

# **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

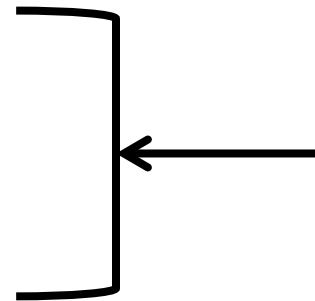
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← Equity considerations

# Eight principles for ethical clinical research

- Collaborative partnership
- Valuable scientific question
- Valid scientific methodology
- Fair subject selection
- Favorable risk-benefit
- Independent review
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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?**

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

- Participation
- Biology
- Societal concern

# 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**

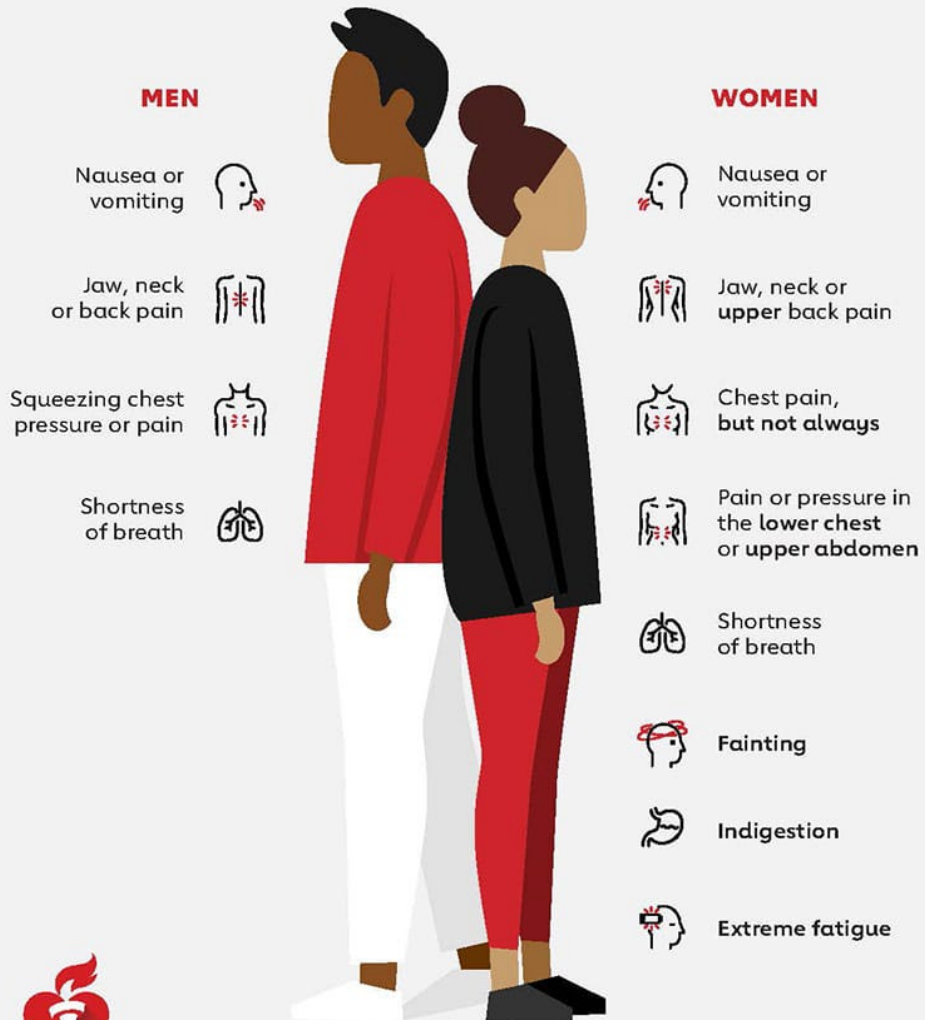
# Potentially differential impact of interventions - **biology**

