

# Diversity & Inclusion in Neurological Clinical Trials: Report from StrokeNet working group

## Current Inclusion Working Group

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# “Pathology of Racism” Key Points

- Segregated care provided to patients of color, undocumented, and poor patients
- Trainees immersed in two-tiered, segregated system
  - “Some patients see residents, other kinds of patients see attendings”
  - Not adequately trained to identify structural factors that lead to worse health outcomes in people of color and people living in poverty
- Academic institutions often turn a blind eye to the long history of medical experimentation forced on communities of color
- Focus on objective quality measures undermines progress in addressing racial healthcare inequities

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## POINTS OF VIEW

### Pathology of Racism — A Call to Desegregate Teaching Hospitals

“We see *such* advanced pathology here,” our guide boasted as she glided through the resident Ob/Gyn clinic. It was 2013, and I was among a nervous gaggle of fourth-year medical students, following the resident on a whirlwind residency interview tour. “We see all the Medicaid and uninsured patients, so it’s, like, really great learning,” she continued. I looked at her in awe, with excitement and near disbelief that I, too, would soon be caring for patients in a clinic just like this one.

Years passed. I worked in many clinics throughout residency and fellowship training. I saw lots of “pathology.” I came to realize that this was a term my tour guide had used when she should have said “injustice.” It was the term she used when she meant to say preventable cervical cancer, untreated abnormal uterine bleeding, absent prenatal care. It was the term she used to talk about the segregated care provided to the Black people, Latinx people, undocumented people, poor rural people, and poor urban people within our academic institutions.

I watched as Black patients turned right and White patients turned left. It was 2020, but it could have been 1950.


Racism was built into the fibers of this academic hospital, but it wasn’t just the racism that caused my stomach to churn. It was the realization that after working in this setting for 2 years, I had grown accustomed to the system. I knew that we were providing segregated care, but I had stopped noticing it, the way you stop noticing a foul odor if you sit in its presence too long. It had become a fact of life. “Oh, that’s a billing thing,” someone had explained simply when I inquired about the segregated clinics on my first day. *A billing thing*. And that was it — just the way things are.

At our medical institutions, we immerse trainees in a two-tiered system. We teach them that some kinds of patients see residents and other kinds of patients see attendings. We teach them that Black patients turn right and White patients turn left. And worst of all, we teach them to pretend not to notice. We teach them to

# Inclusion in Clinical Trials

- **Inadequate involvement of women and racial-ethnic minorities can negatively impact the scientific, economic, and ethical value of a clinical trial**
- NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Trials 1993 – Amended 2001
- 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

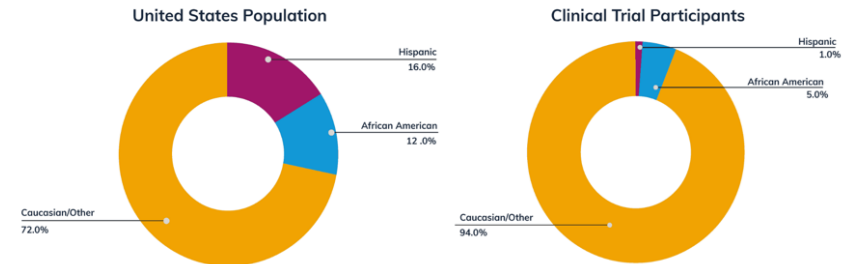
**Inclusion of Women, Minorities, and Children**



By law, Women and Minorities must be included in clinical research studies; in Ph III CT in numbers adequate for valid analysis

By NIH policy, children should also be included in human subjects research unless scientific/ethical reasons (NOTE: Children are < 21 years)  
**NOTE:** difference between children according to HS regulations and children according to inclusion policy

