The (nerdy) joys of health equity research

2019 Cancer Outcomes Breakfast series
University of North Carolina at Chapel Hill

SCIENTIFIC COMMUNITY

Topic choice contributes to the lower rate of NIH awards to African-American/black scientists

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Despite efforts to promote diversity in the biomedical workforce, there remains a lower rate of funding of National Institutes of Health R01 applications submitted by African-American/black (AA/B) scientists relative to white scientists. To identify underlying causes of this funding gap, we analyzed six stages of the application process from 2011 to 2015 and found that disparate outcomes arise at three of the six: decision to discuss, impact score assignment, and a previously unstudied stage, topic choice. Notably, AA/B applicants tend to propose research on topics with lower award rates. These topics include research at the community and population level, as opposed to more fundamental and mechanistic investigations; the latter tend to have higher award rates. Topic choice alone accounts for over 20% of the funding gap after controlling for multiple variables, including the applicant's prior achievements. Our findings can be used to inform interventions designed to close the funding gap.

INTRODUCTION

Despite ongoing efforts at the National Institutes of Health (NIH) to promote a diverse biomedical workforce (*1*, *2*), a 2011 study showed that applications from African-American/black (AA/B) scientists were significantly less likely to receive an R01 award than those submitted by white (WH) scientists, even after controlling for educational background, country of origin, training, previous research awards, and employer characteristics (*3*). Especially concerning was the finding that typical measures of scientific achievement (e.g., NIH-funded training, previous grants, publications, and citations) did not translate into an equal probability of funding across racial/ethnic groups, highlighting the need for further study to guide interventions aimed at closing the funding gap. No significant funding gap for applications from Hispanic scientists or women was identified by the 2011 study; however, a more recent study disaggregating race and gender showed that applications from African-American and Asian-American women were less likely to receive R01 awards, underscoring the possibility of an additive effect for women of color (*4*). These studies raised important questions about fairness in peer review because most of the funding gap for AA/B applicants remained unexplained. Here, we seek to answer those questions by examining the characteristics of applications submitted by AA/B and WH scientists.

The underlying causes of the funding gap have been difficult to identify, in large part because of the complex and multifaceted nature of the application and review process. To address this challenge, we identified six decision points at which differential outcomes might contribute to an overall difference in funding: how frequently applicants submit, whether an application was chosen for discussion by a study section, reviewer-assigned impact scores of discussed applications, final funding decisions made by NIH institutes and centers (ICs), resubmission if the application was not funded, and a previously unstudied factor—choice of topic. An analysis of both new (Type 1) and renewal (Type 2) R01 applications (N = 157,549; attributes summarized in table S1) shows that, although the award rate has dropped for all applicants over the past decade, the funding rate for WH scientists remains approximately 1.7-fold higher than for AA/B scientists [16.1% AA/B versus 29.3% WH in fiscal year (FY) 2000–2006 (*3*) and 10.7% AA/B versus 17.7% WH in FY 2011–2015; Fig. 1].

Complex problems such as this are frequently studied with multivariate regression analysis, which can account for the effect of many independent variables on a single dependent variable. However, interpreting multivariate regression data can be challenging. When one independent variable acts both directly on the outcome and indirectly on another variable, when variables presumed to be independent are highly correlated, or when two or more variables interact with each other in a feedback loop, it can be difficult to decipher which factors make the most significant contributions to an outcome. In addition, real-world data may not provide sufficient power to calculate statistical interactions when a large number of variables act on a relatively small population. For these reasons, we first did simple descriptive analyses to characterize each of our six decision points independently before using multivariate regression analysis to determine how the relevant variables might be interrelated.

RESULTS

Career stage and institutional resources influence the gap in the number of submissions by AA/B and WH scientists

One factor that might be expected to influence whether a scientist receives funding is how many applications he or she submits. From FY 2011–2015, AA/B scientists submitted R01 applications at 83.7% the frequency of WH applicants (Fig. 1 and fig. S1). However, AA/B applicants are unevenly distributed across institutional funding quintiles; 33.9% of all AA/B investigators are from institutions in the lowest quintile, compared with only

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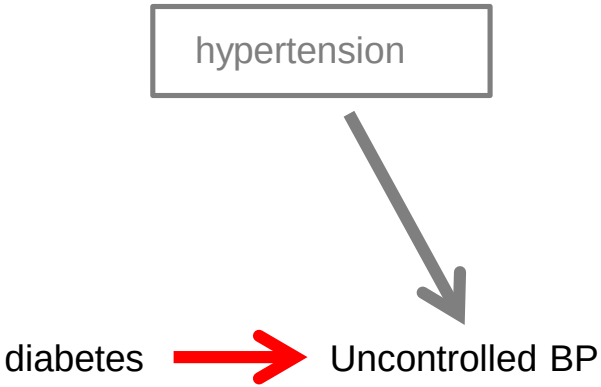
Back to basics:
What was the question again?

Whitney R. Robinson, PhD, MSPH

In collaboration with Julia Ward, MPH; Danielle Gartner, MS; Libby McClure, MS; Mike Fliss, MSW; and Kerry Keyes, PHD

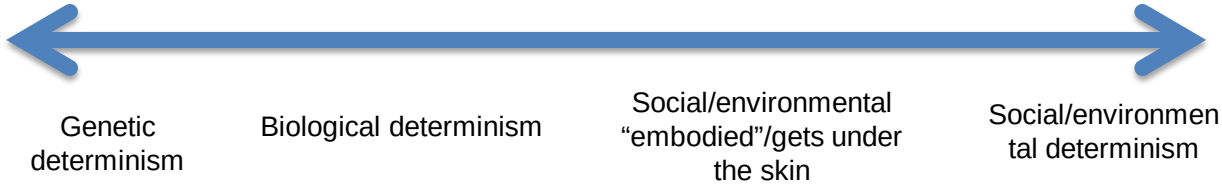
Is the Association of Diabetes With Uncontrolled Blood Pressure Stronger in Mexican Americans and Blacks Than in Whites Among Diagnosed Hypertensive Patients?

Final sentence of paper: "..Because non-Hispanic whites account for the majority of the hypertensive population in the United States, the stronger association of DM with BP outcomes in non-Hispanic whites compared with Mexican Americans reveals that in clinics, health providers need more efforts to weaken the association of DM with uncontrolled BP outcomes by further improving care for DM and BP in non-Hispanic whites while maintaining quality work in non-Hispanic blacks and Mexican Americans to significantly lower the rates of uncontrolled hyper tension and reduce the risk of adverse cardiovascular and renal outcomes in patients with diagnosed hypertension."



