

# 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

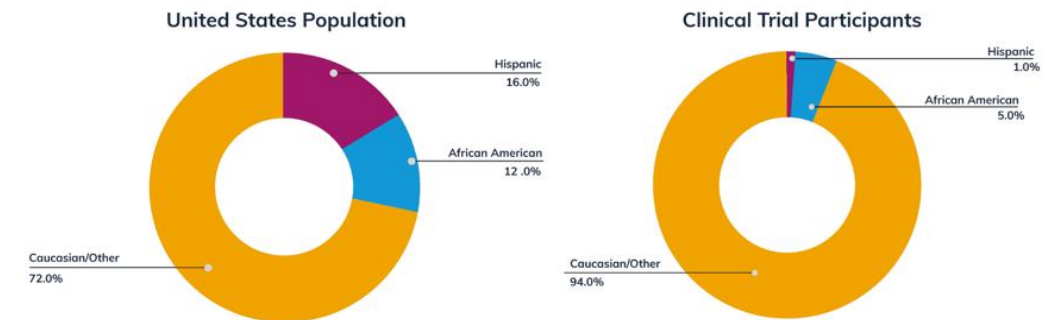
**Inclusion of Women, Minorities, and Children**



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

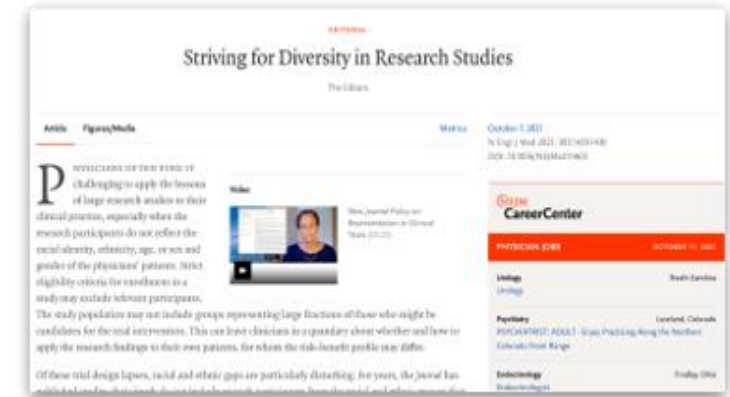
## Underrepresentation in Clinical Trials



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

# “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**



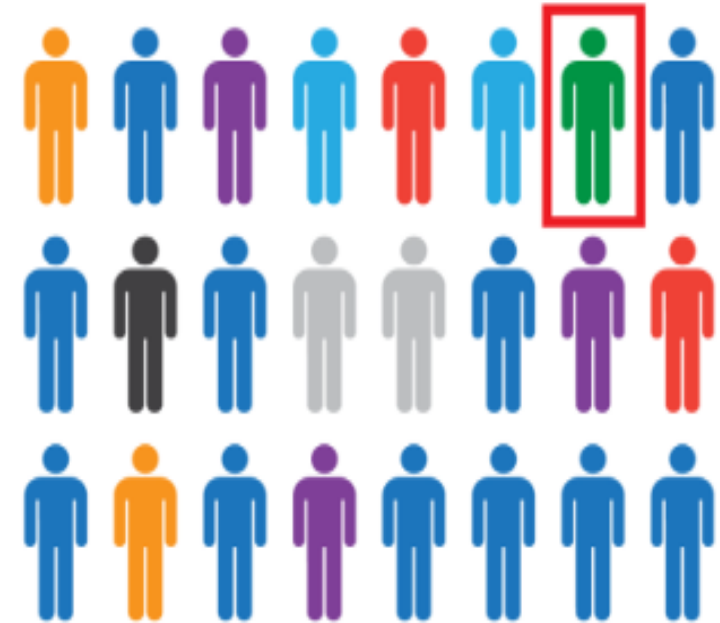
**Table 1. Sample Supplementary Table on the Representativeness of Study Participants.**

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 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

# Investigator Barriers (cont.)

**Table 2. Investigator Identified Best Practices and Recommendations**

Barrier	Theme	Illustrative Quote(s)	Best Practice, Recommendation(s)
Structural and institutional	NIH inclusion policy clarification	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?	Guidance on criteria for optimal inclusion rates A priori minority recruitment and retention budget parameter
	Trial design and site selection	What is the prevalence of the disease? Are you mimicking the prevalence or the racial breakdown of wherever you are conducting the trial?	Best practices on clinical trial design/analysis
	Value of community engagement and partnerships	You have to go to the community to develop those relationships  [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... bridg[ing] trials to communities	Tips/tools on fostering and maintaining equitable community partnerships
	Physician relationships	If the physician believes it's a good choice for [the patient then] he/she is usually more onboard	Primary physician toolkit with active trial information
Recruitment communication	Effective training	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  Recruitment is not based on the recruiter but it is really the psychologies, motivational interviewing, the "human factor"	Communication education Cultural competency training Motivational interviewing
Unique challenges	Clinical environment and patient population	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	Navigating acute clinical trials Guidance on patient denial/stigma

