Published in final edited form as:

AJOB Prim Res. 2012 ; 3(4): 87–97. doi:10.1080/21507716.2012.717339.

What are our AIMS? Interdisciplinary Perspectives on the Use of Ancestry Estimation in Disease Research

Joon-Ho Yu, MPH PhD,

Senior Fellow, Department of Pediatrics, School of Medicine, University of Washington, Box 356320, 1959 NE Pacific St. HSB RR349, Seattle, WA 98195, joonhoyu@u.washington.edu

Janelle S. Taylor, PhD,

Associate Professor, University of Washington - Anthropology, Seattle, WA, jstaylor@u.washington.edu

Karen L. Edwards, PhD, and

Professor, University of Washington - Epidemiology, Seattle, WA, keddy@u.washington.edu

Stephanie M. Fullerton, Dphil

Associate Professor, University of Washington - Bioethics & Humanities, Seattle, WA, smflrtn@u.washington.edu

Abstract

Background—Ancestry estimation serves as a tool to identify genetic contributions to disease but may contribute to racial discrimination and stigmatization. We sought to understand user perspectives on the benefits and harms of ancestry estimation to inform research practice and contribute to debates about the use of race and ancestry in genetics.

Methods—Key informant interviews with 22 scientists were conducted to examine scientists' understandings of the benefits and harms of ancestry estimation.

Results—Three main perspectives were observed among key informant scientists who use ancestry estimation in genetic epidemiology research. Population geneticists self identified as educators who controlled the meaning and application of ancestry estimation in research. Clinician-researchers were optimistic about the application of ancestry estimation to individualized risk assessment and personalized medicine. Epidemiologists remained ambivalent toward ancestry estimation and suggested a continued role for race in their research.

Conclusions—We observed an imbalance of control over the meaning and application of ancestry estimation among disciplines that may result in unwarranted or premature translation of ancestry estimation into medicine and public health. Differences in disciplinary perspectives need to be addressed if translational benefits of genetic ancestry estimation are to be realized.

Keywords

bioethics; continental population groups; interdisciplinary communication; translational research; genetics

INTRODUCTION

Ancestry informative markers (AIMs) are autosomal genetic markers used to probabilistically infer the genetic ancestry of individuals and groups (Shriver and Kittles 2004; Shriver et al. 1997). AIMs are used in the aggregate to infer genetic similarity among individuals, which often correlates with continental origins as well as U.S. racial and ethnic categories (Yang et al. 2005). While AIMs originally referred to a specific set of markers developed and named by the laboratory of Dr. Mark Shriver (Collins-Schramm et al. 2002; Shriver et al. 2003), the term is now generically applied to different sets of selected genetic markers chosen to estimate genetic ancestry or to conduct ancestry estimation (Bamshad et al. 2003; Barnholtz-Sloan et al. 2008; Kittles et al. 2002; Rosenberg et al. 2002). Marker-based ancestry estimation is used in both commercial ancestry tests (e.g., direct-to-consumer (DTC) genetic testing) and in the setting of genetic biomedical research (Royal et al. 2010).

Ancestry estimation has been criticized for its scientific validity and with regard to its potential to harm individuals and groups. Critics argue that ancestry estimation using AIMs in the DTC genetic testing market has limited ability to accurately infer heritage or racial or ethnic background (Bolnick et al. 2007; Davis 2007; Duster 2005; Lee et al. 2009).

Furthermore, the use of ancestry estimation in both commercial and academic settings has been criticized for promoting a biological understanding of racial and ethnic difference and health disparities that contributes to discrimination and stigmatization on the basis of racial and ethnic identity (Bolnick 2008; Bolnick et al. 2007; Caulfield et al. 2009; Davis 2007; Duster 2005; Duster 2006; Lee 2009; Sankar 2006; Weiss and Long 2009). A number of ethnographic studies of genetics disease research have described how ancestry-related practices ‘molecularize’ race from populations to genes to risk (Fujimura, Duster, and Rajagopalan 2008; Fujimura and Rajagopalan 2011; Fullwiley 2008; Montoya 2007).

