Overview of NIH Inclusion Efforts

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March 30, 2023 – NIMHD Inclusive Participation in Clinical Research Workshop
Moving Beyond Inclusion to Intentional Integration to Drive Innovation, Rigor, and Equity

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National Institutes of Health

March 30, 2023 – NIMHD Inclusive Participation in Clinical Research Workshop
Inclusion is in our DNA

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

Distribution of participants by sex/gender, race, ethnicity & age needed to meet study goals

- Beginning in 1980s, NIH and Congress required researchers to include women and racial and ethnic minorities in CTs
- NIH Revitalization Act of 1993
  - Requires researchers to include women and men in clinical trials
- NIH Policy on the Inclusion of Women and Minorities as Subjects in Clinical Research, October 2001

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NIH and Congress Sought to Reverse Men-Only Clinical Studies

The distribution of participants by sex/gender, race, ethnicity, and age needed to meet study goals

• **21st Century Cures Act** expanded inclusion
  - Added **individuals of all ages**
  - Paved way for **pregnant and lactating women**
  - Requires NIH-defined applicable phase III CTs to **report results disaggregated by sex/gender, race, and ethnicity** into ClinicalTrials.gov

• NIH Research, Condition, and Disease Categorization Process (RCDC) Inclusion Statistics Reports publish inclusion data by sex/gender, race, and ethnicity
NIH Inclusion Policies Have Evolved Over Time

1993

NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research

The NIH Revitalization Act of 1993 (Public Law 103–43) directed NIH to ensure women and racial and ethnic minorities are appropriately represented in NIH-funded clinical research.

2016

Inclusion Across the Lifespan Policy

Section 2038(H) of the 21st Century Cures Act requires NIH to update guidelines for the inclusion of women and minorities in clinical research to reflect individuals of all ages included in NIH clinical research.

2019

Expansion of The NIH Inclusion Policy and Guidelines

A provision was made requiring that applicable NIH-defined Phase III clinical trials report results of valid analysis by sex/gender, race, and ethnicity on ClinicalTrials.gov.

https://orwh.od.nih.gov/womens-health-research/clinical-research-trials/nih-inclusion-policies
US Site Enrollment for All NIH-Defined Extramural and Intramural Clinical Research by Sex/Gender
Total US Site Enrollment in NIH-Defined Clinical Research by Racial Categories

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>% Unknown/Not Reported</th>
<th>% More Than One Race</th>
<th>% White</th>
<th>% Native Hawaiian/Pacific Islander</th>
<th>% Black/African American</th>
<th>% Asian</th>
<th>% American Indian/Alaska Native</th>
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</thead>
<tbody>
<tr>
<td>2016</td>
<td>13.8</td>
<td>2.7</td>
<td>63.2</td>
<td>0.8</td>
<td>10.6</td>
<td>7.8</td>
<td>1.0</td>
</tr>
<tr>
<td>2017</td>
<td>12.1</td>
<td>3.0</td>
<td>67.0</td>
<td>0.2</td>
<td>13.7</td>
<td>5.2</td>
<td>0.9</td>
</tr>
<tr>
<td>2018</td>
<td>13.7</td>
<td>2.8</td>
<td>64.2</td>
<td>0.3</td>
<td>14.1</td>
<td>4.0</td>
<td>0.9</td>
</tr>
<tr>
<td>2019</td>
<td>11.9</td>
<td>2.1</td>
<td>65.9</td>
<td>0.2</td>
<td>15.7</td>
<td>5.2</td>
<td>1.0</td>
</tr>
<tr>
<td>2020</td>
<td>16.0</td>
<td>2.7</td>
<td>61.2</td>
<td>0.3</td>
<td>14.9</td>
<td>4.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2021</td>
<td>14.0</td>
<td>2.0</td>
<td>64.2</td>
<td>0.8</td>
<td>13.0</td>
<td>5.0</td>
<td>0.9</td>
</tr>
</tbody>
</table>
Total US Site Enrollment in NIH-Defined Clinical Research by Ethnic Categories

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>% Unknown/Not Reported</th>
<th>% Hispanic/Latino</th>
<th>% Not Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>10.3</td>
<td>14.2</td>
<td>75.5</td>
</tr>
<tr>
<td>2017</td>
<td>12.2</td>
<td>9.1</td>
<td>78.7</td>
</tr>
<tr>
<td>2018</td>
<td>13.1</td>
<td>9.3</td>
<td>77.6</td>
</tr>
<tr>
<td>2019</td>
<td>11.5</td>
<td>9.0</td>
<td>79.5</td>
</tr>
<tr>
<td>2020</td>
<td>13.4</td>
<td>10.9</td>
<td>75.7</td>
</tr>
<tr>
<td>2021</td>
<td>11.8</td>
<td>10.5</td>
<td>77.7</td>
</tr>
</tbody>
</table>
But Underrepresentation and Underreporting Still Exist

- In certain disease research
- Minimal progress – Disaggregation, analysis and reporting of data by sex

Reporting Lags Behind Inclusion

Enrollment for Males and Females in NIH-Defined Phase 3 Clinical Trials (Excluding Sex-Specific Studies) FY2021

- Female: 45%
- Male: 54%
- Unknown: 1%

Inclusion and Analysis by Sex in NIH-Funded Clinical Trials Published in 2015

- Analysis by sex: 2%
- No analysis by sex, no explanation provided: 26%
- No analysis by sex, explanation provided: 72%


NIH Office of Extramural Research, Division of Statistical Analysis and Reporting, 2022
NASEM 2022 Inclusion Report Conclusions

Improving representation in clinical research is **urgent**.