Xuefeng Liu, Ping Song; Is the Association of Diabetes With Uncontrolled Blood Pressure Stronger in Mexican Americans and Blacks Than in Whites Among Diagnosed Hypertensive Patients?, *American Journal of Hypertension*, Volume 26, Issue 11, 1 November 2013, Pages 1328–1334, https://doi.org/10.1093/ajh/hpt109 (FREE ACCESS online)

Theoretical orientations for health disparities research



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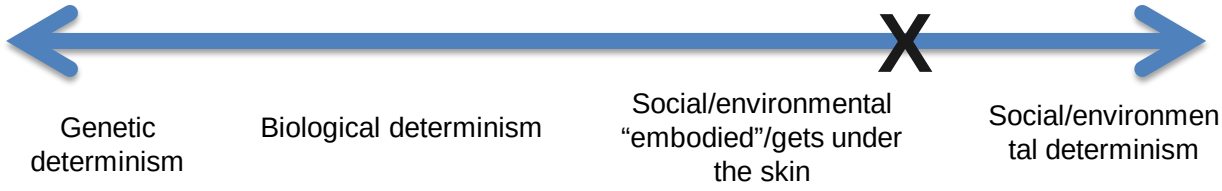

Defining terms: What is a health disparity?

Health disparity (Bravemen): Difference in which disadvantaged social groups–such as the poor, racial/ethnic minorities, or sexual minorities–systematically experience worse health… than more advantaged social groups. “Social advantage” refers to one’s relative position in a social hierarchy determined by wealth, power, and/or prestige.

Braveman Paula. 2006. “Health Disparities and Health Equity: Concepts and Measures.” Annual Review of Public Health vol. 27: 167-194. https://doi.org/10.1146/annurev.publhealth.27.021405.102103

Questions for intervention-oriented disparities work

1. Is there more disease burden in the target group vs. others?

2. Is the distribution of exposure greater in the target group versus others?

3. Is the association between the exposure and the outcome greater in the target group versus others?

“How do we assess a racial disparity in health? Distribution, interaction, and interpretation in epidemiologic studies” (R&R, Annals of Epidemiology). Ward JB, Gartner DR, Keyes KM, Fliss MD, McClure ES, **Robinson WR**

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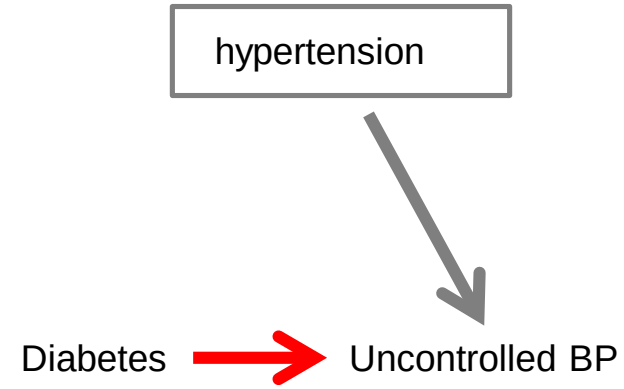

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Prevalence of uncontrolled high blood pressure among people with hypertension, NHANES 1988-1994 – 2011-14

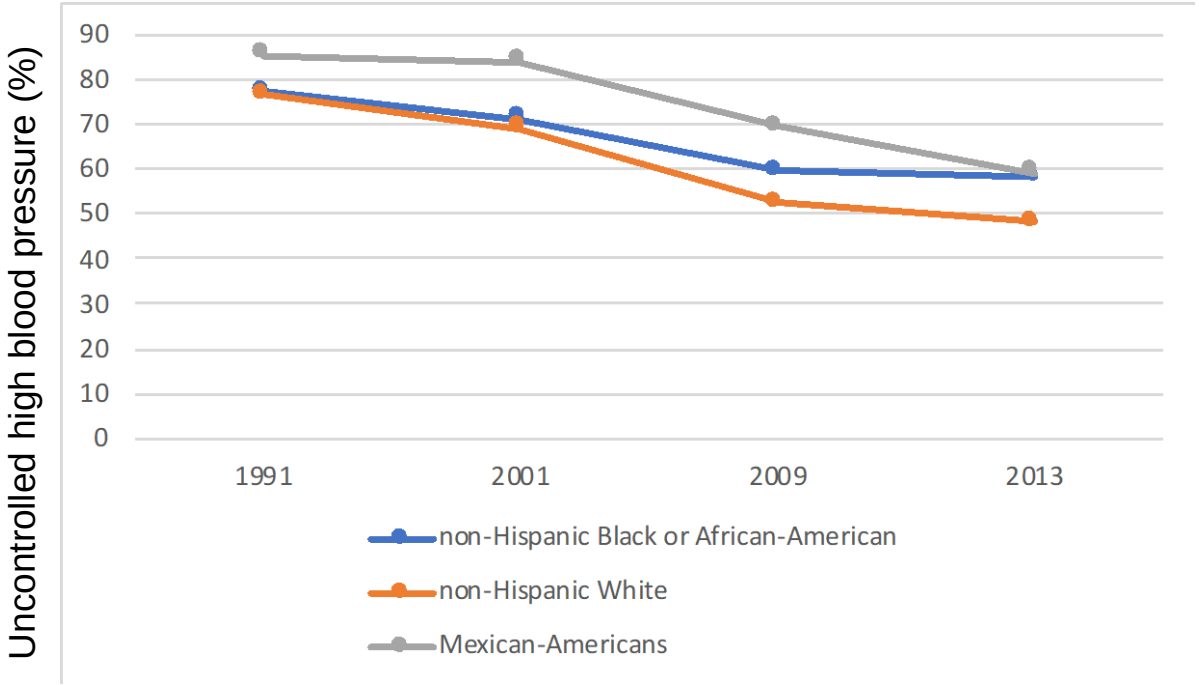

Table 54. “Hypertension among adults aged 20 and over, by selected characteristics: United States, selected years 1988-1994 through 2011-2014” National Center for Health Statistics. Health, United States, 2016: With Chartbook on Long-term Trends in Health. Hyattsville, MD. 2017.

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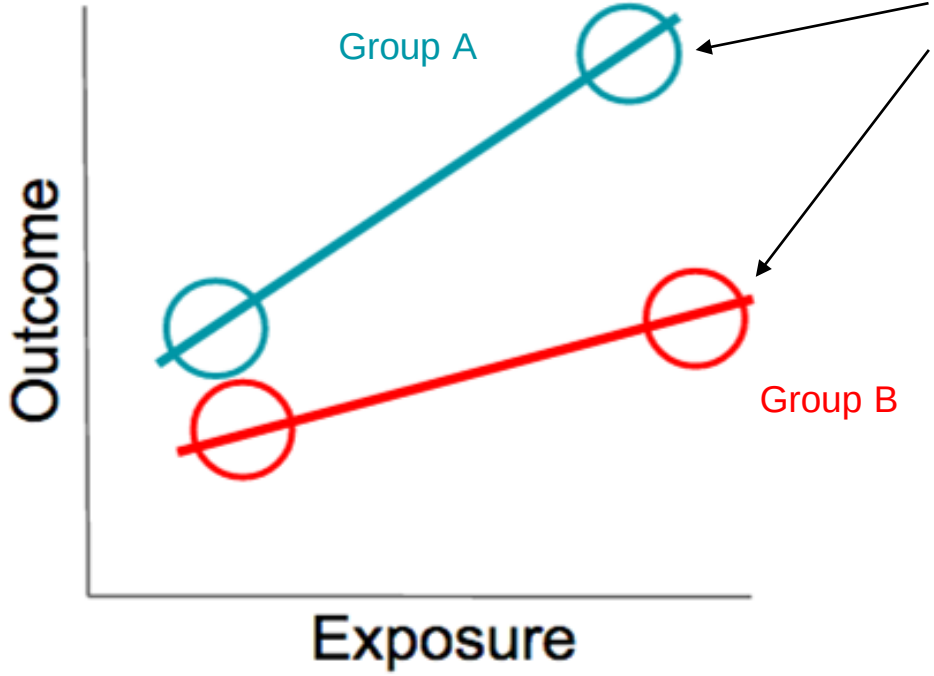

