Strategies Toward Social Justice: Inclusive Participation in the Clinical Research Enterprise

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Inclusion in Clinical Trials & Studies

- Inadequate involvement of women and racial-ethnic minorities can negatively impact the scientific, economic, and ethical value of a clinical trial.

- The National Institute of Health enshrined the need for appropriate representation for women or men or members of minority groups in research outcomes in the Revitalization Act of 1993.

- Racial-ethnic minorities account for one-third of the American population, but account for less than one tenth of U.S. clinical trial participants:
  - Low rates of women and racial-ethnic minorities in neurological clinical trials.
“Striving for Diversity in Research Studies” Key Points

- “Clinicians cannot know how to optimally prevent and treat disease in members of communities that have not been studied”

- Obstacles hinder diversity in clinical research
  - Logistics: Inflexible work schedules, lack of convenient transportation to research center
  - Mistrust: Potential participants fear exploitation/harm by medical establishment

- Dearth of investigators and study staff who are themselves members of minority groups
  - Involvement may increase confidence of potential minority participants and community leaders
  - Mentorship of minority investigators is key

- As of January 1, 2022, NEJM will require authors to prepare supplementary tables containing background information on the disease, problem, or condition and the representativeness of the study group
Challenges to Diversity & Inclusion

How do we?

1. Enhance the screening pool
2. Convert eligible to enrolled
3. Retain enrolled participants
Challenges for Enrolling Diverse Populations: Investigator and Institutional Barriers

Institutional-level Barriers
- Dearth of research from the provider perspective
- Researchers’ attitudes, behaviors, and enrollment procedures can directly impact the success or failure to retain representative populations
- Referral bias between patients enrolled through both hospital and non-hospital platforms
  - Clinical and epidemiological studies based on patients referred from primary to secondary or tertiary care centers may suffer from significant selection bias.

Institutional-level Barriers
- Geographical disconnect between research institutions and organizations serving underrepresented patients
- Lack of meaningful community partnership
- Lack of institutional support

Emre Kokmen, E., et al., Journal of Clinical Epidemiology 1996
Table 2. Investigator Identified Best Practices and Recommendations

<table>
<thead>
<tr>
<th>Barrier</th>
<th>Theme</th>
<th>Illustrative Quote(s)</th>
<th>Best Practice, Recommendation(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural and institutional</td>
<td>NIH inclusion policy clarification</td>
<td>If the African American community makes up 12% of the population and you have 12% of your study patients who are African American, is that adequate? Will you be able to anything with that analysis?</td>
<td>Guidance on criteria for optimal inclusion rates</td>
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<tr>
<td></td>
<td>Trial design and site selection</td>
<td>What is the prevalence of the disease? Are you mimicking the prevalence or the racial breakdown of wherever you are conducting the trial?</td>
<td>A priori minority recruitment and retention budget parameter</td>
</tr>
<tr>
<td></td>
<td>Value of community engagement and partnerships</td>
<td>You have to go to the community to develop those relationships</td>
<td>Best practices on clinical trial design/analysis</td>
</tr>
<tr>
<td></td>
<td>(An academic institution)</td>
<td>[An academic institution] is two miles from the clinic, and the patients are there, the diversity is there but the patients are not traveling to [the institution] and vice versa. I think that is one of the biggest challenges... bridging trials to communities</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Physician relationships</td>
<td>If the physician believes it’s a good choice for [the patient then] he/she is usually more onboard</td>
<td>Primary physician toolkit with active trial information</td>
</tr>
<tr>
<td></td>
<td>Effective training</td>
<td>I would support training to recruit minorities or recruit anyone, recruitment is training people about what are these peoples’ concerns, how do I establish trust, what are the patients’ needs</td>
<td>Communication education</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recruitment is not based on the recruiter but it is really the psychologies, motivational interviewing, the “human factor”</td>
<td>Cultural competency training</td>
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<tr>
<td></td>
<td>Unique challenges</td>
<td>Because neurologic injury occurs, a proxy now has to make a decision about a loved one to enroll in a clinical trial...It’s not your own risk; it’s the risk for a loved one</td>
<td>Navigating acute clinical trials</td>
</tr>
<tr>
<td></td>
<td>Clinical environment and patient population</td>
<td></td>
<td>Guidance on patient denial/stigma</td>
</tr>
</tbody>
</table>