- 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

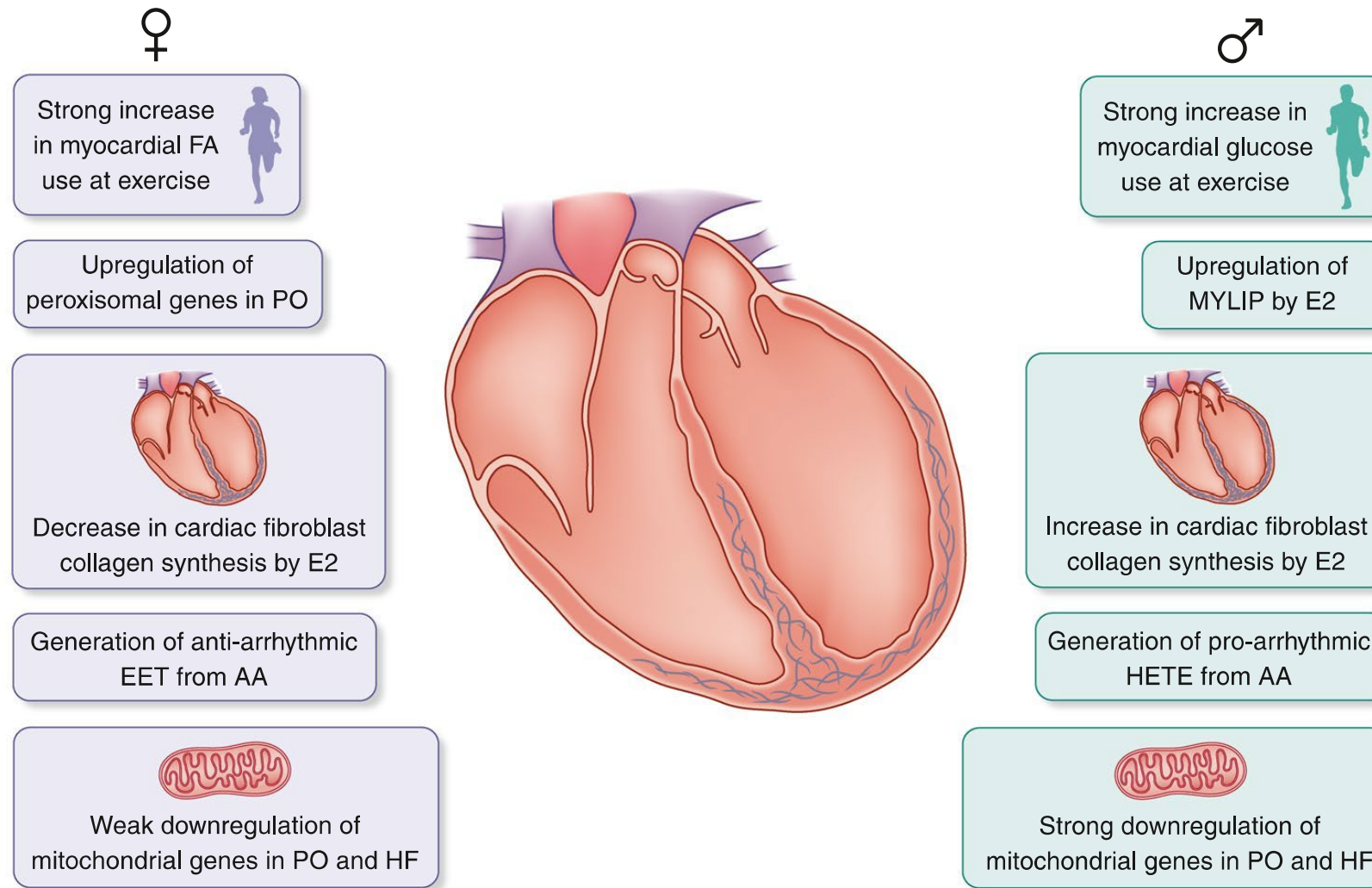
# HEART ATTACK SYMPTOMS: MEN VS. WOMEN

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*  
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**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**