The sizes of the circles represent exposure prevalence

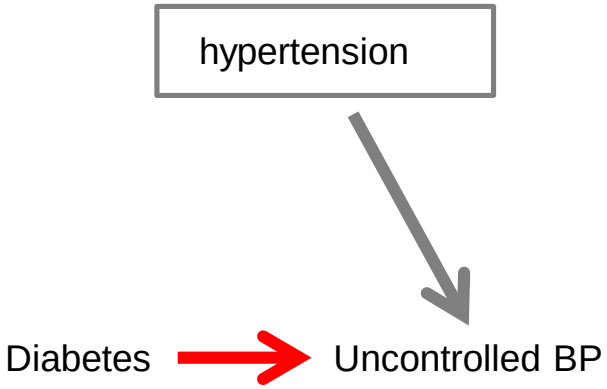

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Table 1. Age-adjusted characteristics of subjects with diagnosed hypertension by diabetes and race in NHANES 1999–2008

Characteristics	Mean or percentage (95% confidence interval)				
	Diabetic	Nondiabetic	Non-Hispanic blacks	Mexicans	Non-Hispanic whites
High cholesterol, %	39.66 (36.36–42.97)	52.97 (50.81–55.12)*	50.19 (46.80–53.58)	49.03 (45.59–52.46)	49.77 (47.47–52.07)
Diabetes	NA	NA	38.03 (35.29–40.78)	41.68 (38.40–44.96)	21.51 (19.69–23.32)*
Albuminuria					

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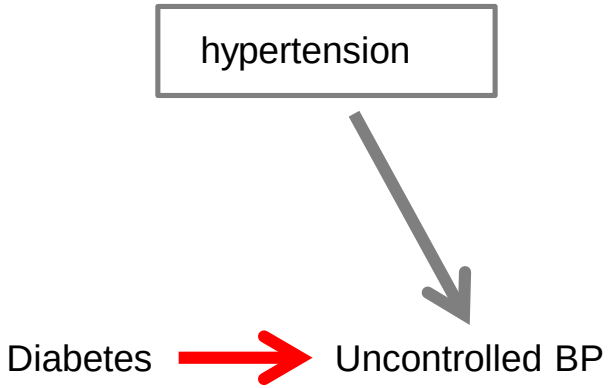

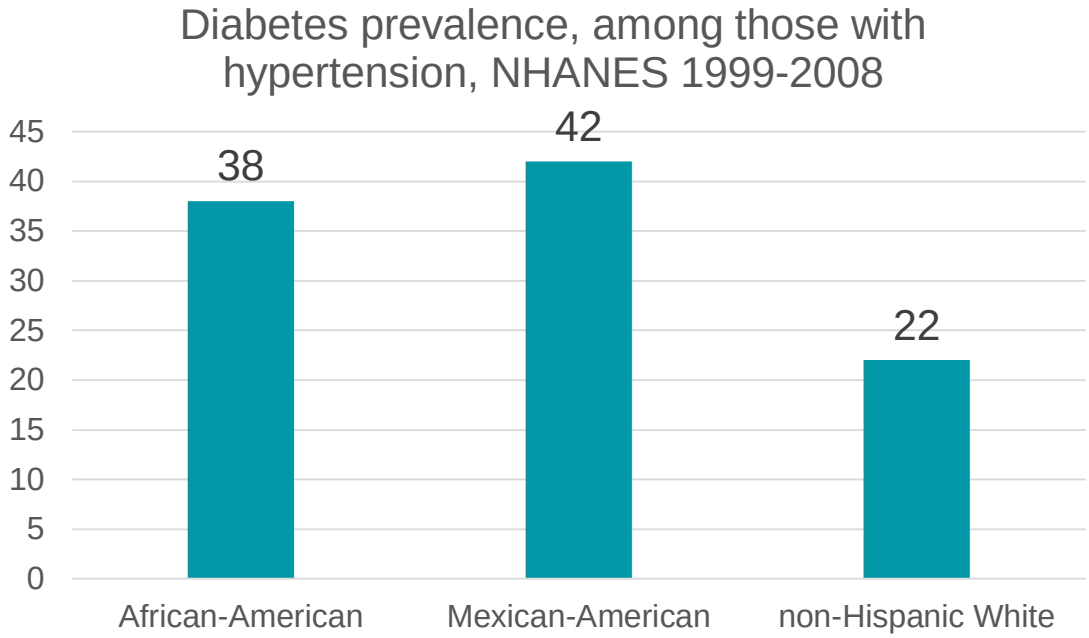

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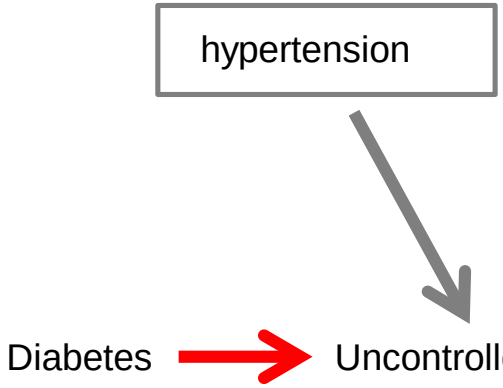

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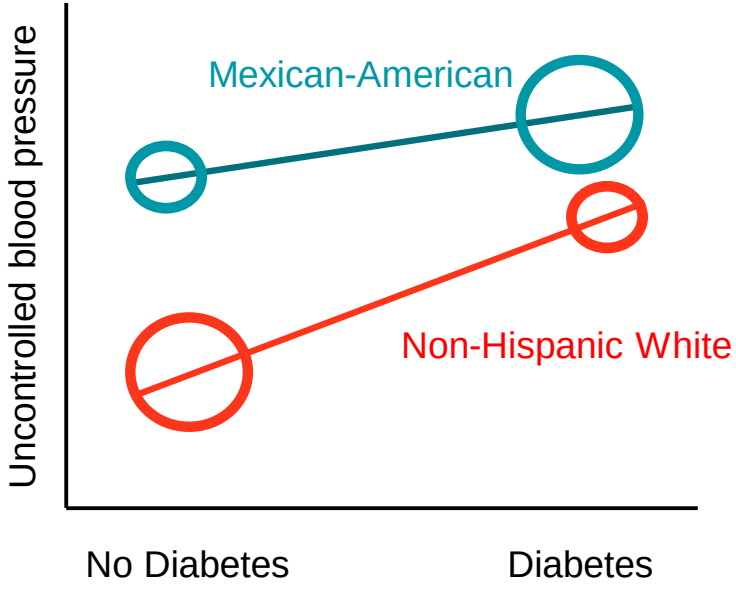

