



# Changing with the Tides:

## Ensuring Recruitment and Retention Success During COVID-19 and Beyond

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# Guide Overview



COVID-19 has thrown a wrench into research conduct, forcing hospitals and universities to transfer their research plans, data collection procedures, survey dissemination processes, and participant engagement methods quickly and nimbly to online venues. In addition, the state of research operations has changed dramatically due to the pandemic. This guide provides key considerations for ensuring diversity in clinical research, how to engage participants better using technology, as well as operational tips for doing research efficiently and more equitably during this time.

*The content in this toolkit is based off presentations and content from the [USC Regulatory Science symposium event](#) from October 2020, and re-opening guidelines from Emory Healthcare and the Georgia Clinical & Translational Science Alliance (Georgia CTSA).*

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# What is Diversity in Clinical Research?

We can categorize dimensions of diversity into intrinsic versus extrinsic factors. Intrinsic factors include genetics, physiological and pathological conditions like gender, age, race, genetic diseases, height, and weight. Extrinsic factors include environmental effects like pollution, climate, socioeconomic status, culture, educational status, language, drug compliance, and more. Increasing this kind of diversity can help us understand differences in disease susceptibility and manifestation, adverse effects, and treatment response, dose, and schedule. For new drugs and vaccines, this is even more critical.

When we are testing a new drug or product, the study population should mirror the characteristics of the population affected by a particular illness or condition and reflect the characteristics of the population intended to use the product. Specifically, we need the inclusion of diverse populations to understand underlying factors like biology, genetics, and metabolism; heterogeneity of treatment effect and safety; interaction with concomitant drugs or biologics, compliance, and comorbidities.

For example, ACE inhibitors are associated with a higher rate of angioedema in Black populations versus non-Black populations. In fact, the risk of angioedema is five times higher in Black populations. A drug called carbamazepine (used for treating epilepsy and bipolar disorder) can cause a serious and sometimes fatal dermatologic reaction in Asian populations. These kinds of risks need to be disclosed in labeling, and we can only know about these risks through diverse participant enrollment.



# Current State of Diversity in Clinical Research

Diversity in clinical research has been an ongoing issue for the last few decades and is only starting to improve with new patient-centric approaches to clinical trial design and greater emphasis on engagement throughout the study lifecycle. For trials to be truly representative of the national population, researchers need to focus on recruitment based on race, ethnicity, sex, gender, age, and geographic ancestry, to name a few factors.

**46,391** study volunteers contributed to clinical trials that resulted in the approval of 48 novel drugs in **2019** alone.

Demographic subpopulations represented:

**9%** of study volunteers were Black/African American

**9%** Asian & **18%** Latino.



Currently, we are seeing a higher participation rate in clinical trials among Caucasians. In a clinical trial snapshot released by the FDA summarizing clinical trial participation from 2015 to 2019, they found that 78% of research study participants in the United States were white. Regarding the gender breakdown, the report states that 51% of participants were female. Although this statistic suggests parity among genders, a closer look into the breakdown of gender in research study participation may suggest otherwise. A 2018 study showed that although female participation accounted for almost half of clinical trials, participation among stages of clinical trials seemed to vary. The study indicated that Phase 1 trials were composed of 22% women, while Phase 2 and Phase 3 trials involved 48% and 49% women, respectively. Although women are more represented in late-stage clinical trials, it is important to have gender equity throughout all stages of clinical research.

Source: [FDA Clinical Trial Snapshot](#) ; [Gender differences in clinical registration trials: is there a real problem?](#)

Historically **underrepresented populations** are getting sick and dying at higher rates than White counterparts during this pandemic.

In addition, individuals in the following groups had **2.3 times** the rate of infection and death: Black, Latino, Pacific Islander, elderly, homeless, incarcerated, institutionalized populations with comorbidities (e.g., hypertension, diabetes, obesity).

Historically, females were excluded from clinical trials due to concerns about hormonal interference and child-bearing potential. In response to the lack of participation of women, the U.S. Food and Drug Administration (FDA) Office of Women's Health (OWH) was established by Congressional mandate in 1994. One of their goals was to promote the inclusion of women in clinical trials and the implementation of guidelines concerning the representation of women in clinical trials and the completion of sex/gender analysis. Now women participate in clinical trials in representative numbers, accounting for over half of participants. Although researchers need to make more progress in this area, these changes are promising.

# Regulatory Considerations for Diversity

The FDA makes sure medical treatments are safe and effective for people to use. However, the FDA does not develop new treatments or conduct clinical trials. Instead, the FDA provides guidance to drug developers in academia (via the National Institutes of Health) and to industry sponsors who conduct the clinical trials. It does state trials should recruit patients that represent the population that has the burden of disease in the real world. Failing to recruit a representative patient population may result in firms having to conduct additional research that could delay the marketing application, approval and launch of a product. The FDA also recommends broadening eligibility criteria to enhance diversity in clinical trials and to better reflect the patients who will be using a drug once it is approved.

In 2020, the FDA released [a document](#) to guide industry sponsors and personnel on how to enhance the diversity of clinical trial populations through trial design, eligibility criteria and enrollment practices, including the following methods:

- Seeking further clarity about barriers to subgroup participation rates
- Implementing efforts to enhance appropriate use of enrollment criteria in clinical trial protocols
- Collaborating with NIH, industry, and other interested stakeholders to broaden diverse participation in clinical research
- Using FDA's communication channels to encourage clinical trial participation by demographic subgroups.





