DIVERSITY IN CLINICAL TRIALS: WHAT NEEDS TO HAPPEN TO MAKE IT HAPPEN

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I was chatting with a friend, a young Black man. We were at Lake Merritt in Oakland, California, on a sunny Sunday afternoon. It was after the holidays, but before anyone younger than 80 had received the COVID-19 vaccine. Our conversation shifted to vaccine clinical trials and the lack of diversity in them.

"You think any Black person is going to sign up for a clinical trial?" he said. "Have you heard about Tuskegee?"

The Tuskegee Study, a 40-year study that former President Bill Clinton later called shameful and racist, is one reason some African Americans won't participate in clinical trials. But it's not the only reason. And the reasons clinical trials underrepresent minorities are as diverse as the populations themselves. Lack of access, lack of awareness and information, lack of interest, and distrust due to racism, discrimination, and exclusion are a few of those reasons, on top of recruitment challenges in general.

To the industry's credit, clinical research has made progress in creating more inclusive clinical trials over the past 20 years. But as our country becomes more diverse, to not recruit trial populations that reflect treatment populations compromises patient health and safety.

Diversity issues in clinical trials also build on a long history of health outcome disparities for people of color. COVID-19 exposed these inequities. So much so that the CDC has declared racism a "serious public health threat."

THE DATA ON DIVERSITY

Multiple studies have evaluated the lack of diversity in clinical trials. Recently, a study published in JAMA Network looked at vaccine trials completed between 2011 and 2020. It found minorities and older adults were consistently underrepresented compared with the overall U.S. population. Nearly half (48.5%) of these studies did not include American Indian or Alaska Native participants.

Table 1: Race/Ethnicity of Participants in Pfizer-BioNTech and Moderna COVID-19 Vaccine Clinical Trials

	Total U.S. Population Age 16+	Pfizer-BioNTech*	Moderna
Total	**258 Million**	**40,277**	**27,817**
Race			
White	73.6%	81.9%	79.4%
Black	12.3%	9.8%	9.7%
Asian	5.9%	4.4%	4.7%
American Indian/Alaska Native	0.8%	0.6%	0.8%
Native Hawaiian or Other Pacific Islander	0.2%	0.2%	0.2%
Ethnicity			
Hispanic	17.6%	26.2%	20.0%
Non-Hispanic	82.4%	73.2%	79.1%

NOTES: *Pfizer-BioNTech data are for all participants globally; of which 76.7% are in the United States. Pfizer results provided for Phase 2/3 trial, Moderna results for Phase 3 trial. The Pfizer trial included those ages 16 and older. The Moderna trial included those ages 18 and older.
SOURCES: Racial/ethnic distribution of total population age 16 or older based on KFF analysis of 2019 American Community Survey data; FDA, Briefing Document: Pfizer-BioNTech COVID-19 Vaccine, December 10, 2020; FDA, Briefing Document: Moderna COVID-19 Vaccine, December 17, 2020

While Pfizer and Moderna made diligent efforts, they underrepresented people of color in their COVID-19 vaccine clinical trials according to Kaiser Health News. This is concerning because data show older adults and communities with ongoing social and structural inequities — Black, Latino, Native American, and Pacific Islander, among others — have higher rates of infection.

While the COVID-19 vaccine trials come close to mirroring the population that will take the vaccine, other therapeutic areas do not. A 2019 study, for example, evaluated 230 oncology trials conducted in the United States between 2008 and 2018. Black and Latino populations were consistently underrepresented and Asian populations were overrepresented. Only white individuals were fairly represented.

Underrepresentation in oncology trials inhibits the development of personalized approaches to treatment based on social factors. It's also interesting to note cancer death rates vary by race. A 2019 Kaiser Family Foundation report found cancer deaths are higher among Blacks than whites: 171 vs. 151.4 per 100,000 U.S. standard population.