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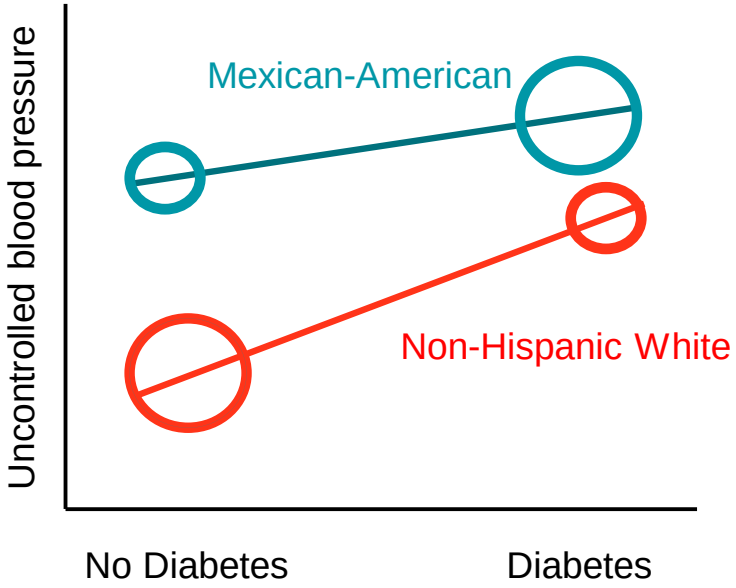
Stratified analyses:
Odds ratios (95% CIs) for uncontrolled blood pressure

non-Hispanic White	non-Hispanic Black	Mexican-American
2.61 (2.02, 3.38)	2.38 (1.77, 3.18)	1.60 (1.01, 2.52)



The Seduction of the Interaction Term

$$\Pr(\text{Health outcome}) = \beta_0+\beta_1(\text{Exposure})+\beta_2(\text{Race})+\mathbf{\beta_3(Exposure*Race)}+\beta_4(\text{Covariates})$$

Final sentence of paper: "..Because non-Hispanic whites account for the majority of the hypertensive population in the United States, the stronger association of DM with BP outcomes in non-Hispanic whites compared with Mexican Americans reveals that in clinics, health providers need more efforts to weaken the association of DM with uncontrolled BP outcomes by further improving care for DM and BP in non-Hispanic whites while maintaining quality work in non-Hispanic blacks and Mexican Americans to significantly lower the rates of uncontrolled hyper tension and reduce the risk of adverse cardiovascular and renal outcomes in patients with diagnosed hypertension."

Ratio of odds ratios

non-Hispanic White	non-Hispanic Black	Mexican-American
ref	0.96	0.53*

Connection of guiding questions to mediation analyses

Guiding question	**Estimate from Mediation Analysis**	**Counterfactual contrast**
Is outcome greater in more disadvantaged group?	Standardized* total effect	Higher rates of uncontrolled hypertension in Mexican-Americans vs Whites
Is risk-producing exposure more common in more disadvantaged group?	Counterfactual Disparity Measure*: Indirect Effect	Predicted difference in uncontrolled hypertension that would have been observed if diabetes rates among Mexican-Americans were fixed to the counterfactual levels they would have taken among Whites
Is effect of risk-producing exposure greater or less in more disadvantaged group?		

Naimi AI, Schnitzer ME, Moodie EE, Bodnar LM. Mediation analysis for health disparities research. American journal of epidemiology. 2016 Aug 3;184(4):315-24.

Resources

- **Advice:**
  - Get to know populations of interest, beyond rates of the disease outcome
  - Partner with experts in the population and in disparities/equity

- **Theoretical literature:** N. Krieiger ecosocial theory, C. Ford's Public Health Critical Race Praxis, K. Crenshaw's intersectionality, J. Phelan and B. Link Fundamental Causes, Thomas LaVeist, Gilbert Gee
  - K. Doll's Grand Rounds: A Race-Conscious Approach to Disparities in Endometrial Cancer for the 21st Century" https://obgyn.uw.edu/news-events/archive (see UW Ob-Gyn archive, May 8, 2019)

- **Empirical Literature:** My work, A. Naimi, J. Jackson, C. Howe, and many others

- **Lay Books:** So You Want to Talk about Race, White Fragility, Blind Spot: Hidden Biases of Good People

Acknowledgements

- This research received support from
  - the National Center Institute (K01 CA172717)

  - the Population Research Training grant (T32 HD007168) and the Population Research Infrastructure Program (P2C HD050924) awarded to the Carolina Population Center at The University of North Carolina at Chapel Hill by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

- Thanks to Mike Griswold, PhD; Jonathan Tingle, BS; and the University of Michigan’s Center for Integrative Approaches to Health Disparities (2P60 MD002249-01 for helping galvanize this work.