Improving representation in clinical research **requires investment**.

Improving representation requires **transparency and accountability**.

Improving representation in clinical research is the **responsibility of everyone** involved in the clinical research enterprise.

Creating a more equitable future entails a **paradigm shift**.
NIH Outreach Toolkit: How to Engage, Recruit, and Retain Women in Clinical Research

The NIH Outreach Toolkit is intended to help principal investigators and their research teams fulfill their responsibilities to include women in clinical research.

- Review of recruitment and outreach best practices
- Information on Federal laws, regulations, and NIH policies on the inclusion of women in clinical research
- Case studies featuring researchers’ experience with including women in their studies

http://orwh.od.nih.gov/toolkit
The Pulse
Monthly Email
bit.ly/ORWHpulse *

Events
bit.ly/ORWHevents

bit.ly/ORWHcovid

The Pulse
Monthly Email
bit.ly/ORWHpulse *

E-LEARNING
• Bench to Bedside: Integrating Sex & Gender to Improve Human Health
• SABV Primer
• SABV Train the Trainer Course
• Intro. to Scientific Basis of Sex- & Gender-Related Differences

*All Bitly addresses are case-sensitive

www.nih.gov/women
Increasing Inclusive Participation in Research

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Disclaimer

The views expressed during this presentation do not necessarily state or reflect those of NIH or the U.S. Government.

Just an FYI.
Lack of diversity in clinical trials is an old problem: An example from a Kidney Cancer drug trial

Race/Ethnicity Reporting and Representation in US Clinical Trials: A cohort study of Registered Clinical Trials (March 2000 – March 2020)

- 20,692 clinical trials – 4.76M enrollees
- 43% reported any race/ethnicity data
- Median enrollees by race and ethnicity
  - White = 79.7% [IQR: 61.9-90%]
  - Black/African American = 10% [IQR: 2.5-23.5%]
  - Latino/Hispanic = 6% [IQR: 0.43-15.4%]
  - Asian = 1% [IQR: 0-4.1%]
  - American Indian = 0% [IQR: 0-0.2%]
- Annual increase = 1.7%

Industry and Academic funding: inversely associated with race/ethnicity reporting

- Industry: lower proportions of racial/ethnic minority enrollees

COVID-19 Emergency and the Scientific Response

More People Of Color Needed In COVID-19 Vaccine Trials
August 23, 2020 - 7:49 AM ET

Large U.S. covid-19 vaccine trials are halfway enrolled, but lag on participant diversity

We Need to Recruit More Black Americans in Vaccine Trials
Pharmaceutical companies and the government must step up their efforts to enroll a diverse group of volunteers.

Clinical trials seek to fix their lack of racial mix
By Patrick Boyle, Senior Staff Writer
August 20, 2021

As COVID-19 vaccines roll out, researchers still seek diverse pool for clinical trials


This Clinical trials awareness day, we can help build a better future to advance medical science.

NIH - National Institutes of Health
What are Solutions to Increase Inclusive Participation in Clinical Research?
Organizational Change and Good Faith Efforts

Hospital/clinic climate

Accessible and inviting research opportunities

Participant/Patient accommodations

Cultural & Community Competence

**Recommendation: Focus on Motivators to Enroll in Clinical Trials**

<table>
<thead>
<tr>
<th>Reasons for Successful Recruitment/Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctor recommendation</td>
</tr>
<tr>
<td>Hope</td>
</tr>
<tr>
<td>Altruism, Advance medicine</td>
</tr>
<tr>
<td>Refusal to give up/no other medical option(s)</td>
</tr>
<tr>
<td>Positive staff interaction(s)</td>
</tr>
<tr>
<td>Access to leading specialist(s)</td>
</tr>
<tr>
<td>$$</td>
</tr>
</tbody>
</table>
## Reasons for Unsuccessful Recruitment/Enrollment