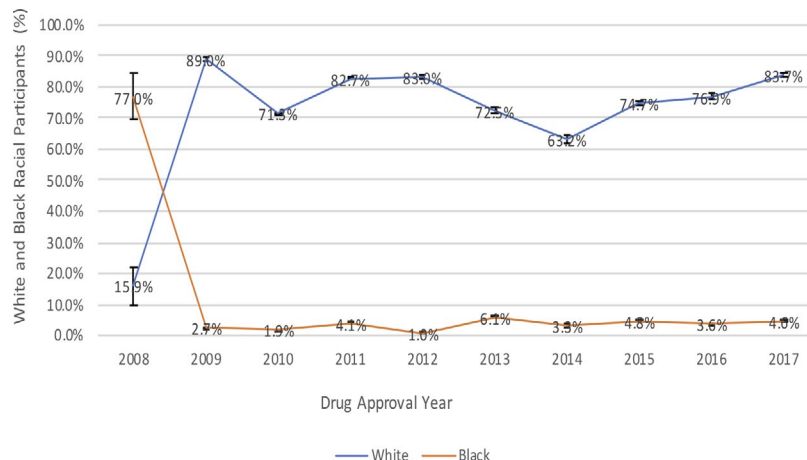
## Underrepresentation in Clinical Trials



\*Sourced from <https://www.sciencedirect.com/science/article/pii/S0146280618301889>

# Importance of Inclusion

- 10-year trends in enrollment of women and minorities in pivotal trials supporting FDA approval of cardiometabolic drugs (2008-2017)
  - 35 novel cardiovascular (n=24) and diabetes mellitus (n=11) drugs were approved during the study period
  - 36% of trial participants were women
  - 81% white, 4% black\*, 12% Asian
  - 11% Hispanic/Latino



\*In trials reporting results for both white and black populations, inclusion of the black minority group remained <10% each year, except for 2008, owing to the predominantly black population in the 1 trial that reported data on racial minorities

Muhammad Shahzeb Khan. Journal of the American Heart Association. Ten-Year Trends in Enrollment of Women and Minorities in Pivotal Trials Supporting Recent US Food and Drug Administration Approval of Novel Cardiometabolic Drugs, Volume: 9, Issue: 11 (2020), DOI: (10.1161/JAHA.119.015594)

# Inclusion Committee

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- NIH StrokeNet Concept Synopsis”. PI to describe diversity, equity, inclusion and retention plan:

Describe the demographics of the patient population under study (gender/sex, race, ethnicity of those with the disease/condition across the life span) and plans to ensure an adequate enrollment of populations that experience health disparities (e.g., study tools, training, outreach, community engagement, types of sites or specialties needed, etc).

- Potential discussion along with concept synopsis at stroke focus area groups
- PI's calling on the inclusion committee:
  - 2 weeks before submission
  - Maybe at study initiation
  - When recruitment is problematic

# “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 requires authors to prepare supplementary tables containing background information on the disease, problem, or condition and the representativeness of the study group

