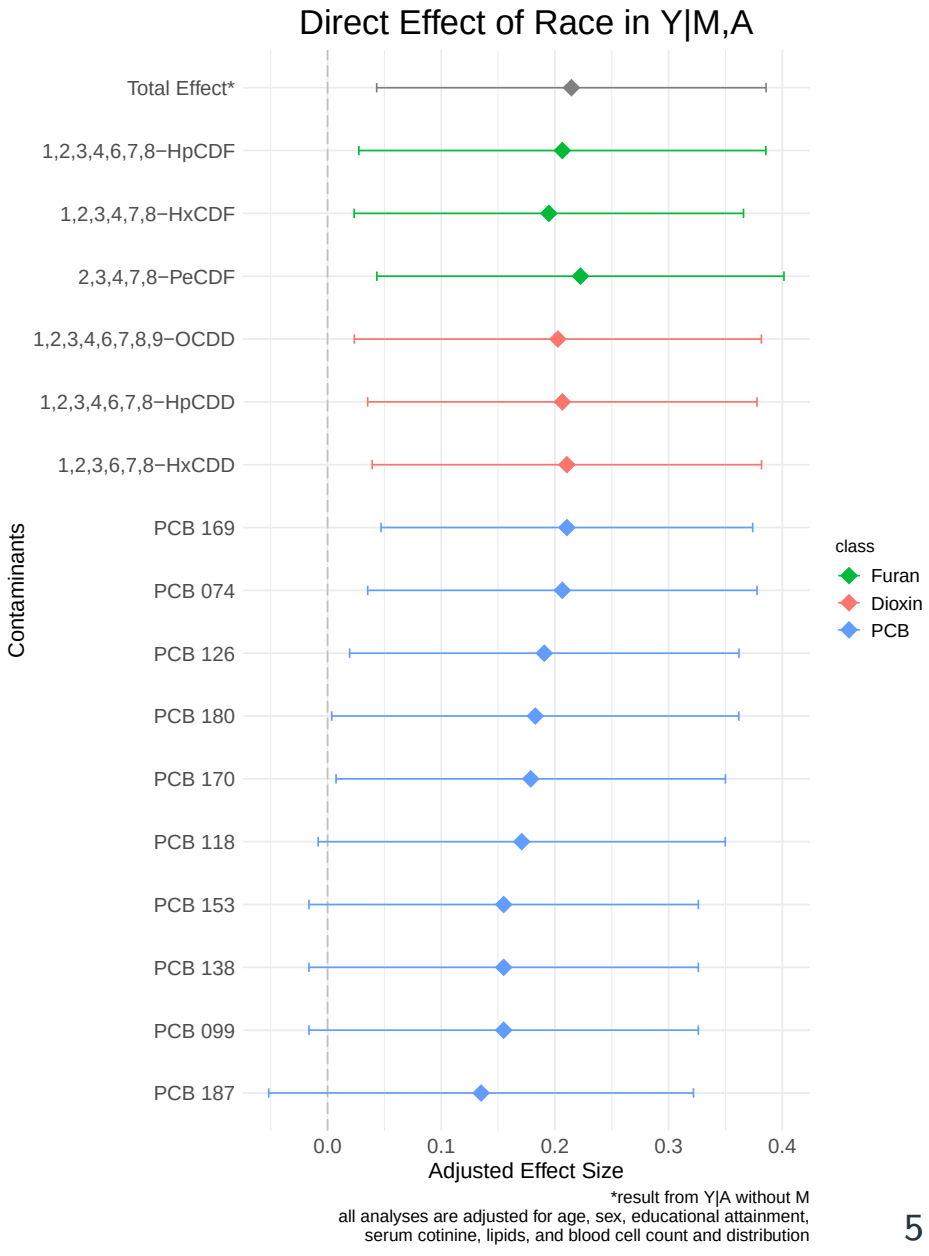
1,169 adults (300 Black and 869 White individuals) from the 1999-2000 and 2001–2002 NHANES cycles with polychlorinated biphenyl (PCB), dioxin, and furan measurements.