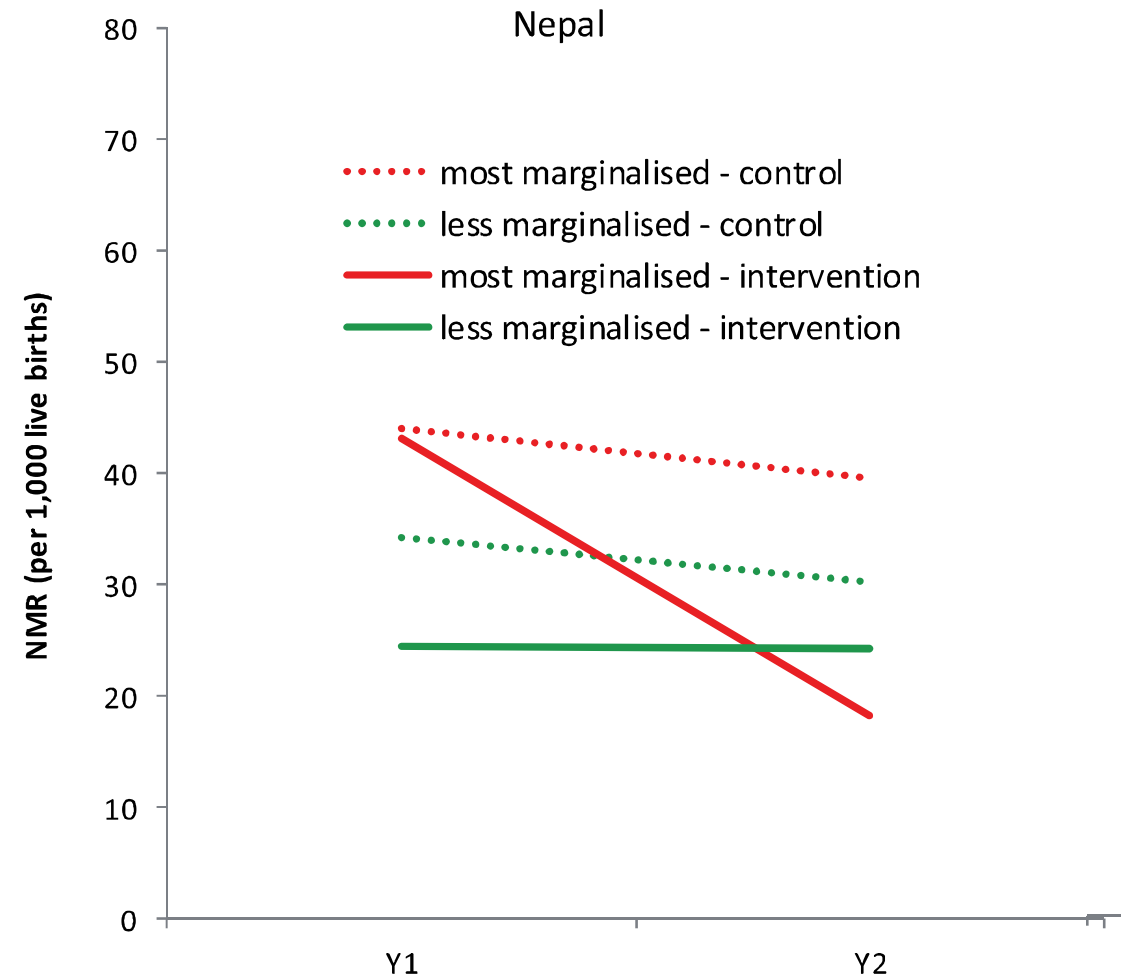


# Potentially differential impact of interventions – **Societal concern**

- 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

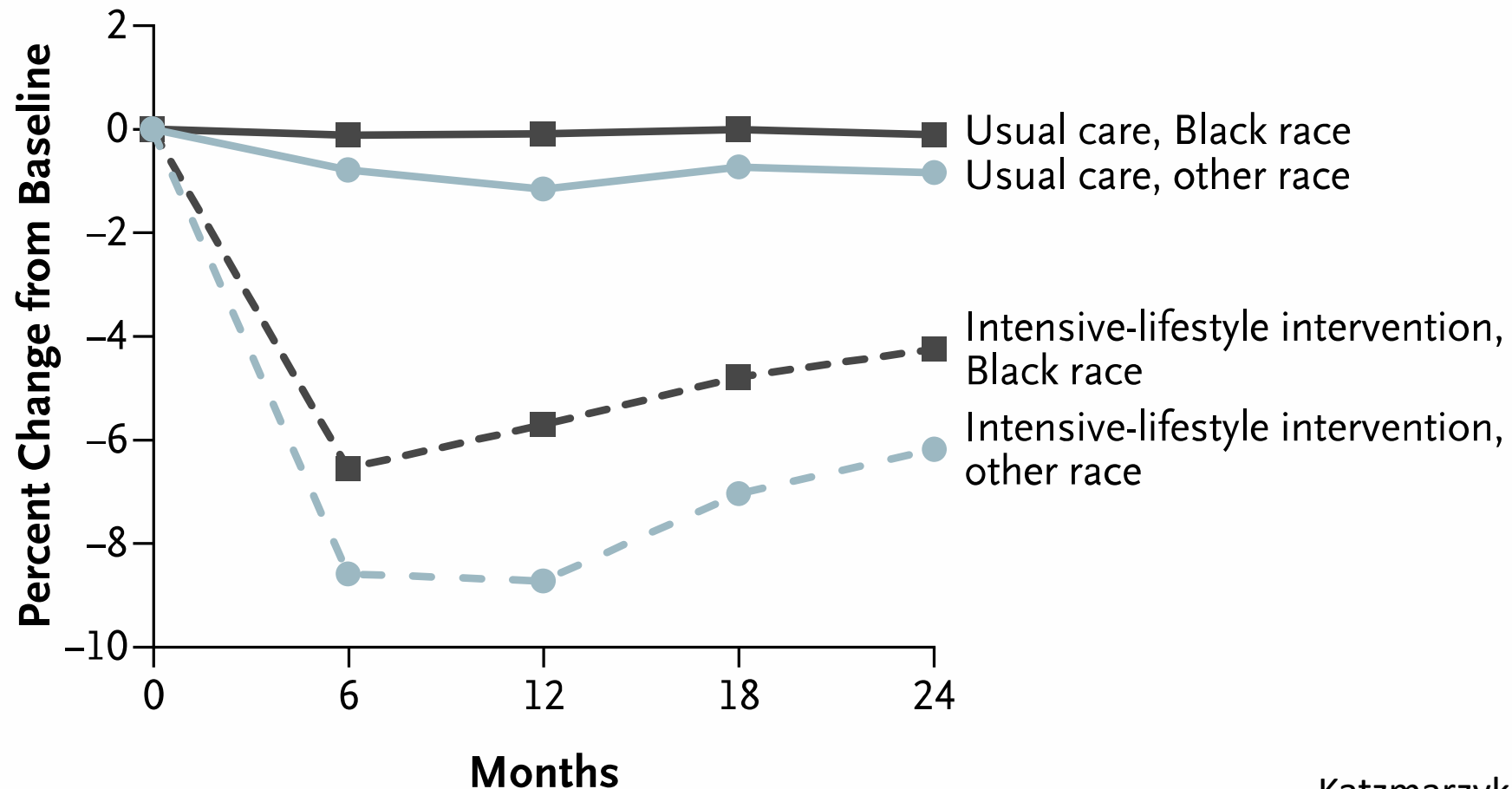
# Effects of a lifestyle-based program for obesity treatment in low-income neighborhoods