THE END

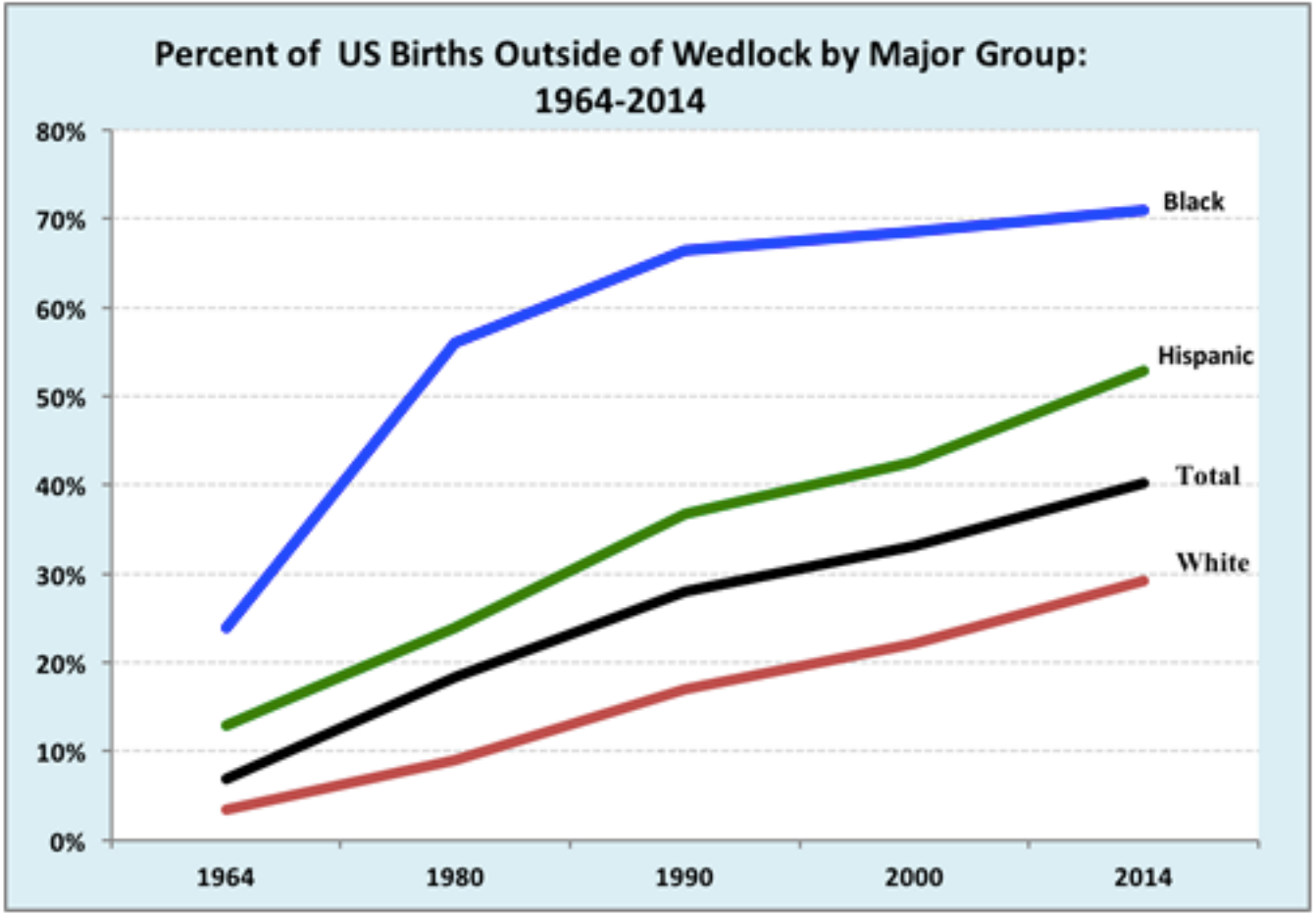
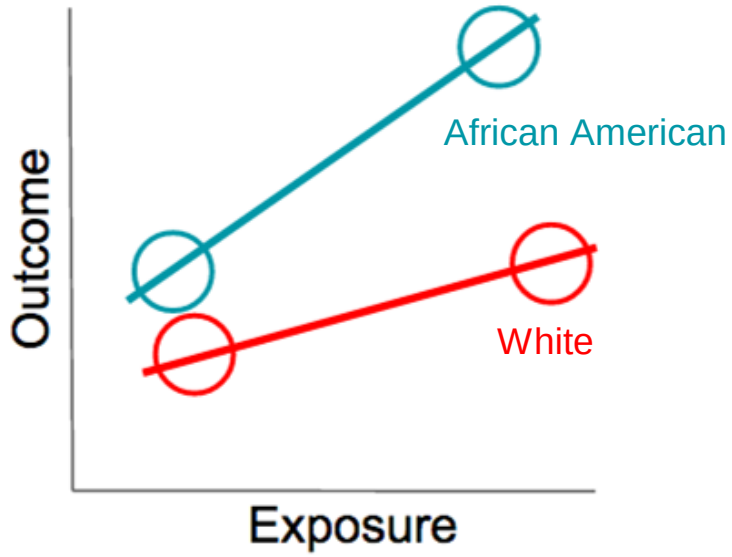

Percent of US Births Outside of Wedlock by Major Group:
1964-2014
80%
70%
60%
50%
40%
30%
20%
10%
0%
1964
1980
1990
2000
2014
Black
Hispanic
Total
White

Figure – hypertension/diabetes example

$$\Pr(\text{Outcome}) = \beta_0 + \beta_1(\text{Exposure}) + \beta_2(\text{Race}) + \mathbf{\beta_3(\text{Exposure*Race})}$$



A significant interaction term.

IOWR: Considerations

- Assumptions:

  No unmeasured confounding, conditional on covariates

  Exposure → Mediator

  Exposure → Outcome

  Mediator → Outcome

  No confounder of the mediator → outcome association affected by prior exposure
- Inefficient compared to Baron and Kenny
- Natural direct and indirect effects

Summary

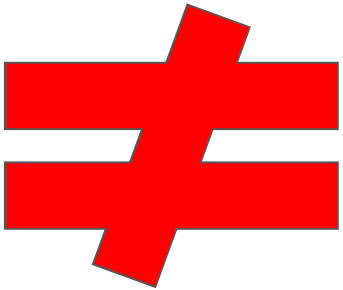
- The significance of an interaction term doesn’t wholly address the question of whether or not an exposure contributes to a racial health disparity.

Recommendations:

- Don’t stop analysis at the interaction term
- Also consider:
  a. Is there an association between the exposure and the outcome? Does it differ by group?
  b. What is the distribution of the exposure in each group?
  c. Is there more disease burden in one group vs. the other?

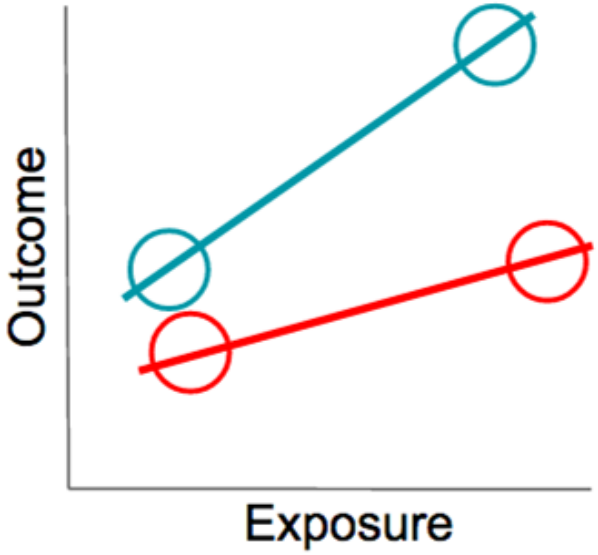
Our central argument

Is the interaction term between race and exposure significant?



Does the exposure contribute to a racial disparity in the outcome?

An introduction to our primary figure



Questions to consider:

- Is there an association between the exposure and the outcome?
  - Slopes of the lines - are they flat?
  - Do they differ from each other?
- What is the distribution of the exposure in each group?
  - What are the sizes of the bubbles?
- Is there more disease burden in one group vs. the other?
  - Is there a difference in the prevalence of outcome between the groups?

