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Viable Strategies to Increase Clinical Trial Patient Diversity

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ABSTRACT

In the United States, the pharmaceutical industry is actively devising strategies to improve the diversity of clinical trial participants. These efforts stem from a plethora of evidence indicating that various ethnic groups respond differently to a given treatment. Thus, increasing the diversity of trial participants would not only provide more robust and representative trial data but also lead to safer and more effective therapies. Further diversifying trial participants appears straight forward, but it is a complex process requiring feedback from multiple stakeholders such as pharmaceutical sponsors, regulators, community leaders, and research sites. Therefore, the objective of this paper is to describe three viable strategies that can possibly increase the diversity of clinical trial participants: (1) Diversification of the clinical research workforce. (2) Adoption of the Diversity Site Assessment Tool, and (3) incorporation of decentralized clinical trial technologies into clinical trial designs.

Introduction

Over the past fifty years, the clinical research industry has developed frameworks and regulations such as the Declaration of Helsinki and the International Conference on Harmonization, designed to protect study participants exposed to new drugs and therapies from possible harm (1-2). Studies have illustrated that a drug's efficacy and likelihood to induce adverse side effects varies among different ethnic groups and subpopulations (3-4). Minorities and underrepresented groups constitute a small percentage of clinical trial participants–yet disproportionately suffer at a higher rate from many of the same diseases being studied (5-7). Therefore, this paper's objective is to illustrate three strategies that can be implemented to increase clinical trial diversity: First, diversifying the clinical research workforce—particularly in patient-facing roles at sites, clinics, and academic medical centers—may provide an avenue to recruiting a larger and more diverse group of patients. Second, the promotion of standardized tools such as the Diversity Site Assessment Tool to allow for accessible evaluation of diverse patient enrollment across all trials in the United States. And third, utilization of technology, particularly decentralized clinical trials along with traditional research methods to drive community engagement at a local level. These three strategies could further raise the interest and enrollment of minority populations in clinical trials, and begin addressing the need to provide safer therapies for all patients.

Develop Actionable Strategies to Increase Clinical Trial Patient Diversity.

A cohort study published by Turner et al., in 2022 demonstrated that clinical trial diversity is modestly increasing (8). The authors analyzed data from 328,452 clinical trials initiated in the United States between 2000-2020; moreover, they excluded studies with a non-interventional study design along with those that recruited patients outside of the United States, thus resulting in only 20,692 eligible studies for analysis (8). The authors further classified those 20,692 studies based on when the studies disclosed ethnicity enrollment data in relation to the passing of two critical Food and Drug Administration amendments: FDAAA 801 and the Food and Drug Administration's Final rule passed in 2017 regarding clinical trial race and ethnicity reporting (8). Of the 20,692 trials, roughly 44% reported race or ethnicity data, but since the creation of the clinicaltrial.gov website from 2008-2018, race reporting increased at an annual rate of 13.5% (8). Likewise, minority enrollment in trials has increased at an annual rate of 1.7% each year, with phase I-IV trials having a greater enrollment of Black and Latino populations than phases II-III (8). The authors conclude that all stakeholders in clinical research must continue providing race data on trial participants to allow the industry to better understand the progress of diversity-related initiatives (8). The relatively low percentages of reported racial and ethnic-related data suggest that the industry strongly needs diversification of trial participants in order to strengthen study data and provide much-needed clinical care to underrepresented populations.

A crucial question is precisely why the Food and Drug Administration's efforts only produced modest gains in the enrollment of diverse patients? One possibility is the dilemma surrounding increased clinical trial diversity is itself multifaceted and requires feedback and contributions from numerous stakeholders, not just within government agencies—but also throughout the clinical research ecosystem and the medical establishment. Regardless, there are tangible solutions that the clinical research industry can employ to further increase patient diversity in clinical trials, a few of which are discussed in the following sections.

The diversity of the clinical research industry itself is one viable option that may increase trust among minority communities and augment the number of diverse trial participants. Diversifying the clinical research staff at research sites, hospitals, and academic medical centers is tenable as these professionals can build rapport within the community and with patients. For example, the clinical research coordinators meet with patients to review informed consent, schedule appointments, and even propose potential clinical trial opportunities. These patient-to-researcher interactions are a starting point for establishing trust at a personal level that may potentially grow into community trust. A recent study conducted by the Tufts Center for the Study of Drug Development illustrated a positive correlation between the diversity of site staff and those of the trial participants regardless of study location (9). By seeing this positive correlation, leaders within the clinical research industry could devise rigorous training programs aimed at developing diverse and passionate research staff, and partner with existing minority clinical research organizations that share similar goals. Ultimately, these trained clinical research professionals could act as liaisons for clinical research at their respective institution or site, and possibly begin reshaping the existing paradigm of mistrust towards the medical community that exists within minority communities.

