

# Diversity & Inclusion in Clinical Trials

**Bernadette Boden-Albala, MPH, DrPH**

Pronouns: *she/her/hers*

Director and Founding Dean, Program in Public Health  
Professor, Department of Health, Society and Behavior, Program in Public Health  
Department of Neurology, School of Medicine  
Susan & Henry Samueli College of Health Sciences  
University of California, Irvine

# “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

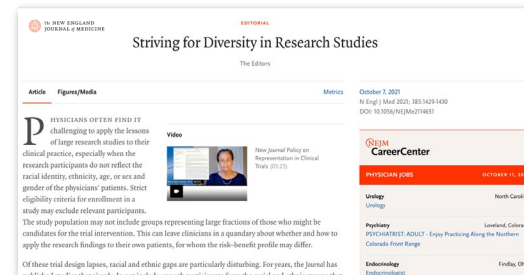


Table 1. Sample Supplementary Table on the Representativeness of Study Participants.	
Category	Example
Disease, problem, or condition under investigation	Heart failure with reduced ejection fraction (HFrEF)
Special considerations related to	
Sex and gender	HFrEF affects men more than women (ratio of 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.

**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.

# “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**

The NEW ENGLAND JOURNAL of MEDICINE

## 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. Matter of social justice**
- 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

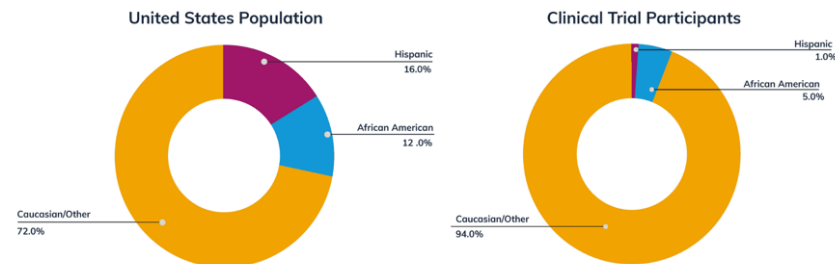
**Inclusion of Women, Minorities, and Children**



By law, Women and Minorities must be included in clinical research studies; in Phase 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

- 38-79% of Pacific Islanders and 40-50% of East Asians estimated to have alleles associated with higher risk of treatment failure or adverse drug events, even on normal dose
  - Hawaiian population comprises nearly half these ethnicities
- CAPRIE study was used to establish the maintenance dosage of 75 mg/day
  - 95% of enrolled study participants were Caucasian (10–20% possess the alleles)

## Bristol-Myers, Sanofi Sued by Hawaii Over Plavix Labeling

Karen Gullo

March 19, 2014 — 9:03 PM EDT Updated on March 19, 2014 — 9:03 PM EDT

Bristol-Myers Squibb Co. and Sanofi were accused in a lawsuit by Hawaii of failing to disclose that the blood-thinning drug Plavix has little effect on 30 percent of the population and puts patients at risk for gastrointestinal bleeding.

Important business  
the day.

is daily newsletter.

email

Sign Up

From 38 percent to 79 percent of Pacific-Islanders and 40 percent to 50 percent of East Asians may respond poorly to Plavix because of a genetic predisposition to inadequately metabolize the drug, Hawaii Attorney General David Louie said in an e-mailed statement. The companies failed to disclose the information to protect their profit from Plavix prescriptions, he said in a complaint today in state court in Honolulu.

# Optimizing Collection of Gender Identity Data

- Consider relevancy to study and ensure research subjects can provide information in a comfortable, private space
- Use the term **sex** when reporting biological factors and **gender** when reporting gender identity, psychosocial, or cultural factors
- Use gender-neutral language in all study materials and avoid gendered pronouns (e.g., use mail carrier instead of mailman, chairperson instead of chairman)
- For gender identity, include a broad range of designations. Example:
  - What is your current gender identity? (Check all that apply.)
    - Male
    - Female
    - Transgender female/trans woman (or Male-to-Female (MTF) transgender, transsexual, or on the trans female spectrum)
    - Transgender male / trans man (or Female-to-Male (FTM) transgender, transsexual, or on the trans male spectrum)
    - Non-binary, genderqueer, or genderfluid
    - Gender identity not listed
    - Don't know/not sure
    - Prefer not to reply

# Optimizing Collection of Race-Ethnicity Data

Is Person 1 of Hispanic, Latino, or Spanish origin?

- ☐ No, ~~not of~~ Hispanic, Latino, or Spanish origin
- ☐ Yes, Mexican, Mexican Am., Chicano
- ☐ Yes, Puerto Rican
- ☐ Yes, Cuban
- ☐ Yes, another Hispanic, Latino, or Spanish origin

What is Person 1's race? Mark one or more boxes AND print origins.

