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Advancing Genomic Research and Reducing Health Disparities: What Can Nurse Scholars Do?

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Abstract

Purpose—Advances in genomic research are improving our understanding of human diseases and evoking promise of an era of genomic medicine. It is unclear whether genomic medicine may exacerbate or attenuate extant racial group health disparities. We delineate how nurse scholars could engage in the configuration of an equitable genomic medicine paradigm.

Organizing Construct—We identify as legitimate subjects for nursing scholarship the scientific relevance, ethical, and public policy implications for employing racial categories in genomic research in the context of reducing extant health disparities.

Findings—Since genomic research is largely population specific, current classification of genomic data will center on racial and ethnic groups. Nurse scholars should be involved in clarifying how putative racial group differences should be elucidated in light of the current orthodoxy that genomic solutions may alleviate racial health disparities.

Conclusions—Nurse scholars are capable of employing their expertise in concept analysis to elucidate how race is used as a variable in scientific research, and to use knowledge brokering to delineate how race variables that imply human ancestry could be utilized in genomic research pragmatically in the context of health disparities.

Clinical Relevance—In an era of genomic medicine, nurse scholars should recognize and understand the challenges and complexities of genomics and race and their relevance to health care and health disparities.

Keywords

Genomic medicine; concept analysis; knowledge brokering; racial categories; health disparities

Health care has largely been driven by developments in biomedical research and technology. Now genomic research is evoking promise of an era of genomic medicine (Doer & Eng, 2012; Green & Guyer, 2011). Genomic medicine incorporates traditional assessment methods, genotyping, and genomic evaluations in predicting disease risk and treatment outcomes. Genomic medicine is relevant to primary care (e.g., family history, risk assessment, and referral), secondary and tertiary care (e.g., risk assessment and

management), and public health (e.g., newborn screening). As novel genomic therapeutic and diagnostic technologies are incorporated into clinical practice, patients invariably will look to nurses for information when making decisions about their health. Because nurses have a vital role in incorporating genomic medicine across all aspects of the healthcare system (Calzone et al., 2010; Jenkins, Bednash, & Malone, 2011), the *Journal of Nursing Scholarship* recently published a series of articles with overviews of clinical genomics and pedagogic methods for incorporating genomics into nursing clinical curricula (Daark-Hirsch, Dieter, & Quinn-Griffin, 2011; Kirk, Calzone, Arimori, & Tonkin, 2011; Lea, Skirton, Read, & Williams, 2011; Williams et al., 2011).

Like most new technology, genomic medicine has social, ethical, and public policy implications that need robust public discourse. In this article, we identify a critical issue in current genomic research as an exemplar for this sort of scholarly engagement. The issue is the scientific relevance and sociopolitical implications for employing racial categories in genomic research in the context of extant health disparities. Unreflective ascriptions of racial categories could render problematic potential benefits of genomic research and may produce unintended boomerang effects that may undermine the successful clinical translation of genomic research. We review the discourse on race in genetic research, and illustrate how nurse scholars could deploy their disciplinary repertoire in concept analysis and knowledge brokering to engage the conundrum of racial identity in genomic research pragmatically, in the context of health disparities.

The Race Controversy in Genomic Research

Current genomic research emphasizes human differences and stratification of patient populations to indicate the genetic underpinnings of disease susceptibility, drug response, and health outcomes. The genomic research literature has a legacy of using race as a proxy for segmenting human populations (Race, Ethnicity, and Genetics Working Group, 2005). Race as a proxy for putative biologic differences began well before the emergence of genomic medicine. Race has long been built into the hypotheses and design of epidemiologic research and in clinical practice as a surrogate for disease risk factors. Yet in the genomic era, the use of race as a proxy for genetic relatedness is contentious because it touches upon the science and politics of race differences. Lee (2009) captured the essence of the problem at the nexus of genomic research and race when she stated that

Without major shifts in how researchers approach population differences in research practice, the much heralded brave new world of genomics may give way to a strangely reminiscent landscape that emboldens notions of racial biologies and oversimplifies understandings of genetic contributions to human health that could ultimately undermine the hopes for equity in healthcare. (p. 121)

