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Physician knowledge of human genetic variation, beliefs about race and genetics, and use of race in clinical decision-making.

Sherrill L. Sellers, PhD [Professor],

College of Education, Health & Society, Miami University, 210 E. Spring Street, Oxford, OH 45056, Office: 513-529-2340, slsellers@miamioh.edu

Brooke Cunningham, MD PhD [Assistant Professor], and

Department of Family Medicine and Community Health, University of Minnesota Medical School, 717 Delaware Street Se, Rm 420, MMC 381, Minneapolis, MN 55414, Office: (612) 624-7244, bcunning@umn.edu

Vence L. Bonham, JD [Associate Investigator]

Social and Behavioral Research Branch, National Human Genome Research Institute, National Institutes of Health, 31 Center Drive Room B1B37-G, Bethesda, MD 20892, Office: (301)594-3973, bonhamv@nih.gov

Abstract

Background: Race in the United States has an enduring connection to health and well-being. It is often used as a proxy for ancestry and genetic variation, although self-identified race does not establish genetic risk of disease for an individual patient. How physicians reconcile these seemingly paradoxical facts as they make clinical decisions is unknown.

Objective: To examine physicians' genetic knowledge and beliefs about race with their use of race in clinical decision-making.

Design: Cross-sectional survey of a national sample of clinically active general internists.

Results: 787 physicians completed the survey. Regression models indicate that genetic knowledge was not significantly associated with use of race. However, physicians who agreed with notions of race as a biological phenomenon and those who agreed that race has clinical importance were more likely to report using race in their decision making.

Conclusions: Genomic and precision medicine holds considerable promise for narrowing the gap in health among racial groups in the US. For this promise to be realized, our findings suggest that future research and education efforts related to race, genomics, and health must go beyond

Corresponding author: Sherrill L. Sellers, Professor, College of Education, Health & Society, Miami University-Oxford, OH. slsellers@miamioh.edu.

Compliance with Ethical Standards:

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educating healthcare providers about common genetic conditions to delving into assumptions about race and genetics.

Keywords

race; genetics; clinical decision-making; physicians

Introduction

Genomic research discoveries will advance the science of precision medicine as innovations lead to better diagnostics, more effective individual therapeutic strategies, and improved clinical decision making tools [1–3]. Researchers' ability to define the role of genetic variation in human disease is growing at an ever-accelerating pace, and genomics is quickly becoming incorporated into some health care services, (e.g. cancer tumor genomic sequencing can inform responses to immunotherapy and genotyping CYP2C19 variants can guide antiplatelet treatment) [4–6]. Further, genomic studies have documented that genetic variants often vary in frequency across ancestral populations [7–9]. However, the correlations between race and genetic variation are imperfect, meaning that not every member of a racial group has the same alleles and everyone with a particular genetic marker does not belong to the same race or ethnic group [10–12]. Thus an individual's race or ethnicity can be flawed surrogates for genetic factors associated with disease causation, disease severity, or course of illness, including drug response [13–17].

Nonetheless the social consequences of race on health are well documented [18, 19]. For example, in the past two decades, hundreds of studies have demonstrated that Blacks receive lower quality medical care than Whites, independent of disease status, setting, insurance, and other clinically relevant factors [20]. While, racial categories have considerable social consequences, scientists disagree on how they think about race, use the concept, and communicate race-related concepts to the public [21].

It may be difficult for providers to reconcile these seemingly paradoxical facts: that genetic differences (i.e., genetic variants) vary in frequency between racial and ethnic population groups and information about a patient's ancestral background can inform genetic basis of disease risk [22]. Yet self-identified or perceived race and ethnicity cannot be used to accurately define an individual's genetic ancestral background, disease risk, or course of illness.

Little is known about how providers navigate the complex and rapidly changing scientific knowledge of race, genetic variation, and health. Given that race does not consistently predict whether an individual will have a particular genetic variant that increases risk of a disease [23], health care providers who know more about genetic variation may be less likely to use race in their medical decision making. Conversely, genetic knowledge may increase providers' use of race, given the growing number of research studies that have identified risk loci associated with common diseases and different frequencies of therapeutic response associated with different racial groups [24–26].

This paper examines associations of physicians' knowledge of genetic variation, beliefs about race and genetics, and self-reported use of race in clinical decision-making. We explore two questions: 1) does knowledge of genetic variation influence use of race in clinical decision making? and 2) do beliefs about the biological and clinical value of race influence the use of the race in clinical care?

