What We’re Talking About When We Talk About Race*

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It has been pointed out repeatedly (1,2) that reported associations between race and illness should be subject to careful scrutiny. Establishing race as an independent risk factor for a disease is even more complicated than the usually difficult task of establishing epidemiologic association. Among the usual difficulties are selection of a representative sample, collection of accurate data, identification of appropriate controls, and adjustment for confounders. Unlike other variables in epidemiologic studies, however, race has complex social and biologic implications.

Viewing race as a social construct is clearly important in epidemiology. Race is linked to a wide range of socioeconomic and cultural factors that impart important modifying effects on health, disease, and the delivery of health care. These factors include income, education, diet, health beliefs, access to health insurance, and exposure to discrimination (3). African American adults are approximately 2.5 times as likely as white Americans to have incomes below the poverty level, and African American children are approximately four times as likely to live in families with incomes below the poverty level. According to the 2000 U.S. Census, 78.5% of African Americans and 88.4% of white Americans over the age of 25 are high school graduates. Differences in college graduation rates are even greater: 16.5% for African Americans and 28.1% for white Americans. The 2000 Center for Disease Control National Health Interview Survey found that although 12.5% of white Americans lacked health insurance, the comparable figure for African Americans was 20%. Apparent racial differences may be markedly attenuated after accounting for confounders such as these. For instance, nationwide studies of patterns of care for heart failure (HF) have found lower rates of angiotensin-converting enzyme inhibitor prescription for African American patients (4,5). In contrast, a recent study of Medicare patients (6), who presumably have lower barriers to gaining access to care, found no racial differences in rates of guideline-based therapy. Race should not be used as a proxy for socioeconomic or cultural factors. When differences in risk factors for a disease are the result of measurable socioeconomic and cultural factors, this causative link should be made explicit.

Race has been viewed in medicine as a biologic construct as well. Race classifies humans on the basis of facial features, hair type, and skin color. The boundaries of these classifications are never explicitly stated and vary across cultures. Thus, there is no standardized method in the medical literature of assigning race. Race may be assigned by the investigator based on the subject’s appearance, or it may be self-assigned by the subject. Self-assignment may be from fixed sets of categories that vary among studies or from an open-ended question. Although racial designations are loosely associated with the continent of origin of an individual’s ancestors, much of the medical literature implicitly attaches a greater genetic significance to race than the available data warrant. Estimates of the genetic variability attributable to individual variation within populations range from 85% to 95% (7,8). Of the remaining genetic variability, only about half is attributable to between-continent differences. Thus, two individuals from different racial groups may very well share more genes than two individuals from the same racial group (9). It has been estimated that approximately 30% of the variable genetic make-up of African Americans is the result of admixture with people of non-African origin (10). Seen in this light, race may have relatively little value as a biologic construct. Exceptions may exist, however. Adrenergic receptor (11) and G protein (12) polymorphisms that may predispose one to HF are more prevalent in African Americans compared with whites. Although further work is needed to confirm the validity of these findings, they may help explain why, for instance, African Americans with hypertension appear to be more likely to develop left ventricular hypertrophy (13). The fact remains, however, that race is an imprecise categorization scheme and is a poor proxy for genomic differences.

In this issue of the Journal, Ruo et al. (14) present evidence that HF patients identified in the medical record as African American are approximately half as likely as those identified as white to have atrial fibrillation (AF). Among 1,373 randomly chosen patients hospitalized with HF during a one-year period, 506 had AF. The prevalence of AF was 19.7% in the African American patients and 38.3% in the white patients. Although relative risks are not reported, the odds ratio of 0.51 for racial prevalence in their final multivariable model suggests that adjustment for age, gender, known risk factors for AF, comorbidity, medications, and HF severity does not substantially alter this relationship. The magnitude of the computed relative risk is striking. How well has the current study avoided the pitfalls of inadequate adjustment for confounding by socioeconomic and cultural factors and of unwarranted assumption of genetic explanations?

With respect to recognizing confounding by socioeco-
nomic and cultural factors, they have studied a sample drawn from a Kaiser Permanente managed care population that has been demonstrated to be representative of the state population. This makes it less likely that black–white differences are the result of socioeconomic factors, but it is unclear whether the African American patients in the study are representative of African American patients in general. Second, although the population studied is relatively homogenous from a socioeconomic standpoint, unmeasured socioeconomic confounders are likely to have been present. Ascertainment of detailed socioeconomic data from the medical record is difficult, and more explicit adjustments would not have been possible with the information available to the investigators.

With respect to possible genetic explanations, the current study is intriguing. First, the direction of the association between race and AF runs counter to that which one might expect if the relationship was based on socioeconomic and cultural factors. The poorer socioeconomic status of African Americans typically is associated with more severe impairment of health status and poorer outcomes, yet the lower incidence of AF among African Americans is a marker of less severe HF. Second, the authors have studied a condition, AF, for which genetic predisposition exists. Familial forms of AF have been described (15), and genetic loci for the arrhythmia have been mapped to chromosome 10 (16), chromosome 6 (17), and perhaps to others (18). Although the existence of a heritable form of AF may suggest the possibility that the findings of the present study reflect distinct genetic differences, the reality is much less clear. The genetic forms identified thus far account for a small minority of cases of AF, and none of the existing AF chromosomal links have been specifically associated with race. Although current understanding of the contribution of genotype to the development of AF is incomplete, it would be premature to conclude that racial differences in AF incidence reflect genetic differences rather than a finding confounded by socioeconomic or cultural factors.

If confirmed, the findings of Ruo et al. (14) may be more important for generating future mechanistic studies than for elucidating epidemiology. Such future studies would collect data that more explicitly account for the socioeconomic status of the patients involved. If predisposition to AF or protection from AF can be mapped to a specific gene or genes, genotyping performed as part of these studies should aid in the identification of relevant polymorphisms. The current study, although limited in its ability to adjust for socioeconomic and cultural confounding and to assess for genetic polymorphisms directly, credibly neither neglects the social nature of race nor uncritically assumes a biologic basis for race. As our society struggles to eliminate race-associated disparities in care and eagerly awaits the advent of genomic medicine, it is absolutely critical that we all know what we’re talking about when we talk about race.

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REFERENCES