<table>
<thead>
<tr>
<th>Lack of doctor recommendation</th>
<th>Complex/intensive protocols</th>
<th>Unclear IRB protections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of Hope</td>
<td>Restrictive inclusion/exclusion criteria</td>
<td>Institutional distrust</td>
</tr>
<tr>
<td>Loss of autonomy</td>
<td>Placebo concern(s)</td>
<td>No/unclear personal/community benefit</td>
</tr>
<tr>
<td>Refusal to give up/no other medical option(s)</td>
<td>Lack of free wrap-around medical care</td>
<td>Language/translation</td>
</tr>
<tr>
<td>Negative staff interaction(s)</td>
<td>Culturally incompetent staff</td>
<td>Invasive requests/procedures</td>
</tr>
<tr>
<td>Insufficient research team diversity</td>
<td>Safety concerns</td>
<td>Inconvenience/lack of accommodations</td>
</tr>
<tr>
<td>Preference for “natural remedies”</td>
<td>Side effects/adverse events</td>
<td>Disrupts daily routine</td>
</tr>
</tbody>
</table>

**Recommendation:** Address Factors that Reduce Enrollment in Clinical Trials
### Strategies: Increasing Trust & Participation in Clinical Trials

#### Research Team Considerations

1. **Multisector:**
   - Scientists, local government, public health departments, health systems, professional societies, community-based organizations, and faith-based organizations

2. Diverse team & staff

3. Set **targets** for recruitment a priori

4. Develop a multifaceted recruitment strategy

5. What does meaningful inclusive participation look like?

#### Strategies

1. Bi-directional community engagement

2. Establish **trust** as the foundation for all efforts

3. Address **social and structural determinants** of health

4. Acknowledge the **longstanding distrust** of institutions and biomedical research

5. Cultural **humility**

6. No “**helicopter**” research

7. **Ask!**
Diversifying Clinical Trials: Address Misconceptions & Modify Approaches

- Misconception that racial and ethnic minoritized groups are:
  - Unwilling to participate in clinical trials
  - “Hard to reach”
- Modify approaches
  - Directed messages
  - Trusted messengers
- Address institutional distrust and trustworthiness
Community Engagement Alliance (CEAL) Against COVID-19 Disparities: Support of Moderna COVID Enrollment

In August 2020 when CEAL began enrollment support of the Moderna (COVE) COVID-19 clinical trial, there was a steady increase in inclusive racial and ethnic minority participation.

Source Moderna: 2020 COVE Study Enrollment Completion-10.22.20
Race and ethnicity

Interim data snapshot - October 21, 2020 - subject to change

- 63% White
- 20% Hispanic/Latinx
- 10% Black/AA
- 4% Asian
- 3% All others
Increasing Trust & Participation in Clinical Trials: Walking the Walk

**Community Voices**

1. **Trust — Here’s What You Shared:**
   - Overall, trust in the healthcare system is low because of current and past experiences.
   - Trust is lowered when doctors and nurses don’t seem to care about every patient.
   - Healthcare is seen as big business — making money is most important.
   - Patients are treated differently based on their insurance and where they live.
   - Doctors and drug companies are working together to push medications.

2. **Healthcare Experiences — Here’s What You Shared:**
   - Overall, most patients had negative experiences with the healthcare systems (e.g., feeling rushed, poor communication, no empathy).
   - Patients with good experiences had doctors who spent more time with them.
   - Deaf and hearing impaired patients prefer live interpreters, and often feel disregarded.
   - High medical bills arrive months after the visit — out of pocket costs are unknown and insurance policies are not clear.

3. **Research — Here’s What You Shared:**
   - Research is important and needed to test new treatments (e.g., drugs).
   - Trust for medical research was broken in the African-American community years ago and hasn’t been repaired.
   - There are concerns about joining research clinical trials testing new medications.
   - Results of studies are not shared with the community, so they are not helpful.

https://doi.org/10.1002/pon.5841


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**Forward Movement Project III**

**Community Voices**

1. **Healthcare Experiences — Here’s What You Shared:**
   - Overall, positive experiences in the U.S. healthcare system (except Puerto Rico).
   - Misdiagnosis, poor management, and long wait times for appointments are problems.
   - Preference for Spanish-speaking physicians and nurses, rather than medical translators.
   - Trust and communication affected by provider behavior (e.g., body language, attitude).
   - Preference for “welcoming” neighborhood clinics, rather than large hospitals.
   - Religion and spirituality are important in both health and healthcare.
   - Most participants are willing to participate in research.

2. **Unmet Cancer-Related Needs — Here’s What You Shared:**
   - Many family or personal cancer experiences but were not clear on cancer screening guidelines.
   - Information on cancer risk factors (e.g., family history) is needed; some awareness of treatment as a risk factor.
   - Screening or medical care delays due to fear “bad news,” deportation, and healthcare costs.
   - Family members often not included in discussions about diagnosis and treatment options.

3. **Barriers to Care — Here’s What You Shared:**
   - Providers and hospital staff, lack cultural competence (e.g., values, focus on family and faith), preference for traditional remedies (and “family rules” care).
   - Unnecessary transportation and parking fees reduce healthcare access.
   - Lack of bilingual staff and low quality translation services.

https://doi.org/10.1002/pon.5841  