Representation and diversity in clinical trials
<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>Among people of color asked to join Covid-19 vaccine trials, worries about inequities run deep</td>
</tr>
<tr>
<td>06</td>
<td>Two Black university leaders urged their campuses to join a Covid-19 vaccine trial. The backlash was swift</td>
</tr>
<tr>
<td>12</td>
<td>New research shows older adults are still often excluded from clinical trials</td>
</tr>
<tr>
<td>16</td>
<td>Women and Black patients are poorly represented in clinical trials, analysis finds</td>
</tr>
<tr>
<td>19</td>
<td>Will Covid-19 vaccines be safe for children and pregnant women? The data, so far, are lacking</td>
</tr>
<tr>
<td>24</td>
<td>Clinical trials need to include more Black and other minority participants. Here’s how</td>
</tr>
<tr>
<td>29</td>
<td>Covid-19 vaccine research must involve Black and Latinx participants. Here are 4 ways to make that happen</td>
</tr>
<tr>
<td>33</td>
<td>Many clinical trials for new cancer drugs didn’t include any data on race</td>
</tr>
<tr>
<td>36</td>
<td>SPONSOR CONTENT Understanding and addressing diversity gaps in clinical trials</td>
</tr>
</tbody>
</table>
In medical parlance, “stat” means important and urgent, and that’s what we’re all about — quickly and smartly delivering good stories. We take you inside science labs and hospitals, biotech boardrooms, and political backrooms. We dissect crucial discoveries. We examine controversies and puncture hype. We hold individuals and institutions accountable. We introduce you to the power brokers and personalities who are driving a revolution in human health. These are the stories that matter to us all.

Our team includes talented writers, editors, and producers capable of the kind of explanatory journalism that complicated science issues sometimes demand. And even if you don’t work in science, have never stepped foot in a hospital, or hated high school biology, we’ve got something for you. The world of health, science, and medicine is booming and yielding fascinating stories. We explore how they affect us all. And, with our eBook series, we regularly do deep dives into timely topics to get you the inside scoop you need.
For decades, clinical trials have been considered the gold standard in medicine. For regulators, providers, payers, and patients to trust a new treatment, it must first be proven safe and effective in a clinical trial.

But clinical trials have historically fallen short in a critical way: They aren’t diverse enough. Many trials fail to recruit people of color as participants. Some studies skew heavily male, and others exclude older adults. Most do not allow pregnant and lactating women to enroll.

It’s an issue that has taken on new significance during the Covid-19 pandemic, which has led to the launch of hundreds of clinical trials testing potential vaccines and therapeutics against the novel virus. Without real representation, it’s difficult to determine how well a therapy might work in certain populations — or whether it might pose an additional risk to a particular pool of patients.

Here, STAT has collected a range of coverage on equitable inclusion in clinical trials. The stories underscore not only the need for a more diverse pool of participants in research, but also lay out the steps it will take to move the needle toward more representative trials.
Clinical Trials. To Go.

PRA's Mobile Health Platform is how we’re integrating clinical trials into the patient’s lifestyle. Our platform brings research to patients everywhere they are through their own devices, in their own spaces, and on their own time through decentralized trials. See how it works at PRAHS.COM/MHP

Let's Go Mobile.
While presenting the Covid-19 vaccine study she’s running, Susan Little was asked for a promise she didn’t have the power to make. A respected local politician refused to support the trials unless Little could ensure that the people of color being prioritized as volunteers would also be prioritized once an effective vaccine was approved.

“They wanted some sort of guarantee that the communities we are asking to participate now are not left behind,” said Little, the infectious disease doctor leading the AstraZeneca vaccine trial at University of California, San Diego.

At another virtual meeting — this one put on by the Chicano Federation — a potential participant expressed a related concern. “If I experience side effects, what happens if I don’t have health insurance?” Nancy Maldonado, the organization’s CEO, remembers someone asking.

Lurking underneath both of those interactions was that old, oh-so-American anxiety about being unable to get medical care. It was just one of the everyday inequalities that made would-be volunteers hesitant as researchers scrambled to include more people of color in their studies — a must to ensure that the shots are equally safe and effective for everyone.
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. Being Black, Latinx, Native American, or Pacific Islander, for instance, means you are more likely to go without health insurance than if you’re white, and that makes a difference. If you want people to sign up as test subjects for experimental vaccines, it helps if they feel comfortable going to a hospital — and are able to take sick leave.

Much has been written on the ever-present specter of the Tuskegee study, which began in 1932, and for good reason. Government scientists recruited hundreds of Black men, falsely promised them free treatment, but instead simply observed without intervention as syphilis destroyed participants’ bodies and lives. Yet the sources of mistrust of Covid-19 vaccine trials aren’t just sepia-toned. The memory of Tuskegee is compounded by instances of racism, alienation, and exclusion all too tangible in 2020.

“This is all playing out in the setting of George Floyd and Breonna Taylor,” said Arleen Brown, a professor of medicine at the University of California, Los Angeles, who has been convening community discussions about the trials. “There was a lot of concern that the powers that be are not going to treat them fairly.”

In emphasizing the need for diversity in these studies, vaccine makers have tried to put their money where their mouth is. The Pfizer-BioNTech team proposed expanding the number of participants in their trial from 30,000 to around 44,000, “to further increase trial population diversity.” Moderna, meanwhile, slowed down its recruitment — a big deal for an operation that’s supposed to advance at “Warp Speed” — out of concern that the pool of volunteers so far was too white.
“Some of our sites, bluntly, are situated in a largely white population. We have had sites in those places that were told, ‘You need to stop now and only recruit from minorities,’” said G. Paul Evans, president and CEO of Velocity Clinical Research, which is running vaccine trials in states across the country. When asked what sort of racial identity would fit the company’s definition of a minority, he said, “What the sponsor’s asking for is … virtually anything that’s not white.”

That doesn’t necessarily sit well with communities often alienated by medical institutions. The framing is delicate. What words you use and how you listen can make the difference between someone feeling heard and feeling like a potential “guinea pig.” That’s a vital distinction that Marvin Hanashiro, a community outreach coordinator at UCSD, is always trying to make clear: “It’s not a way of targeting people, it’s a way of including them.”