- 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**

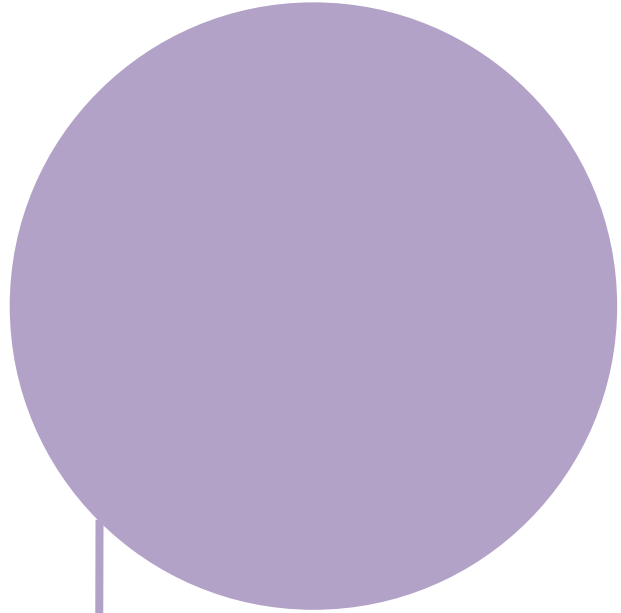
A Change in Weight According to Race



# Potentially differential impact of interventions – Societal concern

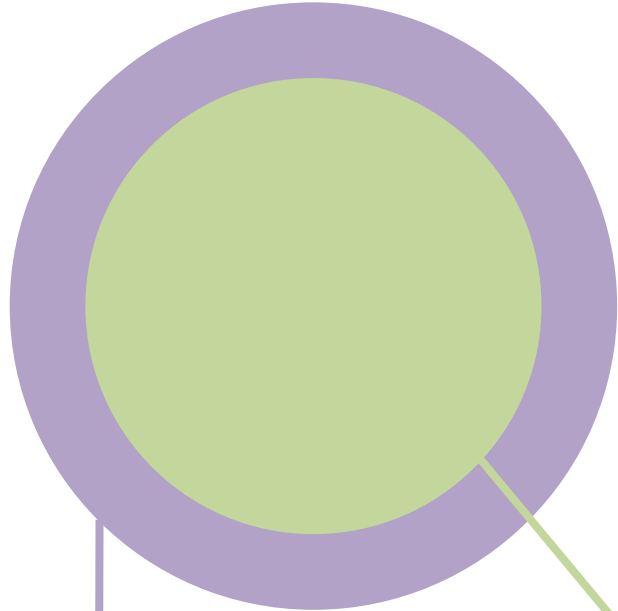
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- Differential intervention effects by social group characteristic
  - An example: Effects of women's group participation on neonatal mortality rate by marginalization
- Differential intervention effects within a traditionally excluded group
  - An 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



