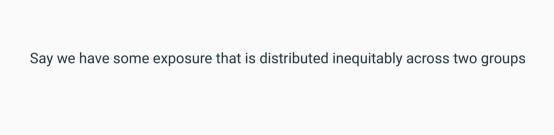
Optimism via causal inference in environmental injustice

Alexander Keil, alex.keil@nih.gov



and that exposure is detrimental to health.

Typically, we can

- 1. Demonstrate inequities in exposures (e.g. compare exposure means)
- 2. Demonstrate that equal *increases* in exposure causes more harm for some groups than others (e.g. stratifed regression analysis)

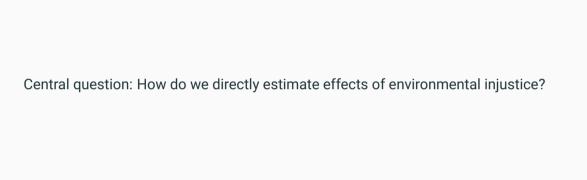
Typically, we do not

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Quantifying effects of injustice requires us to do these things



Thinking causally about environmental injustice

Causal estimates of the effect of injustice is a comparison of the counterfactuals:

A world with injustice the world we have or the one we are headed toward

A world with justice the world we wish to see

Thinking causally about environmental injustice

Causal inference tools allow us to describe a more just world and demonstrate how increasing justice can move the needle on public health problems.

An example with tabular data and old

methods

Effect measure modification: equal *increases* in exposure cause more harm for some groups than others

Effect measure modification is often considered in justice terms: we expect exposures to be worse for some groups because those groups have been subject to historical and contemporary injustices

Results of epidemiologic studies are stratified by racial/ethnic/income/education groups to assess the extent to which exposure (e.g. air pollutants) cause more harm for those who regularly experience racism, relative to those who do not.

Suppose, however, that for at least some individuals that a result of racism is not worse harm (per unit exposure) but instead much higher exposure levels (e.g. siting of new industry, govt unresponsiveness to hazards such as lead solder leaching in water pipes)



Stratified analyses can give the false impression that this inequity does not matter

EMM and exposure distributions

It's seemingly obvious that inequitable exposure across key groups (e.g. environmental injustice) can lead to different public health consequences of exposure. So how can we quantify this?

Effects of exposures, effects of interventions

- · Typically, we study "average treatment effects"
- These can be framed in terms of a randomized trial with 2 arms: "expose everyone" versus "expose no one"
- An alternative design could be "expose half of everyone" versus "expose no one"
- This latter design corresponds to old and seemingly unfashionable¹ concepts like "attributable fractions" or "population intervention effects"

¹An unfair characterization, see: Westreich D. From exposures to population interventions: pregnancy and response to HIV therapy. American journal of epidemiology. 2014 Apr 1;179(7):797-806.

Rescuing EMM for environmental justice

Typically, using stratification to assess effect measure modification considers only "average treatment effects," but these are AN effect of exposure, and not THE effect.

Rescuing EMM for environmental justice

Considered slightly more broadly, effect measure modification assessment using attributable fractions explicitly highlights health disparities that arise due to inequitable distribution of exposures

An artificial example

A population with equity of outcomes and equity of exposures

					Aver treat effec	ment
	Relative sample size	Risk among exposed	Risk among unexposed	Pr(exposed)	RR	RD
Group 1	0.87	0.20	0.10	0.20	2	0.1
Group 2	0.13	0.20	0.10	0.20	2	0.1
Overall	1.00	0.20	0.10	0.20	2	0.1

Inequity in outcomes

Different baseline risks

					Aver treat effec	ment
	Relative sample size	Risk among exposed	Risk among unexposed	Pr(exposed)	RR	RD
Group 1	0.87	0.20	0.10	0.20	2	0.1
Group 2	0.13	0.60	0.30	0.20	2	0.3
Overall	1.00	0.25	0.13	0.20	2	0.13

Inequity in outcomes

Equal RRs, unequal RDs

					Aver treat effec	ment
	Relative sample size	Risk among exposed	Risk among unexposed	Pr(exposed)	RR	RD
Group 1	0.87	0.20	0.10	0.20	2	0.1
Group 2	0.13	0.60	0.30	0.20	2	0.3
Overall	1.00	0.25	0.13	0.20	2	0.13

Inequity in outcomes

Concepts such as "weathering" or multiplicative effects among varying baseline risks can lead to health disparities that are clearly identified in stratified analyses.