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

Variable	Mean ± SD	Range
Age (yrs)	52.37 ± 15.03	21 – 86
N (%)		
<b>Gender</b>		
Female	51 (73)	
Male	19 (27)	
<b>Education</b>		
< High School	6 (9)	
High School	10 (14)	
Some college	24 (34)	
Bachelors degree or greater	30 (43)	
<b>Annual Income</b>		
<\$10,000	19 (28)	
\$10,000 – \$-20000	16 (24)	
\$21,000 –\$40,000	13 (19)	
> \$40,000	20 (29)	
<b>Previously Participated in Research</b>		
Yes	30 (43)	
No	40 (57)	

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

# Best Practices to incorporate into design

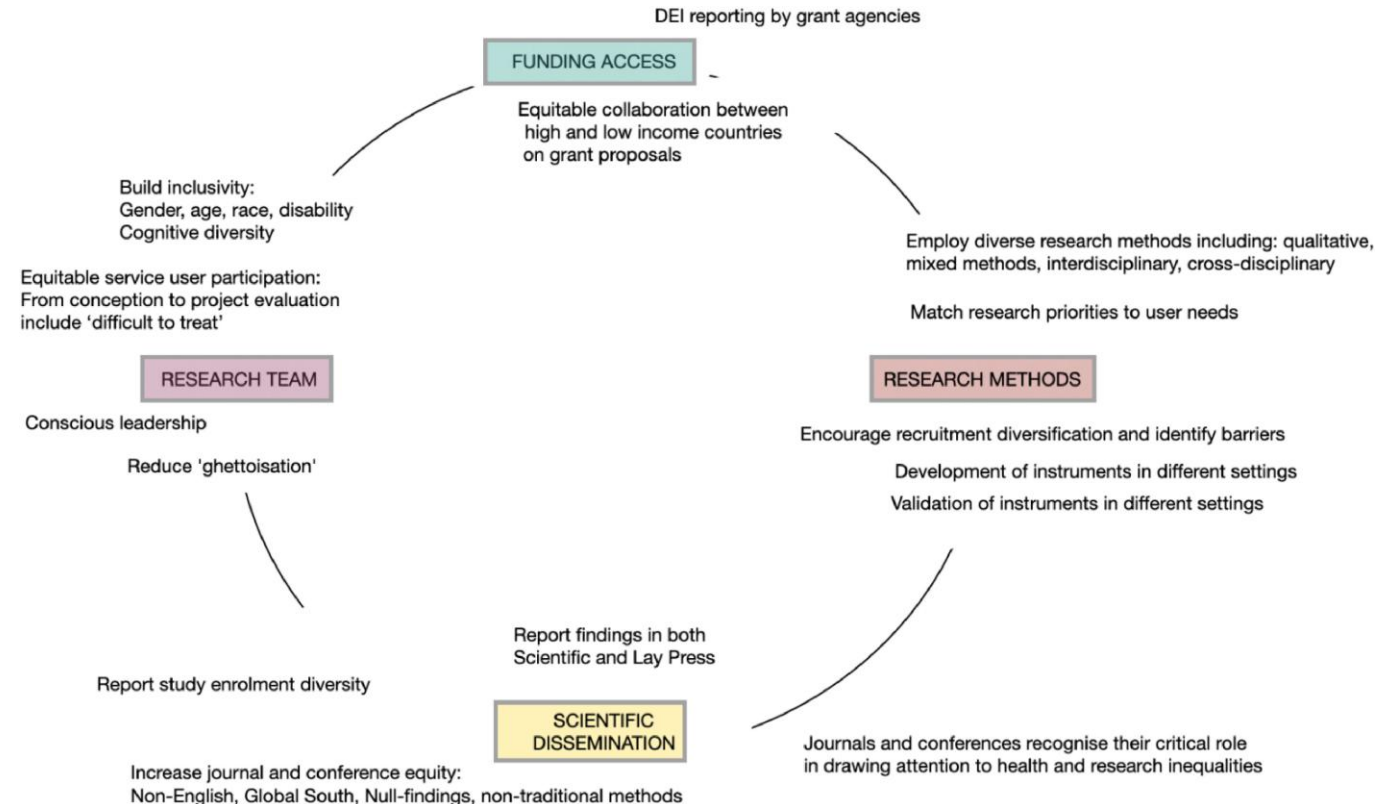
- Importance of family buy-in during the recruitment and enrollment of patients onto clinical studies
- In trials enrolling patients with cognitive impairment and dementia, both the patient and the study partner—most often the patient's primary caregiver—are critical to enrollment decisions. .
- Send 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