The rationale behind this effort is valid, experts say. “That is a goal that we should strive for, to make sure that anything we put forward — a therapy or a drug — is studied appropriately in all populations that will use it, and I think we’re getting there,” said José Romero, the secretary of health for the state of Arkansas and chair of the Centers for Disease Control and Prevention’s Advisory Committee on Immunization Practices, specifying that he was not speaking on the agency’s behalf.

The outreach — to church leaders and social service organizations and unions — is, in some ways, working. The Moderna trial jumped from having 7% Black or African American enrollees in late August to having 13% in mid-September — a testament to the altruism that people like Brown, at UCLA, are witnessing as they broach the subject with community groups.

Yet those advances are highly dependent on geography. “Our phones are going off the hook,” said Devora Torrence, CEO of Centex Studies, who is working on both the Moderna and AstraZeneca trials, estimating that a majority of the volunteers at their site in McAllen, Texas, are Latinx.
Elsewhere, recruiting participants of color is harder, as demonstrated earlier this week, when Pfizer’s latest tally showed that 8% of its trial’s U.S. volunteers were Black, and 0.6% were American Indian or Alaska Native — about half of where those numbers would need to be to represent the breakdown of the U.S. population.

“You really can’t separate participating in a clinical trial from how a person feels the system treats them,” said Onyema Ogbuagu, the infectious disease doctor running the Pfizer trial at Yale. “What surprised me is that it cuts across socioeconomic classes. Even my fellow African American physicians express some concerns you would not expect them to express. It’s percolating in the back of their minds.”

For those who are even less at ease in a clinic or hospital, the worries often run even deeper. The federal government’s involvement in vaccine development makes some would-be participants — many of whom are not U.S. citizens — worry that they may not have control over who gets to see their data, and that that might affect their immigration status, explained Maldonado, the CEO of the Chicano Federation.

The focus on underserved communities is closely tied to the fact that many among them are frontline workers — more likely, by the nature of their jobs, to be exposed to the coronavirus. Yet the logistics can be tough if your employer doesn’t allow you the flexibility that would allow you take time to visit a clinic for injections and follow-ups, or if your local trial site is far from where you live and work.

Even if the logistics do work out, some aren’t sure they want to participate after seeing the government’s indifference to their needs throughout the pandemic.
“There was little response when they were asking for personal protective equipment or sick leave, but suddenly when there’s an opportunity to test out a vaccine, they felt they were being pushed to the front of the line,” said Mona AuYoung, of Scripps Health, who has also been organizing community meetings about Covid-19 vaccine trials.

Little, the researcher at UCSD, has been careful to respond to these concerns as well as she can. She tells potential participants that she does not have the power to guarantee their neighborhoods will be prioritized for an approved vaccine, but that she’ll advocate for equitable distribution. She says that participants will be able to get care for vaccine-related side effects even if they don’t have health insurance.

When building a website, she and her team consulted with their community advisory committee. “Some of the pictures that we picked, they said, ‘That’s a picture of a Latino man, but I don’t identify with it, I think that looks staged, I would rather have something like this,’” Little said. To make participation easier, they’re running the study out of a mobile clinic, a mix of vehicles and tents set up in parking lots in some of the San Diego neighborhoods most deeply affected by the pandemic. Now they’re waiting for the AstraZeneca trial to start back up again in the U.S. Even once it does, though, they will have a lot of work ahead, well beyond giving injections and analyzing data.

“We recognize that building trust is not something we’re going to do in a couple of weeks. This is going to take years,” she said. “We’re not trying to reach out to underserved communities to say, ‘We should talk about the AstraZeneca trial.’ We’re reaching out to build trust, period. It would be great if, along the way, some also volunteered, but we have made no progress if we haven’t built enough trust that people are willing to take a licensed vaccine when it is available.”
Two Black university leaders urged their campuses to join a Covid-19 vaccine trial. The backlash was swift

By Nicholas St. Fleur  @SCIFLEUR  |  OCTOBER 12, 2020

The presidents of two historically Black universities in New Orleans thought they were doing a public service by enrolling in a Covid-19 vaccine clinical trial back in August, so much so they urged their campus communities to consider doing the same.

“I said we should inform our communities because I think there’s something about teaching by example,” said Reynold Verret, a biochemist who leads Xavier University of Louisiana. “We’re two Black men who rolled up their sleeves.”

So Verret and Walter Kimbrough of Dillard University were stunned by the fierce backlash that followed their joint letter to faculty, staff, students, and alumni. Hundreds of outraged commenters flooded their schools’ Instagram, Twitter, and Facebook accounts.

“Our children are not lab rats for drug companies,” said one post. “I can’t believe a HBCU would do this to our people,” said another reply. “Tuskegee, Tuskegee. … Me and mine aren’t first in line,” said another response.
The episode illustrates the challenges historically Black colleges and universities face as they seek to leverage their legacies of trust within African American communities to bolster lagging Black enrollment in Covid-19 vaccine clinical trials. Their recruitment efforts will need to overcome the deep-seated suspicions many Black Americans hold toward medical researchers, pharmaceutical companies, and the government that stem from long-standing racial injustices perpetrated by those institutions.

Now, as the four HBCU medical colleges prepare to host Covid-19 vaccine trials on their campuses, there’s hope their efforts will have more success.

“We’ve engendered a level of trust with communities of color that other organizations, quite frankly, just don’t have,” said James Hildreth, an immunologist and president of Meharry College of Medicine in Nashville. “It’s imperative for us as HBCUs to rise to this occasion because people need us.”

Meharry College plans to begin a trial of a vaccine made by Novavax within the next two weeks, with Hildreth as its first participant. The goal is to enroll 300 at the site, but Hildreth thinks they can enroll 600 people, mostly African Americans. The other HBCU medical schools, Howard University College of Medicine in Washington D.C., Morehouse School of Medicine in Atlanta, and Charles R. Drew University of Medicine and Science in Los Angeles, are planning to start their trials in the coming weeks.