- ☐ White – *Print, for example, German, Irish, English, Italian, Lebanese, Egyptian, etc.* \_\_\_\_\_
- ☐ Black or African American – *Print, for example, African American, Jamaican, Haitian, Nigerian, Ethiopian, Somali, etc.* \_\_\_\_\_
- ☐ American Indian or Alaska Native – *Print name of enrolled or principal tribe(s), for example Navajo Nation, Blackfeet Tribe, Mayan, Aztec, Native Village of Barrow Inupiat Traditional Government, Nome Eskimo Community, etc.* \_\_\_\_\_
- ☐ Chinese
- ☐ Filipino
- ☐ Asian Indian
- ☐ Vietnamese
- ☐ Korean
- ☐ Japanese
- ☐ Other Asian – *Print, for example, Pakistani, Cambodian, Hmong, etc.* \_\_\_\_\_
- ☐ Native Hawaiian
- ☐ Samoan
- ☐ Chamorro
- ☐ Other Pacific Islander – *Print, for example, Tongan, Fijian, Marshallese, etc.* \_\_\_\_\_
- ☐ Some other race – *Print race or origin.* \_\_\_\_\_



# Challenges to Inclusion

---

- Enhancing the screening pool
  - Converting eligible to enrolled
  - Retaining enrolled participants
-

- **Patient-level Barriers**

- Inadequate information on research opportunities and trial requirements
- Burdensome time commitment
- Transportation difficulties
- Language barriers
- Concerns about confidentiality
- General mistrust toward the healthcare system
- **Not asked**

**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.

# Modifiable Institutional Systemic Bias

BIAS	REMEDATION
IRB discordant timelines for non-English language consents	IRB -- same timelines
Lack of community partnerships and information around trials	Trial education and resources transition materials to community beyond Spanish
Disconnect between research institutions and organizations serving underrepresented patients	MOU between academic medical center and primary care or other clinics
Lack of infrastructure investment in trial screening at NIH, Network and institutional levels	Hire Staff/team from community
Structure of inclusion criteria and referrals (e.g., top doppler experts, parents support groups)	Allocation of cost for translation services, communication with community
	Systematic plan around recruitment of subpopulations

- **Current**

Loose requirements including “recruitment and retention plan”

Speaker and consult for specific issues related to trial recruitment

- **Future Recommendations**

- Resource the resource**

- Enhance infrastructure – community website (tailored, narratives, visuals)

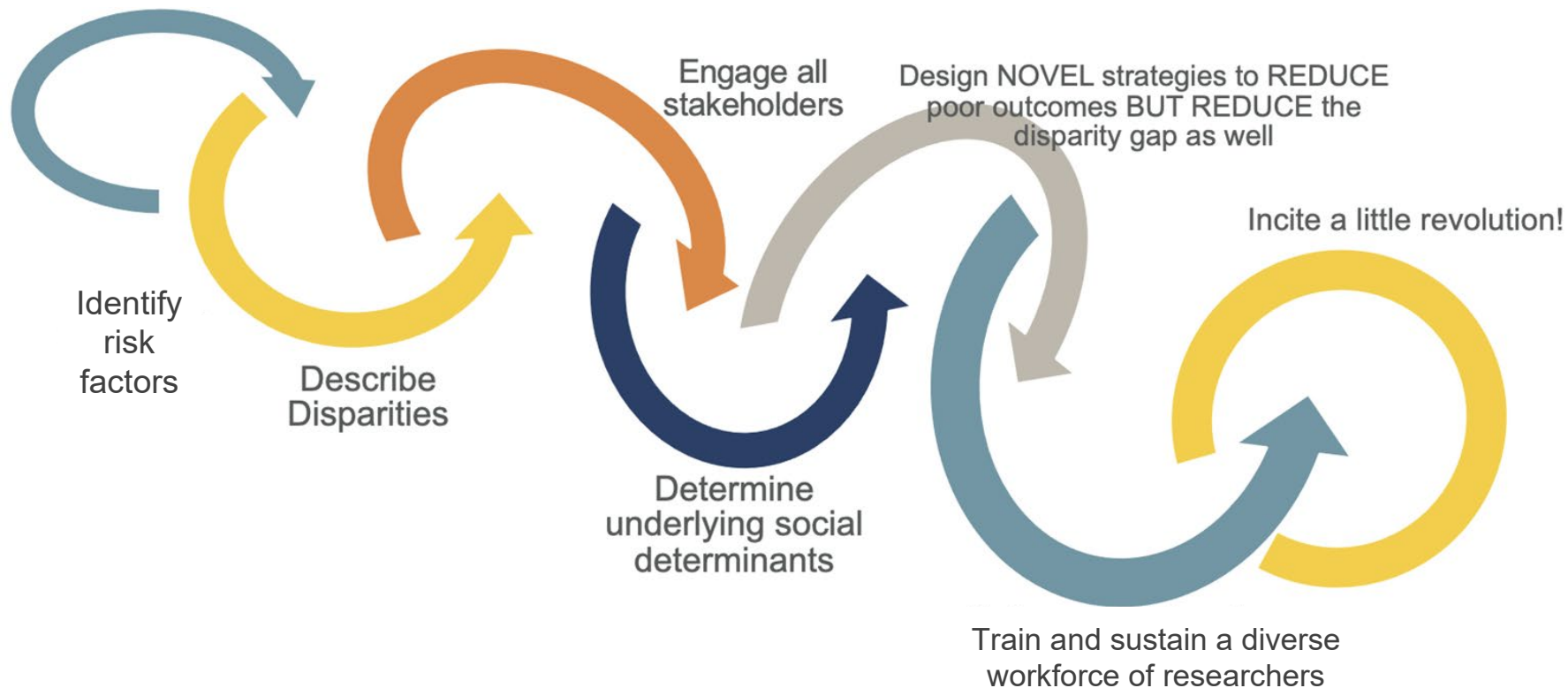
- Faculty/staff development

- True partnership with communities - CBPR training

- Workshop around Inclusion (training to statistics)

- Use CCC's and ADNY 3/4 as models

# Roadmap to Reduce Social Determinants and Bridge the Diversity Gap



# Thank you!

---



[bbodenal@hs.uci.edu](mailto:bbodenal@hs.uci.edu)



949.824.5735