by Denise Myshko

Trial Sites and Patient Diversity

Sponsors, CROs, and sites must work in concert to enroll diverse patient populations. Experts discuss how to address the barriers sites might face.

Having a diverse patient population in clinical trials is important because medicines affect people differently based on age, sex, and race. Biologic, genetic, and even cultural differences between patients can impact how a treatment will actually work in practice.

Industry experts say the racial and ethnic make-up of a trial population should match that of the disease to, hopefully, provide information about how different populations respond to a new drug.

An evaluation by the Food and Drug Administration of the new drugs approved in 2015 and 2016 shows that some groups, especially ethnic and racial groups, aren't always well represented in clinical trials.

In 2016, CDER approved 22 novel drugs. Overall, 31,468 patients participated in these trials. Of these, 48% were women, 7% were African-American, 11% were Asian, and 76% were white. In 2015, CDER approved 45 novel drugs. Overall, 105,826 patients participated in these trials. Of these, 40% were women, 5% were African-American, 12% were Asian, and 79% were white.

And a ProPublica analysis found that in trials for 24 of the 31 cancer drugs approved since 2015, fewer than 5% of the patients were black. African-Americans make up 13.4% of the U.S. population.

"We still have a bias toward a more educated patient population that tends to be middle class or higher who has access to the Internet or is engaged with advocacy groups," says Lisa Dilworth,VP, rare and orphan diseases, Synteract. "In rare diseases specifically, there is inherent bias where we tend to enroll patients who have the privilege of access to information and access to expert centers and access to reimbursement."

Recruiting diverse patient populations can be challenging, especially at the site level. Although sites believe they understand their demographics and their ability to enroll diverse participants, in actuality, they don't, says Diana Foster, Ph.D., VP of strategy and development, Society for Clinical Research Sites and CEO of Total Clinical Trial Management.

"They may lack knowledge, understanding, or consistent training and practices that help them to be able to focus better on enrollment regardless of where patients might be geographically," she says.

Lindsay McNair, M.D., chief medical officer, WIRB Copernicus Group, points out that having a diverse clinical trial involves including other under-represented groups aside from ethnicity.

"For example, most of the drugs used in children are based on data extrapolated from adults," she says. "After decades of pregnant women being specifically excluded from clinical trials the FDA, in recently published guidance, bioethicists and physicians are now encouraging the inclusion of pregnant women in research to have better information about the treatment of medical issues during pregnancy."

Diverse populations should also include the elderly, says Ella Grach, M.D., president and CEO, Wake Research, an organization of investigational sites. "Right now, elderly patients are under-represented in clinical research," she says. "This under-representation is problematic for a number of reasons. Potential variations in pathology of disease might go undetected, as well as differences in responses to new medications."

Barriers to Recruiting Diverse Populations

The barriers to enrolling a diverse participant population are complex. Many studies have looked at these barriers and found that the challenges are systemic (trial availabil-

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LISA DILWORTH
Synteract

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JOE KIM
Lilly

ity), individual (trial access, suspicions about minority groups being taken advantage of in clinical research, etc.), and interpersonal (trust and the provider-patient relationship).

From a pharma company perspective, sponsors expect a level of variation in the recruitment of patient populations at the site level, says Joe Kim, senior advisor, patient experience and design innovation, Lilly. "Not all sites enroll the same numbers of patients. There is mix of patient populations based on demographics. In south Florida you might have a stronger Latino population who comes through a clinic, whereas in Michigan, there would be less diversity."

Location, however, is a key component in making a clinic accessible to patients, he says. "If a clinic is in an ivory tower, only certain types of patients even know how to navigate the logistics or are inclined to enter."

Traditionally, many sites are located in the big academic areas of a city; they're not located in places that will draw a strong minority population, says Nancy Mulligan, executive director, patient and physician services, UBC.

"Patient participation in trials often comes down to questions around convenience: how far away is the site, will the site pay for gas, will there be parking available, does the site have daycare, how many site visits are required?" she says. "There are very few studies where recruitment is easy. Sites may not have the time to put into a community, family-based relationship-building strategy that is required to recruit diverse patient populations."

Ms. Mulligan agrees sponsors and CROs can and should provide sites with additional support for recruiting and keeping patients on therapy. "We have a travel program available to any patient who needs it," she says. "We also have nurses who go to the home or alternate setting such as work place or school. Many sponsors don't use nurses because they think it's too cost prohibitive; but in reality, this helps to take some of the burden off the site, ensure patient contentment and retention, and reduce overall cost."

She says it's also important to plan ahead for recruiting diverse patients. "For many studies I've worked on, recruiting diverse patients was an afterthought," she says. "This strategy should be outlined before the protocol to address the nuances that may arise."

