DIVERSITY IN CLINICAL TRIALS: A WORK IN PROGRESS

Researchers must overcome obstacles to improve representation in retina clinical trial populations.

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Randomized clinical trials represent a high standard of evidence-based medicine and are cornerstones of clinical practice. Yet, the lack of diversity among study participants remains a well-documented challenge throughout many medical specialties. Despite successive statutes, regulatory requirements, policies, and guidance documents, as well as surveys demonstrating overwhelming agreement of the benefits of a well-represented trial, many remain insufficiently diverse in their recruitment.[1-6] The paucity of clinical trial diversity perpetuates rooted disparities in health care, which constrains our ability to properly care for all our patients.

WHY DIVERSITY IN CLINICAL TRIALS IS IMPORTANT

Between 2010 and 2020, the US Census revealed that the US population grew more racially and ethnically diverse;[7] without capturing these demographic changes in scientific research, more individuals will be left with subpar medical care.[7] Diverse populations have diverse needs, and studies show significant racial and ethnic differences in the natural history, progression, and treatment of disease—including in ophthalmology.[8-10] Yet, without adequate representation in medical research, clinicians cannot ascertain how safe or effective a therapy will be for certain populations.

A lack of diversity in clinical trials not only negatively affects those who are poorly represented but leads to financial repercussions. A study published by the National Academies of Sciences, Engineering and Medicine, with subsequent analysis by the University of Southern California Schaeffer Center, showed that billions of dollars will be lost in the next 2 to 3 decades solely from increasing disability, decreased life expectancy, and reduced working years by individuals from poorly represented populations.[11]

To address this challenge at the federal level, Congress introduced the Health Equity and Accountability Act (HEAA) of 2022 to improve the health of minorities in the United States.[1] Building on the DIVERSE Trials Act introduced in August 2021,[2] the HEAA seeks to formalize FDA guidance by mandating that clinical trial sponsors recruit adequately from historically underrepresented groups. This would be accomplished through financial incentives and would require an action plan outlining how a study organizer plans to recruit and retain participants from underrepresented groups.[1] Though not likely to resolve this challenge outright, it represents an important step in the right direction.

HOW ARE WE DOING IN RETINA?

The issue of diversity in clinical trials does not spare the field of retina, and important gaps in the representation

AT A GLANCE

- Of 23 diabetic macular edema and macular edema from retinal vein occlusion phase 3 trials, 96% had different racial/ethnic compositions than the 2020 US Census.
- Many patients may not be aware of the existence of trials due to poor health literacy, cultural considerations, language barriers, or poor outreach.
- Research suggests that the onus of change is on researchers, who must work to establish and foster community-based relationships with each underrepresented group.

of racial and ethnic minorities exist.[12-14] The first challenge is reporting; one study found that, of articles published in the retina literature in 2019, only 43% reported patients' race or ethnicity.[15] If it was reported, it was done so heterogeneously—78 distinct categories of race and ethnicity were identified.[15] In 2016, the FDA published a guidance document that provided explicit recommendations on how to collect and report this information in a standardized format, encouraging study organizers to offer options that mirror what is offered in the US Census.[3]

When retina clinical trials did report full participant demographics, it became clear that there was still much work to be done. Our study found that, of 23 diabetic macular edema and macular edema from retinal vein occlusion phase 3 clinical trials, 96% had significantly different racial and ethnic compositions than what would be expected in the 2020 US Census.[14] In 15 of the 23 clinical trials, the demographic group that was most underrepresented was the Hispanic/Latino population. This was followed by participants who identified as Asian (underrepresented in 10 of 23 trials) and by those who identified as Black (underrepresented in nine of 23 trials).[14]

For Hispanic/Latino participants, this underrepresentation was worse than what was experienced by other groups; nine of the 15 trials had underrepresented this group by greater than 10% from what is expected per the US Census.[16] Given that this is the fastest growing racial/ethnic group in the United States, which additionally experiences a higher burden of diabetes and hypertension (along with individuals who identify as Black), these findings are worrying and highlight the importance of engaging with these communities.[17]

OBSTACLES TO DIVERSE RECRUITMENT

There are many intrinsic and extrinsic factors that affect participation and diverse recruitment. Many patients may not be aware of the existence of trials—or that they are potential candidates—due to poor health literacy, cultural considerations (eg, certain groups may defer to a physician to make the suggestion), language barriers, or poor outreach and patient education on the investigator's behalf. Structural access issues can prevent interested patients from reaching a specialist or a clinical trial site, and a lack of insurance or legal status may prevent or hinder access as well.[18]

The issues of historical research abuse and fear and/or experience of discrimination in the health care setting are complex factors that cannot be ignored. Clinicians should not conflate a lack of implicit trust with a lack of willingness to engage. In fact, patients may feel that the lack of engagement from traditional health care institutions is a manifestation of a lack of concern for their health outcomes.[4]

Financial considerations, be they realized costs or opportunity costs, often play a significant role in a patient's willingness to participate in a clinical trial. Some patients cannot take time off work to attend each trial appointment, which is often longer than the average office visit. Transportation can be a challenge, and many patients depend on family or friends for transportation, which may preclude trial completion.

WHILE NO SINGLE SOLUTION IS GOING TO RESOLVE THE CURRENT SITUATION OVERNIGHT, EVEN SMALL STEPS CAN HAVE A SIGNIFICANT EFFECT.

Even if an individual can navigate the obstacles noted above and reach the screening stage, they may find that they do not qualify due to restrictive eligibility criteria. This often occurs for patients with advanced disease or comorbidities, which tend to affect both older patients and racial/ethnic groups that experience worse disease.

POTENTIAL REMEDIES

While these obstacles may seem insurmountable, clinical trialists and scientists are not without tools and guidance. The literature supports interventions that can improve representation among multiple demographics, and the onus of change is on researchers, who must work to establish and foster community-based relationships.[4] Importantly, the conversations must be bidirectional, and researchers may need to meet individuals where they already receive care such as community health centers (including faith-based and federally qualified health centers, retail pharmacies, or other institutions with long-term community trust [ie, historically Black colleges or universities]).[19] Financial incentives at the national level may help to develop these non-traditional health care spaces into research sites.

Another important initiative is the improvement of diversity among medical and research personnel. This includes changes that can be made locally (eg, increased recruitment at training programs) coupled with actions at the national level (eg, the AAO Minority Ophthalmology Mentoring Program).[20]

One future model found that if clinical trial diversity improved to reduce health disparities by just 1%, the health care system could save at least $100 billion in spending for diabetes and heart disease care alone—not to mention the improved health outcomes for these populations.[11]

(Continued on page 33)

(Continued from page 25)

FIRST STEPS

It is incumbent on all providers to identify and decrease barriers to inclusion for individuals in all underrepresented groups to enhance health outcomes. To neglect this mandate would be to perpetuate negative effects on health equity, medical ethics, and scientific rigor. In an increasingly diversifying world, we cannot leave any patient behind. ■

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