NIH indicates National Institutes of Health.
Designing a study with community for community

- Building trust through uptake of CBPR principles
- Community as partners in research design
- Understand the landscape of recruitment and retention challenges overall, and within specific communities and populations
- Write a recruitment plan that integrates targeted recruitment for underrepresented groups
  - Thinking about power and sample size
  - Don’t just designate 10% of your sample size as nonwhite; THINK ABOUT THE DISPARATE BURDEN OF DISEASE
- Set your budget up for success
  - Include money for translation and community engagement (CAB stipends, transportation fees, babysitting costs, thank you and birthday cards)
Building Trust to Reduce Participant Burden

Trust is not only requisite to enrollment, but likely has a broader impact on participants’ overall research experiences once enrolled.

- Research teams should explicitly strive to continue trust-building with participants and families throughout a study.
- Following through with commitments to participants, maintaining confidentiality, and providing timely compensation and return of research results (whether aggregate or individual) are examples of ways that research teams can build and reinforce participants’ trust in the researchers.
- Eliminating unnecessary procedures, or perception of burden, such as concise and lay-friendly communication of the study purpose, should be developed and tested formally to increase compliance and follow-up.
- Focus efforts to promote clear, ongoing communication about research procedures and, when comprehensive, will not only describe what a participant may expect during a specific procedure, but also explain how specific procedures are linked to the study’s overall goals.
- Clear plan for dissemination.

Strategies to reduce participant burden:

- Inquiries about participants’ personal goals and community goals for research participation can be incorporated into both study enrollment and participant retention protocols.
- Using an electronic consent experience. In a recent study, participants retained more information and preferred the electronic format compared with a typical paper consent.

Gabel, M., et al., Alzheimer Disease & Associated Disorders 2022
Address recruitment and retention barriers as part in design

Patient-level Barriers
- Burdensome time commitment
- Transportation difficulties
- Language barriers
- Testing
- Severe comorbidity
- Adverse events
- Long study duration
- Frequent study visits
- Cognitive impairment and decline over time

Participant satisfaction is driven by various factors:
- Functional status
- Personal relevance to the research
- Perceptive physical and mental health improvements
- Interaction with research personnel
- Ease of testing protocols

Understanding reasons for withdrawal
- Motivational interviewing is key
- Meet people where they are
Barriers and Facilitators Among Black Americans to Participation in AD Biomarker Research

- Researchers conducted focus groups with 70 community-dwelling Black Americans to identify themes.

- Barriers:
  - Mistrust
  - Access to information
  - Fear of the unknown or adverse effects
  - Inconvenience
  - Reputation of researchers and research institutions

- Facilitators (i.e., motivating factors):
  - Relevance of research
  - Altruism
  - Desire to learn more about the disease and ways it may impact the individual’s health
  - Positive reputation of the research institution

Demographic Characteristics of Focus Group Participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>Range</th>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>52.37 ± 15.03</td>
<td>21 – 86</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
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<tr>
<td>Female</td>
<td>51 (73)</td>
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<tr>
<td>Male</td>
<td>19 (27)</td>
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<tr>
<td>Education</td>
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<tr>
<td>&lt; High School</td>
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<tr>
<td>High School</td>
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<tr>
<td>Some college</td>
<td>24 (34)</td>
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<tr>
<td>Bachelors degree or greater</td>
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<tr>
<td>Annual Income</td>
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<td></td>
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<tr>
<td>&lt;$10,000</td>
<td>19 (28)</td>
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<td>$10,000 – $20,000</td>
<td>16 (24)</td>
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<td>$21,000 – $40,000</td>
<td>13 (19)</td>
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<tr>
<td>&gt; $40,000</td>
<td>20 (29)</td>
<td></td>
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<tr>
<td>Previously Participated in Research</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>30 (43)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>40 (57)</td>
<td></td>
</tr>
</tbody>
</table>

Williams, M., et al., Alzheimer Dis Assoc Disord 2010
Facilitators, Challenges, and Messaging Strategies for Hispanic/Latino Participation in AD & Related Dementias Clinical Research

- Researchers conducted narrative literature review (N=210) of the current landscape of Hispanic/Latino participation in clinical research, including the challenges, facilitators, and communication channels to conduct culturally appropriate outreach efforts to increase awareness and participation of Hispanics/Latinos in AD/ADRD clinical research studies.