“By engaging with the four Black medical schools,” Hildreth said, “they will have individuals who look like them, sitting across the table, having these conversations, and we think that’s going to make a huge difference.”

As the death toll passes 210,000, the Covid-19 pandemic has laid bare inequalities within the U.S. health care system and labor force, with a large portion of Black workers employed in essential jobs that put them at risk of infection.
Black Americans are three times as likely as white Americans to contract the disease, five times as likely to end up in the hospital, and twice as likely to die from it, according to the CDC. Had Black Americans died at the same rate as white Americans, some 20,800 Black people would still be alive.

Yet, clinical trials for vaccines are struggling to recruit from their communities. Moderna, one of the drug companies testing a shot, slowed down its trial after failing to enroll enough people of color among its 30,000 participants — though as of last week it said one-third of volunteers were from “diverse communities.” Pfizer and BioNTech reported that 9% of their U.S. clinical trial enrollees are Black and 13% are Latino, while some 72% are white.

“Watching all throughout the summer, you kept seeing stories that say there aren’t enough African Americans in these trials,” said Kimbrough. “You had people like Tony Fauci saying that’s going to be a problem if we create this vaccine and it doesn’t work for Black folks.”

Though people are all nearly identical genetically, people of color might respond differently than white people to a vaccine, especially for a respiratory disease, due to social differences such as exposure to air pollution that disproportionately affects Black and brown communities, or higher rates of chronic diseases such as diabetes or sickle cell.

“How we live and where we live impacts how medicine affects us,” said Kimbrough. “I think that’s a powerful conversation that we need to be having.”

He enrolled in a Phase 3 trial of the Pfizer and BioNTech vaccine after Verret mentioned in a phone call that he’d done the same, through New Orleans’ Ochsner Health system. The study is double-blinded, so neither the participants nor the researchers know whether they received the vaccination or a placebo until the trial is over. (Because the vaccine doesn’t contain any live virus, the participant has no risk of developing Covid-19 from the injection.)
In their letter, Kimbrough and Verret addressed the pain caused by the Tuskegee syphilis study — in which Black patients were told they would be treated for the disease but weren’t — and how it eroded trust between the Black community and health care providers.

“We understand they’re scared, we understand the history,” Kimbrough said, “but we’re not just telling them this, we’re saying, ‘Look, we’re doing this.’”

Outrage poured in nonetheless, fueled in part by a ProPublica story published a day before the presidents’ letter that found Ochsner had sent Black patients infected with coronavirus home to die despite the threat they could spread the disease to other people.

To Tevon Blair, a 2018 Dillard graduate, part of what made the letter unpalatable was the absence of predominantly white local universities such as Loyola and Tulane.

“The red flag in this vaccine trial … is that it is not a city-wide partnership with other colleges,” Blair tweeted.

Myles Bartholomew, 22, a 2020 Xavier graduate who is pursuing his doctoral degree at Brown University in molecular biology, cellular biology and biochemistry, said that from a researcher’s point of view, he understood the importance of encouraging Black people to take part in clinical trials and said the presidents were acting unselfishly.

“And then from a student’s perspective, there’s a lot of panic and trepidation about anything related to Covid right now,” Bartholomew said. He said he would not enroll in a clinical trial for a Covid-19 vaccine and he understands why other Black people wouldn’t either due to distrust of medical research.
“Those horror stories are something that is part of our history as African Americans, so we’d be completely naive to ignore the precedents that have been set,” he said.

The presidents responded to the social media criticism.

“There was some misinformation that was being exaggerated,” said Verret. “The suggestion that there was money being paid to me or Dr. Kimbrough? No. That there was money paid to Xavier. No. That Xavier was requiring that all students be in the trial. No.” He added that any of the standard clinical trial compensation he received — participants are paid a nominal sum for their time — he would donate to his parish.

The presidents’ letter may have helped make some headway in aiding recruitment, said Julia Garcia-Diaz, the principal investigator of the clinical trial at Ochsner. After it went out, she received an email from a woman in her late 60s who said she read the presidents’ note and wanted to sign up.

“Not only was she elderly and African American, but she was a female also,” said Garcia-Diaz. “She ticked all sorts of boxes because women are also underrepresented in clinical trials.”

Kimbrough said if he were to rewrite the letter, he would have addressed it to the general public rather than just his and Xavier’s campus communities.

“That’s a good lesson in terms of messaging,” he said.

The HBCU medical schools have been working to make sure they get the messaging right as they address people’s skepticism. Their outreach includes interacting with faith-based organizations and participating in virtual town halls, like one hosted in September by Howard University’s radio station and The Black Coalition Against Covid-19.
“The major concern that people are expressing is the question, ‘Am I being experimented upon?’” David Carlisle, the president of Drew and an internist, said during the town hall. “I can assure individuals that this vaccine when you are taking it to fight Covid-19 is not an experiment that is being directed against the African American community.”

He added that anyone considering enrolling should first ask their doctor if they should take this vaccine, why, and is this vaccine safe for them?

At Morehouse, Valerie Montgomery Rice, the president and an OB-GYN, is no stranger to recruiting diverse populations into clinical trials. When she helped run a clinical trial for a birth control pill at the University of Kansas in the 1990s, her site was commended for recruiting the highest percentage of minority women in the country. She said she is confident 60% to 70% of the people enrolled in the vaccine trial on her campus will be people of color, because Morehouse has long cared for the community.

“The benefit that is with an HBCU medical college is that we deal with these issues everyday with our community. We are more culturally sensitive and more culturally aware,” said Montgomery Rice. “We have the trust of the community and we’ve earned that trust.”

Nicholas St. Fleur is a University of Michigan Knight-Wallace reporting fellow.
For years, researchers have called out a glaring gap in many clinical trials: Despite having far higher rates of many diseases, older adults are largely excluded from studies testing new therapies that might help them.

For how extensively experts have studied the issue of age disparities, though, it remains a significant problem — and one that has grown all the more pressing during the Covid-19 pandemic, given that the virus has hit older adults particularly hard. An analysis published this week found that older adults are likely to be excluded from more than half of Phase 3 Covid-19 trials on Clinicaltrials.gov — which could make it more difficult for researchers to evaluate doses, efficacy, and safety across all age groups.

