

When are health inequalities unfair?

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Disclaimer

- The views expressed in this talk are my own and do not represent the position or policy of the NIH, DHHS, or US government
- I have no conflicts of interest to declare

This talk

- Focus: equity considerations in the design and conduct of clinical research
- Key points
 - Equity considerations are not a check box – they are woven into principles for ethical clinical research

Eight principles for ethical clinical research

- Collaborative partnership
- Valuable scientific question
- Valid scientific methodology
- Fair subject selection
- Favorable risk-benefit
- Independent review
- Informed consent
- Respect for enrolled subjects

Eight principles for ethical clinical research

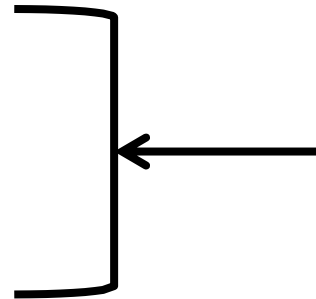
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← Equity considerations

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Equity considerations
(today's focus)

This talk

- Focus: equity considerations in the design and conduct of clinical research
- Key points
 - Equity considerations are not a check box – they are woven into principles for ethical clinical research
 - To make equity considerations explicit and meaningful, it is important to think carefully about when health inequalities are unfair

Today's plan: three guiding questions

- Who should be in the study and why?
- Which health inequalities are unfair and why?
- How do equity considerations influence the study design, analysis plan, and reporting?

Who should be in the study and why?

Changing norm

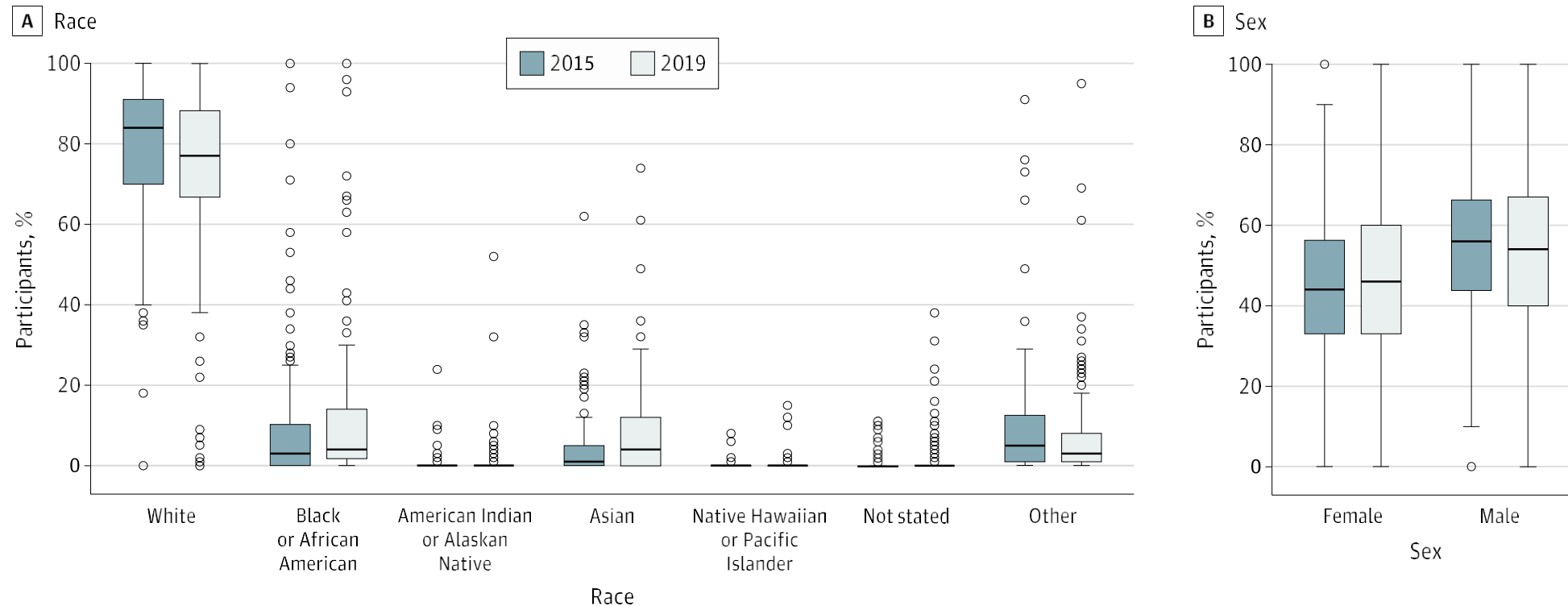
- From exclusion to inclusion
- Study subjects used to be a restrictive, homogeneous group of people
- Study subjects now can/should be anyone, and exclusion requires justification
- An example: NIH guidelines on the inclusion of women and minorities as subjects in clinical research (1994)

Who should be in the study and **why?**

- Participation
- Biology
- Societal concern

Participation

Race and sex representation in randomized clinical trials published in 2015 and 2019*



Middle horizontal lines represent medians; boxes, the interquartile range; and error bars, 1.5 times the interquartile ranges beyond the 25th and 75th percentiles. Outliers are represented by dots.

Participation

- Consideration here is the fair distribution of benefits and burden
- What it means to participate in studies has changed from bearing the burden to accessing to innovations