Location	Overall	White	Black	Hispanic	Asian or Pacific Islander	American Indian or Alaska Native
United States	146.2	151.4	171.0	105.6	92.1	123.6

A 2020 study examined ethnic and racial representation in brain tumor trials. Looking at 342 trials that began after July 1, 2005, and completed by November 11, 2017, the authors found just 28% (97 out of 342) reported on race. Of those that did, whites comprised 85.3% of all participants, while Blacks, Latinos, and Asians comprised 4.4%, 3.1%, and 2.3% of participants, respectively.

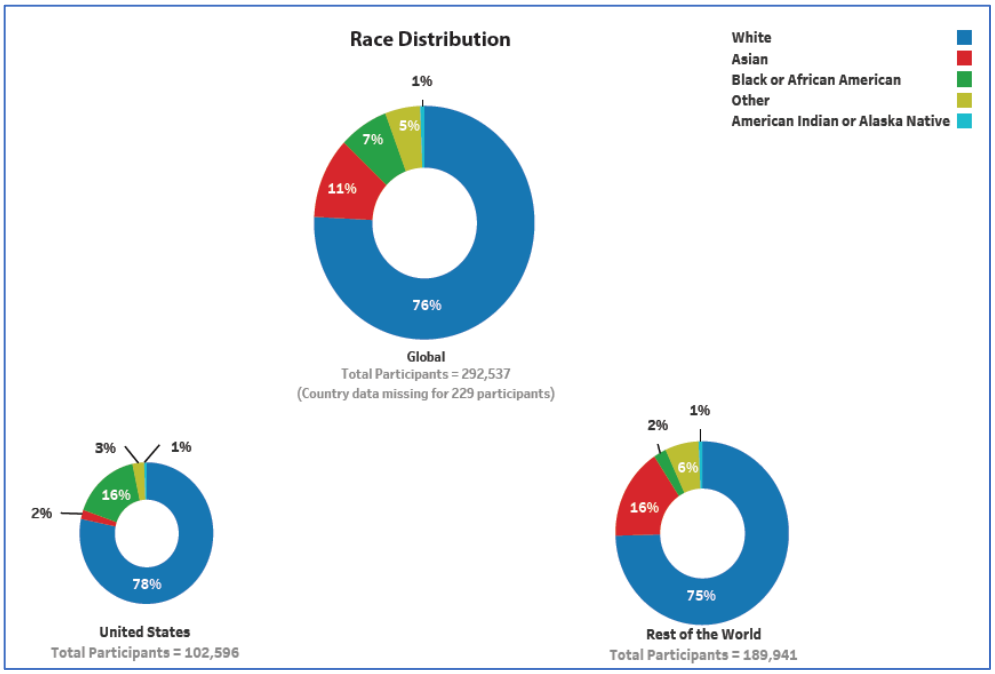
Diversity is needed to understand differences in brain tumor presentation, treatment, and response. Benign brain tumors, the most common type of brain tumor, are more common among Blacks. Malignant tumors are more common among whites.

