

Race, Genetics and Medicine

In the last several months it has become increasingly clear that I am guilty of racial profiling. Before you get too upset with me, consider the following behavior: if I see a patient considering pregnancy, and they appear to be Caucasian, I am far more likely to discuss screening for cystic fibrosis carrier status than sickle cell disease. Rarely do I ask the question formally: “With what racial group do you identify?” before I make this decision. Rarely do I discuss the decision process with my patients. I suspect that I am not alone. This type of provider behavior is reinforced by many national care guidelines, and is embedded in the training of health care providers from their first course in physical diagnosis.

The conscious and sub-conscious binning of individuals by observed physical characteristics is one way to estimate an individual’s personal probability of having certain diseases. Assessment of individuals through the lens of a population sub-group occurs at many junctures in the care delivery process, and rests on epidemiologic data demonstrating that disease prevalence varies among population groups. The logic supporting such an approach is as follows. Particular sub-populations are at higher risk for certain conditions. Effectively distinguishing the sub-population to which an individual belongs helps to define that individual’s probability of developing a given diagnosis. Accurate assignment of risk brings parsimony to the processes of prevention efforts, screening, differential diagnosis formulation, diagnostic workup and, potentially, therapeutic intervention. The binning of individuals by race and ethnicity is only one of a variety of discriminators health care providers routinely employ. The utility of binning individuals depends heavily on the quality of the determinants used to separate populations, and while age and gender are arguably fairly clear-cut, less controversial biological discriminators of disease risk, race and ethnicity are most certainly not.

The wealth of accumulating DNA sequence data from multiple individuals representing multiple population groups is revealing that our understanding of human genetic variation is only rudimentary. Accompanying this realization is a growing acceptance that current definitions of race and ethnicity are poor proxies for estimating the genetic component of individual disease risk. The bottom line is that the DNA of the U.S. population defines the cliché: we are a melting pot. Genetic variability is, in fact, greater between unrelated individuals than it is between racial and ethnic groups. Currently accepted racial and ethnic categories are a blur genetically, and drawing clinically useful boundaries for the purposes of assigning individuals to a group is quite difficult. What effect does this have on clinical care? Fundamentally, it causes errors in assignment of risk because using self-defined race and ethnicity may over or under estimate actual risk. This can result in harms in a variety of ways, but most commonly as a consequence of providing too little (or too much) care.

How might the issue of assigning individual genetic risk in the setting of complex genetic ancestry be resolved? Options include eliminating the use of race and ethnicity as a consideration when deciding whether to offer genetic testing for disease risk or diagnostic purposes. The prototypical example of this approach can be found in the

example of cystic fibrosis carrier screening, where the most recent guidelines suggest genetic screening should be offered in the prenatal setting to individuals of all races and ethnicities. Though in the case of cystic fibrosis screening this approach offers increased sensitivity, screening a larger population clearly results in increased costs. Another approach would be to use genetic markers as a “pre-test” for the ancestry of regions of DNA harboring potential deleterious gene mutations of interest and then to base genetic testing on this ancestral determination. This could be practical when genetic tests are expensive and knowledge of the ancestral derivation of the DNA would determine the most cost-effective testing strategy. An example would be choosing between targeted mutation testing and full sequencing of the BRCA 1 and BRCA 2 genes in hereditary breast and ovarian cancer syndrome in an individual that might or might not be of Ashkenazi Jewish ancestry. However, such a genetic “pre-test” would amount to the morally tenuous use of genetic tests for racial and ethnic profiling.

Clearly neither of these approaches is fully satisfying. The best solution would be the advent of extremely low-cost full genome sequencing techniques that would reveal the entirety of an individual’s genetic variation. This sequence information would allow an individual’s care to be based on their own genetic variations rather than crude estimation of genetic risk. Of course this requires not only the availability of low cost sequencing (which seems possible in the relatively near term) but an understanding of how the individual’s genetic variants interact with each other and the environment to cause disease, a topic for more research – and another column.

What should the health care provider do in light of emerging understanding of race and ethnicity? First, re-examine your own preconceptions regarding race and ethnicity, and how you use them in your practice. You may find that you are doing your patients a disservice. Second, take an appropriate family history, including the ancestral origins of the patient’s grandparents. Third, if you use an individual’s self-identified race/ethnicity in medical decision making, particularly with regard to genetic testing, recognize that the information provided you is less reflective of genetic variation than previously thought. Patients should understand that we have much to learn about genetic variation, and that our current methods for selecting individuals for genetic tests as well as test interpretation are far from perfect. Finally, if you are an educator, examine how you teach your students and trainees to think about approaching the evaluation of patients – make sure that they understand what genomics is revealing about how genetic variation in individuals and in populations relate to one another. With a firm grounding and the current pace of genomic discoveries, they will likely be the generation that resolves the controversies surrounding the use of race and ethnicity in health care.