Inequity in exposures

Different proportions of exposed (say, due to segregation, historical inequities)

					Aver treat effec	ment
	Relative sample size	Risk among exposed	Risk among unexposed	Pr(exposed)	RR	RD
Group 1	0.87	0.20	0.10	0.20	2	0.1
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Inequity in exposures

We intuitively see the injustice just by noting that one group is more highly exposed than another, but **standard statistical interaction assessment obscures** the public health problem².

²We may wrongly focus on the lack of EMM as evidence that there are no justice issues

Now, consider an alternative effect estimate where instead of comparing "everyone exposed" to "everyone unexposed", we compare "actual exposure" to "everyone unexposed"

This effect estimate can be called an "attributable fraction" or a "population intervention RR/RD"

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					•	lation vention t
	Relative sample size	Risk among exposed	Risk among unexposed	Pr(exposed)	RR	RD
Group 1	0.87	0.20	0.10	0.20	1.2	0.02
Group 2	0.13	0.20	0.10	0.60	1.6	0.06
Overall	1.00	0.20	0.10	0.25	1.3	0.03

Unequal RRs, unequal RDs

					•	lation vention t
	Relative sample size	Risk among exposed	Risk among unexposed	Pr(exposed)	RR	RD
Group 1	0.87	0.20	0.10	0.20	1.2	0.02
Group 2	0.13	0.20	0.10	0.60	1.6	0.06
Overall	1.00	0.20	0.10	0.25	1.3	0.03

EMM using attributable fractions can identify health disparities that arise due to "per unit" effects of exposures *OR* unjustly distributed exposures.

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We can extend this idea beyond single, binary exposures...

An example with multiple,

continuous exposures and modern

parametric g-formula approaches

An exposure inequity can be expressed symbolically as

$$p(x|group = 1) \neq p(x|group = 2)$$

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$$p(x|group = 1) \neq p(x|group = 2)$$

The attributable fraction compares the average outcome under the observed exposure distribution (p(x|group)), with the expected average outcome at a "referent" exposure X = 0

An exposure inequity can be expressed symbolically as

$$p(x|group = 1) \neq p(x|group = 2)$$

Alternatively, we could use the exposures of one group as the "referent" exposure for the other group

We could answer questions like "How would the the outcomes of group 2 change if they experienced the same exposure levels as group 1?"

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Using potential outcomes, we can express this symbolically as a causal effect:

$$p(y^{x_{\textit{group2}}}|\textit{group}=2) - p(y^{x_{\textit{group1}}}|\textit{group}=2)$$

We could answer questions like "How would the the outcomes of group 2 change if they experienced the same exposure levels as group 1?"

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Such questions can often be answered directly with g-computation (or the parametric g-formula)

Example: Pesticides, metals and inflammation biomarkers

- Numerous exposure biomarkers, including metals and pesticides, demonstrate racial and ethnic differences in NHANES³⁴
- Both of these biomarker classes are of concern with inflammatory pathways that are hypothesized intermediates for many health outcomes (e.g. cancers)
- Both of these biomarker classes are related to environmental justice concerns related to injustice (e.g. offsite migration of agricultural pesticides, lack of action on lead leeching in water pipes)
- Multiple of these exposures can contribute to inflammatory biomarker levels (e.g. C-reactive protein), leading to a "mixtures" problem

³Nguyen et al (2020) Env. Int.

⁴National Health and Nutrition Examination Survey

Study aims in light of exposure inequeties

- Quantify a health outcome biomarker related health disparity
- Estimate potential impact of reducing exposure disparity on the health disparity

NHANES plasmode simulated data

- Plasmode: Illustrate aspects of a method while preserving as much reality as possible⁵
- Select mixture of 2 organophosphate pesticides and 2 metals with highest detection %
 - Mixture was selected based on prior work on differences in exposure across racial and ethnic groups in NHANES
 - Use measured mixture and confounders in group of participants with complete case data
 - Preserve c-reactive protein/confounder relations
 - Partially simulate c-reactive protein to have known relationship with mixture

⁵it is easy to game simulations to show that a method works in a scenario that never occurs