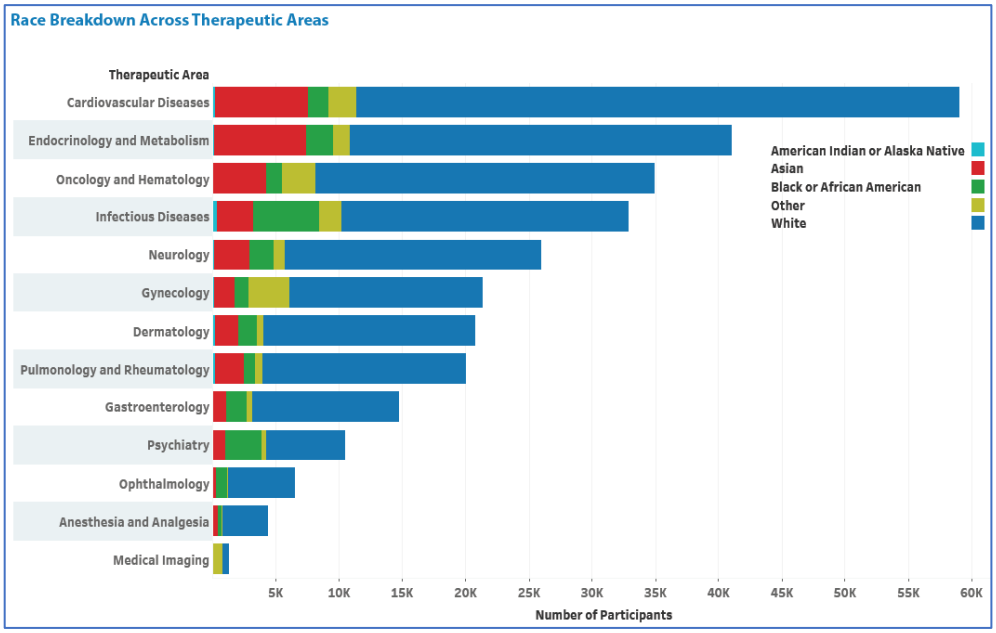
LET'S DO BETTER

In its 2020 guidance document, the FDA advises clinical trial sponsors "work to ensure that eligibility criteria serve the goal of having a representative sample of the population for whom the drug has been developed and examine each exclusion criterion to determine if it is needed to help assure the safety of trial participants or to achieve study objectives." The agency found despite encouragement to broaden eligibility criteria, "racial and ethnic minorities currently compose a small percentage of clinical trial participants relative to the prevalence of disease in these populations."

The FDA's 2015-2019 summary report found that the race distribution of U.S. clinical trial participants as a whole was reasonably diverse. When broken down by therapeutic area, however, some studies fared

better than others. (See charts below. For reference, 2019 U.S. Census data reported U.S. demographics as 76.3% white, 13.4% Black, 18.5% Latino, 5.9% Asian, and 1.3% American Indian and Alaska Native.)





A NOTE ABOUT INTERNATIONAL RECRUITMENT

It's hard to recruit enough participants of any race for a study, much less a group that accurately reflects its underlying disease's affected population. To recruit enough participants — of any race — many sponsors and/or CROs activate sites overseas. That may make it more difficult still to recruit for certain ethnicities.

Ahmed Hamouda, head of operations at RAY, a regional CRO, told CenterWatch that Blacks within and outside the U.S. have different diet, exercise, lifestyle, and acquired immunity, among other characteristics, that impact the generalizability of the data collected. If recruiting from outside the U.S., recruiters must make sure the data match.

International recruitment warrants further discussion, but that's a topic for another day. For this report, we'll keep our focus to U.S. clinical trials.

GENERATING INTEREST, BUILDING TRUST

To encourage a more diverse group of individuals to participate, the life sciences and health care industries will need to work together to a) increase interest in participating and b) build trust in biopharma and clinical research. They go together: if people don't see the value, and if they don't trust the process, they won't want to participate.

The good news: most Americans have a positive opinion of medical doctors (74%) and medical research scientists (68%) according to a March 2020 Pew Research survey. The study didn't break down opinions by race or ethnicity.

The pharma industry didn't fare as well though. A 2017 CISCRP report found Blacks and whites equally trusted pharma "some," while 32% of whites, 28% of Blacks, and 26% of Asians surveyed didn't trust pharma at all.

Even though some distrust exists among all groups, a significant segment of Black and white individuals said they were either "somewhat" or "very" willing to participate in clinical research. A larger segment of the Asian population said they were definitely not willing. It's possible Blacks are willing to participate, but either aren't able to participate or don't know clinical trials exist.