- Challenges:
  - Lack of culturally appropriate outreach efforts
  - Staffing that does not represent participants’ cultures/language
  - Eligibility criteria that disproportionately excludes Hispanics/Latinos
  - Too few studies available in Hispanic/Latino communities

- Facilitators and messaging strategies
  - Approaches that recognize and address the heterogeneity of the Hispanic/Latino ethnicity
  - Tailor outreach activities and programs to address their diverse needs and circumstances

Massett, HA, et al., J Alzheimers Dis 2021
Best Practices to incorporate into design

• Importance of family buy-in during the recruitment and enrollment of patients onto clinical studies

• In trials enrolling patients with cognitive impairment and dementia, both the patient and the study partner—most often the patient's primary caregiver—are critical to enrollment decisions.

• Send cards regularly to celebrate/congratulate the participant on special dates (birthdays, holidays, enrollment anniversary) and to express gratitude for their participation

• Maintain frequent contact with enrollees through newsletter that offers general informational tips

• Make monthly telephone calls to participants to encourage adherence to visits and to monitor adverse events

• Recruitment all day everyday

• Schedule follow-up which are convenient for participants

• Reimburse for travel

• Use motivational interviewing to understanding hesitation for enrollment and reasons for withdrawal
Best Practices for Enhancing Referrals

• **Referral bias** – understanding where referrals come
• **Identifying who is not at the referral table**
  • For example, CREST-2 Lunch and Learns are informal outreach events to meet and share trial information in order to encourage patient referrals to the study.
  • Meeting face to face is key to building relationships between referring physicians and researchers.
  • Engaging local primary care practices can help minority and other underserved populations gain access to top quality care
  • Expanding the team to include health professionals who are serving in clinics around the populations we serve
Building Diversity within Research Teams

• Diversity, equity and inclusivity (DEI) in research teams increases innovation. Greater representation in research team leadership can potentially address knowledge gaps that improve study design.
  • Greater visibility of DEI within research teams can promote trust in the work among potential research participants from diverse backgrounds

• Building the next generation of minority research leaders that will join the workforce in different capacities with the skills and knowledge to lead multidisciplinary teams.
  • Diversity within research team and the research environment will have the added benefits of improving team camaraderie and support, which will go some way to alleviating some of the pressures faced by academic researchers

Asmal, L., et al., Psychiatry Research 2022
Community Health Workers and Promotores

- Community health workers can be partners in clinical trial recruitment strategies. Examples of case studies that showcase the power of using promotores and community health workers:
  - A randomized controlled trial of brief intervention (BI) using peer health promotion advocates (promotores), was conducted among at-risk and alcohol-dependent Mexican-origin young adult emergency department (ED) patients. At 12-month follow-up this study demonstrated significantly improved drinking outcomes for Mexican-origin young adults in the ED who received a BI delivered by promotores compared to those who did not.
  - A culturally informed outreach program was developed that made use of promotores de salud (community health promoters) to increase Latinx SARS-CoV-2 testing. The intervention tested 3.84 times more Latinx individuals per event than controls.
  - After a diagnosis of prostate, breast, or colorectal cancer, Latinos experience higher mortality rates and lower health-related quality of life (HRQOL) in comparison with other ethnic/racial groups. Enhanced patient navigation (PN) improves HRQOL among Latino colorectal cancer survivors.
  - Increasingly, patient navigation services are demonstrating success in improving cancer detection, treatment, and care and in reducing cancer health disparities – especially among Black Americans. A patient navigation program in Baltimore City successfully delivered cancer navigation services to 1,302 urban Black older adults by recruiting, selecting and training CHWs from their community.