A crucial question remains as to how research sites can critically evaluate their diversity outreach efforts. The Society of Clinical Research Sites meets annually and discusses strategies to increase diversity within the clinical trials industry. The consensus from the society's 2022 annual meeting was that the U.S. Food and Drug Administration's guidelines do not propose a standardized methodology for research sites to assess their progress toward achieving diversity in clinical trial enrollment. Therefore, the organization developed The Diversity Site Assessment Tool, which is the first methodology to the authors' knowledge addressing this issue (10). Foster (2020) showed that the Diversity Site Assessment Tool is an extraordinarily reliable questionnaire that sites can use to evaluate their standing across a wide range of areas from site recruitment and outreach to patient-focused services (10). Foster also demonstrated that the individual characteristics of the sites themselves had no statistical relationship to the score, a finding which suggests that the Diversity Site Assessment Tool could be used as a standard to evaluate and compare research site performance (10). Having U.S.-based research sites submit Diversity Site Assessment Tool scores to the Society of Clinical Research Sites for annual publishing could increase the transparency of ethnicity/race reporting for clinical trials, and may provide the industry with a higher level of understanding that may lead to more effective diversity initiatives. For example, researchers could conduct further studies investigating possible correlations between a site's Diversity Site Assessment Tool score and the diversity of their enrollment, and explore the methodologies consistently high-scoring sites employ to improve diversity in enrollment.

Reduce Patient Burden and Implement Technology where applicable.

Other factors may also bar minorities from enrolling in potential trials such as specific study requirements or internet accessibility. For example, some trials may require patients to travel long distances to research sites and may not offer adequate compensation (11). It is important to note that each patient views study travel distance and compensation differently. What is considered appropriate compensation for one patient may not be acceptable for other patients. Furthermore, the average patient may feel that the trial itself is too burdensome due to study design—including the number of visits, diagnostic tests, and visit lengths—or they do not have the resources at home to support the trial itself (11-12). Internet accessibility is still a major problem across the U.S. The Federal Communications Commission reports that approximately 19 million Americans still lack the appropriate access to internet services. This reported number is disproportionately concentrated in rural areas (13). As a result of these issues, traditional clinical trials have suffered from low recruitment and retention, but the COVID-19 pandemic necessitated the acceleration of numerous decentralized technologies (14-15).

Decentralized technologies are new and their effects on minority recruitment and retention have yet to be seen, but they offer an enormous opportunity to make clinical trials more accessible to everyone. Evidence for this can be seen in a recent decentralized and highly successful COVID-19 trial that was conducted by Sedhai et al., at a Virginia hospital whose primary patients come from rural and underserved backgrounds. The study enrolled 51 participants of which 37.5% were female and 62.5% were Black with a median age of 60 years (16). The authors attributed the trial's success to the decentralized model which they assert made the trial more accessible to minorities and impoverished groups (16). Decentralized technologies are also highly favorable among participating patients. For example, Sine et al., conducted a survey assessing whether clinical trial participants' overall satisfaction increased as a result of using a variety of technologies such as e-consents, wearables, and text message reminders (17). The researchers found that using technologies, including wearables and text reminders, increased patient satisfaction and improved their beliefs regarding the overall quality of the standard of care—a conclusion that was statistically significant across all racial groups (17). The study provided evidence that the technologies are popular among Black and Hispanic populations–suggesting a possible avenue to improve patient engagement and retention for underrepresented groups (17). Further research studies must be conducted to confirm the effects of these technologies on the enrollment of minority populations. These findings could suggest that Sponsors may need to diversify their trial design utilizing a combination of decentralized and traditional in-person study visits to capture the widest possible range of study subjects.

Conclusion

The clinical research industry has provided lifesaving medical treatments to patients across the world, but more work must be done to ensure that minority populations are provided with the best possible treatment options. Decision makers within the government, contract research organizations, pharmaceutical sponsors, academic medical centers, and research sites must continue devising and implementing strategies to diversify trial participation in the near future. Diversifying the clinical research workforce, particularly in patient-facing roles at sites, may provide an avenue to recruiting a larger and more diverse group of patients. Additionally, promoting the use of standardized tools such as the Diversity Site Assessment Tool could allow for accessible evaluation of diverse patient enrollment across all trials in the United States, and open the door to more extensive research. Additional methods can also be implemented by establishing research sites in more ethnically diverse locations and utilizing a combination of decentralized and traditional research methods to drive community engagement. These initiatives could raise the interest and enrollment of minority populations in clinical trials, and begin to address the moral imperative of providing safer therapies for all patients.

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