“It is important we have a trial population that reflects the real-world population,” said Ethan Ludmir, a clinician-researcher at the University of Texas MD Anderson Cancer Center who has studied age disparities in clinical trials. “We don’t know if an 18-year-old and a 55-year-old will tolerate [a] treatment differently or respond to it differently.”
That analysis, along with several other recent studies, suggest there’s a need for a course-correction — not just for Covid-19 studies, but for a wide range of research.

Another paper, published this month in *JAMA Internal Medicine*, looked at the inclusion of older adults in cardiovascular clinical trials before and after the National Institutes of Health rolled out what’s known as the Inclusion Across the Lifespan Policy in January 2019. The policy requires anyone applying for NIH funding for studies involving human participants to include a plan for including people of all ages — or explain the scientific or ethical reason why they’re not doing so.

Researchers looked at 97 cardiovascular trials listed on Clinicaltrials.gov and found that before the policy went into effect, one-third of trials had age limits. In the year after the policy went into effect, one-third of trials still had age limits.

Age limits weren’t the only factor that could limit enrollment of older adults. Two-thirds of the trials also used exclusion criteria that weren’t specific to age, but which would disproportionately winnow out older adults, such as having preexisting conditions. Most of the studies also didn’t include endpoints focused specifically on a treatment’s effects on older adults, such as whether older adults were less likely to adhere to the treatment regimen or more likely to experience problems with their mobility.

“Older adults bear a lot of the burden of cardiovascular disease in our country and yet are not always included in the study to see whether the drugs are safe for older adults or effective for older adults or have side effects,” said Colette DeJong, chief medical resident at University of California, San Francisco. DeJong was not involved in the study, but [co-authored an editorial](#) on its findings.
Experts said the NIH plan is the type of policy that will take time to pay off, given how far in advance studies are designed and how early funding — including the NIH grants that would come with policy stipulations — for studies is allocated.

“It’s going to be a few years before we know the effects of the policy... because they only looked at the first year, so time is going to tell us more,” said Kenneth Covinsky, a clinician and researcher who specializes in geriatrics at UCSF. Covinsky co-authored the editorial on the study with DeJong.

In another study, published in October 2019 in JAMA Oncology, Ludmir and his colleagues analyzed the average age of participants in 302 trials for breast, prostate, colorectal, or lung cancer, and compared it with the average age of patients worldwide with those diseases.

“We wanted to assess over the last 20 years or so, whether our cancer clinical trials effectively represent the patients that we see every day in our clinics,” said Ludmir.

On average, study participants were far younger than the real-world population affected by a disease. The biggest age disparities were seen in industry-funded studies and trials testing a targeted therapy. Another troubling finding: Those age gaps seemed to be widening over time.

“Age disparities among cancer trial participants are pervasive, worsening, and associated with industry sponsorship,” Ludmir and his co-authors wrote.

Experts are quick to note that in some cases, the exclusion of older adults from a participant pool is justified. In some cases, there are concerns about comorbidities or patient consent. In other scenarios, there might be risk involved with delivering experimental treatment in combination with other drugs commonly used among older adults.
In the analysis of Covid-19 trials, concerns about compliance — and specifically, the ability to consent to a study — were the most common age-related exclusion. Older participants were also often at risk of exclusion because of other disease diagnoses or technology requirements.

Taken together, experts said the recent findings underscore how often trials exclude older adults, whether directly or indirectly.

And fixing the problems won’t be as simple as changing the inclusion criteria for trials. There are a number of other barriers that affect whether older adults, including enrollment outreach and transportation concerns. Going forward, experts agree clinical trial sponsors will need to think creatively — and carefully — about the best ways to recruit and enroll older adults in a trial.

“It’s imperative that we let patients across all ages have the opportunity to participate in trials and use thoughtful decision-making in who we include and exclude,” Ludmir said.

And he and other experts say that should be a conversation that happens early in planning a study.

“The fundamental question is, if this drug were to be approved, who would it be used [for]?” asked Covinsky.
Amid concerns that clinical trials do not adequately represent patient populations, a new analysis finds a substantial portion of so-called pivotal studies failed to break out data on the race and ethnicity of participants. And at the same time, fewer women participated in trials than might have been expected.

Over a recent 10-year period, only 37% of 775 pivotal trials — which are the late-stage studies used to win regulatory approvals — provided data on ethnicity. And only 73% of the studies broke out participation by race. However, trial sponsors did a better job of disclosing the sex and age of participants — 90% and 83%, respectively.

Meanwhile, more than 252,000 women participated in pivotal trials that were used to support FDA approvals, or 45% of all participants, between 2007 and 2017. But this was roughly 20,000 less than had been anticipated, based on the prevalence of diseases that typically affect women, according to the analysis, which was conducted by the Tufts Center for the Study of Drug Development.
Among the studies that did disclose detailed data, racial and ethnic minorities were sometimes underrepresented. Roughly 24,600 Black people participated in pivotal studies, or 5% of all study participants, which was one-third of what might have been expected given the various ailments affecting this portion of the overall population. By contrast, Asian individuals accounted for more than 8% of all study participants, more than twice what might have been anticipated, according to the Tufts researchers.

The findings are the latest to paint a troubling picture of underrepresentation of large swaths of people in clinical trials. The issue has been regularly probed since a lack of participation – or at least representative data – makes it more difficult for regulators and physicians to understand the extent to which a medicine can help subsets of the population at large.

“Diversity matters a great deal,” said Kenneth Getz, a professor at the Tufts School of Medicine and deputy director at the Tufts Center, which is partially funded by the pharmaceutical industry. For the analysis, the Center reviewed more than 4,700 clinical trials that were conducted for 371 new drugs and biologics that were ultimately approved by the Food and Drug Administration.

“Clinical trials are being conducted with the goal of gathering sufficient evidence to demonstrate safety and efficacy, but they are not including a representative community of patients who may use and benefit by these treatments when they are commercially available. As a result, most clinical trials are not providing definitive guidance on medical treatment dosing and response.”