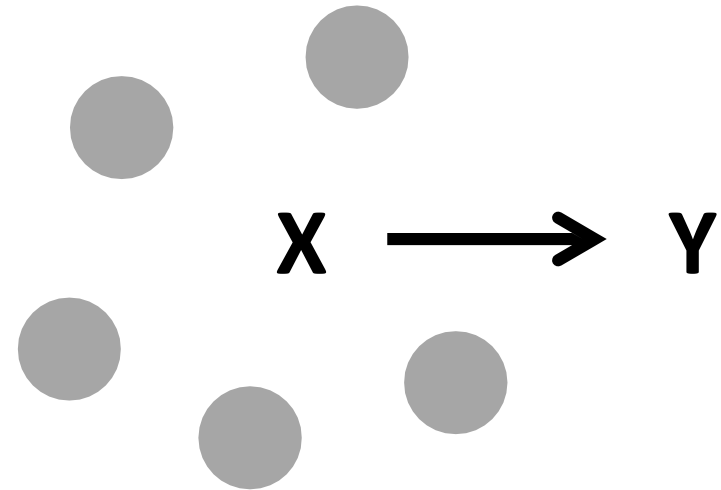
Who should be in the study and **why?**

- Participation
- **Biology**
- **Societal concern**

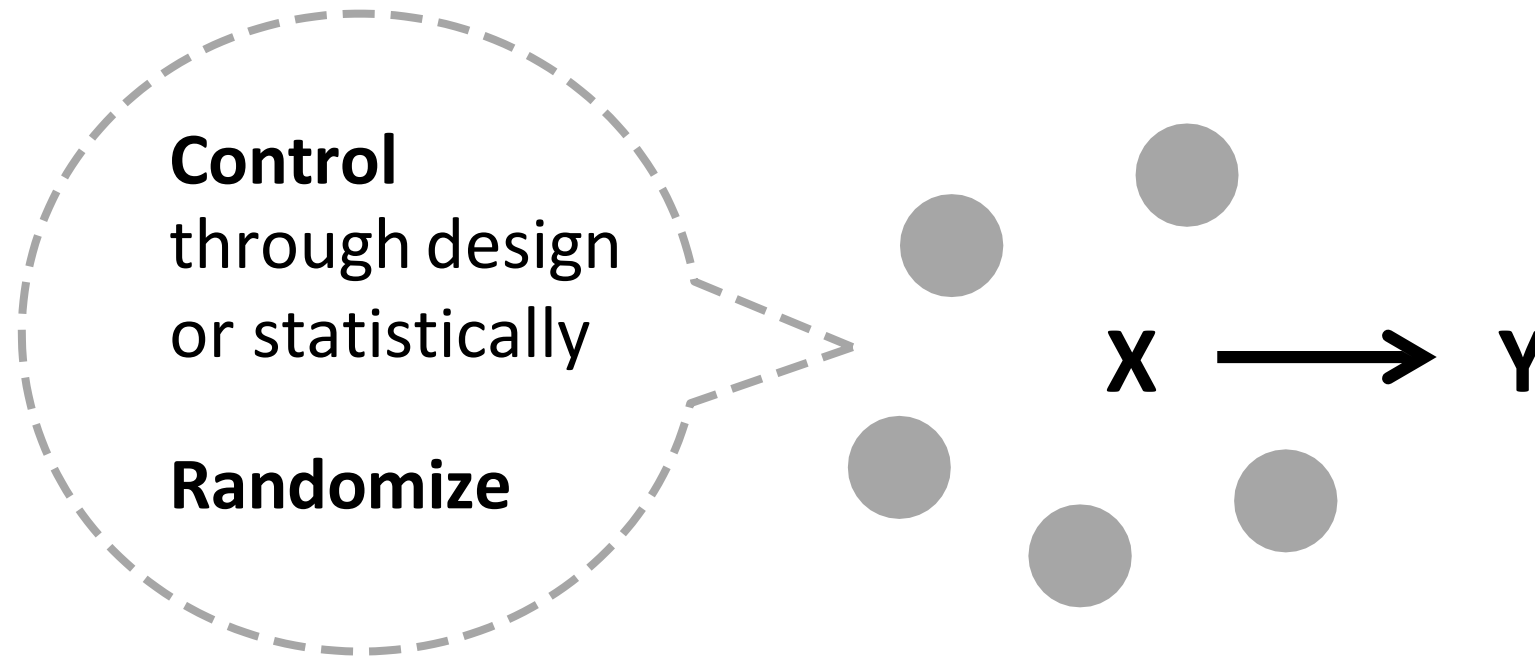
Basics of intervention studies



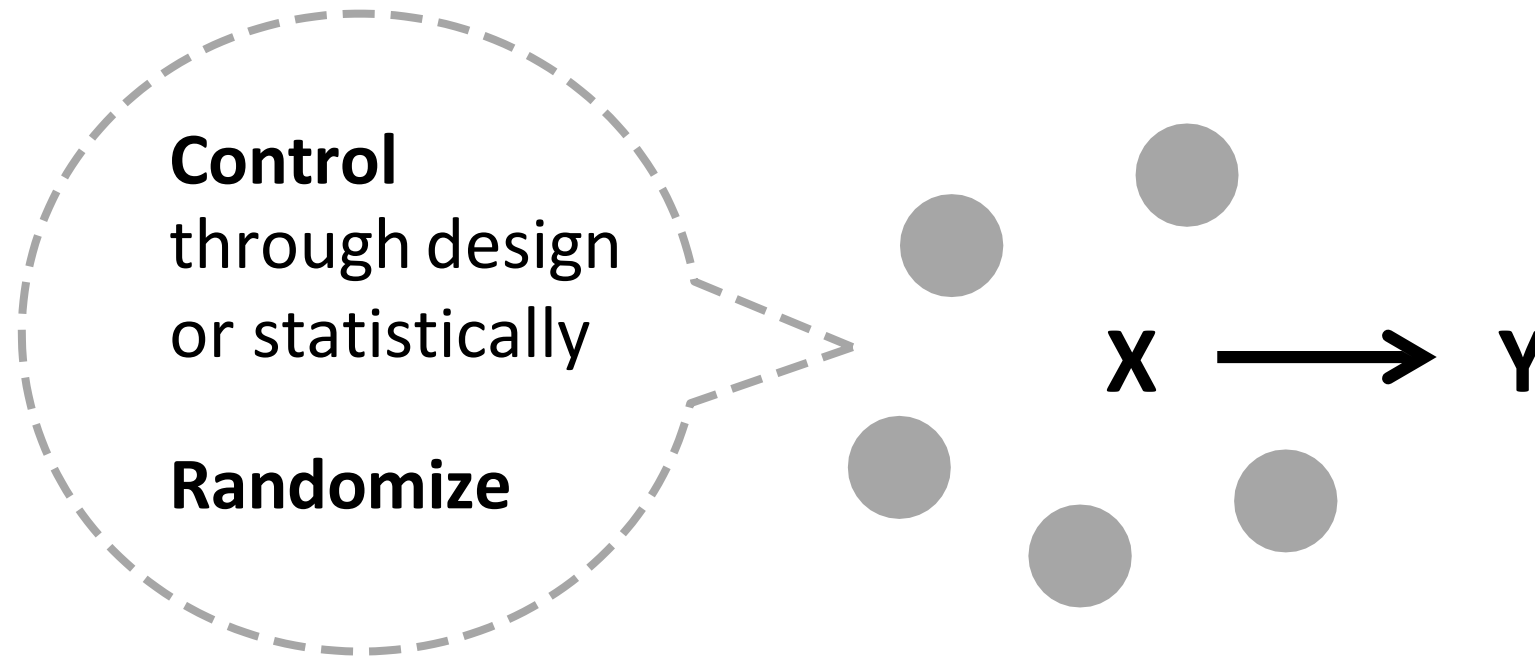
Basics of intervention studies



Basics of intervention studies



Basics of intervention studies



- The greater the disturbance is, the more challenging it is to establish causality
- “Similar” study subjects bring less disturbance
- An assumption: the causality in question ($X \rightarrow Y$) applies to all human beings