Methods: parametric g-formula for time-fixed data

- Regress C-reactive protein on: mixture, racial/ethnic categories, education categories, age BMI, cotinine, gender
- Make predictions from this model with multiple datasets:
 - 1. Observed data ("natural course")
 - 2. Data where the 4 exposures in the mixture are proportionally changed for Black, non-Hispanic participants to have the same geometric mean exposure as White, non-Hispanic participants ("racially equitable exposure")⁶
- Use predictions in these data to estimate: Black/White disparity in C-reactive protein levels in natural course, change in C-reactive protein after hypothetical intervention, change in disparity after hypothetical intervention
- Non-parametric bootstrap to obtain 95% confidence intervals

⁶Focus on these two racial/ethnic groups is for clarity in presentation

Methods aside: parametric g-formula and the exposure distribution

If causal inference is possible (causal consistency), then given the following:

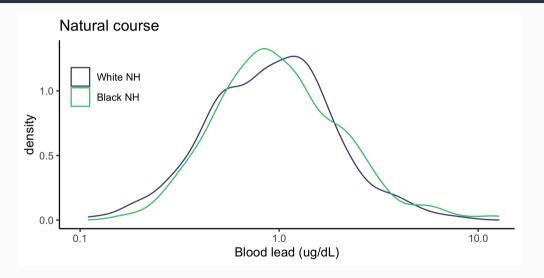
- No side effects of how exposure happens
- No measurement error
- No confounding/selection bias
- No interference

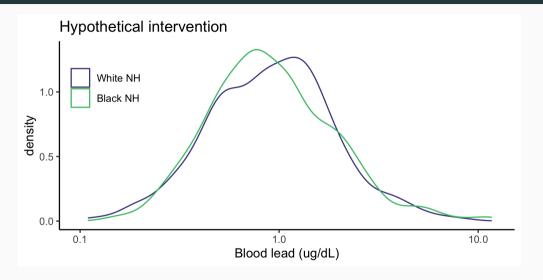
g-computation/parametric g-formula can yield a valid causal effect for *any* exposure distribution, provided that it is possible (positivity) and that the model is accurate at those exposure/covariate combinations (model consistency).

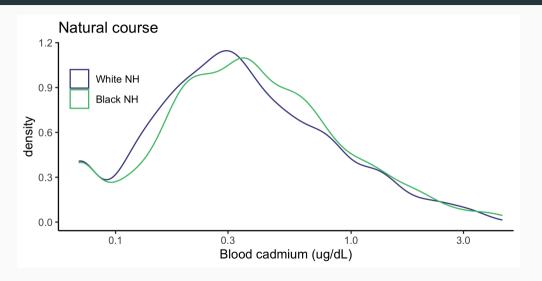
Methods aside: parametric g-formula and the exposure distribution

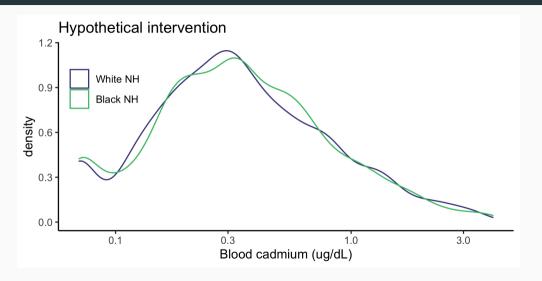
Implications for estimating effects of exposures:

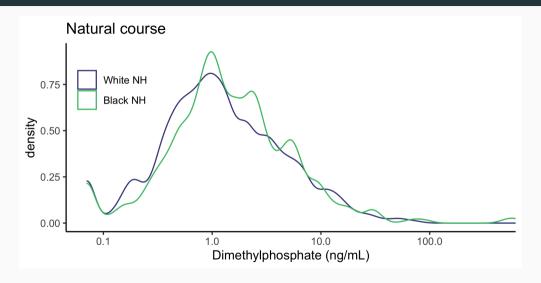
- "per unit" or "per IQR change" contrasts are based on arbitrary models
- G-computation allows us to contrast many possible worlds, including ones with more justice than our own