When examined by therapeutic categories, participation was often very low among racial and ethnic minority groups. By and large, Black individuals were not represented in pivotal trials that studied medicines for pulmonary, rheumatic, or neurological ailments. And Hispanic people were highly underrepresented in pivotal studies of investigational cancer treatments.
There are varying reasons for the disparities. Getz noted that medical literature points to several factors, including distrust of medical researchers among certain minorities, low levels of awareness and familiarity with research practices among some patient populations, limited access to clinical trials, and higher costs to attract study volunteers from minority groups.

This is hardly the first time the problem has been explored. Two years ago, a ProPublica analysis of clinical trial data that had recently been made public by the FDA found that, in trials for 24 of the 31 cancer drugs that approved since 2015, less than 5% of the patients were Black. Yet African-Americans make up 13.4% of the U.S. population.

Also in 2018, FDA staffers published a paper in the Journal of the American College of Cardiology that women accounted for just 34% of more than 224,400 the participants in clinical trials that were used to support approvals for 36 cardiovascular drugs. Representation varied, though, depending upon the specific cardiovascular condition.

The Tufts researchers said this analysis was, to their knowledge, the first to examine whether diversity is adequate based on the prevalence of disease and population census. And it was also the first to measure the trends over time and to quantify the magnitude of shortcomings in industry reporting practices of minorities.

Indeed, year-over-year comparisons can offer differing snapshots.

Last year, the FDA released a report showing the number of women who participated in clinical trials that led to approvals rose to 72% in 2019 from 56% in 2018. But participation among Black individuals fell to 9% last year, a decline from 11% during the two previous years. Participation among Asian individuals declined to 9% in 2019, down from 12% in 2015. And Hispanic individuals accounted for 18% of participants in 2019, up from 14% the year before.
As potential Covid-19 vaccines speed their way through development, manufacturers and U.S. regulators have largely delayed testing in children and women who are pregnant, raising the possibility that experts will lack critical safety and efficacy data in those populations when there’s a pressing need to inoculate them.

Vaccines are always tested first in healthy adults, a population that is most likely to provide a clear picture of whether a vaccine triggers protection. It’s also a population deemed to be at lowest risk should there be side effects from an experimental vaccine.

But the Covid-19 pandemic has triggered a race to vaccinate all Americans as soon as possible, beginning early next year. Even though most experts argue that children and women who are pregnant or breastfeeding won’t be at the front of the line when the first doses become available, others see a need for answers on whether the vaccines are safe and effective in these populations sooner rather than later.
“There’s going to be a huge push to vaccinate children because of schools… so we can open schools more safely,” said Michael Osterholm, director of the University of Minnesota’s Center for Infectious Diseases Research and Policy.

Manufacturers that are testing the vaccines in clinical trials have so far not included pregnant women or women who are breastfeeding. And only one of the vaccine makers that may end up supplying the American market, AstraZeneca, has started to test its vaccine in children.

Meanwhile, given the preponderance of women of reproductive age who work in health care or who are first responders, any plan to put workers from those sectors at the front of the vaccine line has to take into account the certainty that women who are pregnant are among them. At least some may not know it yet at the time they are vaccinated.

“I think that there’s a recognition that if we don’t have a vaccine that we can reasonably offer for safe use in pregnancy, then we’re going to have a real problem in terms of covering the populations that we know we need to cover,” said Carleigh Krubiner, a policy fellow at the Center for Global Development, a think tank in Washington.

Women who are pregnant have historically been left out of all kinds of clinical trials. Krubiner, who is part of a collaboration that has championed the need to include pregnant women in the testing of new vaccines, said this time she knows the issue is on people’s radar, but the studies haven’t yet begun.

“There is certainly a plausible scenario where we have an emergency use authorization [for a vaccine] or a licensed product where there is not any robust data on the product in pregnancy,” she told STAT.
Other populations too are traditionally slower to get invited to take part in clinical trials for vaccines, either because of perceived risks to them or because the data generated when they are vaccinated may not provide the most compelling evidence of efficacy. People who are HIV positive are an example of the former, older and elderly adults, whose immune systems are less effective, an example of the latter.

Both these groups, though, are already being enrolled in clinical trials for Covid-19 vaccines.

A Phase 1/2 clinical trial testing the Oxford University-AstraZeneca vaccine in South Africa includes an arm involving 50 people living with HIV. And a Phase 2b trial of Novavax’s candidate vaccine announced this week in the same nation will enroll 240 people who have HIV and who are medically stable. Under pressure from advocacy groups, Moderna recently amended its plans for its Phase 3 trial to include people with HIV as well.

As they have advanced to Phase 3 trials, various manufacturers testing vaccine in the U.S. have broadened their volunteer pools to include people 65 and older. Moncef Slaoui, co-chair of the administration’s Operation Warp Speed, said at a recent meeting of a National Academy of Sciences committee that the initiative requires all the vaccine projects it is funding to include older adults in their trials.

When asked if the trials are enrolling pregnant women, Slaoui said no.

The Food and Drug Administration indicated to manufacturers that it wanted testing in both these key groups to be conducted when it laid out its guidance for Covid-19 vaccines in June. But the agency stipulated that developmental and reproductive toxicity studies in animals should be conducted before candidate vaccines are tested in pregnant and lactating women.
At least one of the manufacturers, Pfizer, is in the process of conducting these trials, and will present the data to the FDA, a spokesperson for the company told STAT.

Other experts say there are encouraging signs.

Julie Ledgerwood, of the National Institute of Allergy and Infectious Disease’s Vaccine Research Center, said all of the manufacturers are having these types of discussions.

And Kathleen Neuzil, director of the Center for Vaccine Development at the University of Maryland School of Medicine, said she believes “the paradigm has shifted.”

“I think most people feel that pregnant women should be included early. They have the capability of making informed decisions and deciding if they want to be part of a trial,” she said.

Larry Corey, co-leader of the National Institutes of Health’s Covid-19 Prevention Network, said ensuring the vaccines are safe for pregnant women “is of major importance” to the U.S. vaccine development effort.