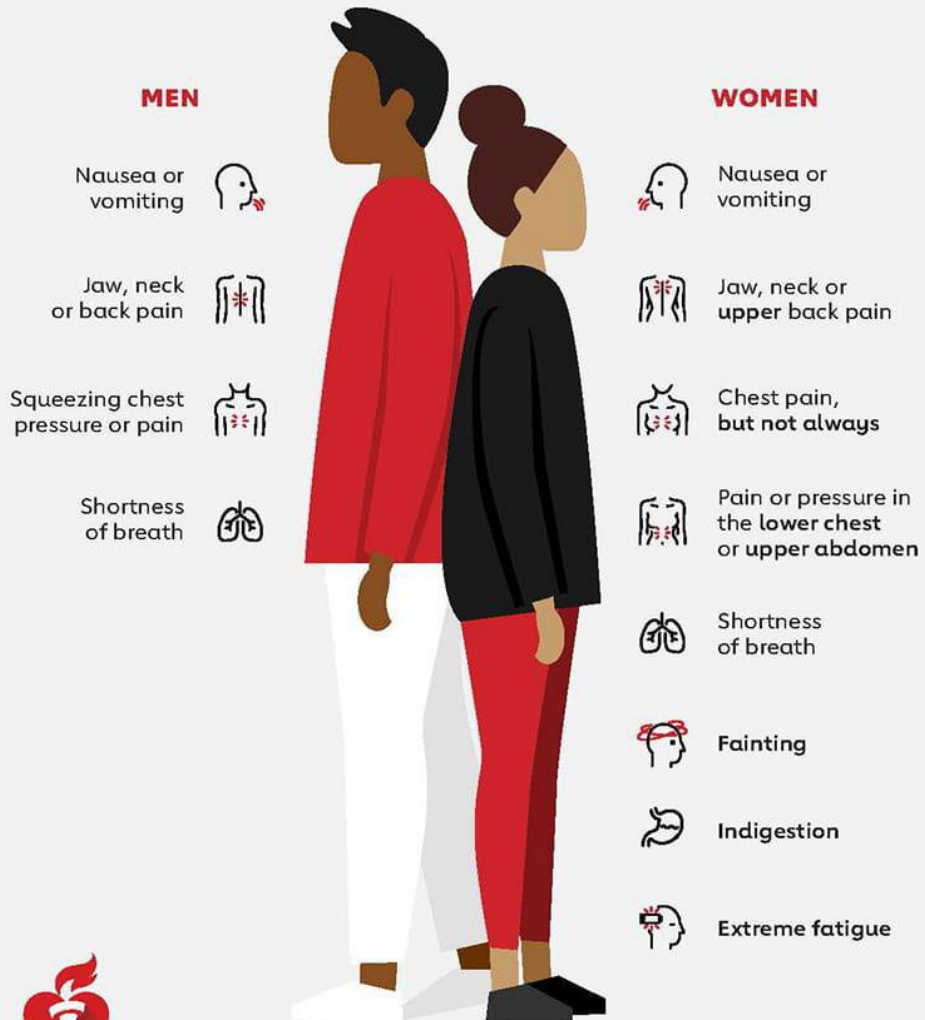
Potentially differential impact of interventions - biology

- The causality in question ($X \rightarrow Y$) may work differently to different groups of human beings because of **biological differences**
- An example: cardiovascular disease by sex

HEART ATTACK SYMPTOMS: MEN VS. WOMEN

By American Heart Association News

The most common symptom of a heart attack for both men and women is chest pain. But women may experience less obvious warning signs.



Source: American Heart Association's journal, *Circulation*
© 2019 American Heart Association, Inc.

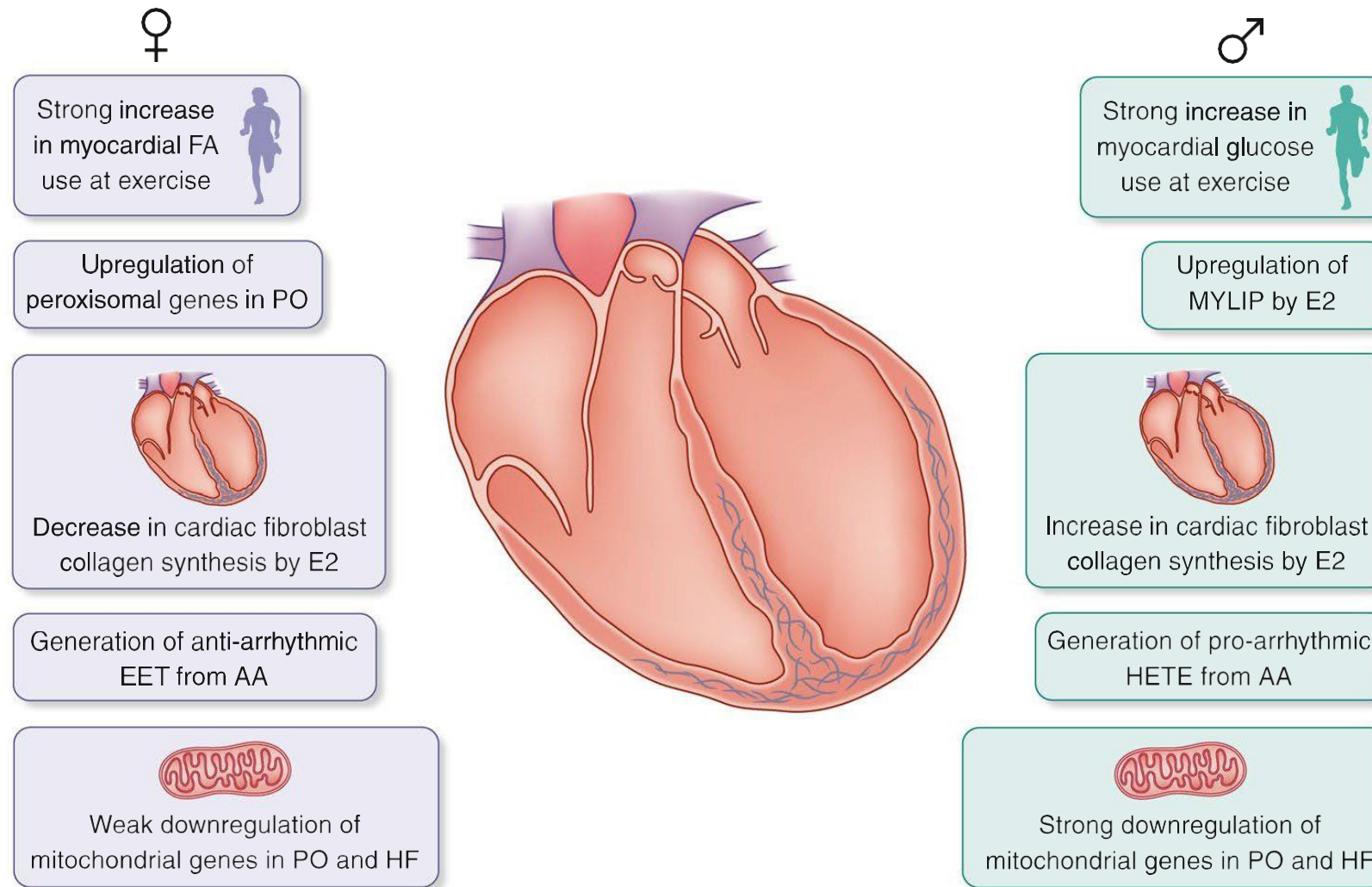


Fig. 2 | Sex-specific features in cardiometabolic disorders. Several mechanisms can be shown to occur predominantly in women or men and to contribute to these disorders predominantly in one sex. AA, arachidonic acid; E2, estradiol; EET, epoxyeicosanoids; FA, fatty acids; HETE, hydroxyeicosatetraenoids; HF, heart failure; MYLIP, myosin regulatory light chain interacting protein; PO, pressure overload. Credit: Debbie Maizels/Springer Nature.

