Essential to Rigorous and Relevant Scientific Research and Health Equity

Notice: These slides are intended for educational purposes only and are not intended to replace the independent professional judgment of the user. Opinions expressed are not necessarily the opinions of the National Institutes of Health (NIH).
Learning objectives

LEARN ABOUT

• Inclusion and its importance in clinical research
• Barriers to recruitment of diverse populations for clinical studies
• Factors that facilitate recruitment and retention of diverse populations
• Reasons sex and gender matter in biomedical research
The NIH is mandated by the Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2 to ensure the inclusion of women and minority groups in all NIH-funded clinical research in a manner that is appropriate to the scientific question under study. The primary goal of this law is to ensure that research findings can be generalizable to the entire population.
The factors that allow someone to participate in a clinical study are called **inclusion criteria**. They are often based on characteristics such as **age, gender, the type and stage of a disease, previous treatment history, and other medical conditions**.
Inclusion achieves more representative studies

- Seeks distribution of participants by sex/gender, race, ethnicity, and age to reflect populations needed to meet study goals
- 42 USC 289a-2 and the 1993 NIH Revitalization Act require researchers to include women and men
- In response to the 21st Century Cures Act, NIH issued the Inclusion Across the Lifespan policy, subsuming its Inclusion of Children policy
  - Requires inclusion of all ages – unless there’s scientific or ethical rationale for exclusion

“Insights garnered from this expanded inclusion approach could enhance reproducibility and generalizability of clinical study findings.”

The importance of Inclusion

- Captures populations more at risk for certain diseases
- Gives more complete picture of the risk and benefit of intervention
- Addresses differences in clinical outcomes because of biological, cultural, social, or economic factors
- Ensures more equitable distribution of participation in research
- Tests safety and efficacy of treatments in people who will use them

That’s why including diverse populations is essential!
Benefits of Inclusion

Advancing in knowledge from research

Creating diversified workforce to design studies, recruit participants, implement findings

Incorporating knowledge into education & training

Providing access to sex/gender-, race-, ethnicity-, and age-appropriate and culturally sensitive care

Implementing new concepts into practice

Changing standards of practice & public health

Photo by Anthony Metcalfe on Unsplash
Barriers to participation of women and minorities:

- Never asked
- Fear and distrust
- Work/family responsibilities
- Expenses & logistical issues
- Lack of knowledge
- Complex consent process
Ways to recruit and retain women and minorities

• Adapt recruitment strategies for cultural and linguistic backgrounds
• Translate materials into appropriate languages
• Enlist culturally and linguistically competent research staff
• Include families and communities in a dialogue
• Partner with community organizations
• Utilize and retain investigators and staff from the targeted communities – to facilitate acceptance and ensure continuity.¹

“Consent should be considered an ongoing process – a dialogue – rather than a discrete act of choice that takes place in a singular moment in time, thus supporting participants in making informed decisions throughout the trial.” ¹

“Successful recruitment strategies for African American women should feature community-based, culturally appropriate approaches.” ²

Why sex and gender matter in biomedical research

<table>
<thead>
<tr>
<th><strong>SEX</strong>¹</th>
<th><strong>GENDER</strong>²</th>
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<tbody>
<tr>
<td>Derived from the chromosomal complement</td>
<td>Multidimensional psychosocial construct</td>
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<tr>
<td>Every cell has a sex (XX or XY)</td>
<td>that integrates roles, behaviors, expressions,</td>
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<tr>
<td>• Begins in utero</td>
<td>and identities of girls, women, boys, men,</td>
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<tr>
<td>• Affects behavior and perception</td>
<td>and gender-diverse people</td>
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<tr>
<td>• Affects health—from disease risk to</td>
<td>• Influences how people perceive themselves</td>
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<td>treatment response</td>
<td>and others and how they act and interact</td>
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¹Exploring the Biological Contributions to Human Health: Does Sex Matter, IOM Report, 2001
Is study population representative of those with disease or condition in wider population?
Case studies on Inclusion practices


- “Facebook Advertising to Recruit Young, Urban Women into an HIV Prevention Clinical Trial”
- “Cervical Cancer Prevention”
- “Treatments for Menopause Symptoms”
- “Caries Prevention in Young Children”
- “Diabetes Prevention”
Why study sex as a biological variable?

To build a knowledge base that better informs the design of clinical research and trials in humans

To deliver personalized care based on studies of both sexes

To maximize return on investment

SABV is an integrating approach for investigations across the biomedical research continuum.
Case Study:
Women’s Ischemia Syndrome Evaluation (WISE)

Multicenter prospective study of 936 women referred for coronary angiography to evaluate ischemic heart disease (IHD), the leading cause of death among women.

• IHD presents treatment challenge because of lack of evidence-based management
• Study aim: Improve diagnostic testing and explore female-specific pathophysiology

• Sex differences exist in IHD presentation and pathophysiology
• Different methods needed to diagnose cardiac ischemia in women than in men
• Results of 10-year follow-up:
  • 1 in 5 died (184) – for a **20% all-cause mortality rate**
  • Of these, 115 (12%) were cardiac deaths – 36 of which (31%) were women without obstructive CAD
  • Lacking obstructive CAD is often seen as clinically benign
  • “Women are most often provided reassurance rather than cardiovascular therapy.”
  • Clinical trials are needed for guidance on women without obstructive CAD

**FINDINGS**

Putting WISE findings in perspective

10-year est. mortality rate for women aged 50 to 59 at baseline scoring low on a mortality index during similar time period: 2.8%

WISE all-cause mortality rate among those with obstructive CAD (≥50% stenosis): 36%

WISE all-cause mortality rate among those without obstructive CAD at baseline: 13%

Proposed American College of Cardiology/American Heart Assoc. Guidelines threshold for initiating lipid-lowering therapy: 7.5%

Case Study: Contemporary heart failure clinical trials

Objective: Determine enrollment patterns by age, sex, and race/ethnicity to compare demographic makeup with that of U.S. epidemiologic studies of specific heart failure (HF) types, among other things.

- Women were underrepresented in cumulative clinical trials (27%) when compared with their representation in general population of HF patients (~50%)
- Enrollment of women was significantly associated with the mean age of participants in HF trials

NIH Inclusion Toolkit: How to Engage, Recruit, and Retain Women in Clinical Research

Helps PIs and their research teams fulfill their responsibilities to include women in clinical research

- Research on recruitment and outreach best practices
- Related Federal laws, regulations, and NIH policies
- Case studies

http://orwh.od.nih.gov/toolkit
Summary

• Integrating sex/gender, race, ethnicity, and age into clinical research is essential to **rigorous** and **relevant** scientific inquiry
• Varied approaches are needed to recruit diverse groups
• Clinical trial participants must represent full spectrum of patients to provide **best information possible**
• Ensuring appropriate enrollment promotes **health equity** – and **better science**
Inclusion Resources

• Inclusion of Women and Minorities
  https://grants.nih.gov/grants/funding/women_min/women_min.htm

• Inclusion Across the Lifespan
  https://grants.nih.gov/grants/funding/lifespan/lifespan.htm