Cherpitel, C., et al., Alcohol Alcohol 2016
DeGarmo, D., et al., JAMA Network 2022
Ramirez, A., et al., Cancer 2020
Bone, L., et al., Prog Community Health Partnership 2013
Training to Optimize the Research Team

- Cultural humility
- Community awareness
- Community engagement
- Motivational interviewing
- Team building
- Ongoing in-services + team debriefing
Becoming culturally competent and practicing cultural humility are ongoing processes that change in response to new situations, experiences and relationships. Cultural competence is a necessary foundation for cultural humility.

What is my culture, and how does it influence the ways I view and interact with others?

CULTURAL COMPETENCE

- Three guiding factors (Tervalon & Murray-Garcia, 1993)
  - A lifelong commitment to self-evaluation and self-critique
  - Desire to fix power imbalances
  - Develop partnerships with people and groups who advocate for others

Cultural Humility

• Cultural Humility
• Tervalon & Murray-Garcia (1993)
  - A lifelong commitment to self-evaluation and self-critique
  - Desire to fix power imbalances
  - Develop partnerships with people and groups who advocate for others

CULTURAL HUMILITY

- Holding systems accountable
  - How can I work on an institutional level to ensure that the systems I’m part of move toward greater inclusion and equity?

- Understanding and redressing power imbalances
  - How can I use my understanding of my own and others’ cultures to identify and work to disrupt inequitable systems?

GAINING CULTURAL KNOWLEDGE
What are other cultures like, and what strengths do they have?

DEVELOPING CULTURAL SELF-AWARENESS
What is my culture, and how does it influence the ways I view and interact with others?
What is Motivational Interviewing (MI)?

- A supportive counseling style used to elicit and strengthen motivation for change
  - MI incorporates asking open-ended questions and using reflective listening

- Successful use of MI for trial recruitment has the potential to:
  - Significantly improve rates of trial participation
  - Reduce disparities that impact generalizability of research

- Meeting patients and investigators/coordinators where they’re at
Motivational Interviewing Training

DECREASE RESISTANCE

REFLECTIVE LISTENING
“It sounds scary…”

AFFIRMATIONS
“I’m glad that you made it here.”

TOLERATING AMBIVALENCE
“…”

SUMMATIONS
“It sounds like you debated what to do, but then made the trip here.”

SELF REFLECTION EXERCISE

CAN YOU IDENTIFY (TO YOURSELF):

• One time when you initiated patient contact but may not have fully committed to engaging the patient?
• One time when you avoided patient contact because you did not feel that you could connect with a potential participant?
• One time when you initiated patient contact even though you were not fully comfortable?

CAN YOU IDENTIFY WHY?
WHAT MIGHT YOU HAVE DONE DIFFERENTLY?

PATIENT TYPES

OPEN
Patient is open and calm when you speak to them.

CONCERNED
Patient is wary but not deeply fearful or angry.

ANGRY
Patient is either deeply fearful or angry.

COMMUNICATION STYLES

DIRECTING
TELLS PEOPLE WHAT TO DO AND HOW TO MOVE FORWARD.

GUIDING
LISTENS CAREFULLY AND OFFERS EXPERTISE WHERE NEEDED.

FOLLOWING
LISTENS TO WHAT IS BEING SAID AND REFRAINS FROM INSERTING ONE’S OWN INFORMATION.

CONTINUUM OF COMMUNICATION STYLES
Build in time for debriefing with the Team

Creating a culture of collaboration and teamwork across all team member.

- Debriefing is considered a critical component of learning to integrate knowledge and improve technical and nontechnical skills.
- Debriefing via peer feedback improved learning of specific skills through repeated and experiential learning, suggesting that it was a useful educational tool.
- Taking the time to step back, reflect and review the situation to improve their practice.
- Putting together scripts for challenges during recruitment.

Rueda-Medina, B., et al., Nurse Educator 2021
Levett-Jones, T., et al., Nurse Educator 2014
Eddy, K., et al., JBI Database of Systematic Reviews and Implementation Reports 2016
A step forward to enhance equity in clinical trials

Being present and actively seeking information to improve your study design and research team is a step in the right direction to improving inclusive participation in clinical trials.
Questions