Potentially differential impact of interventions - biology

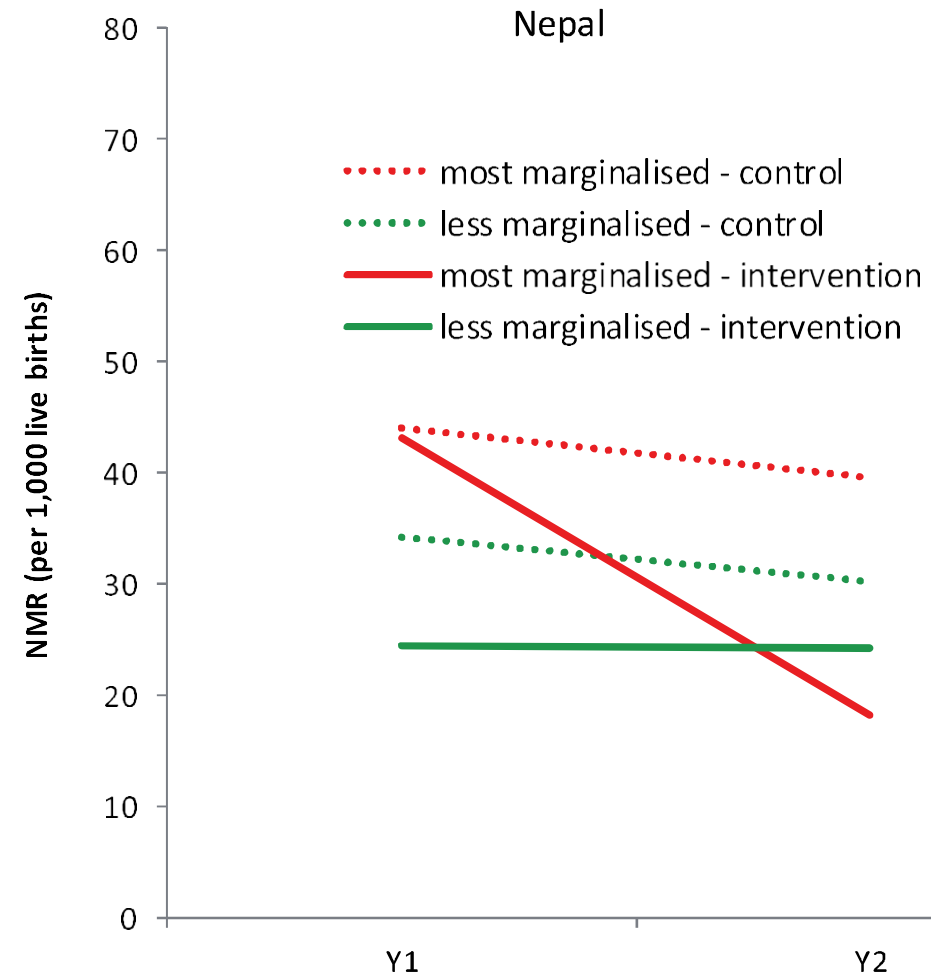
- The causality in question ($X \rightarrow Y$) may work differently to different groups of human beings because of biological differences
- An example: cardiovascular disease by sex
- The primary focus here is **potentially differential causal pathways in different groups**

Potentially differential impact of interventions – Societal concern

- The causality in question ($X \rightarrow Y$) may work differently to different groups of human beings because of **how we organize our society**
- Differential intervention effects by social group characteristic
 - An example: Effects of women's group participation on neonatal mortality rate by marginalization

Effects of women's group participation on neonatal mortality rate by marginalization

- Population: Nepal
- Intervention: A participatory and action intervention with women's groups
- Comparisons: With vs. without the intervention
- Outcome: Neonatal mortality
- Most marginalized: Women who were illiterate and poor
- Less marginalized: The rest of women



Potentially differential impact of interventions – Societal concern

- The causality in question ($X \rightarrow Y$) may work differently to different groups of human beings because of **how we organize our society**
- Differential intervention effects by social group characteristic
 - An example: Effects of women's group participation on neonatal mortality rate by marginalization
- Differential intervention effects within a traditionally excluded group
 - An example: Effects of a high intensity, lifestyle-based program for obesity treatment in primary care clinics in low-income neighborhoods

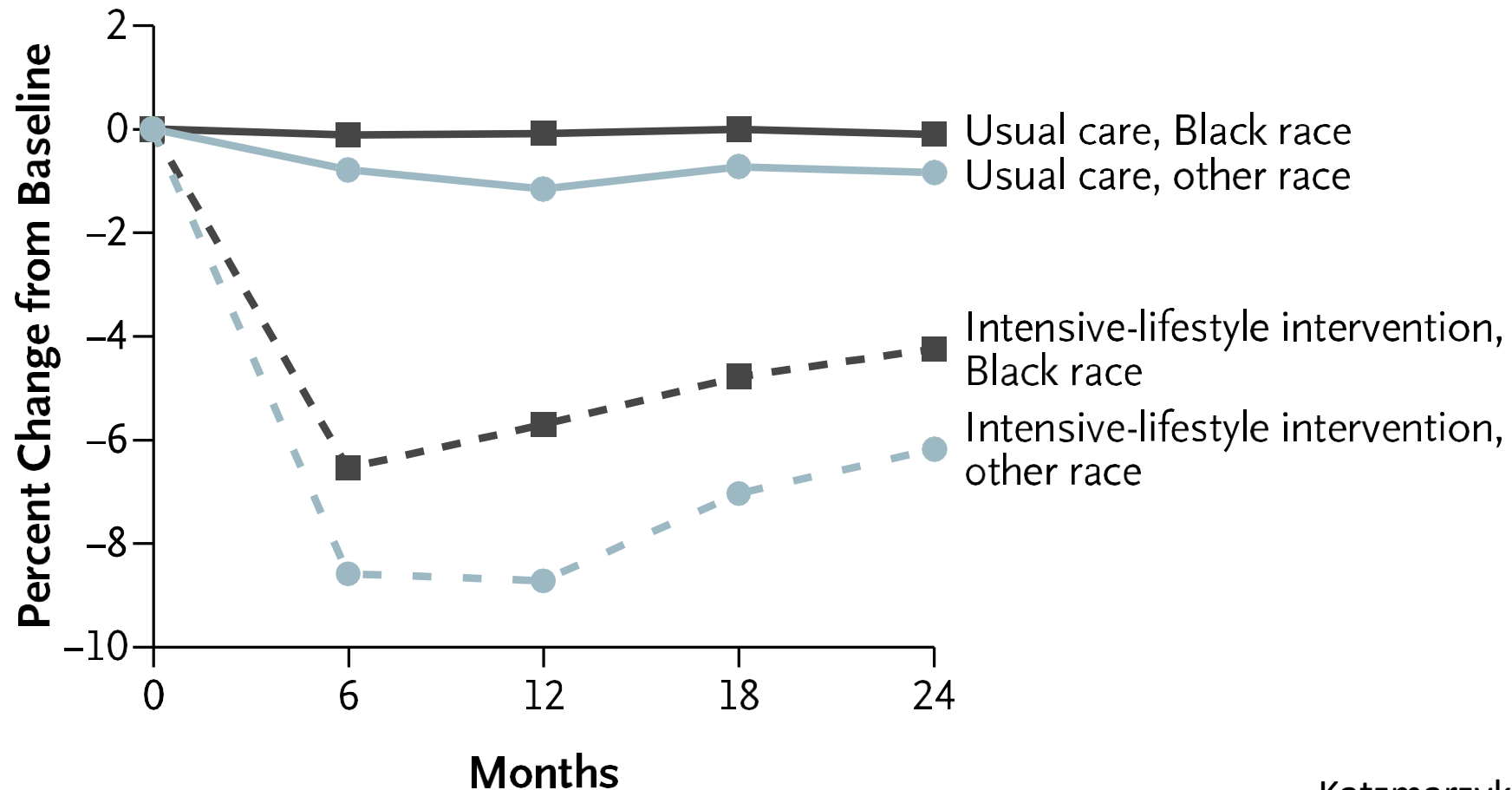
Effects of a lifestyle-based program for obesity treatment in low-income neighborhoods

