

ASK THE EXPERTS

What Are Three Keys to Improving Equity in Cardiac Clinical Trials?

Leaders in cardiac clinical trial research offer their thoughts on how to support and progress the efforts to increase equity among clinical trials.

With **F. Aaysha Cader, MD, MRCP, MSc, FACC, FSCAI**; **Marion Mafham, MBChB, FRCP, MD**; **Megan Coylewright, MD, MPH, FSCAI, FACC**; and **Celina M. Yong, MD, MBA, MSc**



F. Aaysha Cader, MD, MRCP, MSc, FACC, FSCAI

Department of Cardiology
Kettering General Hospital
Kettering, England, United Kingdom
aaysha.cader@nhs.net

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Marion Mafham, MBChB, FRCP, MD

Associate Professor
Nuffield Department of Population Health
University of Oxford
Oxford, England, United Kingdom

Disclosures: None.

Cardiovascular diseases are the leading cause of death in both men and women around the globe. Evidence from cardiovascular trials informs patient care and clinical practice guidelines; however, several groups of patients including women (particularly pregnant and lactating women), BIPOC (Black, Indigenous, and other People of Color) individuals, the elderly, those with multiple comorbidities, and those living in countries with

inadequate trial infrastructure are underrepresented in clinical trials.¹⁻⁴ Clinical trial cohorts generally differ from the populations whose care they hope to inform, because requirements for long-term adherence to trial protocols will inevitably require selection. Despite this, the proportional effects from well-conducted clinical trials are likely to be generalizable to the broader population unless there are substantial differences in the delivery of the intervention or the nature of the target disease in clinical practice. However, unnecessary exclusion of some groups, such as pregnant women, can lead to undertreatment of such populations, while equity of access to research is an important component of a fair health care system.¹

1. Improved trial design to increase equity in trial populations and participant recruitment. Eligibility for clinical trials should be as broad as possible, while maintaining the scientific integrity of the trial and the safety of the study participants. For example, unnecessary exclusion of underserved groups, such as pregnant women, older adults, and those with multimorbidities, is often due to restrictive eligibility criteria of the trial design.⁵ Furthermore, trials can be limited by geography to only large centers in countries with established infrastructure where investigators are already present, thus excluding populations in regions with less-established trial infrastructure (eg, some low- and middle-income countries [LMICs]), often where the burden of

disease might be highest.⁶ Sex- and ethnicity-specific differences in the pathophysiology and metabolism of drugs and interaction with devices may exist.⁷ Most individual trials lack statistical power to assess differences in treatment effects among subgroups; therefore, accurate capture of baseline participant characteristics such as ethnicity or genomic analysis with subsequent individual patient data meta-analysis is important to fully investigate important potential differences between groups of individuals.⁸

2. Remove obstacles to participant recruitment and conduction of trials. Obstacles may be present at multiple levels in the trial process. For participants, reducing the burden of participation by avoiding unnecessary data collection and ensuring patient-centric trial processes for consent, recruitment, and follow-up, designed with patient and public involvement, will facilitate enrollment. There is also a need to build capacity and infrastructure outside of traditional research centers to make participation in clinical trials more accessible to wider populations.⁹

It has been reported that women more often decline to participate in trials owing to a perceived higher risk of harm from trial participation than men. Thus, effective communication of risks may address an important barrier, one that may also be applicable to promoting trial participation in LMICs.^{7,10}

3. A multidisciplinary collaborative approach involving multiple stakeholders. These include trial-

ists, sponsors, regulatory agencies, funders, patient representatives, and advocates, as well as the discussion of strategies to achieve diversity and equity in enrolled populations and appropriate trial design. Diversity in trial leadership and trial teams can influence the diversity in recruitment of participants in clinical trials. Thus, adopting open processes for selection of trial leadership and building the pipeline with adequate mentorship and opportunities for growth, both in investigator-initiated and industry-led trials, are important.⁷

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Megan Coylewright, MD, MPH, FSCAI, FACC

Director, Structural Heart Program
Erlanger Health System
Vice Chief for Faculty Development
Cardiology, Erlanger Heart and Lung
Institute
Member, Erlanger Diversity Council
Associate Professor
University of Tennessee at Chattanooga
Chattanooga, Tennessee
megan.coylewright@erlanger.org
Disclosures: Executive steering committee member for EXPAND TAVR II (Medtronic) and CHAMPION AF (Boston Scientific Corporation).

