VIEWPOINT

Addressing Health Disparities Among Minority Populations
Why Clinical Trial Recruitment Is Not Enough

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Fewer births, declines in mortality related to cardiovascular disease and cancer, and international migration are contributing to unprecedented demographic shifts in the United States. Increasingly, the population is older and more diverse, and in the next 2 decades, racial and ethnic minorities will compose 42% of older adults. Without intervention, existing racial and ethnic health disparities among minority older adults are likely to be exacerbated. The pressing need to address these health disparities is perhaps most evident in Alzheimer disease (AD), which increases in prevalence with age and is disproportionately more prevalent among African American and Hispanic/Latino individuals.

Alzheimer disease prevalence is expected to triple by 2050 and threatens to overwhelm the health system unless significant advances are made. Despite numerous failures of AD drug trials, there remains optimism that some AD treatments may be effective, if started very early, likely in the preclinical (asymptomatic) period. Diagnosis of preclinical AD currently relies on cerebrospinal fluid (CSF) biomarkers and/or molecular or functional neuroimaging, and much of the evidence supporting this approach was generated from studies with fewer than 5% racial and ethnic minorities.[1] Diagnostic tools and therapeutic strategies developed using evidence with so little racial and ethnic diversity could lead to inaccurate diagnosis and/or ineffective treatment for minority patients, thus worsening disparities. For example, studies have found lower CSF tau[2] and higher uptake of radioligands for amyloid[3] in African American individuals compared with white individuals. If these findings are replicated and confirmed in larger studies, there could be implications for use of biomarkers in diagnosis and management of AD. However, even if differences between racial/ethnic groups are confirmed, these findings could reflect differences in risk owing to comorbidities and/or unexamined social factors.

Persistent disparities in AD outcomes have heightened calls for more minority participation in research, which remains low despite the decades-old National Institutes of Health guidelines on inclusion of minority individuals in clinical research and the 2017 National Institutes of Health requirements that phase III clinical trials include valid analyses by race/ethnicity. Researchers are keenly aware of the imperative to increase minority enrollment, but lack of trust, prior research abuses, and ineffective communication with minority communities contribute to low participation.[4] Despite the barriers, successful minority recruitment has occurred using strategies such as hiring staff experienced working with diverse communities, partnering with community organizations, and using communication channels known to reach diverse communities.[4]

While inclusion of minority populations in research is critical, minority recruitment alone is unlikely to provide the evidence needed to understand and address health disparities. Many studies have found an association between AD and years of education, quality of education, socioeconomic status, and neighborhood characteristics.[5,6] Thus, AD studies should be expected to consider these contextual and life experiences, especially among racial and ethnic minority patients who disproportionately are more likely to be socioeconomically disadvantaged. Many studies comparing groups by race/ethnicity use few variables to adjust for socioeconomic factors (eg, years of education and income level), and these insufficiently capture important differences in life experiences between races/ethnicities that could affect risk of disease. Unfortunately, analyzing findings by race/ethnicity without appropriate contextual data could lead to inaccurate, misleading, or stigmatizing conclusions that may detract from the overall goals of diversity in research: to enhance the accuracy, utility, and generalizability of scientific evidence.

Studies of race and ethnicity demonstrate greater genetic heterogeneity within than between racial/ethnic groups,[7] yet there is a common misperception that groups are more genetically homogeneous within racial/ethnic groups. Race, as defined by the US Census and Office of Management and Budget, is a sociocultural construct that is not biologically, anthropologically, or genetically based. Because race is socially determined and dependent on self-identification, it is a fluid construct that can change over time and vary by location and culture.

Although substantial evidence exists to contradict claims that race is biologically based and without evidence that genetic or biological characteristics can be inherently structured into racial categories,[8] long-held assumptions about innate biological differences between races continue to permeate medicine and biomedical research.[9] This is in part because minority race/ethnicity is tightly interwoven with sociopolitical factors, such as systemic racism, discriminatory policies, and access to care, which are linked to biophysiologic changes, such as neuroendocrine dysregulation, cellular aging, and elevated inflammatory cytokines.[10] These biological responses to social factors can contribute to premature morbidity and are not unique to minority populations but are more prevalent owing to the higher burden of psychosocial stress across the life span.