“Engagement with regulatory agencies and the companies are underway to initiate such evaluations,” Corey, a vaccine expert at the Fred Hutchinson Cancer Research Center, said in an email. “Similarly, discussions are underway … to discuss plans for initiating studies in children.”

Outside of the U.S., two clinical trials of a Covid-19 vaccine candidate in China were open to children as young 6 months, according to the clinical trial registry ClinicalTrials.gov. No data from the trials have been published yet. A trial of a vaccine in India was allowing people aged 12 to 65 to enroll.
Osterholm, who has been warning for weeks that the resumption of in-person schooling and the return of university students to campuses would fuel a surge of cases, thinks these studies cannot be done too soon. Already the University of North Carolina has reversed a decision to hold in-person classes after Covid-19 cases among students and staff quickly took off.

Opening schools and keeping them open will require children to be vaccinated, Osterholm said. “That’s why we’ve got to have safety data.”
Clinical trials need to include more Black and other minority participants. Here’s how

By Jocelyn Ashford | JULY 22, 2020

The Covid-19 pandemic and the disproportionate devastation it has wrought on Black, Hispanic, and poor Americans has (again) raised the call for creating inclusive clinical trials that are representative of patient populations. That’s an important goal, but it’s easier said than done.

I work as a patient advocate for Eidos Therapeutics, a biotech company focused on developing a treatment for transthyretin amyloidosis, an underrecognized cause of heart failure with a disproportionate racial impact due to a disease-causing mutation found in 3% to 4% of Black Americans. Part of my job is to help recruit Black and other underrepresented minority participants for clinical trials. I’ve seen the challenges of recruiting Black people to take part in clinical trials, but I’ve also seen how successful it can be.

It’s necessary work. Unless clinical trial participants represent the people who will be using a new therapy, then we can’t know how it will work for those who need it the most. Cardiovascular disease is a good example: Even though heart conditions disproportionately affect Black individuals, they accounted for only 2.5% of clinical trial participants in a global trials report by the Food and Drug Administration.
What’s more, physicians may be reluctant to prescribe new medicines to Black people if investigational trials did not include them, even for diseases such as sickle cell disease or hereditary transthyretin amyloidosis that affect Black people more than others.

I’ve found that one of the first and most important steps to creating an inclusive clinical trial is to engage the target community in discussions around the recruitment plan. By bringing these communities to the table early, we can hear their input instead of making assumptions about how to best reach them. We can hear their concerns and attempt to address them, while educating the communities about the importance of clinical trials, all that’s involved, and the potential to bring high-quality care to their community.

One way to accomplish this is by engaging with community education programs, such as those sponsored by church groups. Eidos partners with the Association of Black Cardiologists to help us understand where our target audiences spend their time and who they trust. With this information, educational opportunities can be established for people to learn in safe places. Approaching trial outreach through tight-knit community groups gives potential participants and their family members an opportunity to learn about information they would have never been exposed to, all from the people they trust.

One of the successful tactics I’ve used to help recruit older Black participants for clinical trials is to engage the younger generation. The family unit is important in the Black community. One obvious place to start is reaching out to historically Black fraternities and sororities. These organized groups of educated, social-minded individuals are looking to give back to their communities and can act as bridges to their parents, grandparents, and the Black community more broadly.
In the Black community, elders often trust younger family members on matters of health, and the younger generation is protective of their elders, so these types of initiatives recognize the dynamics of Black culture and work within those cultural dynamics.

Beyond reaching out to Black people in the U.S., looking overseas to engage individuals of African descent is another option. That can open the door to countries in Africa, as well as in Brazil and elsewhere in Latin America, where Black populations may welcome the opportunity to participate in trials, which can then be more inclusive thanks to their participation.

Engaging investigators is another important strategy. Even simple tactics, like giving physician-investigators a goal for the number of Black participants they recruit, can help fill a clinical trial with a representative population. That’s what the National Institutes of Health does — it says it wants a representative population, and that’s what it gets. Data that represent the racial breakdown in NIH-funded clinical research since 2015 show that there has been a significant increase in the number of Black participants over the last five years. While these trials are still not fully representative (notably of other minority groups), it is an improvement.

Another piece of the puzzle is physician representation at trial sites. Black patients like to see Black doctors, so they should be among the investigators. At trial sites where this is not an option, it’s helpful to include other Black staff members who can meet with patients in addition to the investigator.

While it’s important to recruit Black participants for clinical trials, it’s also important to understand and overcome the barriers to keeping them enrolled. Once enrolled, Black participants tend to drop out of trials at a higher rate than other groups. Based on my work with Black participants, I feel that one reason for this is that some may not be used to people trying to accommodate them, even around basic items like scheduling.
Clinical trial sponsors are keenly interested in ensuring their participants stay on protocol, and so are very accommodating to individuals’ needs. But that message can get lost. If trial participants don’t know to speak up and say they need accommodations around, for example, child care, transportation, or scheduling issues, they’re more likely to drop out. To run a successful inclusive trial, investigators need to encourage participants to be vocal about what they need and then explain how investigators and clinical trial sponsors can help.

Another reason typical clinical trial recruitment strategies often don’t extend to Black participants is the repeated use of certain trial criteria and sites. When planning trials, companies tend to use similar guidelines and work with the same clinical sites time and time again. Establishing trial sites at clinics and medical centers with significant minority populations is a good place to start.

Even when creating criteria for a study, something as simple as carrying over the commonly used target blood pressure level can exclude large portions of racial groups from participation. On average, Black people tend to have higher blood pressure compared to those of European descent. Not adjusting for that difference can lead to inadvertently excluding Black patients from many studies. We must do a better job of looking outside the typical clinical trial site repertoire or reading over exclusion criteria with fresh sets of eyes.

