Diversity in Clinical Trials
Perspectives from the NHLBI

George A. Mensah, MD
Director
Center for Translation Research and Implementation Science
National Heart, Lung, and Blood Institute, NIH, Bethesda, MD

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Orlando

Orlando
Disclosure and Disclaimer Statements

- No conflicts to disclose.
- The contents of this presentation should not be construed as representing an official position of the National Institutes of Health (NIH) or the Department of Health and Human Services.

OUTLINE

1. NIH Definition of Clinical Trials
2. Importance of Diversity in Clinical Trials
3. Promoting Investigator & Patient Diversity
4. Charting the Future Together

Special Greetings from the NHLBI Leadership

- Dr. Gary Gibbons
- Dr. W. Keith Hoots
- Dr. James Kiley
- Dr. George Mensah
- Dr. David Goff
- Dr. Laura Moen
- Dr. Robert Balaban
- Ms. Kate O'Sullivan
- Dr. Amy Patterson
- Dr. Nakela Cook
- Dr. Lenora Johnson

Center for Translation Research and Implementation Science (CTRIS)
OUTLINE

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What is a Clinical Trial? The NIH Perspective

1. A research study involving human participants.
2. Participants are assigned prospectively to an intervention.
3. It is designed to evaluate the effects of the intervention on the participant.
4. The effect under evaluation is a health-related biomedical or behavioral outcome.

https://grants.nih.gov/grants/policy/faq_clinical_trial_definition.htm#5219

To determine whether a study meets the NIH clinical trial definition, answer the following 4 questions

1. Does the study involve human participants?
2. Are the participants prospectively assigned to an intervention?
3. Is the study designed to evaluate the effect of the intervention on the participants?
4. Is the effect being evaluated a health-related biomedical or behavioral outcome?

https://grants.nih.gov/grants/policy/faq_clinical_trial_definition.htm#5219
Inclusion of women & minorities in NIH research

NIH Revitalization Act of 1993, PL103-43 requires:

- Women & minorities be included in all clinical research studies unless there is a compelling rationale for exclusion
- Phase III clinical trials be designed to permit analysis by sex/gender, race and ethnicity
- NIH to support outreach efforts to recruit and retain women, minorities, and their subpopulations

NIH Policy and Guidelines on Inclusion

Goal to ensure individuals are included in clinical research in a manner appropriate to the scientific question under study.

Inclusion of children in NIH research

- Inclusion of Children
  - Children must be included in clinical research studies unless there are scientific or ethical reasons not to do so
  - “Children” ... defined by the NIH as individuals <18 years
    - Applies to application due dates January 25, 2016 or later


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Solutions inspired by diversity of expertise, background, and experiences are often preferred.

Capturing and Leveraging the Benefits of Diversity

*Under-represented Populations in U.S. Biomedical, Clinical, Behavioral and Social Science Research

Challenges and Barriers to Diversity in Clinical Trials

1. Racial & ethnic minorities, rural residents, and low SES persons are under-represented in the clinical trial participant pool.

2. Women and racial & ethnic minorities are under-represented in clinical trial and research investigator pool.

3. Limited "diversity" in clinical trial designs.
Patients Enrolled in Nivolumab versus Docetaxel in Advanced Non-Squamous Non-Small-Cell Lung Cancer Clinical Trial


Overall Survival in Nivolumab vs. Docetaxel in Advanced Non-Squamous Non-Small-Cell Lung Cancer Clinical Trial

Phase I
Purpose: Find out whether a medical approach (e.g., drug, diagnostic test, device) is safe, identify side effects, and figure out appropriate doses.
# of people: Typically fewer than 100

Phase II
Purpose: Start testing whether a medical approach works. Continue monitoring for side effects; get information that goes into designing a large, phase III trial.
# of people: Typically 100-300

Phase III
Purpose: Prove whether a medical approach works; continue monitoring side effects.
# of people: As needed or able to enroll - can be 1,000 or more

Phase IV
Purpose: When a medical approach is being marketed, continue gathering information on its effects.
# of people: Thousands

Demographics of Phase I Clinical Trial Participants at One Northeastern and One Southwestern US Facility

<table>
<thead>
<tr>
<th>Demographic Factor</th>
<th>Phase I Facilities</th>
<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>Northeast</td>
<td>Southwest</td>
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<tr>
<td>Total participants</td>
<td>13,612</td>
<td>8,472</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
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<tr>
<td>Men</td>
<td>5,241</td>
<td>5,006</td>
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<tr>
<td>Women</td>
<td>8,371</td>
<td>3,466</td>
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<tr>
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<tr>
<td>White</td>
<td>10,376</td>
<td>6,210</td>
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<tr>
<td>Black</td>
<td>701</td>
<td>776</td>
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<tr>
<td>Hispanic</td>
<td>1,530</td>
<td>1,080</td>
</tr>
<tr>
<td>Other</td>
<td>705</td>
<td>917</td>
</tr>
<tr>
<td>Total</td>
<td>13,612</td>
<td>8,472</td>
</tr>
</tbody>
</table>

Fisher & Kalbaugh. *AJPH* 2011;101:2217–2222

Demographics of Phase I Participants at One North-Eastern and One South-Western US Facility: Minority Participation in Clinical Research, June 2010

Northeast

Southwest

Total

Fisher & Kalbaugh. *AJPH* 2011;101:2217–2222
Minority participation is much greater than that of whites (63.9% vs. 36.1%).
Blacks participate at 2x the rate expected consideration proportion in US population.
Hispanics are represented at more than twice the expected rate and almost 5x their representation in NIH-sponsored phase III studies.