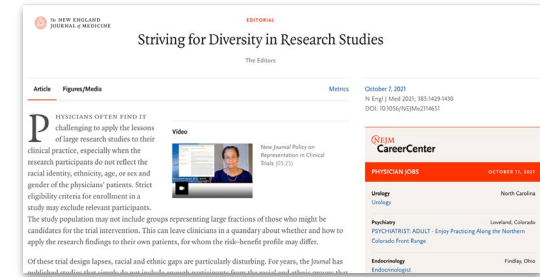


Table 1. Sample Supplementary Table on the Representativeness of Study Participants.	
Category	Example
Disease, problem, or condition under investigation	Heart failure with reduced ejection fraction (HFrEF)
Special considerations related to	
Sex and gender	HFrEF affects men more than women (ratio of 2:1 or 3:1).
Age	Prevalence increases steeply with age; women with HFrEF are older than men with HFrEF.
Race or ethnic group	HFrEF affects Black persons disproportionately in the United States.
Geography	Age and cause vary among countries — patients in Latin America and Asia are younger and more often have noncoronary causes than patients in Europe and North America. Much less is known about heart failure in Africa than in other regions of the world.
Other considerations	In the United States, HFrEF develops at a younger age and more often has a noncoronary cause in Black patients than in White patients. Throughout the world, mortality and hospitalization rates vary widely within and between countries.
Overall representativeness of this trial	The participants in the present trial demonstrated the expected ratio of men to women. Biologic sex was reported by the participants; on the intake survey, they were asked, "What was your sex assigned at birth?" Options were female, male, and intersex. Gender was also reported by participants; they were asked, "What is your gender identity?" Options were woman, man, nonbinary, and prefer not to say. Patients with HFrEF are younger outside North America and Western Europe; thus, the age distribution in the study population is different from that encountered in some countries. The proportion of Black patients who underwent randomization overall was small (4.8%), but among patients enrolled in North America, 18.9% were Black, a somewhat larger proportion than the total population distribution of Black people in the United States. Causes of heart failure and other features such as coexisting conditions and kidney function were consistent with epidemiologic and registry data where these were available from participating countries. No patient was enrolled in Africa.

# Challenges to Inclusion in Clinical Trials

- Enhancing the screening pool
  - Starts with community engagement BEFORE the trial even begins
  - Build awareness about clinical trials AND stroke warning signs
    - Be responsive, not directive
  - Just because your site is in a large, diverse city does not mean that you are guaranteed to recruit participants from underrepresented groups
  - Enhancing the overall number of people in the screening pool will increase the likelihood of eligible participants
- Converting eligible to enrolled
  - Motivational interviewing is key
  - Meet people where they are
- Retention
  - Meet regularly with your research team to discuss participant retention
  - Community advisory boards can help you troubleshoot retention



# What We Are Doing Now

- Inclusion committee is currently not funded
- Consultation activities to assist with recruitment and retention of diverse study populations:
  - Review of recruitment and retention plans
  - Inclusion in-services
  - Recruitment diagnostics
  - Individual site counseling
  - Site selection counseling
  - Motivational interviewing training
  - Identification of unique challenges associated with study protocols
  - Collection of demographics and social determinants of health
  - Retention strategies
  - Structural bias education for physicians and coordinators
  - Demographics and sample size calculations
  - Community engagement strategies

<b>Trial</b>	<b>Consulting Specifics</b>
Efficacy of Home-based Telerehabilitation	Review of R&R plan
ACCESS	Review of R&R plan
ASPIRE	Review of R&R plan
DISCOVERY	Development of R&R plan
VERIFY	Review of R&R plan
CLARITY	Review of R&R plan

Trial	Consulting Specifics
FASTEST (UCI site)	Development and implementation of community consultation plan for EFIC; Development of public disclosure plan for EFIC
DISCOVERY	Site selection; inclusion in-service; retention strategies

# FASTEST: Exemption from Informed Consent (EFIC)

rEVIIa for Acute Hemorrhagic Stroke Administered at Earliest Time (FASTEST)

**UCI** Program in  
Public Health

UCI Health, Orange County, CA

- Focused on language cohorts (English, Spanish, Vietnamese, Korean)
- Leveraged existing partnerships with community groups
- Tabled at FQHC, farmers market, and CBO providing basic services to unhoused individuals
- Conducted bilingual focus groups and presentations at CBO and church meetings
- Advertised in English, Spanish, Vietnamese, and Korean language newspapers and on English and Spanish language radio

*“UCI’s efforts embodied the goals of EFIC to inform the community and allow the community to dialogue with the team.” –Julie Denlinger, FASTEST Project Manager, NIH Strokenet NCC*



Congratulations to all our US sites that have completed their EFIC reports and gained Advarra full study approval. Advarra shared that the FASTEST sites reviewed have been strong! Well done!

