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Genomics and Health Care Disparities
The Role of Statistical Discrimination

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TEN YEARS AGO, 2 EVENTS OCCURRED THAT HAVE transformed biomedical research. In 2001, the draft sequence of the human genome was announced. One year later, the Institute of Medicine released "Unequal Treatment," the first comprehensive report on racial and ethnic health care disparities in the United States.[1] Although the report downplayed the contribution of genetics to disparities, enthusiasm about the human genome spread rapidly to disparities research, creating a new field focused on translating knowledge of human genetic variation into reductions in disparities in health and health care.[2] This Viewpoint examines the potential contribution of 2 pathways in this field—the identification of genetic variation as a cause of disparities and the reduction of clinical uncertainty and statistical discrimination. The terms *race* and *ethnicity* are used to mean socially determined, generally self-reported, categories.

A common hypothesis is that advances in human genomics will reduce disparities by identifying genetic causes of disparities.[2] In support of this hypothesis, racial and ethnic differences in genetic variant frequency have been demonstrated for many diseases. However, translating this evidence into reductions in disparities has proven challenging for several reasons. First, many variants identified have a small attributable risk and explain little of the disease burden in any group, either because of a weak association between variant and disease or because the variant is rare in the population. Second, far more genetic variation occurs within racial or ethnic groups than between groups,[3] and disease-associated variation has no apparent predilection for the 4% to 8% of variation that can be linked to race or ethnicity.[4] Thus, if genomic variation explains a minority of most diseases and is unlikely to be linked to a racial or ethnic group, it becomes unlikely that genomic variation between groups will be a substantial cause of disparities in most common diseases. Third, developing interventions based on this information is challenging. Although prenatal or even premarital genetic screening can reduce the burden of severe diseases if screening influences reproductive decision making, lack of acceptance of these approaches has limited their effectiveness. For other diseases, knowledge of genetic risk factors should increase the ability to target preventive interventions to high-risk individuals. However, the limited effect of genomics on risk prediction for many diseases combined with the relative paucity of effective preventive interventions for some diseases has limited the benefit of such an approach.

Another pathway by which genomics may reduce racial disparities that has received considerably less attention is its effect on clinical uncertainty and statistical discrimination. The need to make decisions under conditions of uncertainty is one of the hallmarks of medicine. This uncertainty arises on 2 levels. For many decisions, there is no credible and consistent evidence about risks and benefits of different interventions. Moreover, even when evidence exists, uncertainty arises about the effect of that evidence on the individual patient. The gap between the average effect in a population and the effect in a specific patient can be substantial, in part because of differences between patients in practice and trial participants and in part because the average effect in a trial masks substantial variation among trial participants.[5]

Under conditions of uncertainty, 2 situations may lead to racial disparities in care. First, clinical decisions become dependent on heuristics, stereotypes, and biases. Although heuristics, or decision shortcuts, can lead to cognitive errors, the real risk of disparities arises from stereotypes and bias.[1] Stereotypes assign characteristics to an individual based on assumptions about group affiliation. Minority stereotypes in the United States may have negative connotations, including beliefs that minorities are less adherent with treatment, less interested in numerical data, or less willing to travel for care.[1] When these negative stereotypes influence decisions, disparities arise. For example, a study of diabetic treatment found that disparities by race and ethnicity were explained in part by differences in clinician beliefs about patient self-management abilities and family competence.[6]

Second, even in the absence of bias and stereotypes, clinical uncertainty can lead to disparities in health care through

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a phenomenon termed *statistical discrimination*. Although one form of statistical discrimination arises from assigning an individual the characteristic of the group, another form arises from greater uncertainty about one group than another. In health care, poor communication between physicians and minority patients may lead to greater uncertainty about the probability that a minority patient has a certain diagnosis or will respond to a certain treatment. In this setting, physicians are less able to "match" treatment to a patient's specific situation, and the patient is less likely to receive appropriate treatment. If the treatment is risky or has a limited benefit, clinicians become less certain that a minority patient meets the treatment threshold and are less likely to recommend treatment.

Reducing clinical uncertainty is an important focus for efforts to reduce disparities. For the first level of uncertainty, this effort requires gathering evidence about clinical effectiveness and translating that evidence into population guidelines. The recent reductions in racial disparities in influenza vaccination and cervical cancer screening have coincided with the widespread acceptance of population-based guidelines for these low-risk interventions.[7] However, for most decisions, information is also needed to address the second level of uncertainty, translating evidence of "average" effectiveness to the individual patient. It is this level of uncertainty for which genomics may have the greatest effects on disparities.

Genomics can reduce uncertainty about the translation of population evidence to individual patients in 3 ways. First, the development of genomically targeted therapies ties the treatment decision to the results of a test for a specific genetic alteration in an individual patient, reducing uncertainty about who should be treated. Second, pharmacogenomics enables prediction of drug response from information about variation in metabolizing enzymes. For example, the decision about pharmacotherapy for depression is difficult because identifying who will benefit from a medication is challenging. This uncertainty may explain, in part, racial and ethnic disparities in depression treatment, despite similar medication effectiveness across groups.[8] However, increasing evidence links response to different classes of antidepressants to genetic variation, which may eventually reduce uncertainty about who should receive pharmacotherapy. Third, genomic information can be useful in risk prediction, including the size of expected benefit. For example, the decision about adjuvant chemotherapy for node-negative breast cancer remains difficult because of small absolute benefit and risk of adverse effects. Racial disparities in this setting are well described, despite similar benefit among minority patients.[9] Breast cancer gene expression profiles correlate with the risk of relapse among women with node-negative, estrogen receptor–positive disease and have been translated into a genetic test to guide decisions about adjuvant chemotherapy. As gene expression profiling reduces uncertainty about who should receive adjuvant chemotherapy,[10] the opportunity for statistical discrimination to influence the treatment decision will also decline.

Over the last decade, the relationship between genomics and disparities has become a national research endeavor. Although genetic variation among racial and ethnic groups has been widely demonstrated, the most effective approach for harnessing genomics to address racial disparities may come from focusing outside the race question. Advances in genomics offer the ability to improve clinical decision making, particularly in settings where uncertainty is high and statistical discrimination, including the use of stereotype and bias, is likely to occur.

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