Methods

Sample

The "Health Professionals Genetics Education Needs Exploration" (HP GENE) survey was developed through focus groups, cognitive interviews, and pilot testing. HP GENE study received institutional review board approval from the National Human Genome Research Institute, National Institutes of Health. From April-December 2010, the HP GENE survey was administered via the web and mail to a national sample of clinically active general internists. The sample was drawn from the SK&A Company AMA Masterfile database. Physicians who were not currently practicing general internists according to their office staff or did not have a current United States mail address were excluded for an identified sample size of 1,738 eligible physicians. Informed consent was obtained from all participants included in this study. Of the 787 total completed surveys, 108 (13.76%) were completed and returned using the paper questionnaire. Analysis indicated no significant differences between mail and web respondents. The overall response rate for the survey was 45.35%.

Measures

The outcome was the Racial Attributes in Clinical Evaluation (RACE) scale. The RACE scale included items related to the use of race in determining genetic risk, medication choice, and how aggressive to be in treatment (alpha 0.86, 7 items). Items included "I consider my patients race when making decisions about which medications to prescribe" and "I consider my patients race in determining genetic risk for common, complex diseases (e.g. kidney disease or diabetes)" [27]. The item response categories were on a 5-point scale (4=all of the time to 0=none of the time). Responses were summed such that higher scores indicated greater self-reported use of race in clinical practice. Bonham and Sellers developed the RACE scale as a tool to measure health care providers' use of race in clinical care, without applying any value-laden assessment of the benefit or harm of its use [27].

The first predictor variable was the Genetic Variation Knowledge Assessment Index (GKAI) [17]. The GKAI is a 6-item knowledge index that measures knowledge of human genetic variation and includes questions such as "There is more genetic variation within populations than between populations" and "Most common diseases, such as diabetes and heart disease, are caused by a single gene variant." The items were scored true/false, with a "don't know" category. "Don't know" was considered an incorrect response for analytic purposes. Scores for GKAI were obtained by summing the correct responses. Higher scores indicated a greater scientific knowledge of human genetic variation.

The second predictor was the Health Professionals Beliefs about Race (HPBR) scale. Beliefs were measured along two domains: beliefs about race as a biological phenomenon

(HPBR-BD) and beliefs about the clinical value of race (HPBR-CD). Items in the biological domain included, “Race is the best proxy clinicians have to identify genetic effects on health” and “A patient’s race provides important information about a patient’s risk of disease.” Items in the clinical value domain included, “A patient’s race can identify patients who can benefit from enhanced screening for certain diseases” and “A patient’s race can identify patients who can benefit from referral to genetic services for certain diseases.” The items were rated on a 5-point scale (5= strongly agree to 1=strongly disagree), with the unsure category coded as a midpoint. Higher scores indicate greater beliefs about relationships between genetics and race. The correlation between HPBR-BD and HPBR-CD is .58 and the two constructs satisfy discriminant validity [27, 28].

The correlation between HPBR-BD and HPBR-CD and the GKAI is .073 and .068 respectively. The correlation between HPBR-CD and GKAI was not significant. While the correlation between HPBR-BD and GKAI is just significant at the .05 level ($p=.045$). More information about scale development can be found in previous publications [27, 28].

Analysis

Multivariate linear regression was used to examine associations of knowledge (GKAI), and beliefs (HPBR-BD and HPBR-CD) with use of race, adjusting for potential confounders. Controls tested for entry into the model were in three categories: 1) physician demographics (age, gender, race, and nativity); 2) physician medical training and clinical experience (years in practice, training (MD or DO), practice area, genetic training, and views about relevance of genetics); and 3) practice characteristics (sex and race/ethnicity distribution and insurance mix of patient panel).

We identified the set of control variables that had statistically significant associations with the outcome ($p<0.20$ criterion) after controlling for other statistically significant control variables in a multivariate stepwise regression model, using backwards elimination with forward checking. Using this process, the model controlled for physician age (in years), nativity (US vs. foreign born), years in practice, internal medicine as a practice area, genetic training during residency, views about relevance of genetics in current clinical practice, MD vs. DO degree, and race/ethnicity distribution of patient panel. Although race of physician was not statistically significant, given the topic under investigation, we added race of physician to the regression model.

Results

Table 1 presents the univariate statistics for variables include in the final model.

Mean age of the respondents was 48.60 years (SD 9.69; Min 29; Max 87). 71% were born in the United States. 67% of the sample was white, non-Hispanic. Respondents had been in practice an average of 16.91 (SD 9.75) years since completing residency. 87% responded that general internal medicine best described their specialty. 11.3% of the respondents indicated that they receive genetics training during their residency training and 71.8% believe that genetics has relevance in their clinical practice. Most (94.2%) held an MD.

Nearly three-quarters of respondents reported that over 20% of their patients served were racial/ethnic minority.