Recently, two of our US sites, received extra recognition for their EFIC community consultation efforts from Advarra. We would like to extend a special acknowledgment to the teams at **UC Irvine (UCI)**, under **Dr. Shah** and **PSC Julia Fong** and **Kaiser Permanente Los Angeles Medical Center**, under **Dr. Sangha** and **PSC Vanessa Audea**. The Advarra reviewer described both sites’ efforts as “excellent”. **AMAZING WORK!**

# Study Implementation

<b>Trial</b>	<b>Consulting Specifics</b>	<b>Challenges</b>
I-ACQUIRE	Lit review to assess state of inclusion in pediatric trials; inclusion in-service; recruitment diagnostics	Enhancement of screening pool
CREST-2	Development of outreach kits for engagement with PCPs; inclusion in-services; recruitment diagnostics; individual site counseling; retention strategies; community engagement strategies	Identification of eligible minority participants
SATURN	Inclusion in-service	Optimizing conversion to enrollment
ARCADIA	Inclusion in-service; site selection	Site selection; optimizing conversion to enrollment; community engagement
ASPIRE	Individual site counseling; inclusion in-services; site selection; community engagement strategies	Optimizing conversion to enrollment; community engagement

- Building a StrokeNet Community of Practice that can tailor recruitment and retention plans to sites' specific needs and address sites' unique barriers and challenges
  - Funding and formal inclusion as part of StrokeNet infrastructure
  - Inclusion committee members sitting on each working group
  - Addition of early career investigators and study coordinators to the committee to ensure sustainability
  - Process for automatic review of all recruitment and retention plans for grant proposals
  - Move beyond focus only on primary and secondary prevention
  - Training infrastructure to address common themes across all trials
- Changes to grant proposal process
  - Sites to demonstrate understanding of the communities they serve
  - Revised R&R template to require description of disease burden across gender and race/ethnicity and a detailed explanation of how sites will meet that distribution in recruitment
  - Budgeted time for inclusion committee members for consultation

# Changes That Need to Occur Simultaneously



- Process
  - Decision to submit protocol with justification of race/ethnic inclusion and sample size (includes standardized collection of race and ethnic identify)
  - Approval of protocol with focus on site selection and detailed description of sites' process for recruitment
  - Study initiation with training on screening, conversion, and retention
  - Study implementation with specific recruitment diagnostics for sites
- Paradigm shift
  - Identify areas of structural bias
  - Continue to enhance StrokeNet's Community of Practice
  - Movement toward meaningful partnerships with community
- Evaluation = defined metrics

# Community of Practice

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- **Historic and systemic exclusion of groups from clinical research is a social injustice that must be addressed in order to advance health equity**
- Systemic change necessitates bringing together communities and interdisciplinary networks engaged in enhancing inclusion.
- The StrokeNet CoP should:
  - Enhance methodologies towards inclusion
  - Implement best practices for diverse recruitment and retention at the investigator and institutional levels
  - Produce rigorous best practices for dissemination and assure fidelity of messages and content
  - Train the next generation of researchers

- Set your budget up for success
  - Include money for translation and transcription
  - Hire culturally concordant research staff and pay them competitively and equitably
  - Include stipends for community action/advisory board members
  - Reimburse participants for transportation, parking, meals, mileage reimbursement for long distances
  - Account for lodging and childcare as needed
  - Provide gift cards to local grocery stores or movie theaters
  - Account for thank you and birthday cards to help with retention
  - Budget for direct mailings
  - Provide competency trainings for research staff
  - Host recognition events (eg, end of study celebration) for participants and staff
  - Plan for unexpected “rainy day” expenses

- Connect people with common goals and interests for the purpose of sharing resources, strategies, innovations and support
- Support the transmission and expansion of knowledge and expertise for leaders, learners and professionals in any field or discipline
- Contribute to a more connected and collaborative global community in a field of expertise