Dr. Grach says it's important when working with older populations to address transportation issues. "We've done a number of clinical studies specifically for the geriatric population," she explains. "One of the ways we accommodated these patients was using local health transportation services that a lot of local hospitals use. We are also in the middle of negotiations with Uber Health."

Industry leaders stress recruiting diverse patient populations should be part of a grassroots effort that involves the community and that aims to build trust in that community.

"Recruitment for special populations must include the elements of trust, talent, transparency, tailoring, and tenacity," says Liz Moench, CEO, managing partner, Patient DTC. "Transparency is central to establishing trust. "

These first two elements are even more important in today's climate of divisive politics, Ms. Moench says. "The recruitment of minority populations in America is against a backdrop of racial and ethnic politics, where mistrust runs high, and whereby the majority of physician investigators are not minority doctors, and also where clinical trial sponsors price prescription drugs out of reach of the minority populations being sought."

Addressing these issues requires talent and tailoring. Study sites need to involve talent from the very minority community needed for clinical trial participation, and minority talent must be involved in tailoring the outreach and communications."

Ms. Moench believes that these barriers can be overcome by pharma companies and sites working together with customized strategies developed from the ground up. "There has to be a grassroots outreach to diverse populations, with the involvement of local minority influencers who are going to stand up and be recognized as spokespeople for a particular cause."

Mr. Kim agrees. "This is not something companies can PR their way out of; diversity recruitment takes real practical change in terms of not just promotional materials that are culturally competent but people on staff at the site who are also diverse," he says. "It takes

Ensuring a diverse population of study participants has to be an active rather than a passive process.

DR. LINDSAY MCNAIR
WIRB Copernicus Group

A more data-driven approach is needed that matches the demand for clinical trial patients from sponsors with the supply available through sites.

BEENU KAPOOR
Cognizant

When sites engage more collaboratively with sponsors and CROs, it creates opportunity for clinical research education on a much larger scale.

ALISSA HANNA
PMG Research

action to dive into the community itself and to be part of it."

For large studies, Lilly requires using at least 25 sites and a minimum of two sites that are "diverse disease sites," which the company defines as having at least 25% of its population as non-Caucasian. Company leaders say after the initiation of this strategy they saw an improvement in the enrollment of African-Americans and Hispanics to clinical trials across oncology, diabetes, and neuroscience.

Helping Sites Recruit Diverse Populations

Representatives from research sites we spoke to for this article say they have a wish list of what they are looking to receive from sponsors and CROs. The first is transparency of goals for recruiting diverse patient populations.

Alissa Hanna, manager of patient engagement, PMG Research, part of ICON Site & Patient Recruitment, says it is beneficial for sponsors to be up front about their preferences for diversity, if any, as early as possible. This allows sites to develop recruitment materials and strategies to address these needs. "Transparency about performance expectations, especially regarding cohorts, as early in the start-up process as possible is crucial to enrollment success," she says.

Lori Wright, CEO, Evolution Research Group, a clinical site organization, says one area of concern is that prior to protocol finalization and site selection, few discussions and decisions about patient recruitment involve the sites.

"Discussions tend to occur between CROs, patient recruitment companies and sponsors," she says. "Many times, by the time a protocol or study makes it to us, there is already a plan in place based on involvement and discussions with a patient recruitment company."

Ms. Wright believes that sites can add value by participating in early discussions as they are the ones interacting with the patients and working within the community.

"I understand that patient recruitment companies may use advanced technology to determine where diverse patient populations may exist," she says. "That is helpful, but without taking into consideration the inclusion/exclusion criteria as well as operational factors, initial outreach efforts may be misdirected, losing valuable time. Many of our key sponsors and CRO partners understand that site feedback is critical and engage with us as early as possible. "

With respect to patient diversification in clinical trials, even the best-laid recruitment plans won't work if there is a lack of communication around expectations.

"We have the indication and the inclusion/exclusion criteria, but if a sponsor is looking for a certain diversity ethnically, it should be communicated to us early in the process and not after subjects have been randomized," Ms. Wright says.

Sites are often the best option to reach out to patients locally, but they often don't have the financial means to do so. Sites would like financial support for things such as patient education and patient support materials.

Ms. Hanna suggests sponsors and CROs can help sites by creating larger-scale education and awareness programs and by making sure study recruitment materials feature diverse representation.

"We collaborate within our practices and physicians, as well as within local communities, but by joining forces we can facilitate extensive programs that will aid in successful patient engagement at the site level and beyond," she says. "Support from sponsors and CROs is helpful for extending our reach."