# Building in Diversity

So, how do you set yourself and your study team up for success when it comes to being representative? Build diversity into the design of the study from the very beginning, starting at the conceptualization phase. This is easier for investigator-initiated studies in which the Principal Investigator is responsible for the study idea and associated procedures. The best way to ensure diversity is to assemble a multidisciplinary team of biostatisticians, research methodology experts, patient engagement experts and research operations personnel. On the other hand, the process varies for sponsored trials in which the company approaches the investigator at a time when the study design is completed, and procedures have already been decided. At this phase, there is not as much that the PI and study team can do to influence the study procedures—but they can do their best to include diverse populations in their research.



Dimensions of diversity go beyond basic demographics like gender, age, race, and the like. Although some factors are genetic, there are some that have implications for the lived experience of the participants. As such, there are other dimensions of diversity to be mindful of like sexual orientation, geography (i.e. if someone lives in a rural, suburban, or metropolitan area), socioeconomic status and more. By enrolling participants who vary in their social, cultural, and economic status, we can begin to include new perspectives into our research.



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## Practical Considerations for Increasing Diversity

One way to increase diversity in clinical research directly is through the workforce. That means hiring research personnel who are like your target population. In terms of the clinical workforce, that means admitting more doctors, nurses, physicians' assistants and other clinical staff into universities and appropriate training programs. Only 36% of doctors are women of any race, according to the Association of American Medical Colleges—and only 5% of all active physicians are Black even though the U.S. population is 13% Black.

In addition to a workforce that is reflective of the population, training and continuing education are also important for all research professionals. Offering training on cultural humility and diversity within research are crucial to making sure we do our best to include all types of people.

Furthermore, healthcare professionals need to have conversations about clinical research participation early and often. Studies show that underrepresented populations are not less willing to participate in research, they are just not approached about taking part in research as often as their White counterparts. They also need the buy-in and support of their trusted healthcare provider to discuss the risks, benefits and experience associated with the study, as well as to answer any questions.

# How COVID-19 Changed Research

In addition to changing our lives, COVID-19 changed how researchers are doing research now and how they'll be doing research in the future. There is now greater emphasis on the participant experience as well as remote data collection and check-ins, use of telehealth, enhanced cleaning and safety protocols, health screening, social distancing, masking, limitations for caregivers and visitors, and more.



Depending on the requirements and processes of your home institution, you may need to screen all participants within 24 hours of their study visit. If the participant reports any symptoms or has disclosed that they may have been exposed to someone who is COVID positive, you should reschedule their appointment. You will also have to make sure you have disposable masks and gloves, face shields, touchless thermometer, extra hand soap, cleaning supplies and clean equipment like iPads, laptops, and pens for facilitating participant data collection. Visitors like caregivers, parents, children and others will usually not be permitted to accompany the participant on their visit. You may also consider designating an area for these individuals to wait for the participant to complete the study visit. Janitorial staff in most institutions have their own robust cleaning protocols, but research teams may want to have additional supplies on hand to disinfect high-touch areas like doorknobs, computer mice, touchscreen devices, and more.

# Participation Challenges

When making the decision to participate, volunteers cite a variety of barriers that make it hard for them to start participating or stay involved for the duration of the study. Research shows that 75% of participants stay involved throughout the whole study, while 14% stopped early and 11% were unsure or didn't remember (of over 3,600 participants surveyed).

So, why do people stop out of studies? The reasons may surprise you, whereas some reasons are expected. Most people lose their eligibility to participate because they become disqualified due to changes in lab values or other complications. In a sample of 506 people, 20% of people became ineligible and thus had to cease participation. For 13% of those surveyed, they cited the location of the study site and the side effects of the study drug as equal barriers that made them reluctant to keep being part of the research. For 11% of those surveyed, they mentioned poor communication and the time commitment to participate as reasons they dropped out. All but one of these barriers are surmountable. Easing the burden of transportation costs, providing compensation for transportation, moving the study site to an outdoor venue or into people's neighborhoods can also help. Study teams can overcome poor communication by sending out regular updates about study progress, frequent reminders about upcoming study visits in the participants' preferred communication method and trying to make study visits as short as possible by conducting some aspects remotely.

*Regulatory Science Symposium Diversity in Clinical Trials in the Time of COVID-19 [PDF]. (2020, October). SC CTSI.*

<https://regulatory.usc.edu/files/2020/10/eBinder-Fall-2020-Diversity-in-Clinical-Trials-in-the-Time-of-Covid-19.pdf>

# Operational Considerations

Study personnel must be flexible above all to ensure optimal participant recruitment and retention. When recruiting and retaining participants, consider offering different or additional forms of compensation whenever appropriate and/or IRB-approved. The best way to understand what your participants need is by having an open listening session.

Scheduling participants may be more difficult now with more people working from home, absorbing additional or new childcare and caregiving responsibilities, and with essential workers taking on longer and more unpredictable hours.

Ride sharing and public transportation were popular method of transportation to and from study sites prior to COVID-19. Now people may have hesitation with these modes of transportation, so research personnel must be flexible when it comes to accommodating their level of comfort. If possible, consider mobile, outdoor recruitment and/or study visits or home visits. In addition, it's important to leave extra time for study visits to account for temperature checking, hand washing, rearranging furniture, and wiping down commonly used objects and surfaces.







## Key Takeaways

Making study participation exciting, inclusive, and as easy as possible will lead to greater success in recruitment and retention, especially during and following COVID-19. Study teams will need to be more agile, flexible and creative than ever to ensure they stay competitive and responsive to participants' needs. In addition, they will need to make a commitment to enrolling and engaging a diverse group of participants so the participants in clinical research reflect the county's population as well as those affected by the condition under examination.

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