Willingness to participate in clinical trials

Race			
	White	Black/African American	Asian
Not at all/not very willing	16%	14%	38%
Somewhat willing	45%	40%	37%
Very willing	32%	40%	16%
I am not sure	6%	7%	10%

COVID-19 may have helped boost the public's opinion of pharma. A spring update to the 2020 Edelman Trust Barometer reported 73% of respondents globally expressed trust in pharma. That is an improvement from the pre-COVID-19 Gallup polls, where pharma consistently received low public opinion ratings. If that lift in public perception proves to be more than a short-term outlier driven by public relief around pharma's ability to deliver a COVID-19 vaccine (studies run hot and cold), now is the time to build on that shift in industry trust.

In its guidance document on diversity, the FDA addresses the trust issue as it applies to clinical trial diversity. A few trust-building practices mentioned include:

- Providing cultural competency and proficiency training to investigators and research staff so they understand how to engage with people of different backgrounds.

- Holding recruitment events often. Hold them when and where it's convenient and comfortable. Instead of hospitals, think community centers, houses of worship, and at public festivals and similar events.

- Holding events during weekend and evening hours to accommodate working adults. Not everyone has health insurance. Not everyone has a doctor who tells them about clinical trials.

- Including sites in locations with higher concentrations of minorities and indigenous populations, as well as neighborhoods where they receive care. Hire diverse investigators and study coordinators to help address language barriers. Plus, people are more likely to trust health care professionals who look like they do.

Leland Allen, M.D., infectious disease specialist at St. Vincent's Ascension in Birmingham, Alabama, recruited a diverse group of 200 for a COVID-19 study because he had developed trust with his patients over many years and because he worked for an organization with deep roots in the city. Sponsors that can identify and activate sites with established, trusting relationships with minority patients could potentially increase their odds of successful recruitment.

ADJUSTING PROTOCOLS

In addition to making sure the trial population reasonably mirrors that of the disease state and using enrichment strategies, the FDA encourages patient-centric practices. Think about your target study populations. Where do they live, work, and play? What are their values? Do research if you need to. Talk to people. Ask questions. Listen.

When developing your outreach strategy, consider where potential participants seek information for clinical trials and where they want to seek it. Those venues vary by condition.

How Respondents Have Heard About Clinical Trials (by condition)

	Lung Cancer	Melanoma	Type 1 Diabetes	Lupus	Multiple Sclerosis	Kidney Disease	GI Disease	Allergy-Asthma
Ads	36%	42%	43%	53%	52%	60%	66%	61%
Advocacy groups	42%	29%	50%	44%	32%	28%	19%	19%
Clinicaltrials.gov	40%	23%	30%	27%	22%	13%	24%	20%
Word of mouth	37%	37%	40%	33%	34%	32%	36%	35%
Medical center/practice	35%	31%	25%	21%	22%	24%	17%	22%
My doctor's office	59%	51%	37%	32%	41%	27%	19%	25%

Source: SCORR-Antidote, "The Patient Perspective on Clinical Trials," (Dec 2018)

From which of the following would you most like to receive more information about clinical trials? (Check all that apply.)

Source	Percent
My doctor's office	73%
Medical center/practice	52%
People who have participated in a clinical trial	49%
Clinicaltrials.gov	47%
Advocacy/nonprofit organizations	42%
Health and wellness information websites (Healthline, WebMD, etc.)	42%
Drug company	22%
Advertisements (printed, online, radio, TV)	21%
Word of mouth (family, friends)	18%

Source: SCORR-Antidote, "The Patient Perspective on Clinical Trials," (Dec 2018)

Most importantly, make it easier for people of all races, ethnicities, and socioeconomic statuses to participate in clinical trials. Many workers can't take time off for multiple clinic visits. Will you have flexible clinic hours? Can they use telehealth or receive home health visits before or after work? If they don't have a computer, will a phone appointment suffice? Can you implement a bring your own device (BYOD) strategy for patient-reported outcomes (ePRO)?

A Pew Research survey said 29% of adults age 65 and up own a cell phone but not a smartphone. Looking at race, 11%, 15%, and 14% of white, Black, and Latino adults, respectively, do not own a smartphone. To include these patients (if eligible), will you provide a provisioned device? These are general patient centricity questions to ask, but they apply to minority recruitment.