Dr. Grach says sponsors and CROs can help sites by financially supporting efforts that will enable more participation by diverse populations. "The transportation service for the elderly and Uber Health comes out of our pocket," she says. "This is a minor thing, but it speaks to the bigger picture about how to create a truly patient-centric approach that makes participation in research convenient for the patient. Minority and disadvantaged populations without transportation or those with limited mobility struggle to participate. But these initiatives are important for the general population as well."

Studies that allow for home health visits would ease this burden on both sites and patients, Dr. Grach continues. "This would drastically increase patient engagement in clinical trials and improve retention."

Ms. Wright says efforts to reduce the burden on patients should be considered as well. For example, reimbursement for transporta-

CISCRP Releases Video to Improve Diversity in Trials

The Center for Information and Study on Clinical Research Participation (CISCRP), has released a new video to increase awareness and knowledge of clinical research among diverse communities. With support from Janssen Research & Development, CISCRP customized a recreational vehicle — called Journey to Better Health -— that visited 10 different Los Angeles community events and encouraged people to learn more about clinical research.

To view the video, please go to: https://www.ciscrp.org/events/aware-for-all/journey-to-better-health-rv/?utm_source=Press%20Release&utm_campaign=J2BH

tion costs should be included in the plan and can also increase the recruitment area for a site. "Our experience has been that certain populations are less likely to drive and public transportation may not be a great option," she says. "In some cases, targeting specialized or ethnically diverse populations has required us to recruit from as far as a three-hour radius."

Dr. Foster says SCRS will be launching a diversity assessment tool to help sites better understand how to train and implement best practices for recruiting diverse populations. "We want to provide the resources to them that will help them work on the areas where they need improvement."

Dr. Grach at Wake Research identified the Hispanic population as one that was untapped at her research organization. The organization invested in a training program for the recruitment department, clinical operations nurses, and those on the front lines working with patients on how to communicate with the Hispanic population.

"We brought in people to work with members of this community," she says. "We now have people in our clinical departments and coordinators who are native-speaking Hispanics. This was a very important factor."

Institutions can make additional efforts to support an infrastructure that encourages and trains a diverse population to be investigators and study team members, Dr. McNair says. "It is also important that sites reach out to the local community with culturally relevant education about clinical trial participation that addresses historical issues and perceptions about research and identifies ways to overcome both real and perceived barriers to research."

Recruiting is always hard. There are very few studies that you can recruit for easily.

NANCY MULLIGAN
UBC

WCG assists sponsors and CROs in identifying clinical trial sites that are located in areas with diverse patient populations. "We can also collate data about investigator history from the WCG Knowledge Base with data from other sources, which can ensure that a clinical trial includes a diverse investigator population, as well," Dr. McNair says.

In addition, WCG has participated in a few projects to help increase the general public's understanding of clinical trials, with the goal of encouraging a more diverse population to consider participating in a study. "We are working with some sponsors and CROs on efforts to support the conduct of virtual trials; trials that are decentralized and either minimize or completely cut out the need for in-person visits to a clinical site," Dr. McNair says.

A more data-driven approach is needed that matches the demand for clinical trial patients from sponsors with the supply available through clinical sites, says Beenu Kapoor, senior director, Cognizant Consulting — Life Sciences. "This requires an open, collaborative technology platform, where sites can make themselves known to sponsors as available and describe their key capabilities, much like LinkedIn provided a new way to find and maintain business relationships in the professional world," she says. "This will lead to an expansion of the investigator pool and access to more diverse patient populations."

Mr. Kim says Lilly is committed to training minority investigators, and has engaged with more than 50 minority oncologists, and the company has partnered with the National Medical Association, which represents African-American physicians, the National Hispanic Medical Association, and the American Society of Clinical Oncology to leverage best practices.

"People tend to trust people who are like them," says Jennifer Miller, Ph.D., assistant professor at Yale School of Medicine, and founder of Bioethics International. "Several studies show the importance of a demographically diverse clinical and investigator workforce, including racial and ethnic diversity, on the quality and cultural competency of care. Expanding trial sites, beyond just the top academic medical centers, and minimizing exclusionary criteria in protocols, could help improve patients' access to trials, especially for elderly, minorities, and rural patients." PV

Barriers Sites Face

The Society for Clinical Research Sites' Diversity Awareness Program was created to identify cultural barriers and support efforts by research sites to recruit diverse populations. A recent survey of sites by the organization revealed important considerations for addressing site awareness and best practices. First, SCRS found that sites' perceived ZIP code demographics do not accurately reflect the Census Bureau's data.

Second, linguistic translations played a major role regarding patient recruitment. Sites with limited linguistic capabilities experienced increased difficulty with patient recruitment and garnering trust.

Third, it was identified that sites with lower racial/ethnic staff diversification experienced limited enrollment of diversified patients. Lastly, the amount of cultural training directly correlated with diversified patient enrollment statistics.

Source: Society for Clinical Research Sites