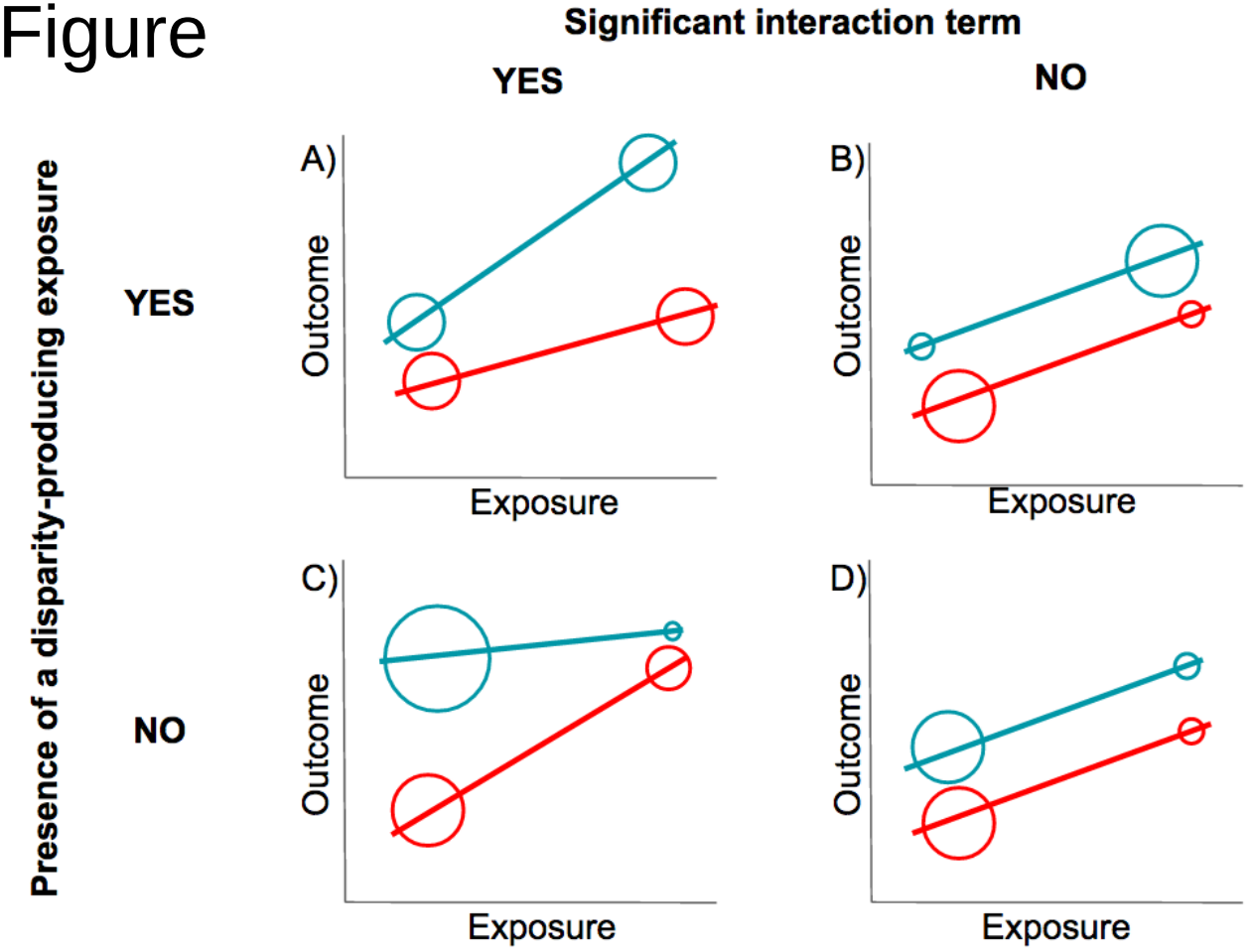
Natural v. Controlled Direct Effects

- **Controlled direct effect:** The effect of exposure on outcome that would be observed if the mediator were fixed to a certain level.
- **Natural direct effect:** The effect of exposure on outcome that would be observed if the mediator in the exposed group were fixed to the counterfactual level it would have taken in the absence of exposure.

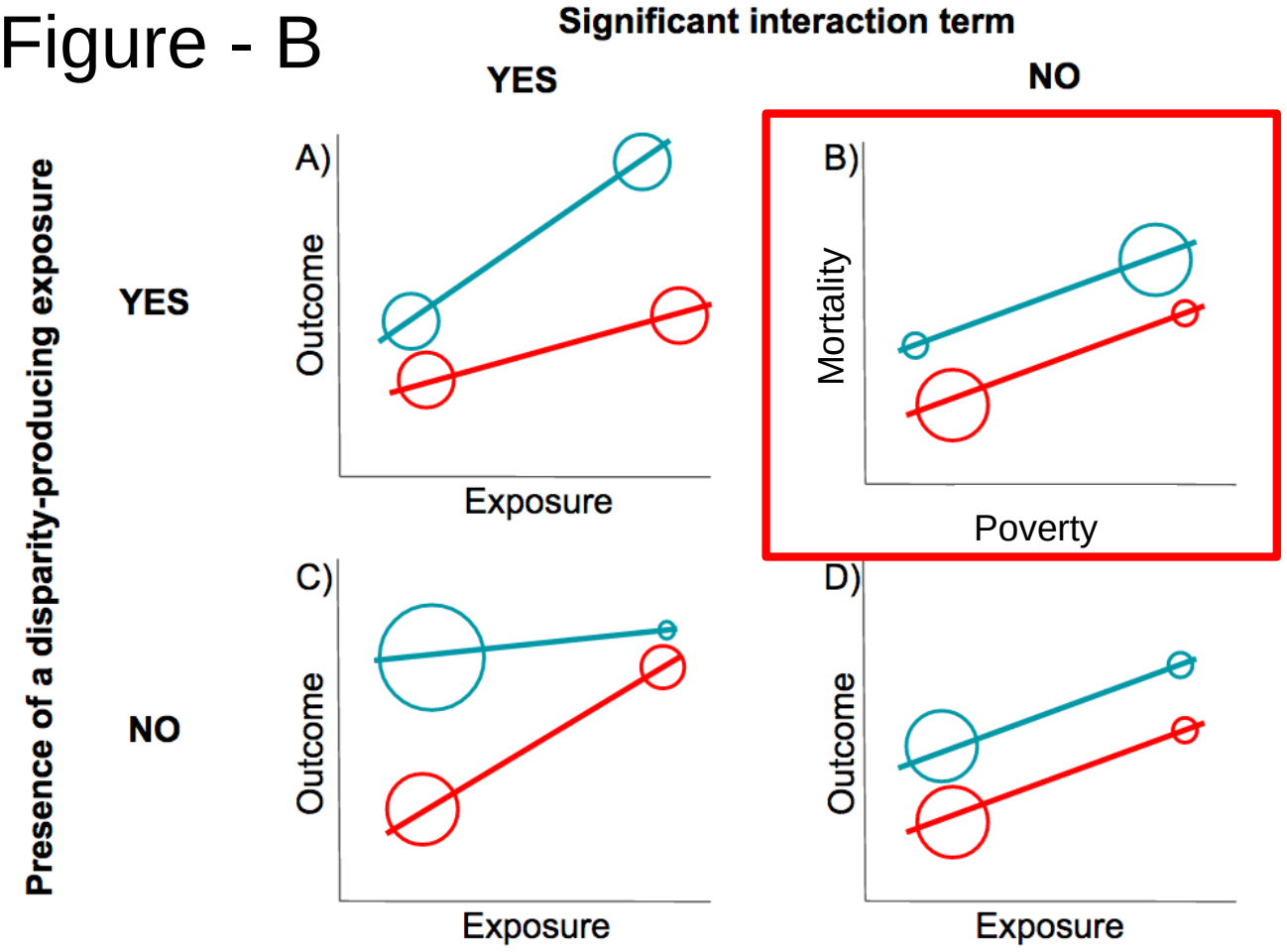
- More on this:

VanderWeele TJ. Policy-relevant proportions for direct effects. *Epidemiology*. 2013 Jan;24(1):175-6.