In light of these concerns, the American Society of Human Genetics (ASHG) formed a task force on ancestry testing in 2007. The ASHG Ancestry Task Force first published a White Paper and then a subsequent longer review in the *American Journal of Human Genetics* recommending that geneticists should be more rigorous in their use of genetic ancestry estimation and that there should be broader scientific and societal discussion about DTC ancestry testing (Royal et al. 2010). Subsequently, the use of ancestry estimation in biomedical research has been described, by one Task Force member, as reflecting “typological rather than Darwinian thinking, raising important issues about the questions that are actually being asked” (Weiss and Long 2009). While this critique recognizes the potential social risks associated with the uses of ancestry estimation in research, it reframes these risks as related primarily to the proper conduct and clear public communication of science, thus implicitly accepting ancestry as ‘good science.’ So long as DTC ancestry testing continues to receive the lion’s share of concern, the potential for research uses of ancestry estimation to contribute to individual and group harms remain relatively unaddressed.

Potential harms must, of course, be considered in the context of established research benefits. Ancestry estimation has potential to aid discovery of genetic contributions to disease and to reduce statistical biases related to the analysis of samples of diverse genetic

backgrounds. Genome-wide assessment of ancestry has been used to identify regions of the genome that harbor disease genes, a strategy known as admixture mapping or mapping by linkage disequilibrium (Briscoe, Stephens, and O'Brien 1994; Darvasi and Shifman 2005; Dean et al. 1994; McKeigue 2005; Seldin 2007; Smith and O'Brien 2005). Ancestry estimation is also commonly used to reduce statistical confounding due to population stratification in genetic association studies (Barnholtz-Sloan et al. 2008; Hoggart et al. 2003; Pritchard and Rosenberg 1999; Pritchard et al. 2000; Rebbeck and Sankar 2005; B. Z. Yang et al. 2005; Ziv and Burchard 2003). The latter technique, in particular, is increasingly regarded as an essential feature of a well-designed study (Chanock et al. 2007).

The scientific benefits of ancestry estimation depend on translation across the disciplines that participate in the translational pathway (Burke et al. 2011; Burke et al. 2008; Maienschein et al. 2008). The analytical advantages of ancestry estimation are most often touted by those who develop AIMs and ancestry estimation methods (Halder et al. 2008; Nassir et al. 2009). The instrumental application (Klein 1990, 1996) of ancestry estimation to genetic epidemiology research (e.g., Aldrich et al. 2009; Kim et al. 2008; Tsai et al. 2005; Wang et al. 2010) requires that ancestry estimation be taken up by a broader community of users (Oudshoorn and Pinch 2003) and that these users exchange knowledge and practices between disciplines. For example, population genetic descriptions of ancestry must be transformed into "markers" of ancestral background best suited to identify and forestall epidemiological confounding. These statistical transformations must, in turn, be further reconfigured to make clear the clinical significance (and ultimate public health benefit) of specific genetic findings.

In this study, we chose to examine this set of interdisciplinary practices that intersect in the application of ancestry estimation to genetic epidemiological research and to explore how scientists with different disciplinary orientations understand the benefits and risks of using ancestry estimation in their work. Specifically, we focused analysis on two questions: First, what sorts of scientists interact in using ancestry estimation in genetic disease research? And second, how do specific disciplinary orientations impact perceptions of the benefits and risks of ancestry estimation? In asking these questions, we focus on the instrumental utility of ancestry and explore how that utility relates to various meanings of ancestry in different disciplinary contexts.

METHODS

Data Collection

This study involved key informant interviews with scientists using or considering using ancestry estimation, and participant-observation of research groups that employ ancestry estimation in their research. Participants were recruited from the authors of primary articles identified from the scientific literature on genetic ancestry estimation as well as through snowball sampling via introductions from interview participants.

Key informants were asked questions in three main domains: (1) the relevance of ancestry to their research; (2) their experiences with the use of AIMs to address population stratification; and (3) their understanding of ancestry, as well as race and ethnicity, more

broadly as categories of difference. These topics provided points of entry for open-ended discussions. In-person and telephone interviews conducted by JY ranged from 30 minutes to two hours in length and were audio-recorded and transcribed for qualitative analysis.

A subset of key informants' labs served as sites for follow-up participant observation. A subset of three sites were chosen because they involved investigators who use ancestry estimation to address confounding but are not otherwise involved in extensive development of ancestry estimation technology or methods (meaning that ancestry estimation was not the major focus of the participant's research), size of research group (because individuals working in isolation would provide limited opportunities for additional interviews/observations), and geographic diversity. Three sites were observed by JY for periods ranging from one to two weeks per site.