The approval of the drug BiDil by the U.S. Food and Drug Administration (FDA) has increased the urgency to address the relevance, societal justifications, and implications of employing racial categories in genomic research in the context of extant health disparities (Krimsky, 2012; Rusert & Royal, 2011; Seguin, Hardy, Singer, & Daar, 2008). Hailed as the first ethnic drug, BiDil is designed and marketed for treatment of heart failure in African American patients only. However, a crucial issue is whether differential responses to drug treatment between racial groups, defined using ostensibly social categories, are attributable primarily to genetic differences. For much of the latter part of the last century, the concept of race was cast mainly as a social construct. In this traditional sense, race distinguishes between groups according to a mixture of physical characteristics (but mainly skin color), which also reflect ancestry and hence biology. In the paradigm case of BiDil, genomic medicine attributes differential response of the drug to genetic differences, using race as a proxy for yet-to-be-determined genes. This brings into sharp relief questions about possible

trajectories of genomic medicine (Pena, 2011). Will the identification of human molecular subgroups map onto current social categories of race and ethnicity? What role do race and ethnicity have on drug specificity? And how will genomic medicine contribute to a more equitable and rational healthcare landscape?

Two Perspectives on Race in Genomic Research

In the biomedical context, two conflicting perspectives on the utility of racial categories in genomic research are available. One perspective denies a biological basis for race, while the other sees race as potentially meaningful biologically. The latter view is held mainly by geneticists who espoused scientific interest in race because of purported evidence of differences between races that are relevant to health status and disease susceptibility (Bowcock et al., 1994; Burchard et al., 2003; Calafell, Shuster, Speed, Kidd, & Kidd, 1998; Mountain & Risch, 2004). Epidemiologic surveys have consistently identified clusters of risk factors and a constellation of disease profiles that are aligned along racial designations. Several racial groups appear to be disproportionately affected by these clustering of risk factors and diseases. In the United States, these special populations include African Americans, Hispanic Americans, Asians and Pacific Islanders, and Native Americans. These researchers thereby support the use of race as a proxy for understanding racial groups' biological predispositions in biomedical research. Accordingly, they cited population genetics studies indicating significant genetic variations both within racial subpopulations and among the five main racial groups defined by continental ancestry. Two arguments are advanced: First, population genetics studies of indigenous groups from around the world have constructed ancestral-tree diagrams showing branching relationships among the various indigenous groups. Numerous types of genetic markers have been consistent in showing that the human population has major branches corresponding to the major racial groups, with subbranches within each racial group associated with indigenous groups (Burchard et al., 2003; Calafell et al., 1998). Second, analyses of genetic clusters have been applied to persons of diverse ancestry with a focus on human differences at multiple genetic loci. These analyses have also consistently resulted in the delineation of major genetic clusters that are associated with racial categories (Mountain & Cavalli-Sforza, 1997; Rosenberg et al., 2002; Stephens et al., 2001). Recently, the arguments validating racial categories in biomedical research do not claim that every person with these identities is included in these categories. Race rather aggregates populations with those social labels (Foster, 2009). Accordingly, racial populations represent differing genetic histories evidenced by high variability across populations in allele frequencies for some putative disease-associated gene variants. The presence of rare variants is identified in some populations and not others. Consequently, racial population histories can be important in designing genetic studies (Adeyemo & Rotimi, 2010).

The proponents (mostly social scientists), who deny any biological underpinning to race, view the concept as denoting historical, socioeconomic, and cultural experiences (Cooper, Kaufman, & Ward, 2003; Goodman, 2000). The enormous genetic diversity among any given racial group makes race an imprecise proxy for individuals' genotypes. Racially targeted therapies presume that the frequencies of genotypes that determine disease susceptibility or influence drug efficacy and response are meaningfully and predictably different for each race. But the science supporting this assertion is inconclusive. While not gainsaying the existence of genetic variants that are almost exclusively found in one racial group, which may give rise to important clinical differences, this alternative scientific perspective alludes to other gene variants that are differentially distributed among racial groups (e.g., 10% may have the variant in one group, 40% may have it in another group) as proof of genetic heterogeneity across racial groups. These proponents are skeptical of most methods for establishing race that are used in routine clinical practice, particularly with

genetics. They claim that the flux of human populations over time and the increasing admixture of genetic material between previously isolated racial groups make the link between “apparent race” and underlying genetics increasingly complex. In the United States, various estimates for the average percentage of non-African genetic material in African Americans range from 16% to 26%, while the amount of non-African genetic material in a person self-identifying as African American may range from 0 to 80% (Nebert & Menon, 2001). Studies of population admixtures in Brazilian and other South American populations show that many members have significant genetic material from three ancestral lines: White, Black and indigenous (Pena, Di Pietro, Fuchshuber-Moraes, Genro, & Hutz, 2011). Cluster analyses of people living in Africa show several genetically distinct clusters. A seminal study of African ethnic groups found most Ethiopians situated in a population group otherwise contained Norwegians, Armenians, and Ashkenazi Jews (Rosenberg et al., 2002). Human immigration has affected the worldwide distribution of sickle cell disease to increase the incidence of the disease in European countries that traditionally had experienced lower sickle cell disease prevalence (Lê et al., 2010).