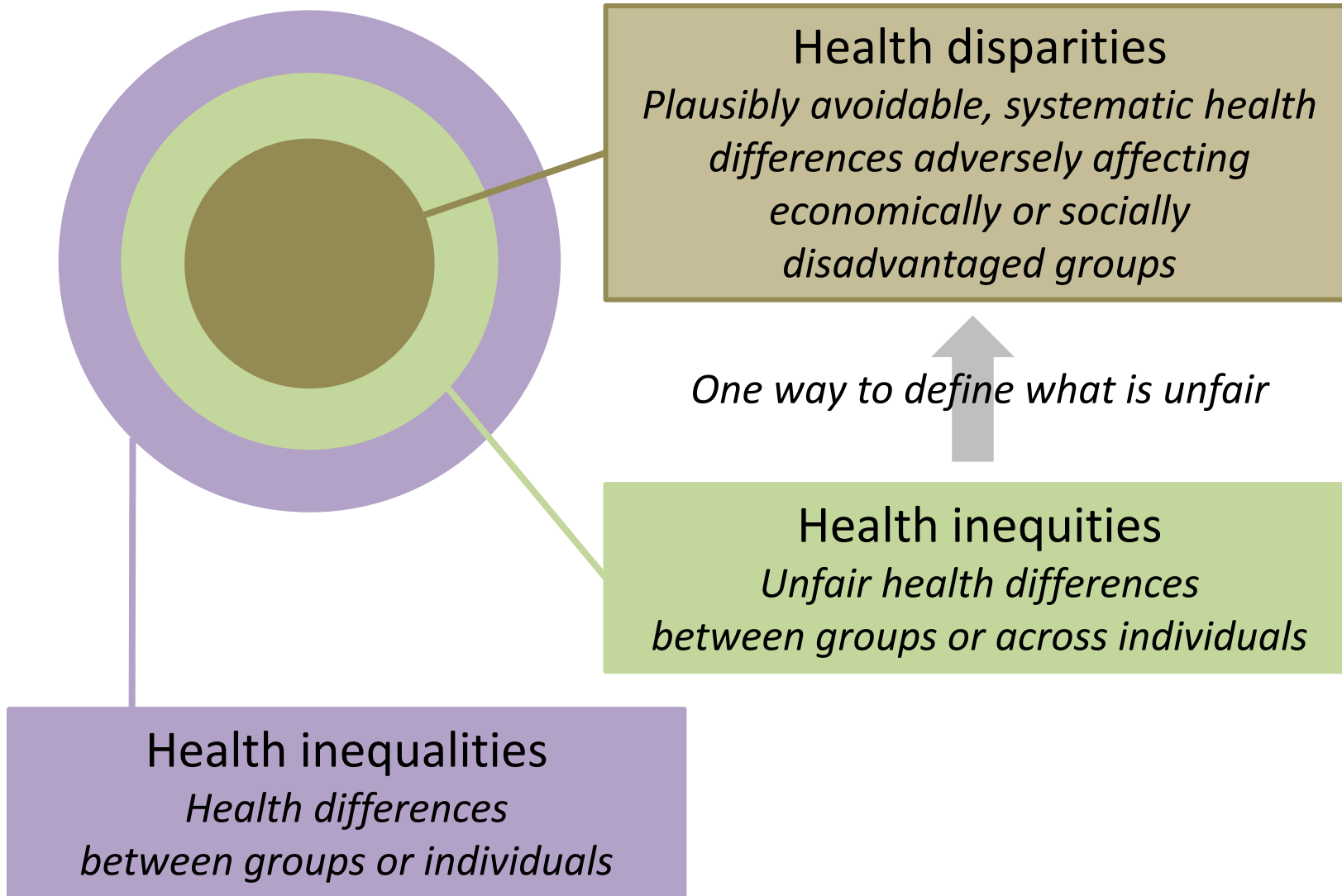
Health inequalities  
*Health differences  
between groups or individuals*