Methods

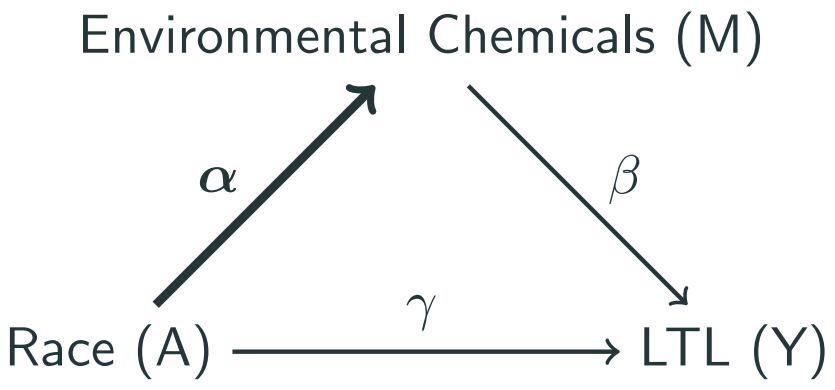
- LTL was assayed using quantitative polymerase chain reaction.[17]
- Exposures with more than 50% below their respective detection limits are excluded from the analysis. Non-detects for the remaining 16 exposures are multiply imputed using censored likelihood multiple imputation.[18]
- We characterize single-pollutant mediation effects by constructing survey-weighted mediation models while accounting for NHANES's stratified cluster sampling design and multiple testing.
- In the imputation and mediation models, LTL and all environmental exposures are always log-transformed then standardized.
- Mediation models are adjusted for age, sex, educational attainment, serum cotinine, lipids, and blood cell count and distribution.