Race-Based Medicine and Social Justice

The United States has disparities in healthcare accessibility, quality, and treatment provided for racial minority groups, which serves to cloud the discourse on race and genomic medicine. Race has underpinned group discrimination, prejudice, marginalization, and even subjugation. Many generations of researchers, under the guise of science, have tried to arrange human populations on the basis of geographical ancestry and ethnic or racial characteristics, and correlate human groups with behavior or intelligence. Now, racial and ethnic groups are being classified on the basis of genetic susceptibility to diseases or differential drug responses. Race often travels with discrimination in the United States, and diverse stakeholders are alarmed that race-based medicine such as BiDil reinforces false notions of racial biologies and oversimplifies public understanding of genomic contributions to human health. It could ultimately undermine the hope for equity in healthcare (Bowser, 2004; Rusert & Royal, 2011).

Still other stakeholders have embraced genetic explanations as underpinning health disparities for which a morally infused public policy response is warranted. They framed race-based genomic therapeutics in terms of social justice, redressing long-standing demands for science to attend to the health needs of racially disadvantaged groups (Kahn, 2005). The Association of Black Cardiologists co-sponsored the trial to test the efficacy of BiDil in treating heart failure in African Americans. The National Medical Association and the Black Congressional Caucus supported the drug’s approval by the FDA. Consequently, BiDil became more than a drug involved in the reduction of hypertension—it became a paradigm of race-based medicine deployed for redressing historical inequities in healthcare delivery.

The Stakes and Consequences of Race-Based Genomic Medicine

The United States has sizeable disparities in the incidence of many common diseases disproportionately affecting ethnic and racial minority populations (Kempel, Percy, & Wagener, 2002). Genetic factors are increasingly being examined in an effort to discern these racial and ethnic disparities in many common health conditions (White, Koehly, Omogbehin, & McBride, 2010). For example, recent genomic epidemiologic research suggests that common polymorphisms in a number of genes may increase genetic susceptibility to the harms of environmental exposures such as cigarette smoking and increase the risk for diseases such as lung cancer in ethnic minority populations (Liu, Zhou, & Christiani, 2005). Mechanic and colleagues (2007) have suggested that common genetic variations in TP53 may account for increased risk for lung cancer and worsened lung cancer

prognosis among African Americans. African Americans are also more likely than Whites to carry a less efficient DNA damage-induced G2-M checkpoint, which may be associated with an increased risk for lung cancer among African Americans (Zheng et al., 2005). In prostate cancer, differences in the expression profiles of immune-response genes is seen between tumors in African American and European American men and could have implications for utilization of immunotherapy treatment (Wallace et al., 2008). However, the extent to which self-identified racial minority individuals are assumed to be genetically predisposed to a remarkably high number of chronic diseases when few genetic data have been systematically analyzed and various social and environmental factors remain inextricably intertwined is particularly troublesome for some stakeholders (Gravelee, 2009; Kempel et al., 2002). Race as a proxy to guide clinical decisions may not be as accurate as direct assessment of both the genomic and environmental factors in predicting treatment (Bonham & Knerr, 2008). Healthcare practices that fixate on molecular and genetic differences as an explanation for racial disparities in health may also prematurely deflect attention from known social determinants of health: economic class, social conditions, and environmental factors, among others. With the BiDiL case, some Blacks with heart failure may individually benefit from BiDiL, but the Black community as a whole may suffer if this leads to an uncritical acceptance of the erroneous notion that differences in human genetic characteristics, their adherent social meanings, and racial disparities in health outcomes are observable at a molecular level.

Paradoxically, genomic “race-based” medicine could potentially exacerbate health disparities by increasing the already relatively high levels of distrust racial minority groups have toward the medical and scientific professions (White et al., 2010). The potential of race-based genomic medicine to increase health disparities in this way depends on public perception about race. Unreflective use of racial categories in reporting genetic findings could exacerbate both medical and popular misconceptions about genetic contributions to health disparities among racial groups. It could inhibit racial minority groups’ participation in genetic research. Racial minority groups are reported to be concerned about participating in research linking genes, race, ethnicity, and health outcomes. African Americans tend to hold low levels of belief about medications deemed to be effective specifically for African Americans. They also have high levels of suspicion regarding the safety and effectiveness of race-based medications (White et al., 2010). Thus, the moral claim that race-based medicine addresses extant injustices may inadvertently reinforce the notion in the public imagination that genomic medicine is a race-based healthcare delivery paradigm.

