Invited Commentary

Disentangling Ancestry From Social Determinants of Health in Hypertension Disparities—An Important Step Forward

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We are having difficult but necessary conversations about racial/ethnic health disparities in cardiovascular (CV) medicine. Instead of an implied assumption that racial/ethnic disparities in CV disease (CVD) morbidity and mortality are driven by inherently biologic differences across racial/ethnic groups, we are beginning to acknowledge as a medical and research community that race is what it has always been: a social construct. The disproportionate effects of the coronavirus disease 2019 pandemic, subsequent economic crisis, and police-sanctioned violence on Black people in the US have forced us to confront the definition of race. It is clear that systemic racism, or structural inequity defined by race, limits access to economic stability, quality health care, and safe, well-resourced environments, which are reflected in the social determinants of health for Black people in the US.[1] There are important questions to tackle as clinicians and scientists begin to unravel the elements of race and structural racism that influence CV health. For instance, an important question is how and whether we should use race in predictive models defining clinical risk, such as the Get With the Guidelines-Heart Failure Risk Score for determining risk of in-hospital heart failure mortality or the Society of Thoracic Surgeons Short-term Risk Calculator for mortality risk in cardiothoracic surgery.[2] Another fundamental question is how we can examine the association of ancestry with CVD outcomes, given that ancestry coexists but is not synonymous with race.

Editor's Note

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In this issue of *JAMA Cardiology*, Rao and colleagues[3] provide an important step forward in addressing this second question by examining the association between West African ancestry and trajectories of blood pressure control and associated physiologic markers, composite CV events, and all-cause mortality, using data from self-identified Black participants in the Systolic Blood Pressure Intervention Trial (SPRINT). This type of study is particularly timely because Black adults in the US are disproportionately affected by hypertension and its negative sequelae, including coronary artery disease, stroke, and chronic kidney disease. Moreover, recent data show that hypertension control among non-Hispanic Black adults has remained consistently lower than for non-Hispanic White adults from 1999 to 2018, with a decline in hypertension control across all racial/ethnic groups in the US since 2013.[4] Therefore, identifying the role of West African ancestry in hypertension-associated outcomes could elucidate how genetic factors may contribute to racial/ethnic disparities in hypertension. By examining data from SPRINT, a multicenter clinical trial from 2010 to 2012 in which participants 50 years and older with hypertension and elevated CV risk were randomized to either intensive or standard blood pressure control, the research team was able to examine outcomes in a study designed to provide equitable access to health care and medications across racial groups. The authors defined West African ancestry by biallelic ancestry informative markers, which were genotyped in a subset of SPRINT participants (n = 2569). The reference populations for these ancestry informative markers were individuals in HapMap[5] of Yoruba background from Ibadan, Nigeria (as an established proxy for West African ancestry), and European American control participants. The ancestry informative markers were used to define the proportion of West African ancestry, which ranged from 30% to 100% among the study population. Across tertiles of West African ancestry proportion, there were no significant differences in the trajectories of blood pressure, kidney function, or left ventricular mass in self-identified Black individuals with intensive or standard treatment. Additionally, there were no significant differences across West African ancestry tertiles in the association between intensive (compared with standard) treatment with SPRINT's primary outcome, which was composite adverse CV events. Finally, greater West African ancestry was associated with an 8% lower risk of adverse CV events, which remained after adjustment for confounders (adjusted hazard ratio per 5% greater West African ancestry, 0.92 [95% CI, 0.85-0.99]), and West African ancestry had no significant association with all-cause mortality in this SPRINT cohort.

As the authors[3] note, these findings highlight that social and environmental factors, as opposed to West African ancestry, likely play more critical roles in determining racial disparities in hypertension control and subsequent CVD events in the US. This work is an important start to disentangling the role of ancestry from social determinants of health in race-based hypertension disparities. However, we should acknowledge the limitations of existing genomic data that define African ancestry and admixture for self-identified Black individuals in the US. Until recently, there was a paucity of genomic data on the populations across the African continent, which has limited our ability to account for the rich genetic variability of populations on the continent when inferring African ancestry.[6] The Human Heredity in Health (H3Africa) Consortium is an example of critical efforts in building genomic data resources and genomic research and training capacity on the continent, with a particular focus on CVD research.[7] Efforts to diversify available genotypic data must continue as we move towards more tailored, genomic-based medicine. Moreover, we can gain a deeper understanding of the biology of adversity with interdisciplinary, collaborative approaches in epidemiologic studies or clinical trials of therapeutic options that integrate detailed phenotyping of social and environmental exposures with exploration of biologic pathways that may be most affected by adverse social and environmental conditions.[8] For instance, future studies can further examine the role of epigenetics in

hypertension disparities or posttranscriptional or posttranslational genetic modifications that can occur because of adverse social and physical environment exposures.[9] Future work could also examine the interaction between social and environmental stressors and cellular or molecular signaling pathways that promote hypertension risk and serve as potential intervention targets. Finally, there is a need to not only identify specific biologic mechanisms by which social and environmental factors promote health disparities but capitalize on community-based participatory research and similar principles to engage communities in designing tailored, multilevel interventions that promote systems-level changes for reducing hypertension disparities.[10] Why is community engagement so crucial? Community-academia partnerships in the design, implementation, and dissemination of interventions lead to inclusive involvement of vulnerable populations and greater sustainability of intervention effects. Thus, if we are to move beyond racial health disparities and toward health equity, we must continue taking steps in shifting the paradigm away from race as a potential determinant of CVD risk and toward social determinants of health.

ARTICLE INFORMATION

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