## Developing the CoP

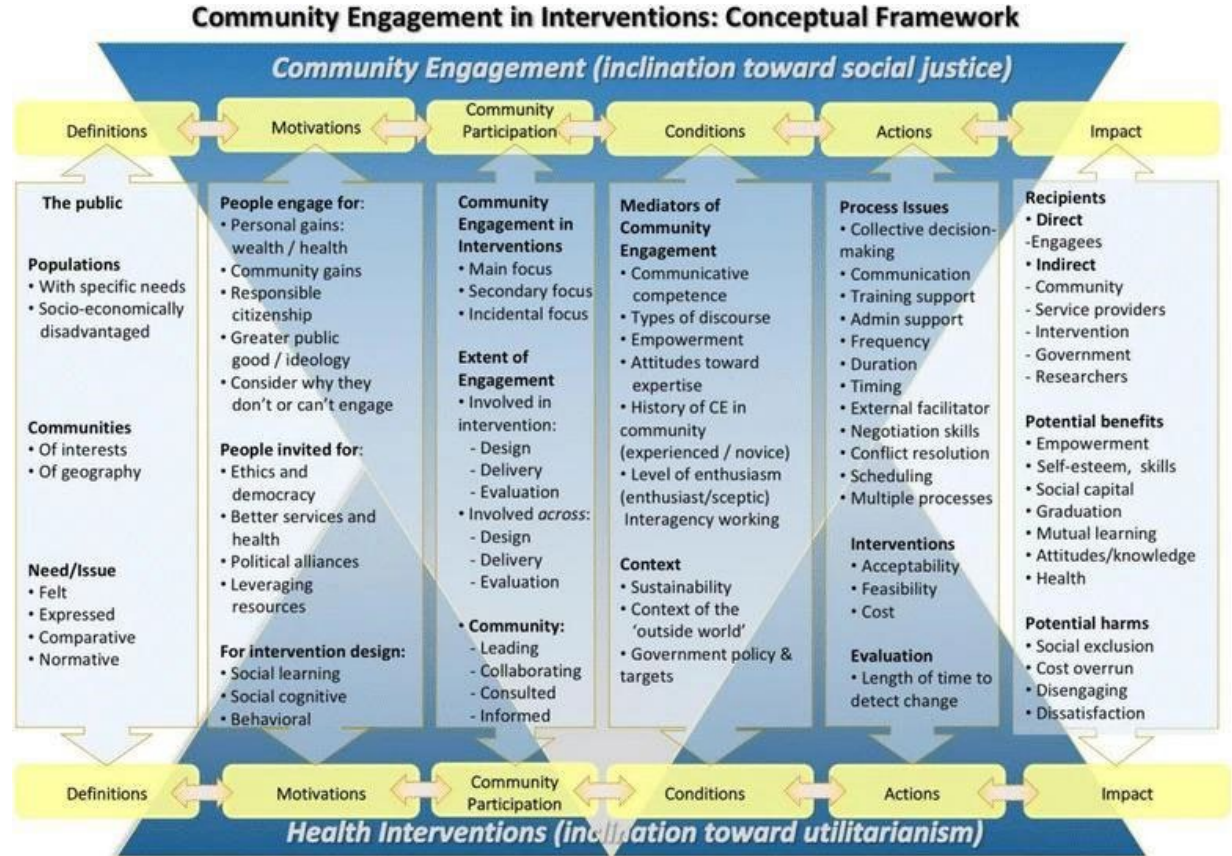
- Define the CoP
  - Reflect and plan as a group
  - Expand beyond original members
  - Identify processes and practices that engage members
  - Determine how leaders will be identified and supported
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- CoP can include seasoned investigators, trainees, students, community members from multiple disciplines

# Community Engagement

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# Engaging in Community Conversations

- Relies on targeted goals developed directly with community for social justice reform
- Requires:
  - Training to inform about issues
  - Curriculum to focus dialogue
  - Collaborative leadership models for the sharing and use of resources
  - Ethics of hospitality, patience, and reconciliation
  - Role models to demonstrate how and why issue is valuable