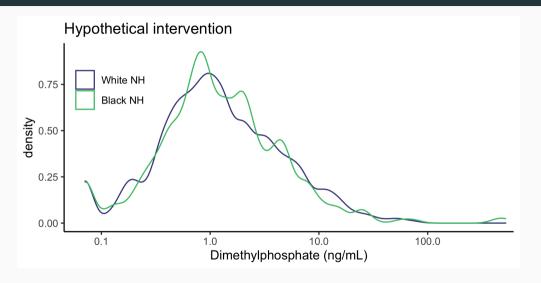


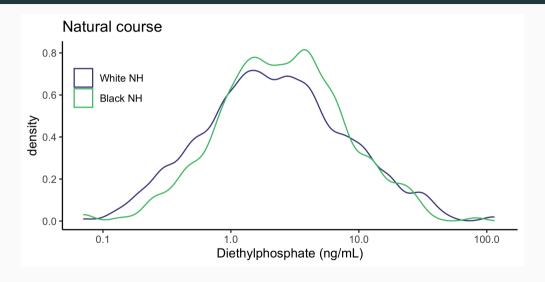


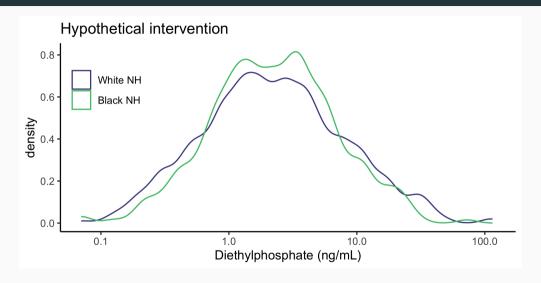












Results: linear regression model for C-reactive protein in plasmode data

	Estimate	Std. Error	t value	Pr(> t)
Intercept ^a	-2.3054	3.0371	-0.76	0.4479
Blood lead (ug/L) ^a	0.0681	0.1429	0.48	0.6341
Blood cadmium (ug/L) ^a	0.8063	0.4569	1.76	0.0778
Urine dimethylphosphate (ng/mL) ^a	0.3609	0.0100	36.02	0.0000
Urine diethylphosphate (ng/mL) ^a	0.2023	0.0236	8.57	0.0000
Age (y)	0.0840	0.0810	1.04	0.2998
Age^2	-0.0008	0.0008	-0.97	0.3327
BMI (kg/m^2)	-0.0952	0.1345	-0.71	0.4793
BMI ²	0.0060	0.0018	3.27	0.0011
Serum cotinine (ng/mL)	0.0026	0.0022	1.17	0.2426
Race/eth: Other Hispanic	0.1802	0.9366	0.19	0.8474
Race/eth: Non-Hispanic White	0.7741	0.7776	1.00	0.3197
Race/eth: Non-Hispanic Black	0.6892	0.8047	0.86	0.3919
Other Race - Including Multi-Racial	0.3606	0.8491	0.42	0.6711
Ed: 9-11th grade	0.3762	1.0349	0.36	0.7163
Ed: High school	-0.2750	0.9504	-0.29	0.7724
Ed: Some college	-0.9314	0.9211	-1.01	0.3121
Ed: College graduate or above	-1.1434	0.9833	-1.16	0.2451
Female	0.8313	0.4614	1.80	0.0718

^aCoefficients set in plasmode simulation

Results: g-computation

	Estimate	Std.Err ^a	95% CI ^b
Under natural course			
Mean CRP, White NH	5.79	0.41	(5.04, 6.62)
Mean CRP, Black NH	7.76	1.03	(6.10, 10.24)
Disparity	1.97	1.10	(0.16, 4.60)
Under hypothetical intervention			
CRP change among Black NH	-0.54	0.31	(-1.29, -0.09)
CRP change in study sample	-0.12	0.07	(-0.29, -0.02)
Change in disparity	-0.54	0.31	(-1.29, -0.09)

^aBootstrap standard error

 $[^]b$ Bias corrected bootstrap percentile method

Discussion: observations

- Parametric g-formula: directly assess impact of reducing exposure inequity
- EMM arose entirely due to exposure distribution differences between Black NH and White NH participants.⁷
- · Small inequities in many exposures can lead to large disparities in outcomes
- · No fancy black box: all estimates arose from the underlying linear model
- Causal assumptions required for causal interpretation (but that holds for g-computation AND regression modeling - both are equally creditable)
- This framing forces us to specify what we mean by equity and justice and prioritize where changes should be made

⁷We could relax this assumption with a more flexible model

Contact me at: alex.keil@nih.gov

Materials to re-create analysis in R: https://github.com/alexpkeil1/ej