Racial categories will continue to serve as tools to explain differences in disease incidence and health disparities. In the United States, biomedical researchers are mandated to include racial and ethnic minorities in all federally funded research, and to use racial categories prescribed by the U.S. Office of Management and Budget. These socially and politically construed categories are fluid and subject to change in shifts of racial concepts. Critics argue that the mandated inclusion of racial and ethnic categories are rather vague yet encourage researchers to conflate racial and ethnicity identities with genetics. Guidelines that carefully promote reporting the basis of racial and ethnic variable classification in genetic research have been suggested (Bhopal, 2006; Kahn, 2006).

What Can Nurse Scholars Do?

The linchpin for the emergence of appropriate underpinnings of genomic medicine is for genomic research to identify putative human genetic factors across all human populations with the sensitivity and specificity to characterize genuine human dispositions for the purpose of guiding genomic medicine. However, the search for specific variables that cause clinically important differential findings among racial groups would require decades of

scientific research. The burgeoning genomic enterprise will continue to amass vast amounts of data on the molecular underpinnings of disease susceptibility and drug response. For the foreseeable future, classification of genomic data will center on racial and ethnic groups because genomic research is population specific. Therefore, it is imperative that we clarify how putative racial group differences should be elucidated in light of the orthodoxy that genomic-infused solutions may be available for racial health disparities. Undoubtedly, nurse scholars could join other stakeholders, including biomedical researchers, bioethicists, clinicians, and public policy analysts, in this important task. More specifically, nurse scholars could deploy their expertise in concept analysis to elucidate how race is used as a variable in scientific research and use knowledge brokering to delineate how race variables that imply human ancestry ought to be utilized in genomic research pragmatically in the context of health disparities.

Understanding the Race Variable Conceptually and Contextually

What race as an intellectual construct means or ought to mean in genomic research should be a subject for nursing scholarship. Concept analysis, an important tool in the nursing profession repertoire, could be deployed for this important task. There are two ways in which nurse scholars use concept analysis: theoretical and colloquial concept analysis (Risjord, 2009). Briefly stated, theoretical concept analysis makes explicit how certain concepts are represented in specific scientific literatures. Colloquial concept analysis characterizes the representation of certain concepts within specific groups. While colloquial concept analysis focuses on people, theoretical concept analysis focuses on literature. These two forms of concept analysis adduce different kinds of evidence and choice of methods in making patterns of concept usage explicit. Nurse scholars could then interrogate and document how racial variables are used among different scientific disciplines and how they are specified in scientific literatures. Concept analysis is the first step in clarifying patterns of usage explicit for critical analysis and reflection. Nurse scholars would examine the types of racial categories used in scientific investigations, disciplinary-specific practices for assigning racial categories, characteristics of racial categories, and interpretations of racial categories. The utility of concept analysis is problem clarification—a first step in the process of problem resolution.

Knowledge Brokering and Pragmatic Use of Race Variable

In an ideal world, specific genetic alleles and environmental history could be used to identify subgroups with clusters of clinical response to guide genomic medicine. The challenge for genomic research is specifying and weighting potential scientific benefits against the prospective social harms and risk of geneticization of specific populations when racial categories are used in biomedical contexts. Conceptual frameworks that could weigh the scientific benefits of population-specific genetics research against the potential risk of population geneticization could advance genomic medicine. However, because different stakeholders will argue for different ways of using genomic association as causation in accounting for the potential benefits and harms, the use of social identities in biological contexts is a critical space for knowledge brokering.

Knowledge brokering is an active process aimed at facilitating linkages between research, practice, and policy communities (Gerrish et al., 2011). A knowledge broker is an intermediary (Ward, House, & Hamer, 2009) who helps bridge activities linking diverse stakeholders, facilitating their interactions so that they are able to better understand each other's goals and professional culture, influence each other's work, forge new partnerships, and promote the use of research-based evidence in public policy decision making. Nurse scholars are equipped with appropriate skills to function as knowledge brokers in configuring the underpinnings of genomic research in the context of reducing health

disparities (Reutter & Kushner, 2010). The nursing profession has decades of experience dealing with the fragile relationship between the social identities and health disparities in scholarship and clinical practice (Giddings, 2005; Giger et al., 2007; Pesquera, Yoder, & Link, 2008; Smith, 2007). Nurse scholars are also aware of the dilemma of race, especially regarding the allocation of public goods and services (Harrison & Falco, 2005; Miller, 2007). Promoting equity in healthcare no doubt synchronizes well with the nursing profession's historical and ideological roots (Cohen & Reutter, 2007; Falk-Rafael, 2005).