- Our scoping review of CE in neurological trials found that only 35 stroke trials between 2000-2021 utilized CE
- Most focused on primary and secondary prevention
- CE strategies used in neurological trials:
  - Collaboration with community partners (41%)
  - Culturally-tailored materials and mobile health (39%)
  - Community health workers (34%) – most commonly used strategy in stroke trials
  - Collaboration with faith-based organizations and local businesses (27%)
  - Focus groups/health needs assessments (21%)
  - Community Advisory Boards (18%)
  - Personnel recruited from target communities (18%)
  - Caregiver/social support (12%)

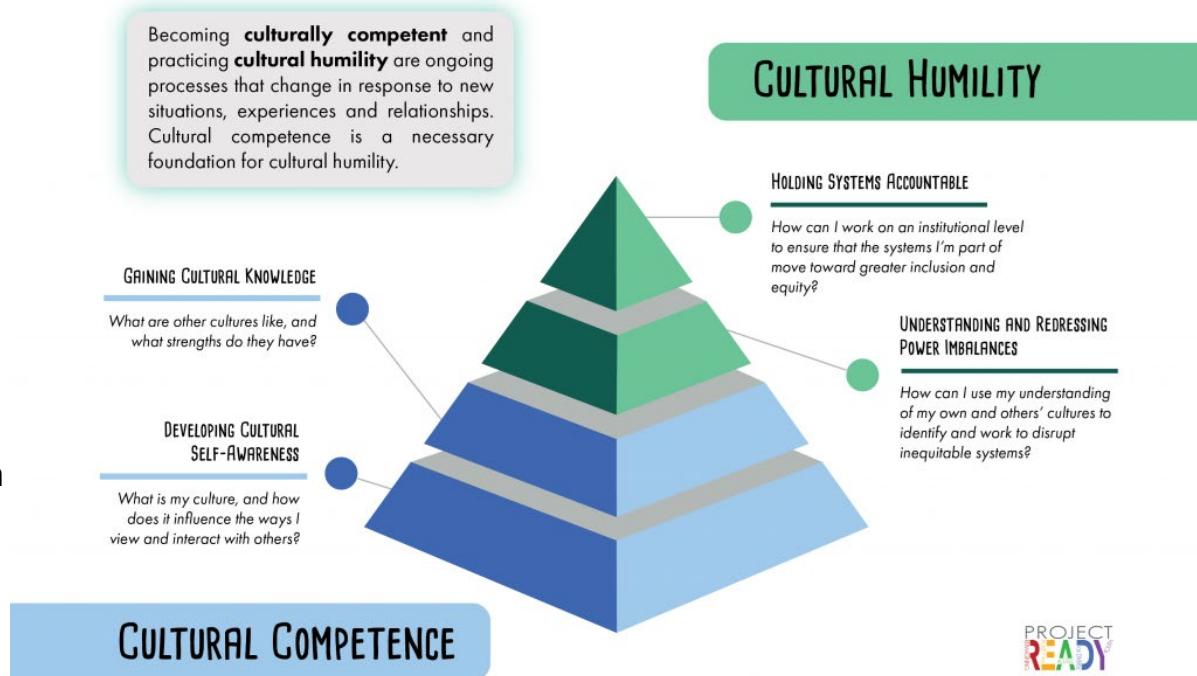
# CBPR Challenges

- The extent to which we can achieve any of the community based participatory research (CBPR) principles will vary based on content, purpose, scope, and participants involved
- Each principle is a continuum -- a goal to achieve
- No one is there yet
- It's up to you to make connections with the community and to talk about stroke/stroke studies
  - What does it mean to participate in trials?
  - Is there a budget for multiple languages
  - Partner - look for investigators with experience in community engagement (CTSAs, FQHCs)



# Cultural Humility

- 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







# Questions?

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# Thank you!

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