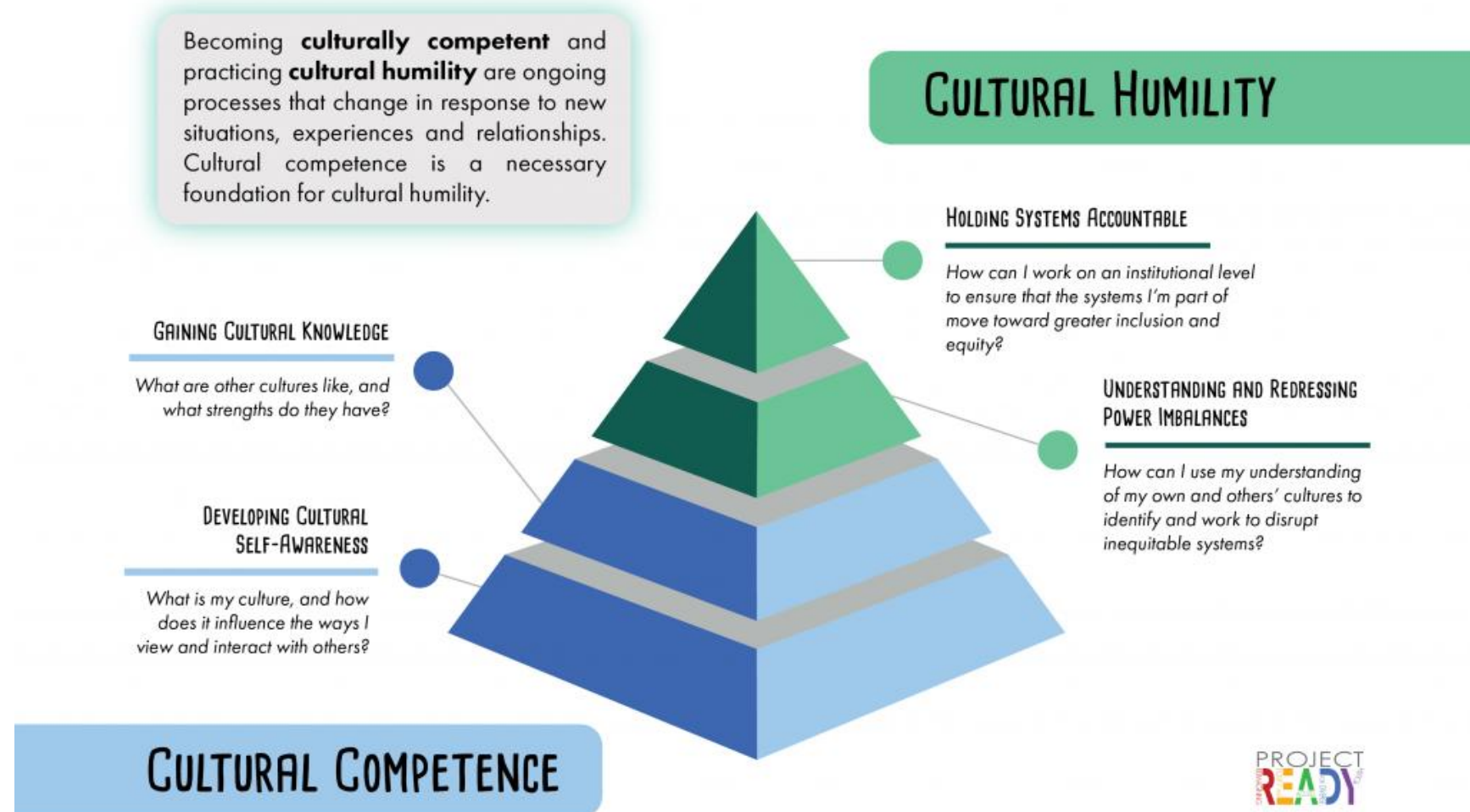
# Training to Optimize the Research Team

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- Cultural humility
- Community awareness
- Community engagement
- Motivational interviewing
- Team building
- Ongoing in-services + team debriefing

# 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




# 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

GUIDING  
Listens carefully and offers expertise where needed.  


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 SELECTION 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

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# 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





# Questions