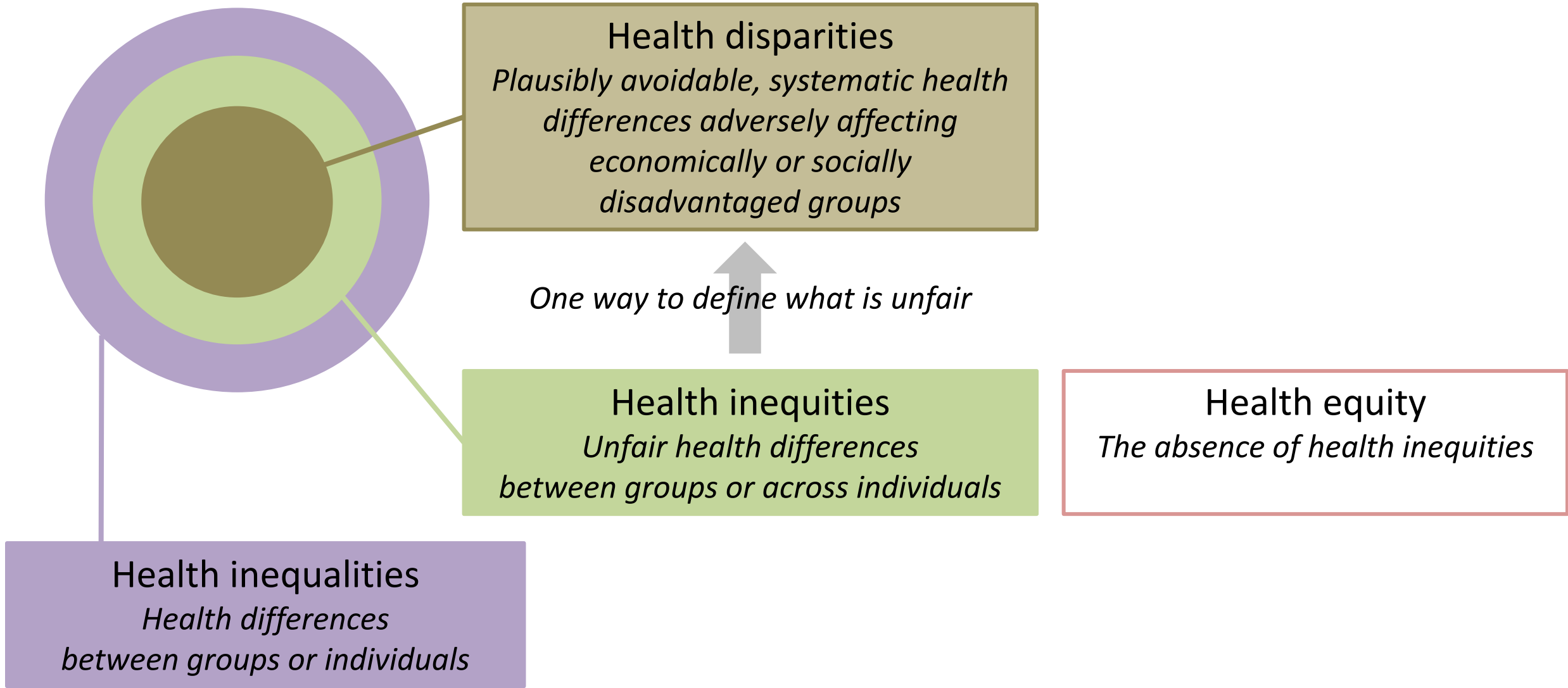




Health inequalities  
*Health differences  
between groups or individuals*

Health inequities  
*Unfair health differences  
between groups or across individuals*





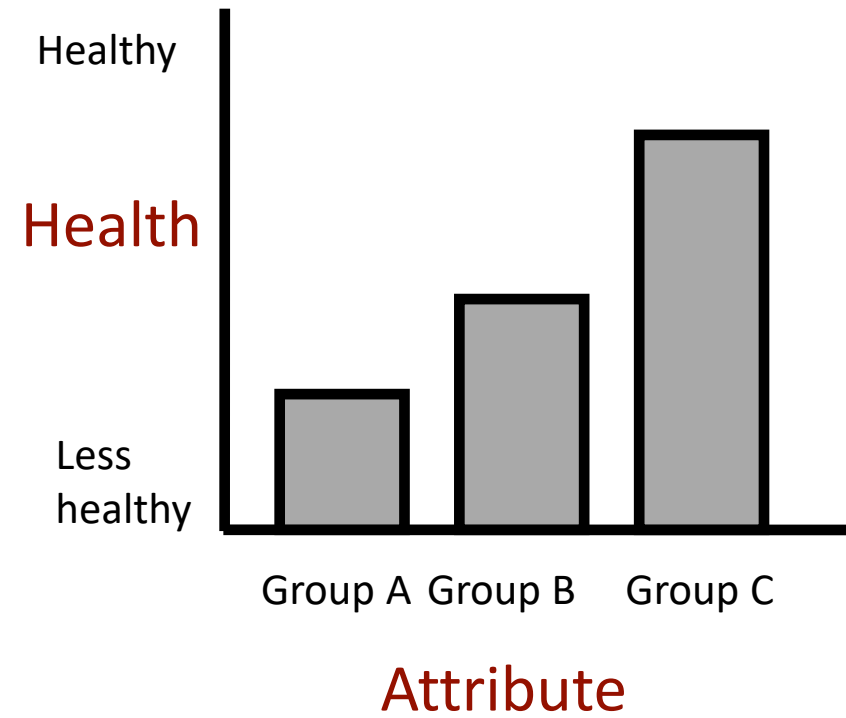
# Who should be in the study and why?

- Participation
- Biology
- Societal concern

**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 variable to continuous variable)
- 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