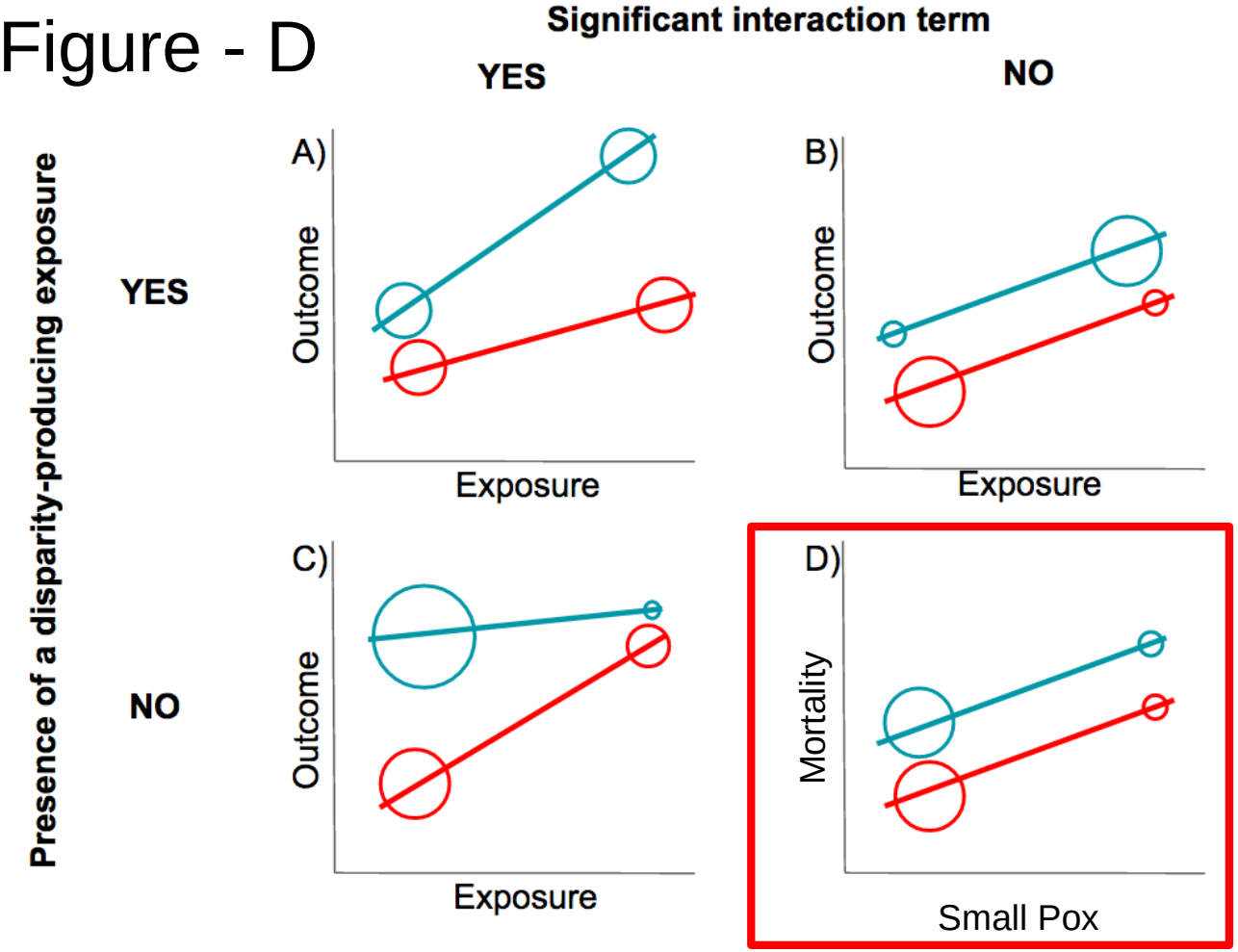
Primary Figure



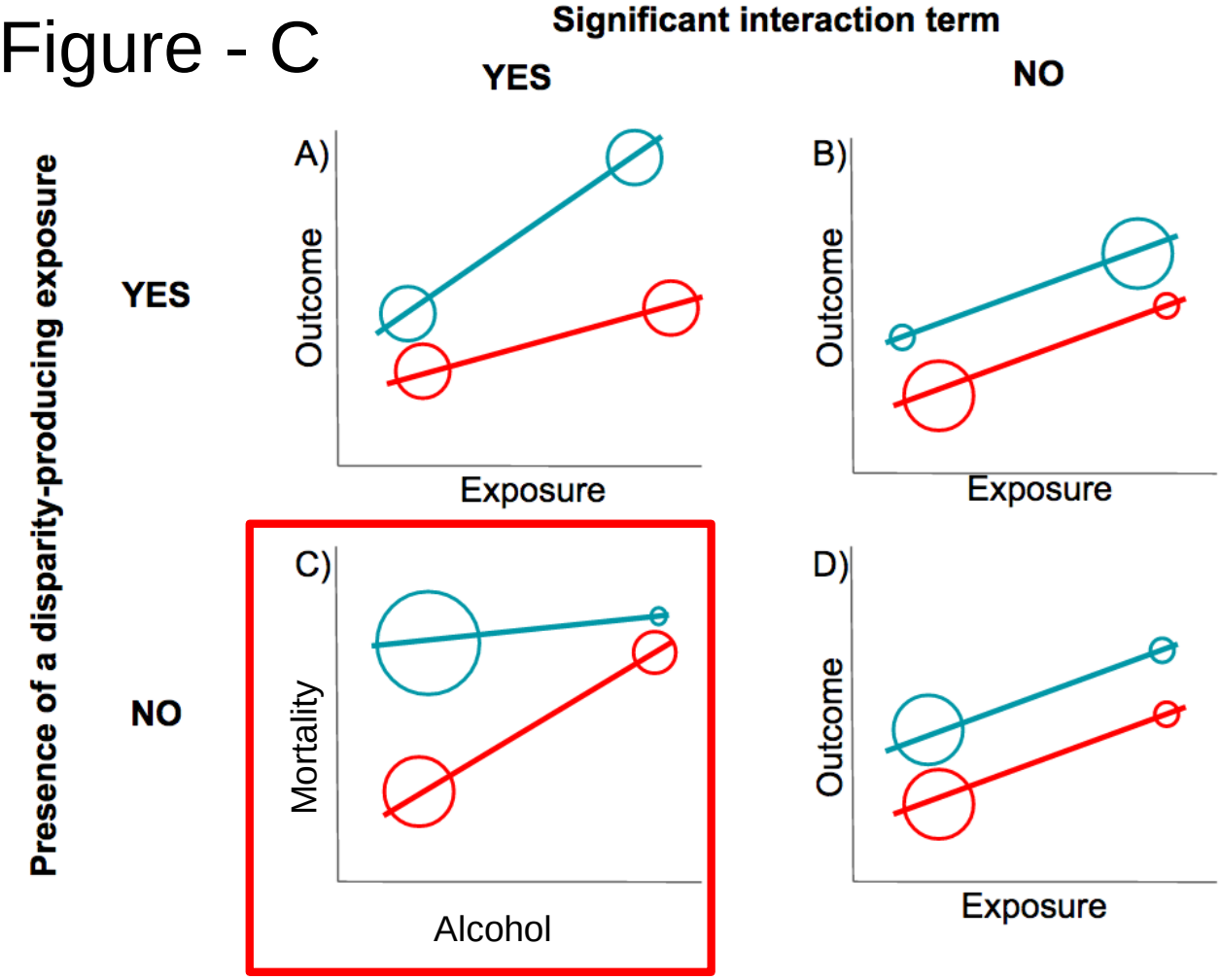
Primary Figure - B



Primary Figure - D



Primary Figure - C



Documenting racial health disparities in epidemiologic studies

Differential Association of Birth Weight with Cardiovascular Risk Variables in African-Americans and Whites: The Bogalusa Heart Study

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BMI were also analyzed. The interaction of birth weight with ethnicity was also assessed. A separate model was con-

1). The interaction of ethnicity with birth weight was signif-icant for all outcome variables except diastolic BP and HDL.