1. Know your numbers. The first step is transparency with your own research team about the importance of equity through representation in clinical trials. Host a

meeting in which you present the latest literature on the well-documented disparities in cardiac clinical trials with regard to representation of women and people of color. Remind staff it cannot be explained by prevalence of the disease, nor differences in the aging population. Then, engage the team to review the internal numbers for patients recruited into clinical trials at your institution. Brainstorm barriers and engage facilitators locally to enroll more patients in underrepresented groups. Encourage group study of the literature that outlines best practices for recruitment. Implement new ways to identify and recruit patients.

2. Invest in staff. The current system of cardiac clinical trials is working as designed to get the results we see. How do we change the system to offer different results? This will take time, attention, and investment in resources. Be honest with your research team about this need. Invest in staff to be able to assist with additional tasks. Note whether the research staff reflects the diversity you hope for in recruitment. If not, how can you leverage additional staff in your institution—and support them with resources for their work—to reach the goals you have prioritized?

3. Identify your goals; trade-offs may be required to get there. When running cardiac clinical trials, our first focus is most often on recruiting as many patients as possible, as quickly as possible. This approach has led to the disparities we see today in clinical trials. What trade-offs are required? It may be creating new clinics for research recruitment that give patients and families more time to ask questions or feel part of a

larger community. It may mean team members spending more time together reviewing patient lists and contacting referring clinicians and patients themselves with formal invitations to participate. There are many innovative strategies, and recognizing that it will take time and effort will aid in examining the trade-offs needed; ultimately, this will lead to greater sustainability of efforts.



Celina M. Yong, MD, MBA, MSc

Associate Professor of Medicine
Stanford University
Director of Interventional Cardiology
VA Palo Alto Healthcare System
Stanford, California
cyong@stanford.edu
Disclosures: None.

If we hope to apply the findings of our cardiovascular clinical trials to all our patients, we need to prioritize including participants who represent the entire patient population we serve.

1. Go where the patients are. Many clinical trial sites are located at prestigious university centers where leading researchers work; however, some patient populations may not routinely receive their care at these locations. When designing multisite trials, trial leadership must prioritize including trial sites in areas enriched with diverse patient populations. A study of two United States national coronary stent registries showed that studies with research sites in geographic regions with more racial and ethnic diversity performed as well as nondiverse sites across key performance metrics, suggesting that we can achieve diversity in our trial representation without sacrificing volume or quality of trial metrics.¹ Decentralized trial design can also allow for diversified recruitment even when the infrastructure for a local trial site is not possible. Additionally, natural language processing approaches to methodically match patients with appropriate trials have the potential to reduce bias in recruitment.

2. Diversify the principal investigators. In a study of cardiovascular clinical trials listed on clinicaltrials.gov in the last decade, we found that trials with a female principal investigator were more likely to recruit a higher proportion of female patient participants than trials led by a male principal investigator.² More research is needed to understand the degree to which this is attributable to increased access to different patient populations or different ways of connecting with patients that lead to enhanced diversity in enrollment. We have much to learn from diversifying clinical research leadership, including potential strategies that can be applied more widely to all patient recruitment approaches.

3. Alignment across the clinical trial spectrum. Researchers cannot solve this problem alone; improving equity in clinical trials requires collaboration from the entire scientific and clinical community. All funding institutions, both public and private, should require intentional study design and reporting to ensure equitable recruitment. Editorial boards should prioritize adequate patient representation as a metric for a high-quality trial design worthy of a high-impact publication. Then, clinicians need to be aware of how well the published trials represent their own patients, so they can help communicate the most relevant findings to the patients they are intended to inform.

Ultimately, it is only when all of us—researchers, funding institutions, editorial boards, patients, and clinicians—align on the importance of diversity as a key criterion of scientific quality that will we be able to reach the goal of equity in cardiovascular care. ■

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