Inclusion and Diversity in Clinical Trials: Actionable Steps to Drive Lasting Change

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Duke Clinical Research Institute

Duke Health
Outline

• State of Diversity in Clinical Trials in the U.S.
• Diversity in Clinical Trials as a National Priority
• DCRI Think Tank Approach
• DCRI Think Tank Results
• Summary and Discussion
Participation in Clinical Trials of New Molecular Entities and Therapeutic Biologics by Race (2020)

Average Percent Participation

- Women
- White
- Black or African American
- Asian
- Hispanic

U.S. FDA Drug Trials Snapshots Summary Report. 2020
Participation in Clinical Trials of New Molecular Entities and Therapeutic Biologics by Race (2020)

- Women: 53 NME or Biologics, 32,000 participants
- White: 53 NME or Biologics, 32,000 participants
- Black or African American: 20
- Asian: 10
- Hispanic: 30

U.S. FDA Drug Trials Snapshots Summary Report. 2020
Racial and Ethnic Minorities Underrepresented in Pancreatic Cancer Clinical Trials

Herremans et al. Gastroenterology. 2021
Racial and Ethnic Minorities Underrepresented in Pancreatic Cancer Clinical Trials

Yet, Black individuals have 19% higher incidence of pancreatic cancer compared with other racial groups and have higher age-adjusted mortality (13.3 vs 11.0 per 100,000)

Herremans et al. Gastroenterology. 2021
Underrepresentation of Older Adults in Cardiovascular Clinical Trials Despite NIH Inclusion Policy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
<th>Prepolicy (n = 47)</th>
<th>Postpolicy (n = 50)</th>
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<td>33 (70)</td>
<td>34 (68)</td>
<td>.81</td>
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Underrepresentation of Women and Racial Minorities Impacting Cardiovascular Guidelines

Increasing Racial Diversity, US Census 2010-2020

Diversity Index: Likelihood that two people chosen at random from population will be of different races

https://www.census.gov
Shifting Demographics of the United States
National Priority: Regulatory perspective

• Published 2020
• Recommendations for trial sponsors on increasing enrollment of under-represented groups
• Improve accessibility
• Broaden eligibility criteria
National Priority: Regulatory perspective

- Demographic inclusion data of clinical trials for approved New Molecular Entities and original biologics
National Priority: Funding Agencies

• Published by National Academies of Sciences
• Seeks to delineate the causes of and the solutions to health inequities in the United States
• Offers community based solutions

Baciu et al. 2017
National Priority: Industry

• Many companies working towards improving diversity in clinical trials
• Merck participating one such initiative in collaboration with Novartis
National Institute of Health: Community Engagement Alliance (CEAL)

“To provide trustworthy, science-based information through active community engagement and outreach to the people hardest-hit by the COVID-19 pandemic, with the goal of building long-lasting partnerships as well as improving diversity and inclusion in our research response to COVID-19”
National Institute of Health: Community Engagement Alliance (CEAL)
DCRI Think Tank

• Organized and sponsored by the Duke Clinical Research Institute
• Held virtually April 28-29, 2021
• Attendees selected by Think Tank faculty and staff of the DCRI
• Representatives from each organization had opportunity to extend invitation to others
DCRI Think Tank: Methods

• Representatives from:
  • U.S. Food and Drug Administration
  • National Institutes of Health
  • Academic institutions/Clinical investigators
  • Pharmaceutical and device companies
  • Community-based organizations
  • Data analytics companies
  • Patient advocacy groups
DCRI Think Tank: Key Questions

• What are the best practices for participant engagement with underrepresented populations during study design, recruitment, and trial execution?
• How can we create mutual benefit and value that drives sustained engagement and retention of underrepresented populations?
• How can the use of digital approaches increase diversity and retention, and how can we ensure that we use technologies to eliminate, rather than increase, disparities?
• What are the characteristics and strategies of sites and teams that consistently achieve inclusive enrollment?
• What concrete steps can be taken to develop a more inclusive, diverse network of trial investigators and leaders?
DCRI Think Tank: Methods

• Clinical trials considered broadly according to NIH definition
• Following FDA Center for Drug Evaluation and Research approach, Think Tank focused on gaps in representation of racial and ethnic minorities, women, and older adults
• In accordance with the AMA guidance, racial and ethnic groups discussed reflect race and ethnicity as a social construct, influenced by cultural, economic, and political forces with little biologic or genetic basis
Inclusion and diversity in clinical trials: Actionable steps to drive lasting change

Michelle D. Kelsey, Bray Patrick-Lake, Raolat Abdulai, Uli C. Broedl, Adam Brown, Elizabeth Cohn, Lesley H. Curtis, Chris Komelasky, Michael Mbagwu, George A. Mensah, Robert J. Mentz, Amesika Nyaku, Stephanie O. Omokaro, Judy Sowards, Kendal Whitlock, Xinzhi Zhang, Gerald S. Bloomfield
Build Partnerships with Participants and Communities.