The mean score on RACE was 13.86 (SD=5.57; Min=0 Max=28), indicating that physicians in our sample were moderately likely to employ race in their clinical decision making processes. The mean score for the GKAI was 3.58 (SD=1.17; Min=0, Max=6), suggesting that respondents had a fair knowledge of human genetic variation. Mean score for HPBR-BD was 10.97 (SD=3.41; Min=4, Max=20), indicating respondents did not hold strong beliefs about race as a biological phenomenon. In contrast, respondents held comparatively stronger beliefs about the clinical value of race and genetic variation for understanding individual and group-level risk for disease, with a mean HPBR-CD score of 11.66 (SD=2.40; Min=3, Max=15).

Table 2 presents the regression model. Physician age was associated with RACE, with older physicians being more likely to use race in their decision making. Physician's self-reported race was not associated with use of race in clinical decision making. Physicians who were born outside the United States were more likely to use race than those born in the United States. Years of practice was not associated with RACE. Those who reported internal medicine as their specialty were more likely to use race compared to those in other specialties. Physicians training in genetics was not associated with RACE; although those who viewed genetics as relevant in their current practice scored higher on the RACE scale. MDs, compared to DOs, were less likely to use race in their decision making. Respondents whose patient panels were 20% or more racial/ethnic minority scored higher on the RACE scale.

No association was found between knowledge of human genetic variation and use of race in decision making. Both belief measures were related to RACE. Respondents who had higher biological belief scores and those who had higher clinical belief scores had higher scores on RACE. The predictors explained 39% of the variation in the model, and the model was statistically significant, F-value=38.49, p-value <0.0001.

Discussion

This study examined two questions related to knowledge and beliefs about race and genetic variation and use of race in decision making. For the first question, we found that knowledge of human genetic variation was not associated with use of race in clinical decision making. This finding is somewhat surprising. We expected that physician's use of race depended on their depth of knowledge and background about the relevance of genetics in human health. We thought that physicians with more knowledge of human genetic variation would use race less. This was not the case and suggests that other factors may influence using race in decision making.

In answer to our second question, we found that beliefs about the biological and clinical value of race were associated with use of race. Specifically, agreement with views about race as a biological phenomenon and about its clinical importance was associated with increased use of race. This finding suggests the need for additional research on role of racial beliefs in

clinical decision making. Greater knowledge about physicians' beliefs about race is important because these beliefs could result in inappropriate differences in clinical care. For example, there is a growing body of research that suggests even unconscious beliefs may contribute to racial disparities in health care [29–31].

The aforementioned helps address one puzzle related to our sociodemographic controls. Although physician's race was not significantly associated with use of race, having a larger minority patient panel was. This finding suggests that participants in this study find that race is still important in helping to identify patients that may be at increased risk for disease, poorer outcome, or lack of response to treatment. For example, there are recommendations to screen patients differently by race for colon cancer, to treat hypertension differently in African-Americans and Whites, and discussion about using different lab cutoff to diagnosis diabetes for different racial groups. These recommendations by expert groups to diagnosis and treat disease differently in different racial groups may explain why physician's race was not significantly associated with use of race [32–36].

Race can be important in understanding social identity, life experiences, and disease risk of a patient. Race also can be used to stereotype a patient's social identity, life experiences, and disease risk. Race can provide information about a patient's genetic ancestry and genetic disease risk. Self-reported and perceived race may not correlate with a patient's genetic ancestry. Race must be used cautiously and based upon an understanding that the concept is fluid and based upon political and social constructs. A similar caution must be considered in the use of genetic ancestry which is based upon how populations are defined (e.g. continental geographic, country, ethnic group). The linkages between self-identified race, genotype, and health are inexact.

Race is not a biological absolute, but instead is a complex set of categories that are produced and reproduced historically, socially, and politically [37,38]. These categories change over time and differ across locale. Although race is not a biological absolute, it has an enduring connection to health and well-being, morbidity, and mortality [39]. Racial disparities in health persist across time despite changes in diseases, improvement in health care delivery, and advancement in our knowledge of salubrious health-related factors. These disparities persist independent of socioeconomic status (SES) [39–41]. Given this complexity, it is important to understand the use of race and genetic ancestry in medical training [42]. An over-reliance on race may lead physicians' to make assumptions about patients' social circumstances. Our findings indicate that it is important to examine beliefs about race as one of several characteristics below the surface of the clinical relationship [43–49].