Lack of trust in research
Lack of awareness
Lack of interest in research
Lack of information
Research considered risky
Lack of access

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Important findings from the Research America! 2017 Survey on Public Perceptions of Clinical Trials

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Although 80% of Americans have heard of a clinical trial, Most Americans have never participated in one.

Have you ever heard of a clinical trial?
- Yes: 15%
- No: 80%
- Not sure: 5%

Have you or anyone in your family ever participated in clinical trials?
- Yes: 9%
- No: 91%
- Not sure: 18%

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Most Americans have never heard their doctor talk to them about clinical trials; but are likely to participate if informed by the doctor.

Has your doctor or other health care professional ever talked to you about medical research?
- Yes: 7%
- No: 93%
- Not sure: 19%

If your doctor had a clinical trial for you and recommended you join, how likely would you be to participate in a clinical trial?
- Very likely: 1%
- Somewhat likely: 41%
- Not likely: 15%
- Would not participate: 43%
- Not sure: 15%
Diversity Matters to NIH in Multiple Ways

NIH-Wide Strategic Plan
Final Year 2010-2015
Enhance Stewardship
- Recruit/retain a diverse outstanding research workforce
- Enhance workforce diversity
- Enhance innovation
- Enhance impact through partnerships
- Ensure rigor and reproducibility
- Reduce administrative burden

Center for Translation Research and Implementation Science (C-TRIS)

Lack of Diversity in Biomedical Science Careers

Gender gap in academic medicine (2016)
At the current rate of improvement, attaining gender parity will take a very long time (48 years nationwide)

*Clinical and basic science departments combined
Diversity and Quality of Science

- 2.57 million scientific papers between 1985-2008 (authors with U.S. addresses); 11 scientific fields
- Surnames of co-authors – ethnic diversity
- Controlled for # authors; population density etc.

Papers written by a diverse groups:
- Receive more citations
- Published in journals with higher impact factors

- Similar finding for gender diversity


NIH Scientific Workforce Diversity

Strategies to Date: Targeted Mainly to Individuals

**Intramural**
- Recruitment strategies and tools
  - Diversity in applicant pool
  - Outreach to diverse candidates
  - Reducing implicit bias
- Retention strategies
  - Build community
  - Mentoring groups
  - Professional development
- Postdoc recruitment and retention
- Graduate student partnerships

**Extramural**
- Diversity Program Consortium
  - BUILD
  - NRMN
  - CEC
- Eliminate R01 funding disparities
- Fairness in peer review
- Evaluate existing programs
  - Diversity supplements
- National strategy for sustainability
  - Hubs of Innovation in scientific workforce diversity

Institutional Commitment to Diversity: Promote Transparency and Accountability

- Systematic review and transparency of hiring and promotion procedures, policies
- Transparency: collect and publicize aggregate diversity metrics
- Provide tools to Divisions, Departments for enhancing recruitment and retention
- Evaluation of impact

NIH Addresses Challenges in the Science of Diversity

1. Among scientists, what is the impact of diversity on the quality and outputs of research?
2. Which evidence-based approaches to training and retention in biomedical research work? And in which contexts?
3. Identifying psychological and social factors that mitigate individual and institutional barriers to workforce diversity.
4. Develop a scalable strategy to effectively disseminate and sustain diversity within the nationwide scientific workforce.
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A Focus on Populations & Health Systems With Implementation Research Outcomes as Primary Endpoints

Hybrid Study Designs in the Assessment of Intervention Effectiveness and Implementation

Assessing Intervention Effectiveness: A Focus on Proximal & Distal Outcomes
1. NIH has provided a new definition of clinical trials; ensuring familiarity with this definition is crucial.

2. Full compliance with this definition is necessary to be competitive for current NIH Clinical Trial research grants.

3. A lack of diversity is seen at several levels in the clinical trial enterprise (participant, investigator, trial design levels).

4. Racial & ethnic minorities are under-represented in Phase III clinical trials at the participant & investigator levels.

5. Many of the reasons often cited for racial and ethnic minority underrepresentation in clinical trials may not be accurate and deserve re-examination.

6. Recent survey data show that most Americans have never participated in clinical trials even though awareness levels are high.

7. Most Americans indicate they are likely to participate in clinical trials if informed of trials by their doctor.
8. Strategic partnerships between professional organizations and NIH can help accelerate diversity in the clinical trial investigator pool.

9. New funding opportunities for investigator-initiated Phase II and above clinical trials (PAR-16-300 and PAR-16-301) are now available.

10. NIH remains fully committed to advancing the science, diversity, and impact of clinical trials.

Acknowledgements

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Contact Details

George A. Mensah, MD
george.mensah@nih.gov

- [Twitter (CTRIS): @NHLBI_Translate](https://twitter.com/NHLBI_Translate)
- [Twitter (professional): @ProfMensah](https://twitter.com/ProfMensah)