- Population: Primary care patients **living in low-income neighborhoods**
 - Intervention: High intensity, lifestyle-based program for obesity treatment
 - Comparisons: Intensive-lifestyle program vs. usual care
 - Outcome: Percent change in body weight
-
- Major finding: Percent change in body weight at 24 months (95% confidence interval)

Intensive-lifestyle group	Usual care group	Difference
-4.99 (-6.02 to -3.96)	-0.48 (-1.57 to 0.61)	-4.51 (-5.93 to -3.10)

Effects of a lifestyle-based program for obesity treatment in low-income neighborhoods **by race**

A Change in Weight According to Race



Potentially differential impact of interventions – Societal concern

- The causality in question ($X \rightarrow Y$) may work differently to different groups of human beings because of
- Differential intervention effects by social group characteristic
 - An example: Effects of women's group participation on neonatal mortality rate by marginalization
- Differential intervention effects within a traditionally excluded group
 - An example: Effects of a high intensity, lifestyle-based program for obesity treatment in primary care clinics in low-income neighborhoods
- The primary interest here is **differences across groups or how a traditionally excluded group fares**, and this interest derives from concerns for **unfairness or inequity**

Terminology

- Health inequality
 - Differences or variations in health across individuals and/or groups
 - No ethical judgement
- Health inequity
 - Those inequalities in health across individuals and/or groups that we judge ethically problematic, unfair
- Health disparity
 - = health inequality (Kawachi, Subramanian, Almeida-Filho 2002)
 - = health inequity (National Institute on Minority Health and Health Disparities)

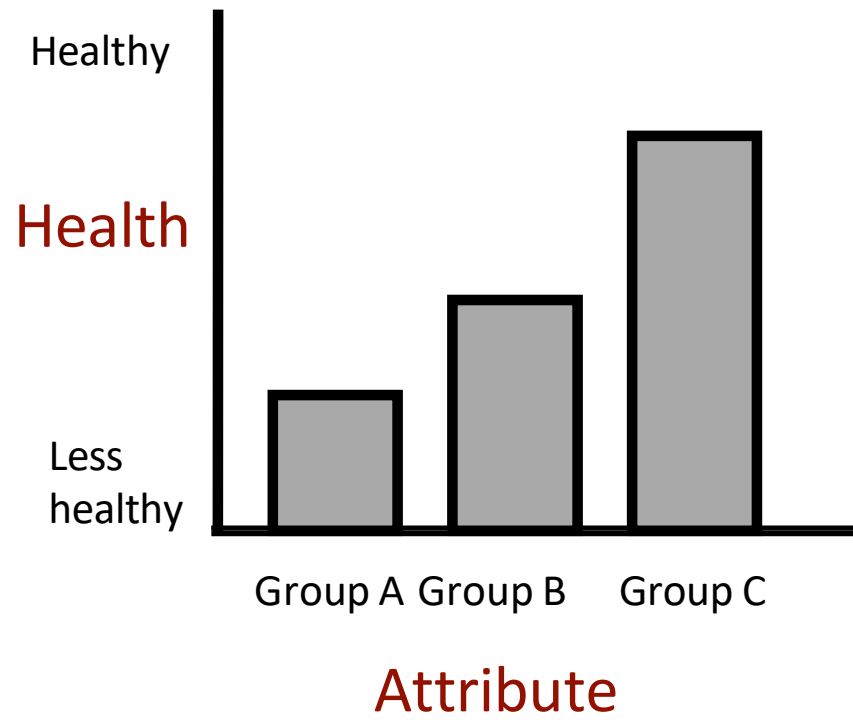
Who should be in the study and why?

- Participation
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Which health inequalities are unfair and why?

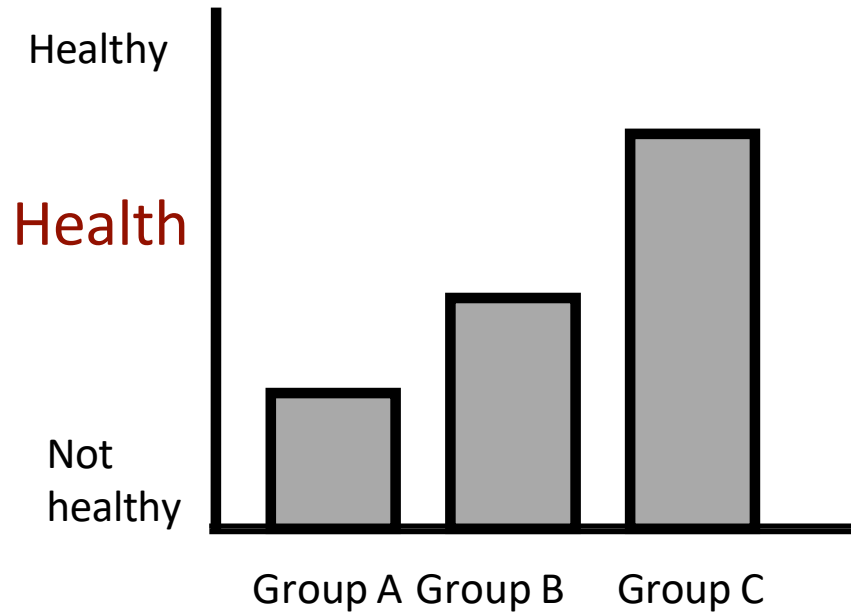
Including diverse study subjects for societal concern

- Often operationalized to include or focus on historically overlooked social groups
- Groups selected signify social disadvantage and power imbalance
- Examples of groups
 - NIH guidelines on the inclusion of women and minorities as subjects in clinical research (1994)
 - “A minority group is a readily identifiable subset of the US population which is distinguished by either racial, ethnic, and/or cultural heritage”
 - PROGRESS-Plus: **P**lace of residence, **R**ace/ethnicity/culture/language, **O**ccupation, **G**ender/Sex, **R**eligion, **E**ducation, **S**ocioeconomic status, **S**ocial capital, and additional context-specific personal or setting characteristics (Jull et al. 2017)
- The common thread: bivariate approach