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TABLE 1. Mean (SD) of baseline characteristics and biochemical measurements of the study population according to gender and race

	Male			Female		
	African-American	White	*P*	African-American	White	*P*
Number	203	386	–	222	344	–
Age	13.5 (3.5)	12.7 (3.3)	0.01	13.5 (3.4)	13.0 (3.4)	0.08
Birth weight (g)	3213 (538.0)	3454 (474.5)	< 0.01	3053 (520.4)	3342 (503.9)	< 0.01
BMI (kg/m^2)	21.3 (5.7)	20.5 (5.1)	0.08	21.5 (5.8)	21.1 (5.6)	0.97
Systolic BP (mmHg)	106.0 (10.7)	102.7 (10.2)	< 0.01	104.7 (9.8)	102.3 (9.2)	< 0.01
Diastolic BP (mmHg)	64.1 (9.2)	62.3 (9.5)	0.03	65.1 (9.3)	63.7 (8.9)	0.07

Other Measures & Approaches - A Primer

- Contingency Table
- Absolute: Rothman's I (IC)
- Relative: RERI (ICR)

Rothman's I = $(R_{11} - R_{10}) - (R_{01} - R_{00})$

RERI = Rothman's I / R_{00}

- Oaxaca-Blinder Decomposition

$$\Pr(\text{Outcome}) = \beta_0 + \beta_1(\text{Exposure}) + \beta_2(\text{Race}) + \beta_3(\text{Exposure*Race})$$

	Referent Race/Ethnicity	**Index Race/Ethnicity**
Unexposed	Doubly "unexposed" $R_{00} = \beta_0$	Singly "exposed" $R_{10} = \beta_0 + \beta_2$
Exposed	Singly "exposed" $R_{01} = \beta_0 + \beta_1$	Doubly "exposed" $R_{11} = \beta_0 + \beta_1 + \beta_2 + \beta_3$

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Racial health disparities

Differences in disease burden and healthcare quality between racial and ethnic groups that are due to the systematic social disadvantage resulting from belonging to a racial or ethnic minority group

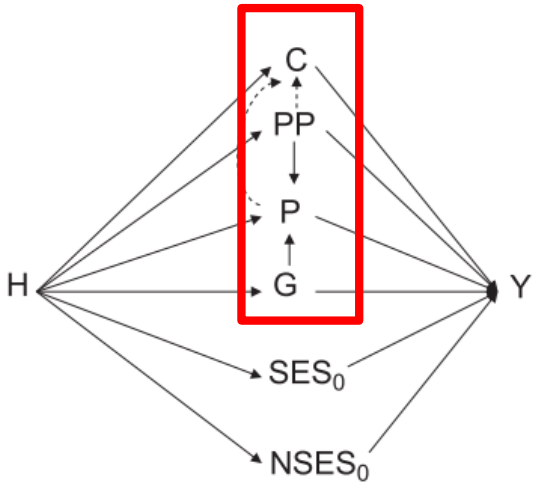

FIGURE 2. Diagram illustrating cultural context (*C*) that may be influenced by physical phenotype (*P*).

introduction

- Variables that don’t fit a new PO framework
- Race/ethnicity – genetic determinism, biological determinism, social determinism
- Conceptual reading from Thomas LaVeist (if time)
  - In Epi, See also Nancy Krieger, Chandra Ford, Gilbert Gee, Jay Kaufman, among others
  - Great literature in sociology, social medicine, history, anthropology
- What purpose is this variable serving?
  - Confounder
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Documenting racial health disparities in epidemiologic studies

Is the Association of Diabetes With Uncontrolled Blood Pressure Stronger in Mexican Americans and Blacks Than in Whites Among Diagnosed Hypertensive Patients?

Xuefeng Liu[1] and Ping Song[2]

Table 1. Age-adjusted characteristics of subjects with diagnosed hypertension by diabetes and race in NHANES 1999–2008

	Mean or percentage (95% confidence interval)					
Characteristics	**Diabetic**	**Nondiabetic**	**Non-Hispanic blacks**	**Mexicans**	**Non-Hispanic whites**	**Total**
Count	1,753	4,155	1,767	951	3,416	6,134
Age, y	62.69 (61.74–63.64)	59.84 (59.12–60.57)*	56.34 (55.41–57.27)	56.53 (55.13–57.93)	61.57 (60.76–62.37)*	60.54 (59.88–61.20)
Sex						
Female, %	55.21 (52.46–57.96)	56.82 (54.82–58.81)	63.27 (60.90–65.65)	55.98 (52.80–59.16)	54.85 (53.06–56.64)*	56.27 (54.69–57.85)
Education						
High school or below, %	63.40 (59.53–67.28)	51.87 (49.15–54.58)*	66.19 (62.68–69.70)	78.51 (75.46–81.57)	51.79 (48.38–55.21)*	54.83 (52.13–57.52)
Family poverty income ratio	2.52 (2.40–2.63)	3.01 (2.92–3.10)*	2.28 (2.15–2.42)	2.09 (1.89–2.29)	3.04 (2.93–3.14)*	2.89 (2.80–2.97)
Smoking						
Former smoking, %	39.08 (36.31–41.86)	37.35 (35.52–39.19)	29.53 (27.32–31.74)	31.66 (28.26–35.06)	39.79 (37.98–41.61)*	37.97 (36.51–39.43)
Current smoking, %	19.26 (17.09–21.44)	19.61 (17.99–21.24)	24.79 (22.24–27.34)	17.18 (15.20–19.16)	19.11 (17.41–20.82)	19.72 (18.28–21.16)
Alcohol use, %	55.96 (52.17–59.75)	66.29 (63.29–69.29)**	53.82 (50.07–57.58)	60.31 (55.88–64.74)	65.65 (62.49–68.81)*	63.69 (60.93–66.45)
Body mass index, kg/m^2	33.44 (32.97–33.92)	29.76 (29.51–30.01)*	31.70 (31.36–32.05)	30.73 (30.33–31.13)	30.40 (30.14–30.66)*	30.60 (30.39–30.81)
Serum cholesterol						
Mean, mg/dl	194.04 (190.69–197.39)	204.99 (203.25–206.73)**	203.20 (199.75–206,64)	200.66 (197.42–203.90)	202.29 (200.30–204.28)	202.24 (200.55–203.93)
High cholesterol, %	39.66 (36.36–42.97)	52.97 (50.81–55.12)*	50.19 (46.80–53.58)	49.03 (45.59–52.46)	49.77 (47.47–52.07)	49.69 (47.74–51.65)
Diabetes	NA	NA	38.03 (35.29–40.78)	41.68 (38.40–44.96)	21.51 (19.69–23.32)*	24.49 (22.94–26.04)
Albuminuria						