Additional participant-observation was conducted at three key national and international research meetings. These sites provided a view of how ancestry estimation was being used and discussed in different communities of researchers. In October 2007, JY attended and observed research presentations at the American Society of Human Genetics conference in San Diego, California. In 2008, JY attended the Annual Meeting of the American College of Epidemiology, for which the theme was the Dawn of Evolutionary Epidemiology. Finally, in 2008, JY also attended a meeting jointly convened by the National Human Genome Research Institute (NHGRI), National Cancer Institute (NCI), and National Center on Minority Health and Health Disparities entitled "Understanding the Role of Genomics in Health Disparities: Toward a New Research Agenda."

Data Analysis

Interview transcripts and field notes were coded for themes using Atlas.ti v.6.0. A constant comparison method of analysis was used in which data were reviewed as they were collected in order to identify emerging themes (Glaser 1965). Thus, the first five interviews were coded at the outset to learn if the interviews were soliciting desired information and to determine initial themes from the interviews. These results were then used to inform the remaining interviews and participant-observations, shape additional data collection, and refine the trajectory of inquiry. Not all topics were probed equally in every interview. In order to solicit more in-depth responses from participants, discussions focused on topics that the participant initiated or on which the participant was willing to elaborate.

Our analysis here focuses on responses related to disciplinary and interdisciplinary dimensions of ancestry estimation. In particular, we focus on participants' perceptions of the utility of ancestry estimation and their understanding of the relationship between race and ancestry in this context. A summary of codes pertaining to this analysis and their frequencies are described (see Supplemental Table 1:). Each group of coded quotations was evaluated for common themes and subthemes.

All aspects of this study were reviewed and approved by the University of Washington Institutional Review Board and informed consent was obtained from all participants.

RESULTS

Key informant interviews were conducted with 22 scientists who had used, or were considering using, AIMS to address population stratification in genetic association studies (Table 1). Of the 22 participants, 12 were identified through the scientific literature and 10 through snowball sampling. Participants were a mixture of senior, established investigators and recent investigators including one doctoral candidate and four post-doctoral fellows. An equal number of participants were male or female. Six participants were foreign-born and received a portion of their professional education outside of the United States.

Nine participants were asked if they would be willing to serve as field sites for this study – all agreed, three were observed. All three sites had at least one group of investigators actively using AIMS or other ancestry-based approaches in population-based studies of common conditions including stroke, heart disease, and diabetes; and more rare conditions including birth defects and pre-term birth. All three sites were working with data drawn from African-, Hispanic/Latino-, and European- American populations.

In this study, participants identified themselves primarily as population geneticists, epidemiologists, and clinician researchers, categories not exhaustive of all those who use ancestry estimation in research (for instance, one could also include biostatisticians). We consider these self-described categories as disciplines.

Participants used these categories to describe themselves and to distinguish different perspectives with regard to genetic ancestry estimation and its implications. Further, although the three research groups visited in this study were chosen based on their experience using ancestry estimation to address confounding by population stratification, all sites involved teams comprised of all three disciplinary elements among others. While a clinician-researcher might have also self-identified as a medical specialist (e.g., pediatrics), the role of a clinician-researcher, relative to population geneticists and epidemiologists, was most salient to these respondents use of ancestry estimation. The interactions between these disciplinary perspectives contribute to the practice of genetic epidemiology and play an important role in bringing meaning to perceived benefits and harms of genetic ancestry estimation.

A summary of our findings is presented below (see also Table 2).

Disciplinary migrants: Population geneticists among clinician-researchers

In some forms of interdisciplinary research, disciplinary “migrants” serve as agents who travel across disciplinary boundaries sharing knowledge and methods (Chubin 1976; Klein 1996). We found this to be the case in the practice of genetic epidemiology, in which junior investigators (defined in this study as those who had acquired faculty positions within the last few years or postdoctoral fellows still in training) often served as experts on genetic ancestry, whereas senior investigators (defined as Principal Investigators (PIs) and those who led research groups) were less experienced in the use of ancestry estimation. These junior experts were almost always trained in population genetics and were recently recruited into a clinically-oriented research group to provide their expertise on population structure

(i.e., patterns of genetic variation within and between populations) and to help clinical investigators conduct epidemiologic studies. These individuals, while clear about their training in population genetics, viewed themselves professionally as located in-between disciplines. As one key informant trained in population genetics explains:

And now I'm here and I'm still in this like intermediate position within genetic epidemiology and hard core population genetics... so for an epidemiologist I'm an ultra, ultra hard core (laughter) population geneticist that only cares about history and demography... and for population genetics I then like sell my soul to the devil and I'm collaborating on things related to disease. (Population geneticist, P10, 156:2)

Several study participants, trained in population genetics, had made a similar disciplinary transition through their postdoctoral training and were working in research groups lead by clinician-researchers. In this role, population geneticists often established the meaning of genetic ancestry and, for other lab members, possessed the dominant expertise on how one should use it. As they worked with their clinical research colleagues on genetic epidemiology studies, they served to educate clinicians on the applications of ancestry estimation to genetic association studies, as well as questions of racial difference. Population geneticists in this study often made a clear distinction between race and ancestry, wherein the utility of race is limited strictly to its surrogacy for genetic ancestry. As this population geneticist explains:

While I'm looking at race or ethnicity, and the answer is I'm actually looking at neither, I'm looking at your genetic ancestry. And that, in those terms, I'm only interested in the geography of where your genome came from. And as a scientist... I could care less how you define yourself. (Population geneticist, P40, 170:5)

Distinguishing between race and ancestry in this way was regarded as critical to many informants because one of the expressed benefits of using genetic ancestry in scientific research is to “move beyond” the use of race (Bonham, Warshauer-Baker, and Collins 2005) as a variable for stratification (Shields et al. 2005). Of course, moving beyond race also meant moving beyond the *controversies* that surround the use of race in genetics research. As one informant opined:

“I think we think ancestry has very different implications than race/ethnicity. Already there's a distinction when you say that. If I said genetic ancestry, I don't think it would be as controversial if I had said race/ethnicity” (Epidemiologist, P03, 149:8)

Other respondents believed ancestry to be less controversial in that “[r]ace has that nasty overhang to it” (Clinician-researcher, P31, 165:13) or because “race is a loaded term” (Population geneticist, P40, 170:7).

The desire to move beyond controversies associated with using race in genetics runs deep; some informants described genetic ancestry estimation as a strategy to actively eliminate race as a useful variable in genetic research. According to these informants, the scientific utility of ancestry over race, coupled with the controversy surrounding the use of race in genetics, effectively relegates race and ancestry to separate corners.

Clinician-researcher: enthusiastic, yet reliant on population geneticists

In contrast to population geneticists serving as analytical experts, clinician-researchers often served as principal investigators of research projects conducting genetic epidemiologic analyses, but had limited understanding of and direct experience with genetic ancestry or its estimation. These downstream users of ancestry estimation rarely conducted analyses of genetic data and relied on others with expertise in biostatistics and genome analysis. As one clinician-researcher put it, “it’s [ancestry estimation] a long stretch. The people that do this think about it very carefully, I mean this is just as big a sort of technique as doing genotyping” (Clinician-researcher, P31, 165:15). There are of course exceptions, and a few AIMS developers are themselves clinician-researchers, but the clinician-researchers we spoke with were often the most distant from the actual practices involved in using genetic ancestry in genetic epidemiology research.

While the clinical and public health applications and implications of ancestry testing remain under-developed (American Society of Human Genetics 2008; Royal et al. 2010), the clinician-researchers we spoke to expressed great expectations for genetic ancestry in healthcare. As an example:

As a clinician, I’m most excited about those [ancestry] results being brought into the clinic. A patient walks in, we could do a blood test to identify their ancestry and based on that predict, okay out of five drugs I could prescribe which one is likely to work best. You have [this disease] but how severe is it likely to be down the line based on your ancestry? What we need to do is correlate the ancestry data, other genetic marker data, medication history, and disease progression into one huge database, run the super computer and see which associations hold and that will help us with our clinical decision-making. (Clinician-researcher, P14, 160:11)

Notably, clinician-researcher participants in this study mostly took for granted the use of race in clinical decision-making and often used the terms race and ancestry interchangeably in our discussions. Accordingly, these participants viewed ancestry as relevant to medical practice in much the same way that race is often regarded as relevant. They cited ancestry as an indicator for follow-up genetic testing to avoid adverse drug responses, viewed genetic ancestry as a potential factor to consider in decisions concerning increased screening or monitoring, and conveyed the importance of considering ancestry to avoid missing a possible diagnosis, even as they voiced concerns about the prospect of patients bringing their DTC ancestry test results into the clinic. Almost all the possible applications identified by clinician-researchers in interview responses involved a direct substitution of genetic ancestry for race or ethnicity. The point is that clinicians with the greatest expectations for ancestry estimation were also perhaps the least well-informed; thus it is not surprising that clinicians involved in conducting genetic epidemiology studies reported relying on the expertise of population geneticists. From this perspective, the job of population geneticists is not only to provide expertise on genetic ancestry but more broadly to teach clinicians “how they should think about race” (Population geneticist, P05, 151:42).