Challenges of the bivariate approach

- Increasing number of groups is identified as important
- Within-group variation and intersectionality are often overlooked
- Concerns for intersectionality will increase the number of groups
- The group definition can change (e.g., from binary sex to continuous sex)
- Reasons why the selected group characteristic signify concerns for unfairness and inequity are often intuitive and implicit
- Many bits of information lack a coherent picture

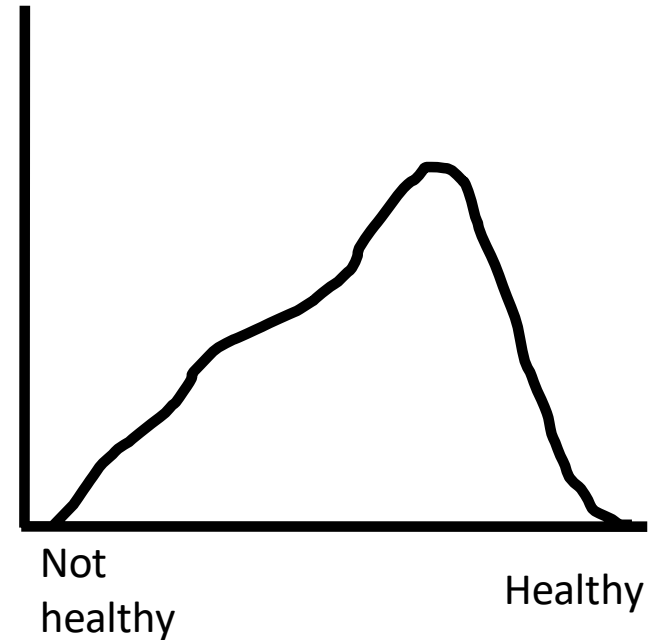


Attribute

Bivariate/group approach

Epidemiology and public health

Population frequency

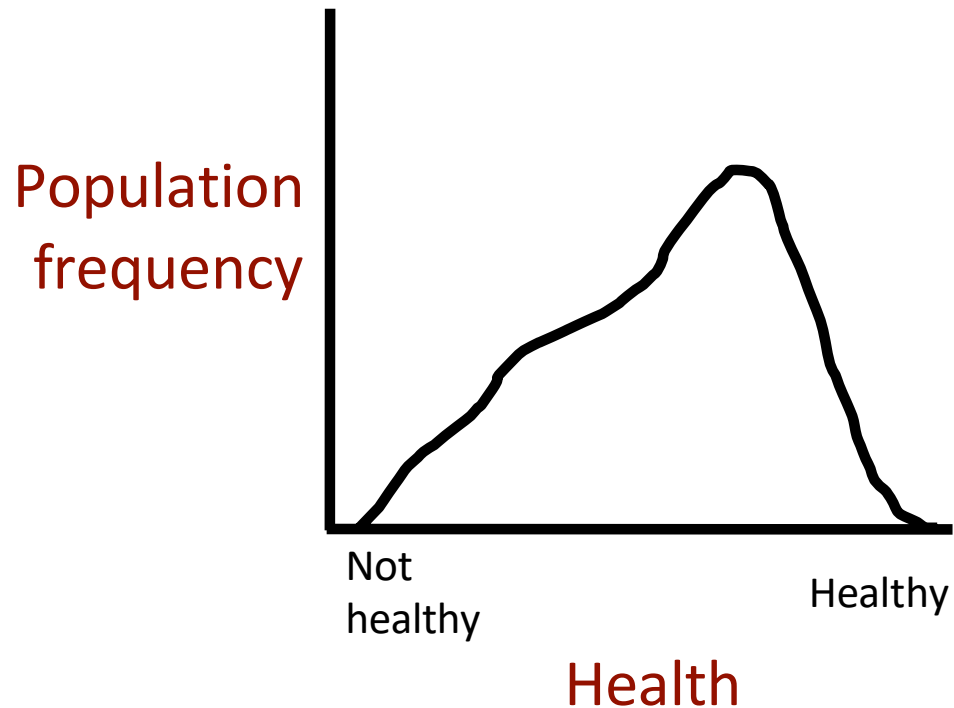


Health

Univariate/individual approach

Health economics

Is health inequality across individuals unfair?



- For some, yes
- For many, no – only part of inequality is unfair

Selected views on which health inequalities are unfair

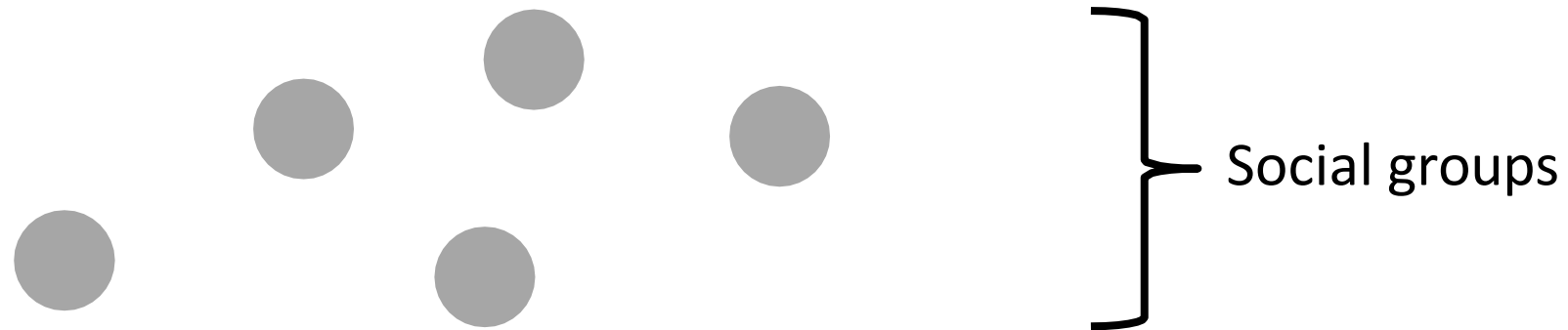
- Equal opportunity for health (or luck egalitarianism)
 - Health inequalities due to factors beyond individual control are unfair
- Policy amenability
 - Health inequalities due to factors amenable to policy interventions are unfair
- Remediability and compensability (Hausman)
 - Remediable and incompensable health inequalities are unfair
- Fair distribution of social determinants of health (Daniels extending Rawls)
 - Health inequalities are unfair when they result from unfair distribution of social determinants of health

Including diverse study subjects for societal concern informed by philosophical literature

- Making implicit explicit
- More practically, we can better:
 - articulate which groups to choose and why
 - understand the importance of intersectionality
 - Synthesize findings across studies as a cohesive story