Unconscious bias within the medical community can also hinder trial recruitment. Physicians may not even think to suggest to their patients of color that a clinical trial is an option if they assume their patients are not interested or have a negative perception of clinical trials. Training works to help physicians and investigators think past their biases, proactively encourage their Black patients who might qualify for clinical trials to participate, help educate them about the process and the clinical studies, and make it clear that patients should never be afraid to ask questions.
As many of us in biotech and pharma push for more equal representation across our industry, we need to ensure that it’s a priority in our clinical trials as well. With the right focus and commitment, clinical trials can and should be inclusive, leading to improved studies and access to experimental medicines for more Black patients.

*Jocelyn Ashford is the director of patient advocacy at Eidos Therapeutics, a BridgeBio company.*
Covid-19 vaccine research must involve Black and Latinx participants. Here are 4 ways to make that happen

By Kathryn Stephenson & Bisola Ojikutu | JUNE 26, 2020

The development of a Covid-19 vaccine is progressing at an incredible pace, breaking down barriers to the invention, manufacture, and testing of potential vaccine candidates. The Department of Health and Human Services says it aims to have “substantial quantities of a safe and effective vaccine available for Americans by January 2021.”

To achieve this goal, each of the five leading Covid-19 vaccine candidates will need to be tested in approximately 30,000 people — a total of 150,000 research participants in the next six months. This will be a massive and unprecedented undertaking.

Equally unprecedented is the opportunity that Covid-19 vaccine development presents to break down barriers to the engagement of Black and Latinx individuals in clinical trials research. Ideally, vaccine trials should include participants from communities that have the highest risk of infection. In the case of Covid-19, those at-risk communities are disproportionately Black and Latinx. To match local demographics of Covid-19, Black or Latinx individuals would need to comprise up to 40% of vaccine trial participants nationwide.
Clinical trials also establish the safety and effectiveness of new interventions, and there is no guarantee that the effects of an intervention will be the same across populations. Contemporary medical studies point to disparities in response rates to pharmacological therapies by race and ethnicity. No one knows for sure if such variances are products of the socioeconomic realities faced by trial participants, a variety of environmental factors, or genetics, but they are real.

Yet past experience shows that Covid-19 vaccine trials will likely have challenges meeting enrollment targets like these. In 2019, for example, the Food and Drug Administration approved 11 new cancer drugs based on clinical trials that enrolled just 4% of Black participants, despite the fact that Black individuals account for 13% of the U.S. population and have the highest death rate for most cancers.

Most clinical trials are designed to enroll racially and ethnically diverse groups of participants and honestly aim to do that. But it’s a hard goal to achieve. The hours that clinics are open are too limited for people of color whose employers prohibit taking off work; study budgets don’t always pay for interpreters and translations that would facilitate participation by non-English speakers; study protocols often exclude individuals with chronic illnesses like diabetes and hypertension, which disproportionately impact people of color.

The pressure to enroll participants and quickly accumulate data can be intense, especially in a pandemic, often eclipsing the goal of equitable representation.

Another barrier to equitable clinical trial participation is the pervasive structural racism that is intricately woven into the fabric of our society. The U.S. has a shameful history of unethical experimentation on Black men and women, from experimental surgeries performed without anesthesia on enslaved Black women to the misappropriation of cervical tissue from Henrietta Lacks and the infamous Tuskegee syphilis study.
This history has led to understandable and pervasive mistrust of clinical research. It is no wonder that Black and Latinx patients often say to us, “I don’t want to be a guinea pig in your experiments.”

Layered on top of this are strong anti-immigrant and sometimes xenophobic views that keep Latinx individuals and others who weren’t born in the U.S. away from contact with health care institutions, including research groups.

A recent survey conducted by the Pew Research Center demonstrates how this sordid history and ongoing structural inequity could affect clinical trial participation: Even if a Covid-19 vaccine were available today and proven effective, only 54% of Black adults would be willing to take it, compared to 74% of white adults. The statistics would likely be equally dismal for participation in Covid-19 vaccine trials.

Everyone in medical research shares the responsibility to promote equitable representation in Covid-19 vaccine trials. Here are some ways we can do this:

**Step 1.** Acknowledge the problem. We must recognize the importance of enrolling Black and Latinx participants in these studies, even in the context of unprecedented rapid enrollment. Studies must report the demographics of trial enrollment while they are ongoing.

**Step 2.** Provide appropriate funding to trial sites to support diversity initiatives. It takes money to translate informed consent forms, reimburse participants for transportation, staff clinics on weekends and nights, and advertise in a broad array of neighborhoods and media outlets. It also takes money and institutional will to build a diverse research workforce that reflects affected communities and is representative of the country as a whole.
Step 3. Address research mistrust by engaging communities now, at the beginning, not when it’s time to share the final results. This means investigators need to meet with local stakeholders in Black and Latinx communities, host webinars and virtual town halls, do interviews on community radio, and put themselves out there on social media.

Step 4. Pay people back for trusting in the medical research community. We need to make any successful Covid-19 vaccine that comes out of this herculean research effort accessible to everyone in this country — regardless of race, ethnicity, or the ability to pay for it. The fair and transparent distribution of an effective Covid-19 vaccine is paramount.

Vaccines can be transformative. They have the potential to provide medical shelter against deadly diseases like Covid-19, allowing communities to safely emerge from this pandemic and rebuild.

The recent protests against racism in the United States are calls to medicine and science too: Black and Latinx communities must be a part of the critical endeavor to develop a vaccine for Covid-19.

Kathryn Stephenson is the director of the clinical trials unit in the Center for Virology and Vaccine Research and an infectious disease physician at Beth Israel Deaconess Medical Center in Boston. Bisola Ojikutu is the director of the Community Engaged Research Program in the Harvard Center for AIDS Research and an infectious disease physician at Brigham and Women’s Hospital and Massachusetts General Hospital.
One-third of the clinical trials that led to new cancer drugs approved between 2008 and 2018 didn’t report on the race of trial participants — and even studies that did report on race often had far fewer black and Hispanic cancer patients than might be expected, given the makeup of the cancer patient population.

That’s according to a new study, published in JAMA Oncology, that looked at 230 clinical trials that supported oncology drugs approved by the Food and Drug Administration. Of those studies, just 145 reported on at least one race of trial participants. Just 18 broke the data down by the four major racial groups — white, Asian, black, and Hispanic — in the U.S. The study’s authors say their findings highlight the clear need for better reporting and representation in cancer trials sponsored by the drug industry.