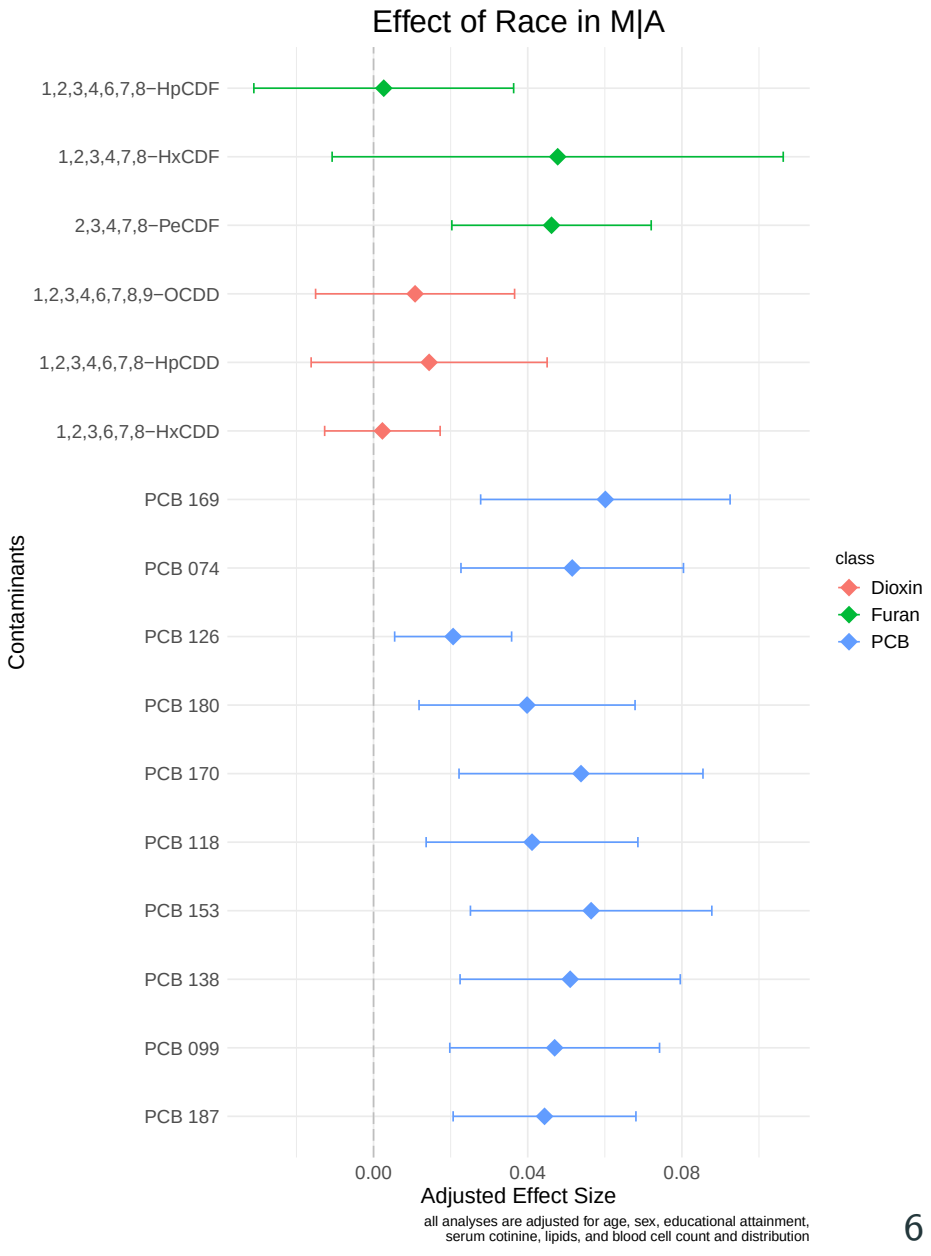
Mediation Analysis: $Y|M, A$



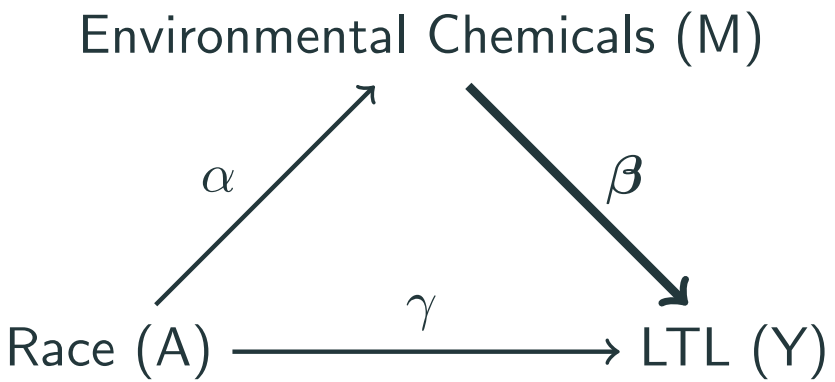


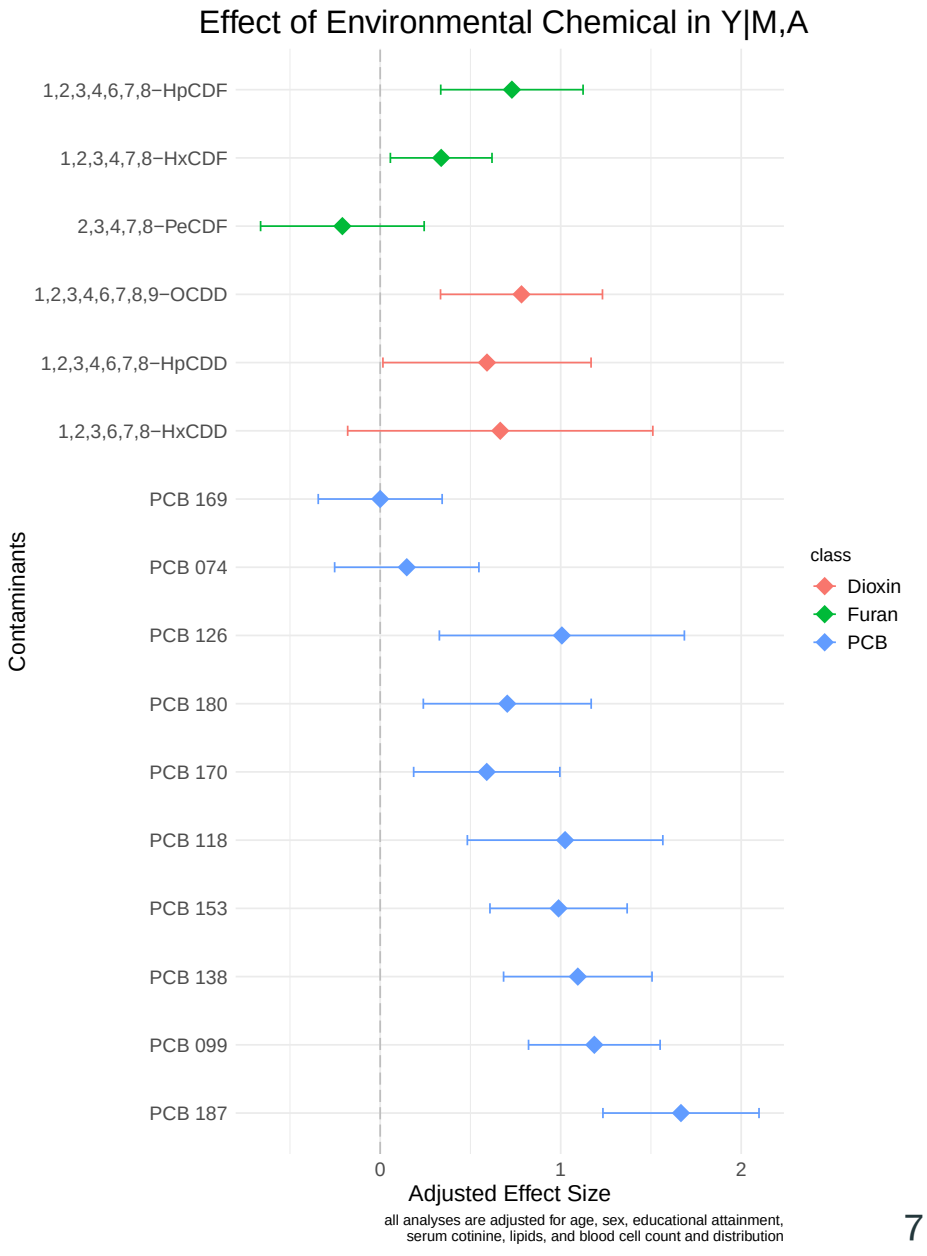
Mediation Analysis: $M|A$



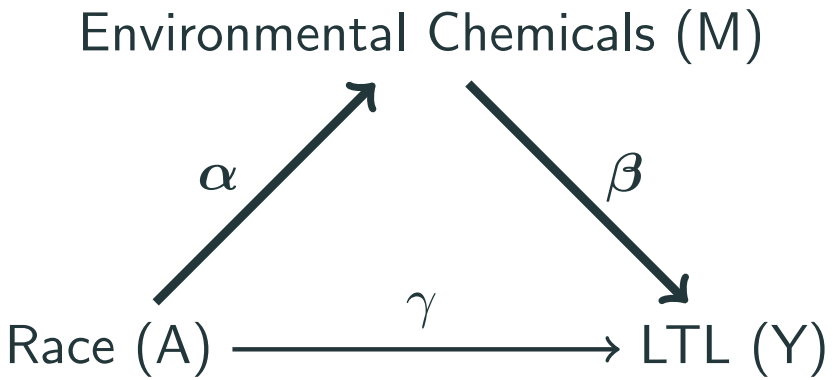


Mediation Analysis: $Y|M, A$

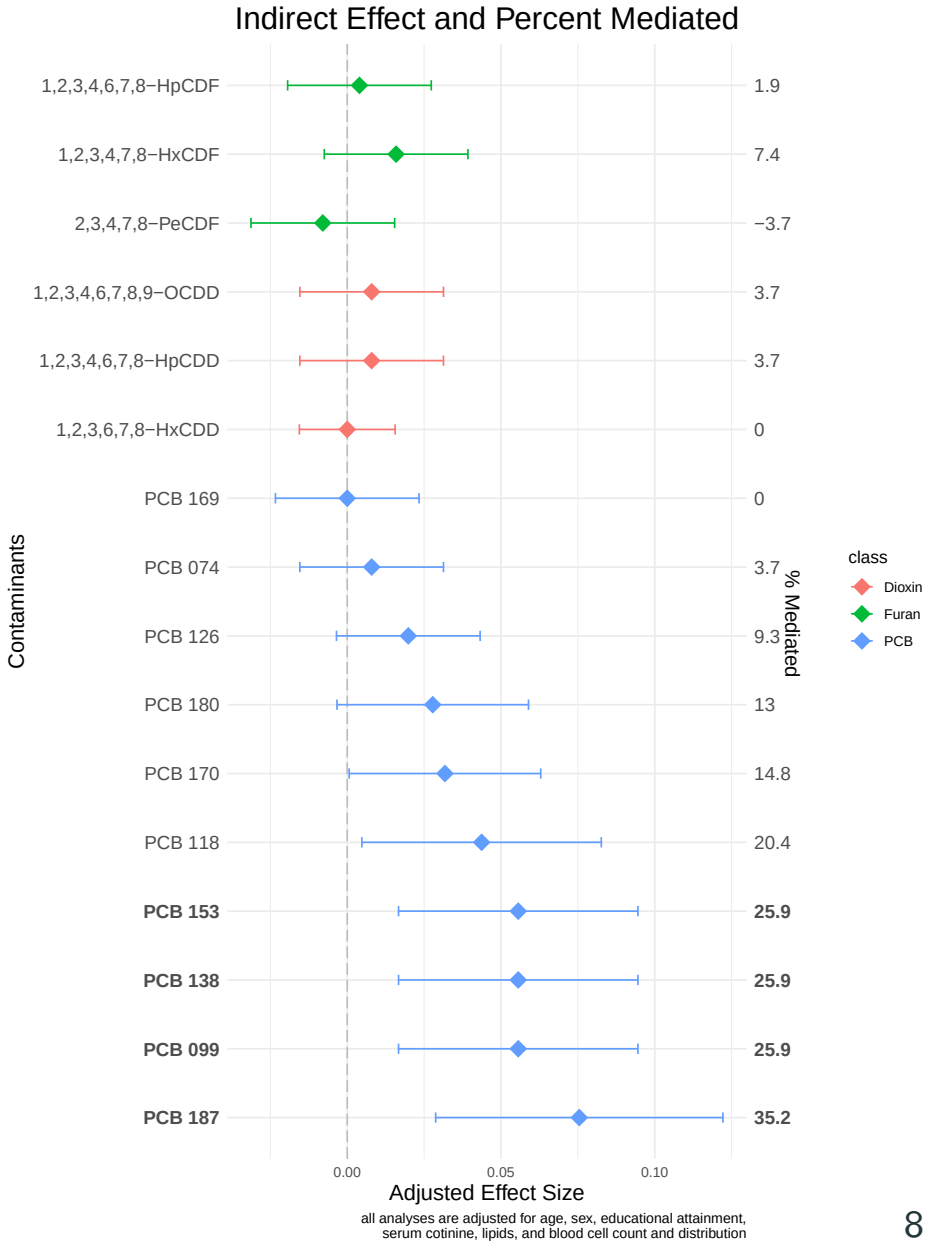




Mediation Analysis: Indirect Effect



$$\text{Percent Mediated} = \frac{\text{Indirect Effect}}{\text{Total Effect}} \times 100$$



Conclusion

- **Conclusion:** Some evidence of a mediation effect among the PCBs.
- **Next steps:** Multi-pollutant mediation analysis methods which quantify a global mediation effect due to exposure mixtures.
- **Big Picture:** Racial disparities in cancer incidence and mortality.[19,20,21,22]

Thank You!

Contact: bossjona@umich.edu **or**

ekrobe@umich.edu

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