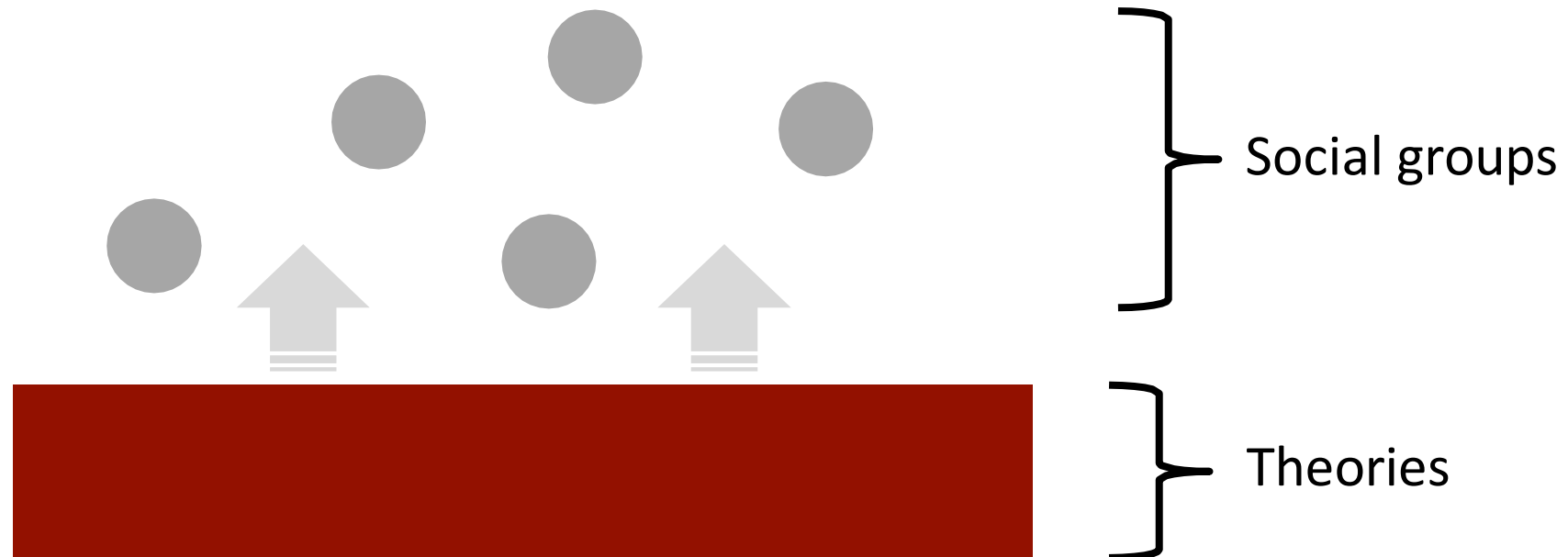
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How do equity considerations influence the study design, analysis plan, and reporting?

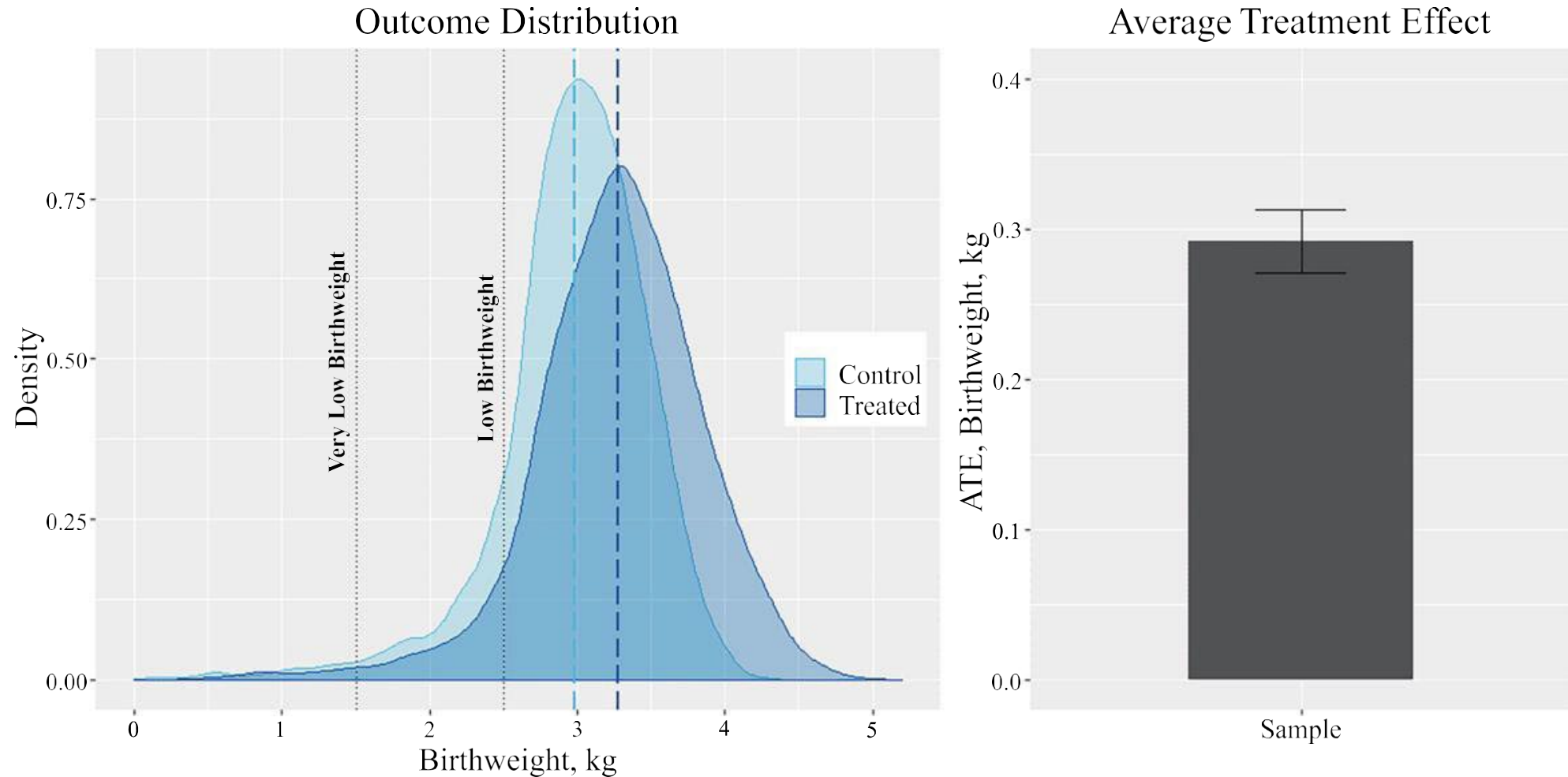
Reasons why study subjects should be diverse inform study design, analysis plan, and reporting

- Participation
 - Fair subject selection is the primary concern
 - If there is no reason to suspect or be interested in potentially differential intervention effects due to biology or societal concern, no additional considerations for the study design, analysis plan, and reporting may be necessary
- Biology
 - The study design, analysis plan, and reporting should meet the objective of examining potentially differential causal pathways in different groups
- Societal concern (equity)
 - The study design, analysis plan, and reporting should meet the objective of identifying differences across groups that indicate unfairness or inequity
 - “Health equity-relevant randomized trials” (Jull et al. 2017)
 - “Equity-informative methods” (Cookson et al. 2021)

How do equity-relevant/informative studies look like?