Both clinician-researchers and their migrant population geneticist collaborators encountered challenges in their interdisciplinary exchanges. First, there were difficulties distinguishing

between an understanding of ancestry as a continuous variable and the prevailing typological understanding of race and ethnicity among clinician-researchers.

For [informant's clinical collaborators] to think of race as anything other than a bin is very, very difficult. Or my challenge is, so far is just to push the idea that it's continuum, you can't think of blacks and whites as two distinct bins. We need to take into account the inter-group variability, the within group variability. And that continuum that you might find when looking from one person to another, and I just run up against a block. (Population geneticist, P05, 151:14)

This conceptual barrier appeared to reflect a difference in the translational objectives of the two disciplines. As one population geneticist points out “ultimately, it all comes down to what I said right in the beginning – we [population geneticists] study populations but we [clinician-researchers] treat individuals” (P05, 151:41). This challenge involves deciding how to translate genetic ancestry-based information for medical care often organized along racial lines. As one clinician-researcher echoes, this “huge societal challenge between distinguishing between individuals and populations” (P02, 147:2) hinges on the relationship between ancestry estimation and racial identity. This translation depends on one's assumptions about the meaning of genetic ancestry and its practical utility for both one's research and clinical practice.

Epidemiologists' ambivalence toward genetic ancestry

The growing influence of ancestry estimation on the practice of genetic epidemiology is readily observed in the genetic association literature (Aldrich 2007; Chanock et al. 2007; McCarthy et al. 2008). The study of genetic ancestry as a population genetic question and its application to the problem of population stratification in the design of genetic association studies go hand in hand. The epidemiologists we spoke with discussed the application of, and methods involving, ancestry estimation with great interest. Epidemiologists who have traditionally focused on specific disease studies recognize a growing need to be better informed about ancestry and its implications for analysis of study samples.

Despite the clarity with which genetic ancestry estimation has been described as a useful tool for the practice of genetic epidemiology, we also found evidence that epidemiologists are ambivalent toward genetic ancestry and resist its wholesale substitution for race in genetic epidemiologic studies. Epidemiologists in our study, for example, reported feeling external pressure from funders to use genetic ancestry estimation to control for confounding but were concerned over additional genotyping costs. Thus, rather than assuming the relevance of ancestry estimation to their studies, several epidemiologists shared that they routinely conducted unpublished analyses “taking a look at” genetic ancestry profiles of their study populations, the correlation between genetic ancestry estimations and self-reported race, and exploring whether adjustment with ancestry estimates affected their results. While these practices sometimes make their way into publications, these internal checks were more often conducted to check the validity of self-reported race, determine the extent to which population structure may be present, and/or decide between using self-reported race or genetic ancestry in a publication. Possibly reflecting the controversial nature of some practices that equate genetic ancestry and race, participants expressed ambivalence

with respect to publishing ancestry estimation results or association results using ancestry estimation.

In addition to these practical concerns, epidemiologists' ambivalence toward ancestry estimation also appeared to reflect a belief that race is important not only in its use to delineate genetic background differences, but also on account of its value as a broad demographic variable with specific epidemiological meaning.

This is me as an epidemiologist, but I personally think self-report just does a wonderful job, I mean it captures so many ways of, you know, what we eat, and our culture and that sort of thing, and I just – something like genetic ancestry isn't going to tell us that. (Epidemiologist, P12, 158:19)

Thus, differences between population genetic and epidemiologic understandings of the meaning and utility of ancestry estimation relative to racial identity may involve different understandings of epidemiological knowledge and how it is produced. For example, uncertain interpretation of results from studies using genetic ancestry estimation was cited as a practical barrier to particular ancestry estimation practices. The challenge of interpreting the meaning of a principal component (i.e., a statistical transformation of genetic variation data) in the context of generating useful disease risk information was often cited as a reason for not using Principal Component Analysis (PCA)-based methods such as Eigenstrat (Price et al. 2006):

The high risk genotype with 5% higher Native American ancestry, that's meaningful whereas if I were using a principal components to adjust for it [said with indignation]? It's just an adjustment factor, there's no interpretation. You cannot interpret, really, principal components factors. "We included the first four factors, four principal component factors in our regression analysis to adjust for population stratification," that's about it. It has no meaning. So that's a disadvantage of a principal components analysis. The interpretation is very difficult. (Epidemiologist, P03, 149:29).