Limitations

Self-report is an imperfect method of assessing complex psychosocial constructs. The limitations of self-reported items are well-known, including recall bias, over- and under-reporting, and social desirability bias. We measured self-report of a practice behavior (i.e., use of race), adding another level of abstraction. Additionally, the discourse about race in general, and race and genetics in particular, can be contentious. We do not know how the general social milieu might have influenced survey responses. Also, our design was cross-

sectional which limits the ability to draw causal inferences. We do not know, for example, whether a stronger belief about the association between race and genetics leads to greater use of race in clinical practice or vice versa. Last, the response rate reduced statistical power and may have limited generalizability of the study findings. Although the response rate is not uncommon in physician surveys [50, 51] and additional analysis shows the similarity of the demographics between the sample and the AMA database of physicians [27], this limitation speaks to the need for further research with larger more representative samples.

Conclusion

This study makes several important contributions. There is a paucity of literature regarding how health care providers understand and use information about race and genetics in their clinical decision-making. To our knowledge, this study is one of the few to report empirical data of physicians' knowledge and beliefs about relationships among race, genetic variation, and disease, and their use of race in clinical decision-making.

Physicians often link race to genetics and, despite ongoing debates about the appropriateness of doing so, diagnostic tests continue to be developed and approved that use race [52]. The promise of the genomic era is "precision medicine," which routinely will tailor prevention and treatment strategies to a person's individual genome [53]. Some question whether this tailoring will end the use of race in clinical decision-making [54], yet this remains uncertain, particularly because this study suggests physician use of race as an heuristic, rather than knowledge of genetic variation, play a central role in the use of race.

Genomic medicine will impact health care delivery, but its transformative potential may be limited by pre-existing beliefs. Although the relationship between beliefs and knowledge needs to be future explored, our findings suggest that future research and education efforts related to race, genetics, and health must go beyond simply educating healthcare providers about common genetic conditions to delving into assumptions about race and genetics. Places to start include the re-examination of common practice, such as reporting laboratory test results by race; and requiring authors to state explicitly their hypotheses about the ways in which race influences health in research articles. Further, educating health professionals about "race" will require instruction in the history and sociology of race in the medical curriculum. Although race is a social construct, it is still important in helping to identify patients that may be at increased risk for disease, poorer outcome, or lack of response to treatment [55].

Clearly, neither race, ethnicity, nor genomics are comprehensive predictors of an individual's health. Health is multifactorial, influenced by genomics, personal behavior and choices, the environment in which a person lives, and the resources available to maximize one's opportunity for a good outcome (e.g., quality of schools, access to high quality health care, income and wealth). Advancing health equity will require balancing the promise of genomic sciences with the realities of contemporary racial hierarchies [56].

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TABLE 1.**Sample Characteristics**

Physician's Demographics	
US Born (%)	70.9
Self-reported Race (%)	
White, non-Hispanic	67.14
Minority	32.86
Physician Medical Training & Clinical Experience	
Years in Practice [mean (SD)]	16.9 (9.8)
Internal Medicine (%)	87.0
Current Genetics Has Relevance (% Agree)	71.8
Had Genetics Training in Primary Specialty Residency (%)	11.3
Type of Degree (%)	
MD	94.2
DO	5.8
Patient Panel Over 20% Minority (%)	74.0
Outcome & Key Predictors	
RACE [mean, (SD)]	13.8 (5.6)
Knowledge Score [mean (SD)]	3.6 (1.1)
Biological Beliefs [mean (SD)]	11.0 (3.4)
Clinical Beliefs [mean (SD)]	11.7 (2.4)

TABLE 2.

OLS Regression Analysis Associations of Physician Knowledge of Genetic Variation and Beliefs about the Biological and Clinical Importance of Race with Use of Race in Clinical Decision-making.

	(b) [†]	(se)
Physicians' Demographics		
Age	0.111 *	0.046
Self-reported Race: White, non-Hispanic vs. Minority	-0.517	0.444
US Born vs. Foreign Born	-1.178 **	0.403
Medical Training & Clinical Experience		
Years in Practice	-0.076	0.046
Internal Medicine Specialty vs. Other Fields	1.422 **	0.518
Genetic Training in Residency vs. No Genetic Training	0.775	0.541
Current Genetics Relevance: Disagree vs. Agree	0.697 ***	0.137
MD vs. DO	-2.354 **	0.804
Patient Population: Greater than 20% Minority vs. Less than 20% Minority	1.079 **	0.394
Knowledge	0.085	0.157
Biological Belief	0.509 ***	0.056
Clinical Belief	0.725 ***	0.078
Intercept	-2.379	2.246

R-squared for this model= 0.391; F-value=38.49, P-value <0.0001

[†] coefficient gives the change in the RACE score for every 1 unit increase (e.g. every additional point in score for biological beliefs) or between the indicated group and reference group (e.g. genetic training in primary residency vs. no genetic training).

* P<0.05,

** P<0.01,

*** P<0.001