The Lessons COVID-19 Taught Everyone About Clinical Trial Diversity

The COVID-19 pandemic has affected just about everyone. Throughout this struggle, the world has learned many lessons about things like public health, leadership and resilience.

During the latter half of 2020, the world also got a close-up look at how important diversity in clinical trials is. When a disease impacts certain populations disproportionately, in theory those populations need to be well-represented in clinical trials as researchers study and identify possible treatments.

That's much easier said than done, the world found out.

COVID-19 provided irrefutable evidence that our economies, our healthcare systems and our governments privilege certain groups over others. And clinical research just happens to sit at the intersection of all those issues.

COVID-19 Exposed Healthcare's 'Deepest Fault Lines'

Around the world in 2020, billions of people invested their hopes in American pharmaceutical companies and their abilities to develop a vaccine with unprecedented speed. That companies like Moderna and Pfizer were successful is a near-miracle, and that must be acknowledged.

What's more, those companies faced real challenges in recruiting 30,000 people to take part in the phase III trials.

To understand why, you must first understand which demographic groups bore the brunt of the COVID-19 pandemic in America. As Rachel Nania at AARP notes:

- People 65 and older account for 80 percent of COVID-19 deaths.
- COVID-19 infection rates are two to three times higher among people of color, and hospitalization rates are four to five times higher.
- The mortality rate among Black Americans is twice that of white Americans.

Black Americans, Latinx people, indigenous peoples and Pacific Islanders also are less likely to have health insurance, Eric Boodman at STAT writes. Health insurance provides an important safety net for clinical trial participants, and without that safety net many people of color didn't feel able to participate in those drug trials.

At the same time, people of color are more represented in front-line, essential jobs — jobs in which workers might feel less able to take sick leave to participate in a trial (or to self-quarantine, or to stay home to care for a loved one).

"That the communities hardest hit by Covid-19 have also been woefully underrepresented in clinical trials is no coincidence, and in racing to find 30,000 participants who could represent an even broader population, pharma companies have found themselves face to face with health care's deepest fault lines," Boodman writes.

Diversity and Representation in the COVID-19 Vaccine Trials

Historically, people of color have been underrepresented in clinical trials in America. The COVID-19 vaccine trials' recruitment challenges were merely another facet of an old problem.

"African Americans represent about 13% of our population but fewer than 5% of those who participate in clinical trials," says Marjorie A. Speers, a retired executive and global leader in human research protections. "That is of concern because when a new drug or device is tested, we don't know whether it's going to respond the same way, in terms of safety and efficacy, in people who are genetically different."

Moderna executives recognized this during the enrollment stage of its phase III trial, and the company actually slowed enrollment in early September 2020 "to ensure it has sufficient representation of minorities most at risk for the disease," Meg Tirrell and Leanne Miller at CNBC reported at the time. (Moderna shares fell 8 percent on that news, too, Tirrell and Miller reported.)

In the end, both the Moderna and Pfizer/BioNTech trials achieved more representative enrollment figures — again, a small miracle given the speed at which this was all happening. Alan McGreevy at the University of Winnipeg has the final figures:

- The Pfizer/BioNTech study enrolled 43,000 participants, 42 percent of whom identified as “Asian, Black, Hispanic/Latinx or Native American.”
- The Moderna study enrolled 30,000 participants, 37 percent of whom “are from racialized and ethnic minority groups.”

The FDA’s November 2020 Guidance

Meanwhile, in November 2020 the FDA published its final guidance on encouraging better clinical trial diversity. That guidance offers several suggestions, including:

- How sponsors can encourage more diverse patient populations by thinking through the logistical challenges that might prevent a person from participating.
- How technology can give participants more ways to participate remotely.
- How sponsors can reach out earlier to patient advocacy groups, especially for trials that investigate treatments for rare diseases.

In summarizing that guidance, Stephen Hahn, FDA commissioner of food and drugs, notes how disparities in healthcare impact certain people in different ways. “This difference in impact illustrates why we must encourage developers of any medical product such as treatments or vaccines for COVID-19 – as well as medical products more broadly – to endeavor to include diverse populations to understand their risks or benefits across all groups,” he writes.

“To further promote and protect public health, it is important that people who are in clinical trials represent the populations most likely to use the potential medical product.”

Hahn’s remarks point to the larger context in which all of this is embedded: Unequal access to healthcare for some, unequal treatment in the workforce, unequal representation when it comes to public health policies.

Tuhina Neogi, Boston Medical Center’s chief of rheumatology, says clinical trials represent an important area in which researchers and healthcare professionals can strive for health equity.

“In many regards, research that involves our patients will be directly contributing to the understanding of health disparities and how systemic inequities contribute to adverse health outcomes,” Neogi says.

Recruitment Quotas and Community Engagement Aren't Enough

Neogi and Hahn both argue that early community engagement helps enroll representative patient populations. But engagement often faces tall hurdles and old fears, themselves rooted in painful truths.

As the Boston Globe editorial board points out, "[t]he presidents of two historically Black universities in Louisiana wrote a joint letter in September [2020] to their campuses underscoring the 'importance that a significant number of black and brown subjects participate' in Phase 3 vaccine trials 'so that the effectiveness of these vaccines be understood across the many diverse populations that comprise these United States.'"

That letter elicited angry social media reactions from some Black Americans, who perhaps remember how studies like the Tuskegee Syphilis Experiment carried on for 40 years under direction from the USPHS and the CDC.

Clinical research must address some fundamental doubts before trials can regularly enroll representative patient populations. That starts at the top. Sponsors and drug companies need to understand how some Black Americans might never trust a clinical researcher, or how a Latinx food service worker with a rare condition might never feel they have the necessary safety net to take time off of work to participate in a trial.

“It seems obvious that a diverse workplace would lead to a better understanding of the positioning of a diverse consumer base,” the team at Couch Health in the U.K. writes. “But if pharma companies maximise how much they understand and connect with a diverse audience, they’ll be more likely to achieve success.”

Likewise, pressure from the research community can hold trials accountable for the makeups of their patient populations. “[Sponsors, regulatory agencies, research funders, medical journals, and peer reviewers] can deem it unacceptable for proposals or manuscripts to fail to justify the demographic makeup of a study population,” Daniel B. Chastain, et al. write in The New England Journal of Medicine.

It’s only via these larger, holistic changes that clinical trial diversity can become a reality. COVID-19 showed us how important representation in clinical research is. Now, the entire industry must make trial diversity a priority if we want to realize a world in which everyone — whatever their race, sex, culture, age, gender or background — is allowed to pursue the happiest, healthiest lives they can.

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