“It’s important to recognize that this problem is there and this problem is persisting over the years,” said Dr. Kanwal Raghav, an oncologist at MD Anderson Cancer Center and an author of the study.
For trials that did report on race, there were notable disparities in the makeup of participants. White patients accounted for 76% of study participants, while Asian patients accounted for 18%. But black patients made up just 3% of participants in clinical trials for approved cancer drugs during that time, and Hispanic patients accounted for just 6%. The proportion of black and Hispanic patients in cancer trials did improve somewhat during the decade the study examined, though not considerably.

Black and Hispanic patients, in particular, were underrepresented in trials that led to cancer drug approvals. There were far fewer black and Hispanic patients in cancer clinical trials than would be expected, given the share of cancer patients who are black or Hispanic. Raghav and his colleagues say that’s problematic, particularly for trials that play a pivotal role in patient care.

“When you come across clinical trials that establish FDA approval or standard of care [for a new drug], they should definitely be representative of the population it’s used to treat,” Raghav said.

Another striking finding: Different racial groups were more likely to enroll in different types of trials. White patients were more likely to enter larger, randomized, later-stage trials with multiple arms. Minority groups, on the other hand, were more likely to enter smaller, non-randomized trials with just one arm. It’s not clear why, exactly, that’s the case. But taken together, Raghav said the findings raise questions about what the disparities might suggest about how researchers recruit for and run clinical trials.

“You do a trial of cancer patients across the country, you should see that kind of proportional representation. If it’s not being done, why is it not?” he asked.
The National Institutes of Health requires studies it funds to have racial representation that’s proportional to the patient population. But most human trials that contribute to drug approvals are funded by the drug industry. The Food and Drug Administration does recommend that trial researchers collect and report data on the race and ethnicity of participants and has also said study sponsors should enroll patients who reflect the patient populations that would benefit from the drug. But the findings show there’s room for improvement when it comes to representation in industry-sponsored research, Raghav said.

“The issue here is not where the funds are coming from,” Raghav said. “The issue here is doing the right thing. … There should be more efforts made to increase participation of all racial subgroups.”
Clinical research participants are not necessarily representative of the populations that will ultimately receive the new therapy, if or when it’s approved. Generally speaking, clinical trial participants tend to be privileged, have the ability to take time off of work, and have access to medical centers. They tend to be, in reality, middle-aged Caucasian men.¹

Limiting the scope of research in this way is simply not good science. We need a platform that allows us to expand access to all patients, providing a more inclusionary process for women and minorities.² We need to test drugs on a diverse, representative population to understand how the biology works in everyone.

The health care industry can better connect with patients as well as ensure broader access to clinical research, better inclusion and diversity, and increased availability of investigational therapies to all by decentralizing the existing research paradigm.

LIMITATIONS TO THE CURRENT MODEL

Traditional clinical research is site-dependent and creates a high burden on patients. It requires them to travel to physical sites, resulting in time off of work, time to travel, and other inconveniences.¹
The current research paradigm’s limitations and the gaps in accessibility make it challenging for clinical research to reach a representative group of patients.¹ This means that potential patients do not receive the care option of clinical research, nor can they participate in science that could save lives.

**BARRIERS FOR UNDERREPRESENTED PATIENT POPULATIONS**

Participating in a clinical trial is often particularly burdensome for patients with rare diseases. Because the expertise is so specialized, they may need to travel hours — or across multiple states or even countries — to a site where the research can be performed. This creates a burden on the patient and their caregivers and families, who need to adjust their schedules and routines in order to seek treatment. The added cost and time create more challenges and stressors to an already challenging and stressful situation.³

Additionally, language barriers inhibit access to information when looking at underserved populations such as Asian Americans, Latinx, and Pacific Islanders.⁴ Other barriers to seeking clinical care for these groups and for African Americans include mistrust, competing demands, lack of access to information, and health condition stigma.⁵

**BREAKING BARRIERS WITH PATIENT-CENTRIC APPROACHES & ADVANCED TECHNOLOGY**

We need to increase the number of sites that target these groups in order to increase the diversity of patient populations in clinical trials.⁶ We can find ways to bring more diverse patients into a trial with the use of technologies such as mobile health platforms. By using a bring-your-own-device approach, patients can get the care they need through familiar devices, right at their fingertips. Regardless of where a patient is physically located, their socioeconomic status, gender, or ethnicity, they can participate in a clinical trial from anywhere. This lowers the barriers of entry and ensures everyone has access to the best possible care.⁷
PRA’s Mobile Health Platform is making care more accessible to all patients – watch our video and learn more at PRAHS.COM/MHP

ENGAGING & PROTECTING PATIENTS WITH TECHNOLOGY

More and more patients have been asking to participate in health care remotely. Covid-19 exacerbated that need, due to site closures and challenges for higher risk populations to receive in-person care. We have seen a sharp increase in modalities such as telehealth visits across disease states. This further highlights the need for research and care options using a decentralized or virtual model. Mobile health platforms specifically answer this need by enabling greater access to patients where they already are.

SUMMARY

We’re already seeing technology use change how patients get their health care delivered. Clinical research needs to mirror that use. For example, technology allows for the decentralization of clinical trials, thus bringing research directly to patients on their own mobile devices. This allows us to reach a more diverse and representative patient population wherever they are. Not only does this help provide access to groups who’ve otherwise struggled with access, decentralized trials will also create better science, and therefore provide clinical trials as a care option for underserved patient populations.

Read more about how decentralized trials and a patient-centric approach can help bridge the diversity gap.

1 Schliebner, S. The Burden of Clinical Trial Participation. Rare Disease Patient Survey, 2018. PRA Health Sciences. Data unpublished


3 “Standard of Care.” Legal Information Institute, Legal Information Institute, www.law.cornell.edu/wex/standard_of_care

6 Ashford, J. Clinical trials need to include more Black and other minority participants. Here’s how. 2020