Surveillance of Resource Allocation for Health Disparities and Genomic Research

Pragmatically, nurse scholars acting as knowledge brokers could influence how public dollars are assigned when race and genetics are posited as variables in major public health disparities research initiatives. Genetic research that ameliorates health disparities is considerably valuable. Therefore, researchers have often characterized the importance of their work in terms of advancing our understanding of health disparities. It has been suggested that researchers may overstate the potential benefits of their research, especially when the primary impetus for the research derives from the researcher's need to acquire increasing scarce scientific research dollars (Sankar, Cho, Condit, & Hunt, 2004). However, this suggestion has not been substantiated by empirical evidence.

Nonetheless, as knowledge brokers, nurse scholars could highlight the importance of including all the determinants of health (patients' social and genetic environment) in studies using genetic variations to unravel causes of health disparities among racial populations. Scientific review panels or technology assessment committees with nurse scholars could ensure that proposed genomic research studies aimed at ameliorating health disparities among disadvantaged racial groups are configured precisely in ways that are cognizant of the risks and benefits of geneticizing race. Unreflective use of racial identities may lead researchers to neglect other variables, such as socioeconomic, lifestyle, and environment factors, that may be important to variation in health disparities and are easily confounded with racial categories. Nurse scholars could highlight whether researchers reflectively weigh the potential scientific benefits against testable population-specific risks of geneticization when racial categories are used to recruit participants in genomic research. Nurse scholars could ensure that racial identities are treated as analytic categories and are explicitly qualified with respect to the criteria used to define racial characteristics, that the study samples are really representative of the larger racial populations, and that the scientific rationale for using these racial categories are made explicit. Nurse scholars should alert stakeholders to the nonbiological events and environmental forces that shaped the contemporary manifestations of the racial categories used in proposed studies (Foster, 2009; Knerr, Ramos, Nowinski, Dixon, & Bonham, 2010). As knowledge brokers, nurse scholars could ensure that the use of race in health disparities biomedical research be held to a high standard of proven efficacy and narrowly tailored and used only when better proxies such as specific genomic markers are not available. That is, racial categories should be used in genomic research when such categories have a high likelihood of successful prediction of disease risks or differential drug responses. In essence, nurse scholars would ensure that social responsibility and good science go hand in hand.

Conclusions

Genomic research endeavors and genomic medicine have brought to the fore the old debate on the biologic import of race. Current racial categories have associated liabilities in some ethnic and racial populations. A race-based genomic medicine paradigm may compound or attenuate racial group health disparities. A genomic revolution is in the making, and nurse scholars worldwide plus other stakeholders have time to help determine how best to harmonize the creative energies of genomic research in addressing health disparities. Nurse

scholars must engage our understanding of race and genetic variations within the context of health disparities. Health inequalities exist among defined racial groups in many societies, and potential health disparities are within the context of genomic medicine to require proactive attention. Promoting equity in health care has roots in the nursing profession's historical and ideological roots. Nurse scholars are positioned for leadership in reducing health disparities. This overarching mandate in the context of genomic healthcare requires nurse scholars to have a stake in how race (both social identity and human ancestry) ought to be used in scientific investigations. The type of data and their collection methods underpin such genomic studies, and the context of discoveries should be issues of nursing scholarship. This mandate's dual approach is first to understand how biomedical researchers conceptualize, interrogate, and incorporate race into their scientific investigations, and second to bring the nursing disciplinary repertoire to broker critical pathways in which clinical translation of genomic research could evolve an equitable genomic healthcare landscape.

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Clinical Resources

- American Anthropological Association. About RACE: A Public Education Project. <http://www.aaanet.org/resources/a-public-education-program.cfm>
- New England Journal of Medicine Series on Genomic Medicine. <http://www.genome.gov/27541912>
- Practical Approach to Teaching Genomics for Primary Care APNs: Web Genomic Resources for APN Educators. http://www.medscape.com/viewarticle/740623_sidebar1