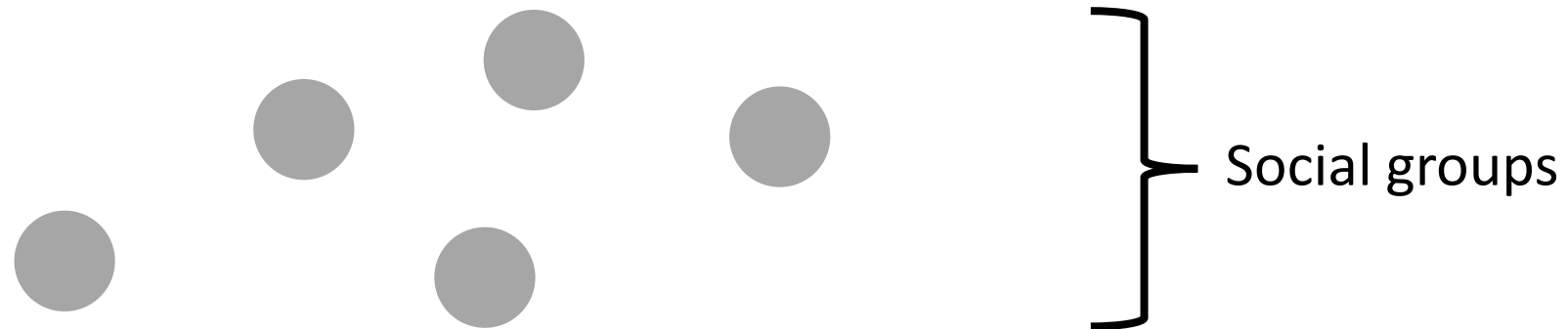


# Deeper philosophical discussion is needed to include diverse study subjects for societal concern

- 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

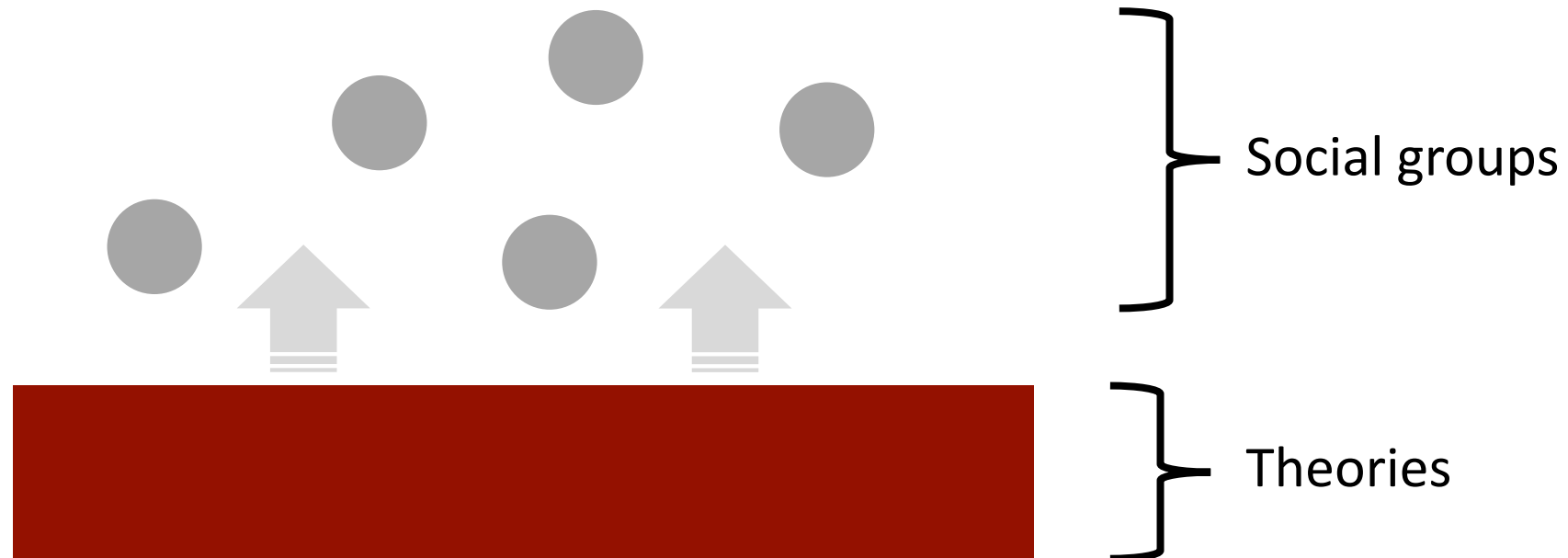
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**How do equity considerations influence the study design, analysis plan, and reporting?**

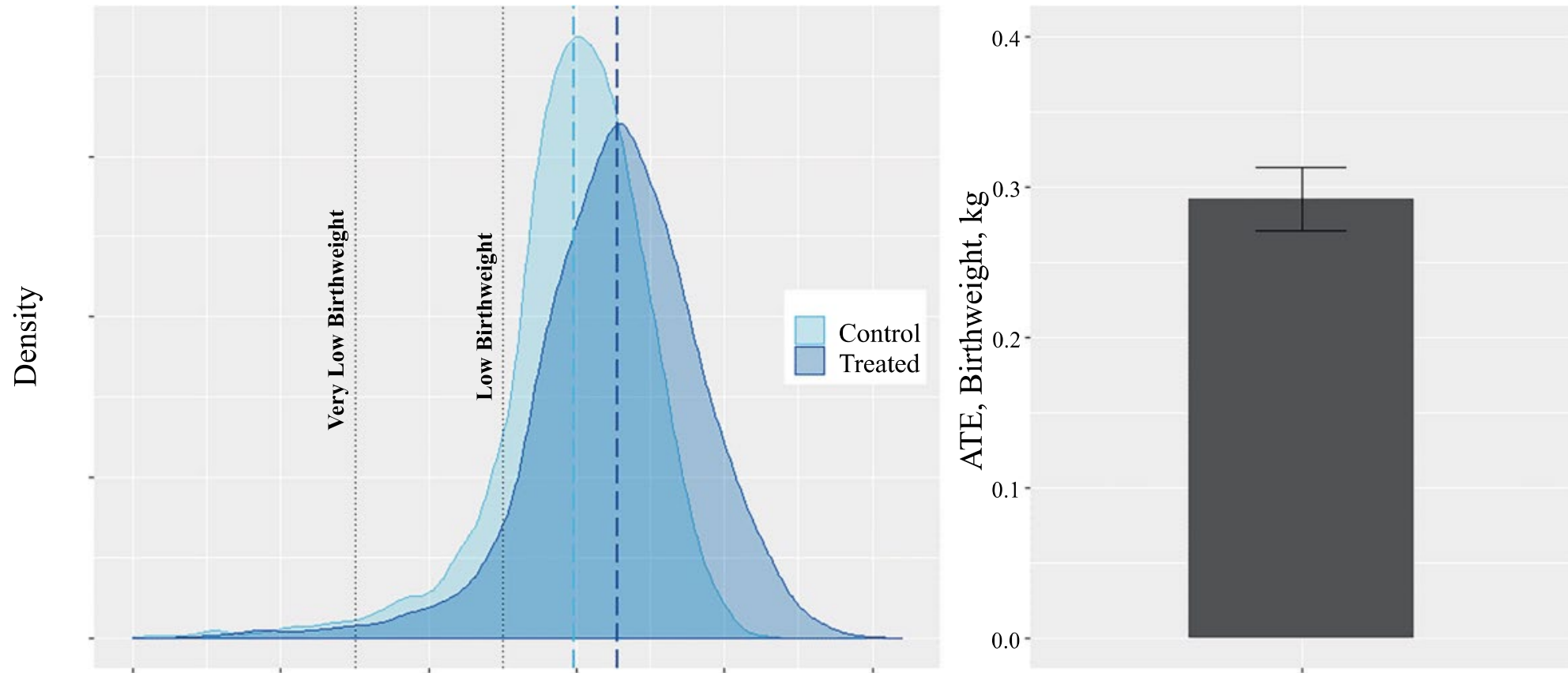
# Reasons why study subjects should be diverse inform study design, analysis plan, and reporting

