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How to build trust and achieve diversity in clinical trials

By Taylor Davidson

Clinical trial sites and sponsors have long struggled with a lack of diversity in their trials. Black, Hispanic, elderly, and disabled patients are consistently underrepresented in clinical trials throughout the United States,[1] and this underrepresentation can have devastating effects on treatment efficacy.

Race, ethnicity, age, and gender affect how patients respond to new treatments. In fact, roughly 20% of new drugs have differing effects depending on a person's race.[2] Yet, until recently, new treatments were often approved after being tested on populations that were from 68% to 83% White.[1]

This is changing with the U.S. Food and Drug Administration's (FDA's) new diversity and inclusion guidance, which requires many trials to create a Race and Ethnicity Diversity Plan.[3] New treatments can now be rejected because they were not tested on a diverse patient population. Inclusion is now a regulatory requirement as well as an ethical imperative.

Ensuring all patients have equitable access to clinical trials is not simple. It requires clinical trial organizations to think deeply about the historical causes of these inequalities. Clinical trial organizations must build trust and increase access using community sites and technology.

Underrepresented Patients

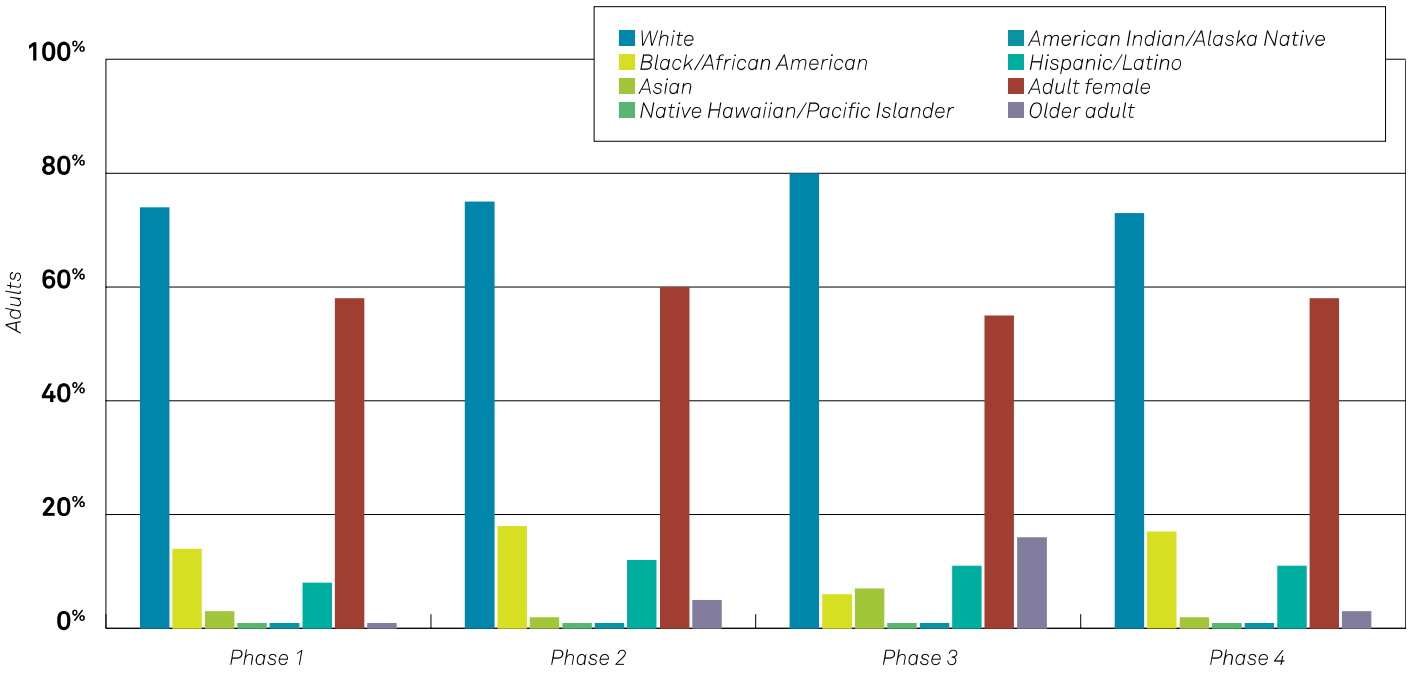
Clinical trials have consistently struggled to recruit participants who are diverse in age, ability, and race. In the United States, between 2011 and 2020, 60% of vaccine trials didn't include any patients over 65 years of age.[4] However, 16% of the U.S. population is 65 or older, and that number continues to climb. These patients are also eligible to receive vaccines that were not tested on their age group.

Clinical trials also often exclude patients with disabilities, even when it would be safe and feasible for participants with certain types of disabilities to join. In one review, 84.1% of clinical trials that excluded patients with disabilities did not explain why they had done so, making it impossible to tell whether the exclusion was justified by safety concerns.[5]

Finally, and of greatest concern to the FDA, clinical trials often fail to have sufficient racial diversity. In the United States, Black people make up 13.4% of the population but only 5% of clinical trial participants.[1] Hispanics make up 18.5% of the population but only 1% of clinical trial participants.