Improve Accessibility of Clinical Trials.

Improve Representation Among Clinical Investigators.
Build Partnerships with Participants and Communities
When Offered to Participate

- Among 35 studies, N=9759 patients offered clinical trial participation
  - 55% (95% CI: 49.4-60.5%) of those approached agreed to enroll
  - Black patients: 58.5% (95% CI: 46.8%-69.7%)
  - White patients: 55.1% (95% CI: 44.3%-65.6%)

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Despite this apparent willingness, only 8% of individuals with cancer in the U.S. enroll in clinical trials.

Build Partnerships with Participants and Communities

• Community engagement particularly effective for recruitment of racial and ethnic minority groups

• In systematic reviews, community involvement and partnership with community-based organizations *universally* cited as key to success.

• Beneficial for participant retention (65% retention rate across community-base participatory research studies).

De las Nueces et al. Health Serv Res 2012
Heller et al. Contemp Clin Trials 2014
Build Partnerships with Participants and Communities

Level of community engagement

- Researchers inform community of the project and may solicit feedback from them
- Communication flows freely between stakeholders throughout the project
- Community participates actively in key aspects of the project
- Community and researchers collaborate on every aspect of the project; decision-making and ownership are shared
- Community leads and owns the project with collaboration from researchers
Build Partnerships with Participants and Communities

• What is the reputation and involvement of my work in the community?

• Does the outcome of this study benefit health in the community?

• When did we ask for input? When did you talk to the community, at the start or just for engagement/recruitment?

• When and how will I return results?

• Are you a trusted and generous community resource?

• Can you link the community to services where needed?
Improve Accessibility of Clinical Trials
Improve Accessibility of Site Networks and Research Infrastructure

• Decentralized clinical trials to reduce geographic barriers
• Leverage community infrastructure already in place
• Use of digital tools
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### Accessibility of Clinical Trials

<table>
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<th>Cancer Type</th>
<th>Patients, No.</th>
<th>&lt;30 min</th>
<th>30 min to &lt;1 h</th>
<th>1 h to &lt;2 h</th>
<th>2 h to &lt;3 h</th>
<th>3 h to &lt;4 h</th>
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<td>40981</td>
<td>24.9</td>
<td>29.3</td>
<td>27.8</td>
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<td>Prostate</td>
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<td>26.4</td>
<td>33.9</td>
<td>11.5</td>
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<td>1.3</td>
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<td>Colorectal</td>
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<td>21.1</td>
<td>26.7</td>
<td>33.6</td>
<td>13.3</td>
<td>2.9</td>
<td>2.4</td>
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<tr>
<td>Non-small cell lung</td>
<td>157183</td>
<td>28.1</td>
<td>33.5</td>
<td>28.7</td>
<td>8.1</td>
<td>1.2</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*Number and geographic distribution of patients with metastatic disease approximated by using cancer-specific mortality data from wonder.cdc.gov.*
Number of Clinical Trial Sites per 10,000 persons

Seidler et al. Clin Invest 2014
Improve Accessibility of Site Networks and Research Infrastructure

• Decentralized clinical trials to reduce geographic barriers
• Use of Digital Tools
• Leverage community infrastructure already in place
Digital Health Technology

• Identified by FDA as key strategy to enhance diversity in clinical trial.
• Digital Tools: electronic sensors or devices that detect and measure a physical characteristic and transmit to a study database.
• Increase engagement
• Decrease participant burden
Digital Health Technology: Use with Caution

- 97% of Americans own cellphone, 85% own smartphone
- Internet access limited in rural areas
- Private space to discuss medical information
- Digital literacy
Improve Accessibility of Site Networks and Research Infrastructure

- Decentralized clinical trials to reduce geographic barriers
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Improve Representation Among Clinical Investigators
Representation of Women Authors in Heart Failure Guidelines and Clinical Trials

Reza et al. Circ Hear Fail 2020
Prioritize diversity in the clinical research workforce

- Hiring individuals from under-represented groups
- Offering support and mentorship of their research endeavors
Build Engagement and Partnerships with Participants.

Improve Accessibility of Clinical Trials,

Improve Representation Among Clinical Investigators