- 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?

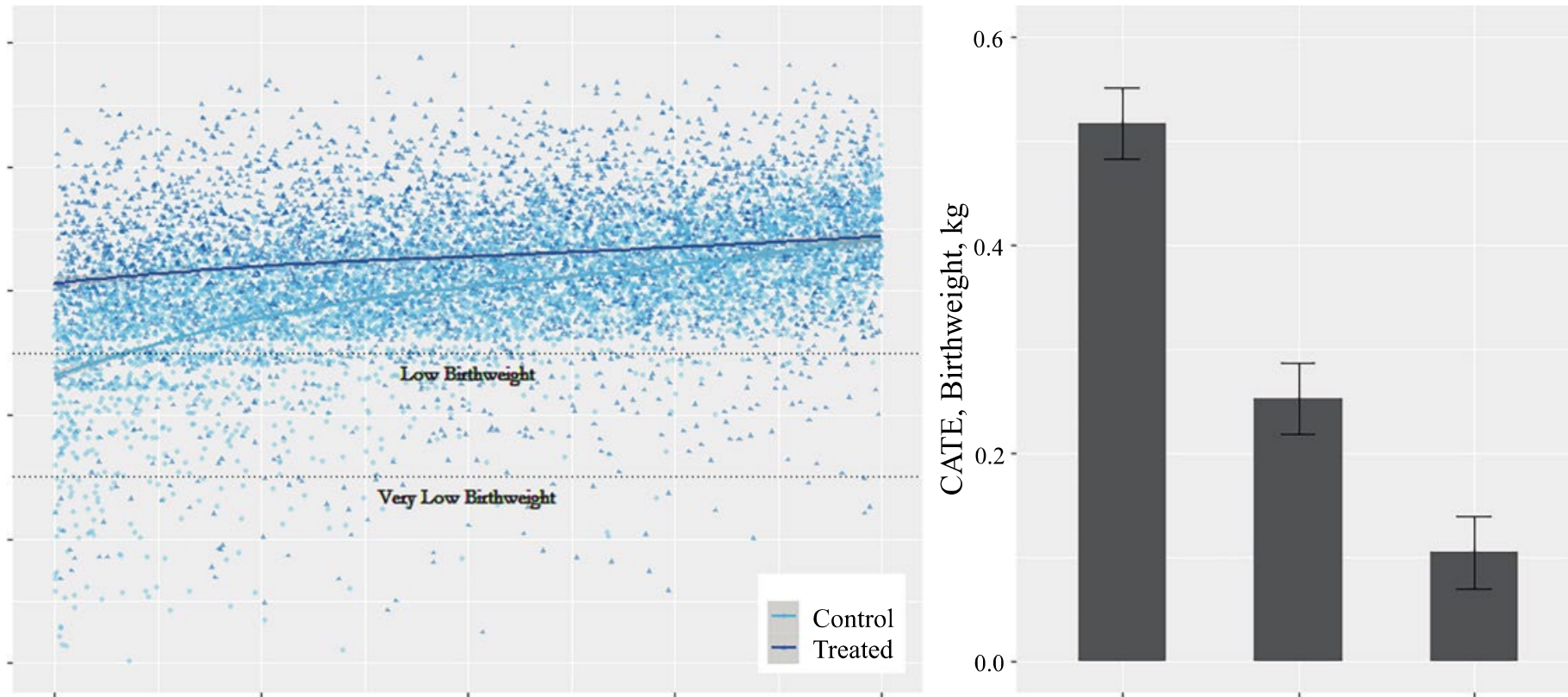
- A hypothetical example: Cookson et al (2021)
  - Population: A low-income country
  - Intervention: Antenatal dietary education and supplementation program
  - Comparison: Babies whose mothers received the intervention vs. babies whose mothers did not receive the intervention
  - Outcome: Birthweight

# 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

# Summary

- 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?
- 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

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