Race, particularly in the United States, is associated with markedly different life experiences as well as social and economic opportunities that affect health. Painful legacies of overt racism, abuse, and trauma continue to negatively affect minority communities.

Native American communities experienced historical traumas including exploitation and forced removal from their land, resulting in a ripple of economic, cultural, and social losses that continue to disadvantage their communities today. Such injustices are not limited to the distant past. In the 1950s and 1960s, most schools in the southern United States were racially segregated, and many public places, including hospitals, had separate entrances for African American individuals, if they were allowed to enter at all. There were substantial differences in the quality of the education at schools for African American individuals in the South, many of which operated on split terms to allow 2 months off in the fall to pick cotton. In 2002, *Unequal Treatment*, the landmark Institute of Medicine consensus report, found that racial and ethnic minorities in the United States receive lower-quality health care even when adjusting for insurance status, income, age, and severity of conditions. Racial bias, prejudice, and stereotyping by health care clinicians were found to contribute to these differences in care.

To mitigate health disparities, more comprehensive research assessments are needed to disentangle the myriad factors contributing to them. Researchers must begin with sufficient numbers of racial and ethnic minority participants, and ideally, the study sample should reflect the population of people with the disease. For example, if Hispanic/Latino individuals have higher incidence of AD, that should be expected in the study. Race and ethnicity should be collected by self-report using questions that allow individuals to identify as multiracial or multiethnic. Because only 22% of older adults born outside of the United States speak English, language spoken at home and English proficiency should also be collected. As important, researchers should collect contextual and environmental information that may explain or be associated with racial differences. The **Box** shows variables that would be useful in assessing individuals in an AD study.

Adapting and expanding data collection to more accurately assess environmental and sociocultural factors affecting health is critical not only for addressing health disparities but also for science more broadly. Less than 25% of the global population is of European ancestry; thus, studies primarily comprising white individuals lack generalizability, particularly if groups with the highest disease burden are excluded. Basic scientists and clinical investigators must learn to consider and identify social determinants of health and integrate these factors into hypothesis generation and study design. Social scientists and individuals experienced with minority health should be valued members of clinical research teams, not solely because they will help with minority recruitment but also because they may improve the quality of the science more broadly. By increasing the diversity of research participants and integrating the contextual information needed to understand diverse life experiences, we will finally begin to address the racial/ethnic differences in health and disease.

Box. Key Sociodemographic Information to Understand Social and Environmental Factors Relevant to Alzheimer Disease Disparities

Demographic and Social Information to Collect in an Alzheimer Disease Study

Race/ethnicity: Self-reported; should allow individuals to select more than 1 group[a]

Primary language: Spoken at home (or preferred language)

Education: Total years of education; school characteristics (public vs private, rural vs urban vs suburban); parents' total years of education

Annual household income: Current and at age 40 years

Perceived social class: Occupational prestige, housing type, sources of income

Neighborhood characteristics: Walkability, availability of healthy foods, social cohesion, and neighborhood violence[b]

Perceived discrimination: 9-item Everyday Discrimination Scale[c]

[a] A single question for race and ethnicity minimizes missing data from individuals who do not identify a race and acknowledges ethnicities other than Hispanic/Latino.

[b] Christine PJ, Auchincloss AH, Bertoni AG, et al. Longitudinal associations between neighborhood physical and social environments and incident type 2 diabetes mellitus: The Multi-Ethnic Study of Atherosclerosis (MESA). *JAMA Internal Medicine*. 2015;175(8):1311-1320.

[c] Williams DR, Yan Y, Jackson JS, Anderson NB. Racial differences in physical and mental health: socio-economic status, stress and discrimination. *Journal of Health Psychology*. 1997; 2:335-351.

ARTICLE INFORMATION

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