Figure 1

Demographic Representation by Vaccine Clinical Trial Phase



Source: JAMA Netw Open. 2021;4(2):e2037640. doi:10.1001/jamanetworkopen.2020.37640

In this cross-sectional study of 230 U.S.-based clinical trials with 219,555 participants, undertaken by the Journal of the American Medical Association *in 2021, Black or African American, American Indian or Alaska Native, Hispanic or Latino, and older adults were underrepresented and women were overrepresented compared with the U.S. population.*

The Barriers

Multiple reasons account for this lack of diversity. Historical abuses, such as the Tuskegee syphilis study and the theft of Henrietta Lacks' cells, cause justifiable mistrust of medical research for people of color.[6,7] Even today, more than half of patients fear that clinical researchers will discriminate against them because of their race or ethnicity.[8]

A lack of diversity among researchers can also lead to a lack of diversity among participants.[9] A reported 40% of clinical trial participants would like to hear from a researcher who shares their background but do not have that option.[8]

Additionally, underrepresented patients lack access to clinical trials.[10] In the United States, over 70% of the population lives more than two hours away from a major research site.[11] This makes it difficult for elderly people, people with disabilities, people who work strict hours, or people who rely on public transportation to join trials.

Hala Borno, MD, an oncologist at the University of California in San Francisco, studies the gap between real-world demographics and clinical trial enrollment.[12] An expert in building diversity for clinical trials, she advocates for clinical trials to take place at community sites in underserved areas instead of at research sites in major cities.

Dr. Borno also co-authored a study in *Contemporary Clinical Trials Communications* in Fall 2020 that looked at the racial and ethnic makeup of COVID-19 trials and compared it to the disease burden in the United States at that time.[13] Results showed that Black patients were underrepresented in all studies relative to the affected population in each city where the study took place. This raises an important concern—how the COVID-19 pandemic had both negative and positive impacts on clinical trial diversity.

The Pandemic's Impact

From February to May 2020, the number of clinical trials initiated in the United States dropped by 43% due to the pandemic.[14] Outside the United States, the number of clinical trials initiated dropped by 23%.

The pandemic also impacted ongoing studies. Completed trials fell by 5.1% in 2020 compared to 2019.[15] The most extreme difference came in the summer—27.4% percent fewer trials were completed in July 2020 than in July 2019. With fewer clinical trials running, fewer patients had access to new treatments.

The impact of COVID-19 caused clinical research studies to significantly struggle with participant enrollment:

- 20% of patients with cancer said they were less likely to enroll in a clinical trial than they were before the pandemic.[15]
- 60% of research sites said they were having challenges with patient recruitment since the pandemic began.[16]

The challenges the pandemic created for patients were even more difficult for underrepresented patients.[17] For example, patients older than 65 were at high risk for complications from COVID-19, which made enrolling in any trial difficult.

People who were already battling an illness also hesitated to risk exposure to the virus by traveling to research sites. Patients who might have been willing to enroll struggled to do so because of travel restrictions.

Yet, as Dr. Borno rightly points out, COVID-19 vaccine trials needed to be inclusive to determine if the vaccine would work for the global population. The methods Pfizer and Moderna used to improve their lack of diversity contain lessons for how all clinical trials can improve their inclusion and equity.

Diversity at Community Sites

When confronted with how to recruit diverse clinical trial participants in spite of a pandemic, clinical trial organizations turned to past success stories, like the SPRINT blood pressure trial.[18] Spearheaded by Thomas Ramsey, MD, this trial worked with 19 coordinating centers across five health networks.

The SPRINT trial included:

- 102 participating community sites
- 15,000 participants (>9,000 trial minimum)
- 50% of participants from racial and ethnic minorities

Pfizer used similar methods to ensure diversity in its COVID-19 vaccine trials. Pfizer reached out to 153 community clinical trial sites across the United States, Argentina, Brazil, South Africa, Turkey, and Germany.[19] These local sites enrolled more than 46,000 participants, and approximately 42% were Asian, Black, Hispanic, or Indigenous/Native American, with only 58% non-Hispanic White.

Though these numbers do not fully represent the global population, they come much closer than clinical trials typically do (see "Patient Comfort Levels").

Clinical trials include complex regulatory requirements that prove challenging for small community sites. That is where technology comes into play.

How Technology Helps

Small community sites often do not have the technology or personnel to run trials on their own. But they can do so with regulatory and technology help from sponsors, contract research organizations (CROs), and coordinating centers.

When Pfizer wanted to improve their trials' diversity by reaching out to local sites, they turned to remote connectivity software.[20] This software allows them to instantly see documents and data from all their global trial sites.

During and after the pandemic, technology proved it could help with:

- Speeding up communication between sites and sponsors, coordinating centers, or CROs
- Providing reports on site progress
- Collecting data from participants
- Training site staff[21]

For example, coordinating centers sent online study start-up kits with binder and folder setups and document templates to community sites.[22] The investigators at the coordinating center also used video conferencing, webinars, and training videos to share their expertise with staff at small sites.

Remote connections between community sites and sponsors presented advantages for clinical trial teams and for patients. Community sites received funding and experience from getting involved in research, and the sponsor gains access to a wide, diverse participant population. Most importantly, patients who had never joined trials finally had access to the latest treatment options.

Patient Comfort Levels

Because participants were able to join clinical trials at pharmacies or doctors' offices in their own neighborhoods, the studies did not feel unfamiliar and intimidating. Trials also became accessible to patients who could not take time off work, had to care for children, or did not have a car.

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Reaching Out

Improving the diversity of clinical trials makes new treatments likely to be approved and effective for all patients who use them. However, increasing the diversity of clinical research requires building trust and making trials accessible.

As the COVID-19 vaccine trials proved, clinical trial organizations can begin by reaching out to local community sites. When these sites get involved in clinical trials, patients have access to a clinical trial site near their homes and staffed by physicians they trust. Technology powers connections between sponsors and local sites. By combining technology and accessible sites, clinical researchers draw close to bringing medical advances to all patients who need them. GPJ

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