All clinical trial participants deserve reasonable compensation for their time. Communicate the financial considerations and logistics up front. Will you provide or reimburse for transportation, lodging, child care, meals, and other expenses? Will you cover costs for family members and/or caregivers?

COVID-19 showed the life sciences industry that decentralized trials can work, and their use of mobile technology and connected health platforms helps ensure willing, eligible patients can participate regardless of race, ethnicity, age, gender, or socioeconomic status.

The additional benefits of decentralized trials in terms of time- and cost-efficiency, as well as patient enrollment and retention, are well documented. As the industry works out the kinks to adopt this trial design long term, it must do so with the flexibility to broaden access for all patients.

THE WORD ON THE STREET

The author sent out a survey through her social networks to get input from people who had no ties to the life sciences industry. This is a snapshot of the feedback she received:

WHAT ADVICE DO YOU HAVE FOR CLINICAL RESEARCHERS ON HOW TO BRING MORE DIVERSITY INTO CLINICAL TRIALS?

- "Hire more diverse researchers who can relate and be more effective in different communities. Representation counts."
- "Enable easy participation for target communities, like low-income neighborhoods, areas lacking transportation, places speaking little English, people without internet access, easier participation for people challenged in many ways (physically, mentally, etc.)."
- "Solicit participation using TV networks with predominantly minority audiences: Telemundo, Zee TV, etc."
- "Talk to minority physicians who care for minority patients so their doctor can better explain the pros and cons."

Limitations: Extremely small sample size. Respondents recruited from one of the author's personal social media accounts and a public speaking group. Most respondents live in the San Francisco Bay Area.

TOOLS OF THE TRADE

Technology may hold a key to broadening eligibility criteria. A study in Nature used an AI tool called Trial Pathfinder to analyze electronic health records of 61,094 patients with advanced non-small cell lung cancer. The researchers found that many common eligibility criteria, including exclusions based on laboratory values, had minimal effect on trial outcomes. The researchers reported they could more than double, on average, the pool of eligible patients for oncology trials using the tool.

Elligo Health Research®, a healthcare-enabling research organization, offers IntElligo® Research Stack technology to connect the best health care experts with the best research technologies and infrastructure. The tool searches EHRs for health care practices frequented by patients who fit the target study criteria. This type of technology could help sponsors or CROs zero in on minority populations.

"Innovations in healthcare technology have helped researchers more accurately project patient populations and created new ways to reach patients who might participate in trials," says Elligo CEO John Potthoff. "For participants in certain geographic locations or in hard-to-reach socioeconomic groups, wearables and direct shipping of medications allow patients to participate from home, which helps bridge gaps."

CONCLUSION

As researchers develop more gene therapies, rare disease treatments, and precision medicines, an accurately diverse population will be even more important to get the full picture of a treatment's safety and efficacy. "Age, comorbidities, gender, geographic location, race, ethnicity, and lifestyle may all affect how someone responds to treatment," says Potthoff. "The medical community knows this, but sites may not account for these differences."

Building diversity is also the morally and ethically right thing to do. By investing time, money, and energy into creating a more inclusive clinical trial environment, sponsors bring potentially life-changing and even lifesaving new medicines to people who need them — *all* people.

About the Author

Heather R. Johnson is a scientific writer for SCORR. She brings more than 20 years of professional experience as well as industry expertise in clinical trial technology and operations, medical device, and digital health. Therapeutic area knowledge includes neurology, psychiatry, orthopedics, digestive health, oncology, and rare disease. Her writing career includes ample diversity: she has interviewed Beyonce and B.B. King and written about plastic bags and ball bearings. (Plastic bags are way more interesting than ball bearings, and Beyonce was very nice.) She lives in Oakland, California — the fourth-most diverse city in the U.S. with more than 125 languages spoken among its 450,000 residents. (Back to Top)

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