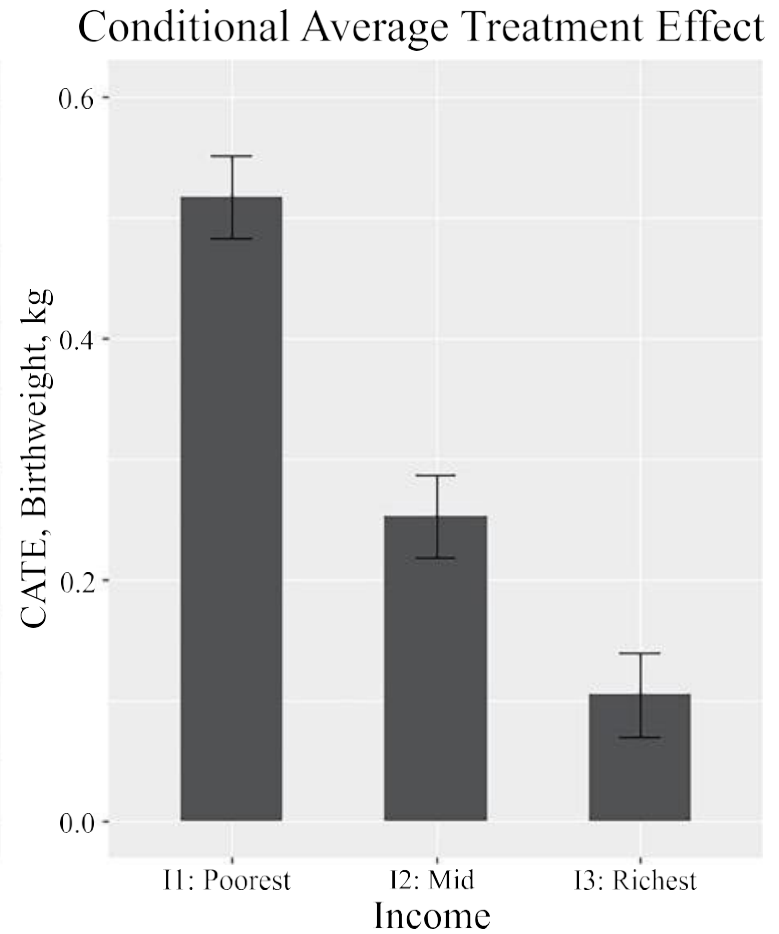
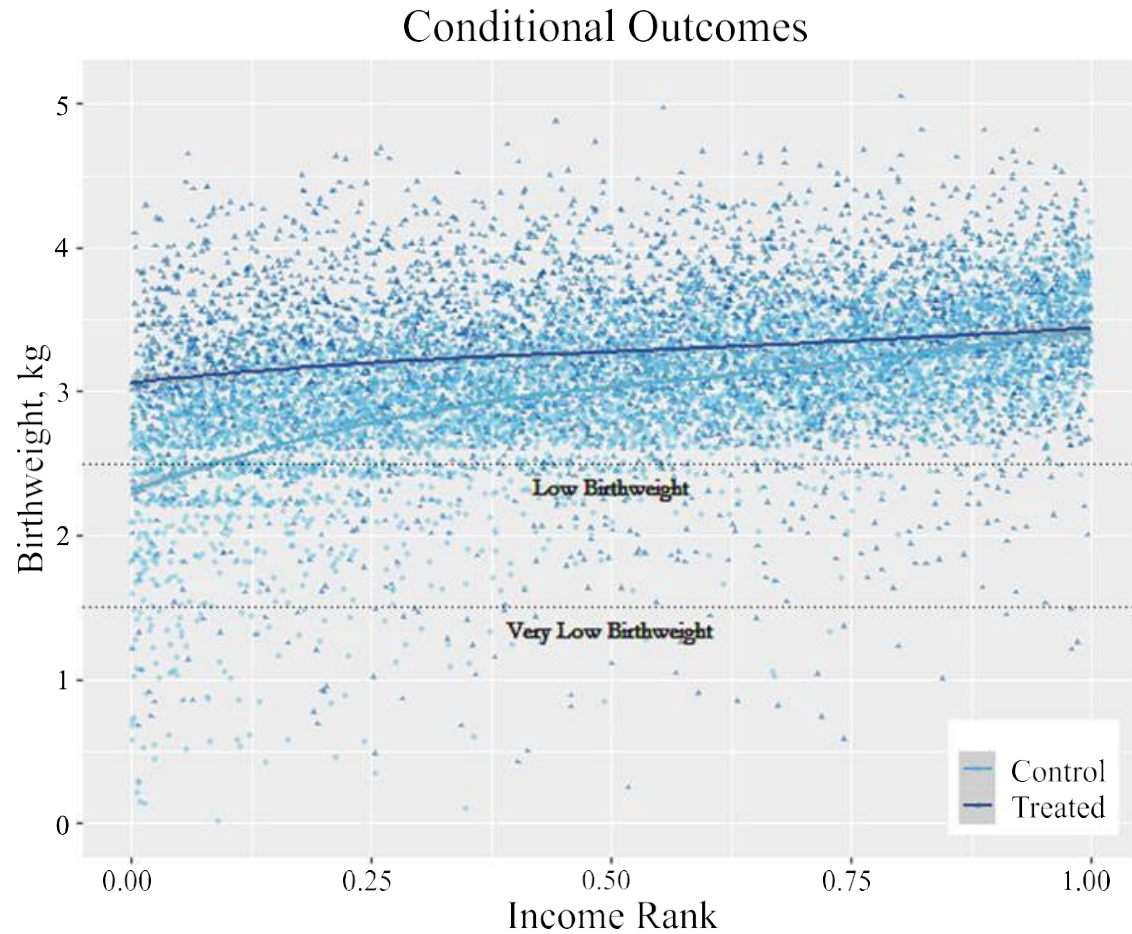
- A hypothetical example: Cookson et al (2021)
 - Population: A low-income country
 - Intervention: Antenatal dietary education and supplementation program
 - Comparison: Babies whose mothers received the intervention vs. babies whose mothers did not receive the intervention
 - Outcome: Birthweight

Traditional (non-equity-relevant/informative) study – average treatment effect



Equity-relevant/informative study

– conditional average treatment effects

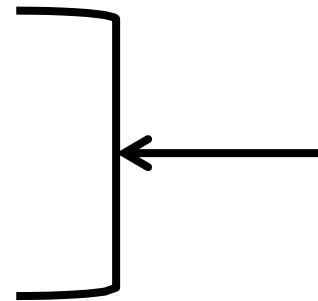


Challenges of equity-relevant/informative studies

- Sample size
 - Larger sample size is needed from typically smaller groups
 - As long as diverse sociodemographic characteristics are reported, studies can be equity-relevant/informative post-hoc
 - Combining data from many studies (meta-analysis)
 - Using Bayesian methods that use established evidence to overcome small samples
- Cost
 - NIH guidelines on the inclusion of women and minorities as subjects in clinical research (1994) state costs cannot be the reason for exclusion
- Complexity

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Summary

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