

EDITORIAL COMMENT

Equitable Global Representation in Cardiovascular Guidelines and Clinical Trials

Lacunae Remain

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In sub-Saharan Africa (SSA), an epidemiologic transition is well underway, with cardiovascular diseases (CVDs) poised to overtake communicable diseases as the leading cause of death by the next decade.¹ The pattern of CVD in the region also significantly differs from high-income countries (HICs) in Europe and North America. For example, the most common etiologies of heart failure (HF) in SSA include hypertensive heart disease and rheumatic heart disease, compared with ischemic heart disease in HICs. Furthermore, patients in SSA tend to be both younger and suffer worse outcomes from CVD.² These epidemiologic differences underscore the need for clinical guidelines that apply to these regions, which may be facilitated in part by their adequate representation in the literature.

The representation of African countries in cardiovascular literature is abysmal, despite them carrying the greatest burden of CVD.³ This is reflective of a broader trend of under-representation of low- and low-middle-income countries (LMICs), to which most of SSA belongs. While LMICs contribute almost 60% of global CVD death rates, they account for only 2.8% of the total CVD research output.⁴ Influential literature, such as randomized controlled trials

(RCTs) and systematic reviews are predominantly led by HICs and involve these countries' populations.⁵⁻⁷

In this issue of *JACC: Advances*, Hudson et al⁸ present a timely addition to the growing literature on inequitable regional representation in cardiovascular research. Here, they analyzed the representation of SSA-based populations in RCTs cited by the European Society of Cardiology guidelines on HF and acute coronary syndrome. They found that only 11% of all RCTs involved LMIC-based sites. Furthermore, only 14% of HF trials and 8% of acute coronary syndrome trials involved SSA-based sites, making SSA the least represented global region. A disheartening revelation was that South Africa, an upper-middle-income country, was the only country from the entire region represented. However, as the authors note, there were limitations to the study, including the lack of granular data on the number of participants and lack of analysis of other society guidelines, both of which may have provided greater insight.

Decentralization of RCTs, with LMIC-based populations being involved, and with LMIC-based researchers included in trial leadership are steps in the right direction to address problems pertinent to these regions, and also promote broader applicability of their recommendations. Ensuring equitable involvement of LMICs in RCT leadership can also curb exploitation of LMIC populations, which can receive potential future benefits resulting from these studies.⁹ It can also help with research capacity-building in these countries.⁶ However, researchers in LMICs face numerous challenges to conducting research, including heavy clinical obligations with limited protected research time, limited funding, lack of trained personnel, and bureaucratic barriers.¹⁰ HIC-based institutions and researchers can help

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ameliorate some of these barriers with dedicated grants for LMIC researchers and institutions, knowledge exchange programs, and formalized mentorship efforts.¹¹ This study appears to be an example of a fruitful collaboration, being co-led by HIC- and LMIC-based authors, with funding support from a HIC.⁸ Progress will be slow, but will undoubtedly improve the quality of research and knowledge dissemination.

Overall, the Hudson et al⁸ analysis provides a baseline for future assessment of the representation of LMICs in CVD RCTs and guidelines. Their thoughtful work will hopefully provide further

impetus for efforts to ensure adequate global representation in influential cardiovascular literature.

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REFERENCES

1. Minja NW, Nakagaayi D, Aliku T, et al. Cardiovascular diseases in Africa in the twenty-first century: gaps and priorities going forward. *Front Cardiovasc Med*. 2022;9:1008335.
2. Yuyun MF, Sliwa K, Kengne AP, Mocumbi AO, Bukhman G. Cardiovascular diseases in sub-Saharan Africa compared to high-income countries: an epidemiological perspective. *Glob Heart*. 2020;15:15.
3. Noubiap JJ, Millenaar D, Ojji D, et al. Fifty years of global cardiovascular research in Africa: a scientometric analysis, 1971 to 2021. *J Am Heart Assoc*. 2023;12:e027670.
4. Qureshi NQ, Mufarrih SH, Bloomfield GS, et al. Disparities in cardiovascular research output and disease outcomes among high-, middle- and low-income countries - an analysis of global cardiovascular publications over the last decade (2008-2017). *Glob Heart*. 2021;16:4.
5. Ramanan M, Tong SYC, Kumar A, Venkatesh B. Geographical representation of low- and middle-income countries in randomized clinical trials for COVID-19. *JAMA Netw Open*. 2022;5:e220444.
6. Rubagumya F, Hopman WM, Gyawali B, et al. Participation of lower and upper middle-income countries in clinical trials led by high-income countries. *JAMA Netw Open*. 2022;5:e2227252.
7. Bhat V, Ozair A, Bellur S, et al. Inequities in country- and gender-based authorship representation in cardiology-related Cochrane reviews. *JACC Adv*. 2022;1:100140.
8. Hudson JA, Sanga L, Jobe M, et al. Sub-Saharan Africa's contribution to clinical trials in international acute coronary syndromes and heart failure guidelines. *JACC Adv*. 2024;3:101383.
9. Dal-Ré R, Ndebele P, Higgs E, Sewankambo N, Wendler D. Protections for clinical trials in low and middle income countries need strengthening not weakening. *BMJ*. 2014;349:g4254.
10. Dakhil ZA, Cader FA, Banerjee A. Challenges in clinical research in low and middle income countries: early career cardiologists' perspective. *Glob Heart*. 2024;19:13.
11. Kalra A, Kumbhani DJ, Hill JA. Cardiovascular science India tour: impacting cardiovascular disease in South Asia. *Circulation*. 2020;141:159-160.

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