This concern has elicited at least one recent attempt to clarify the meaning of a PCA correction (Ma and Amos 2010). Furthermore, the meaning of a risk estimate when controlling confounding using ancestry can be misunderstood and misapplied to inform meta-analyses of variant-disease risk. In the passage below, one participant describes what he views as an instance in which epidemiologists misinterpret the results of a study for which ancestry adjustment has been conducted.

So epidemiologists look at this table which is a paper done by geneticists, epidemiologists see the risk and they put it in their table, they put it in their meta-analysis, and I'm like you can't put it in there. They don't listen to me and it's clearly not a comparable test to the others. Few people see it as another confounder that people adjust for and I see it as, it wasn't a test for risk, it was asking a specific question about the relationship between admixture and the variant. (Genetic epidemiologist, P01 146:11)

The concern expressed reflects a distinction between two different applications of ancestry estimation and subsequent interpretation of results. Per this informant's account, the

epidemiologists erroneously viewed these results as suggesting a valid association with ancestry when, in fact, the analysis was actually designed to learn if a signal between a particular locus and phenotype (identified through admixture mapping) could be attenuated with ancestry adjustment. The respondent is suggesting that this difference in interpreting results may be due to these epidemiologists' lack of familiarity with admixture mapping versus the more common practice of using ancestry estimation to reduce confounding due to population stratification. Ultimately, this potential for misinterpretation as well as the contingencies of ancestry estimation led this individual to question the utility of using ancestry in preference to race for controlling confounding due to population stratification.

DISCUSSION

This study demonstrates that disciplinary orientations and, practically speaking, scientific purposes are important considerations in understanding how and why scientists use ancestry in their research as well as what benefits and harms they anticipate from their use. All too often scholarship on race, ancestry, and genetics reduces to definitional debates across disciplines (Fullerton et al. 2010; Sankar 2008) – what IS race or ancestry, what counts in one category or the other? By taking an interdisciplinary perspective, the question shifts from what IS race and ancestry to what do scientists DO with race and ancestry? Prior conceptual and empirical investigations of race and ancestry in disease research have shown that the ways in which these phenomena are conceptualized can critically shape their application and use (e.g. Fujimura et al. 2011; Fullwiley 2008). In contrast, this analysis investigates what scientists do with ancestry and race in an effort to infer scientists' explicit and implicit understandings of these concepts. The utility of ancestry estimation depends on the scientific question at hand, the populations studied, and available genetic markers (Barnholtz-Sloan et al. 2008; Via, Ziv, and Burchard 2009). Thus, when asked whether and, if so, how one should use genetic ancestry estimation in research, epidemiologists in this study often gave a contextual response – “it depends.” For these users, the contingency of genetic ancestry lay not in its feasibility, but in its application. Yet, in this study we identified another dimension of this contingency – “It depends” on disciplinary purposes and perspectives.

The practice of ancestry estimation facilitates scientific work across disciplines and, in this context, serves to forge interdisciplinary research (Bowker and Star 1999). Yet, disciplinary misalignments are evident in the application of genetic ancestry to genetic epidemiologic research and suggest significant challenges for the ultimate translation of genetics for health benefit (Burke et al. 2008). In our sample, and presumably more broadly, population geneticists possessed the greatest authority over the meaning and application of genetic ancestry estimation. Population genetics has come to influence epidemiology practice in a variety of ways, including supplying ancestry estimation as the solution to the problem of confounding due to population stratification (Price et al. 2010). Population geneticists are also playing a greater role in clinical research collaborations as the role of genetics in common diseases has become a more important etiological research question. Conversely, clinician-researchers depend heavily on population geneticists to explain the relationship between race, ancestry, and genetics. In this way, ancestry-related research has perhaps been strengthened by collaborations between population geneticists and clinician-researchers, and

as a result, may have encouraged clinician-researchers' enthusiasm for ancestry estimation. This study suggests that this relationship inadvertently contributes to promoting a technical criteria fallacy (Veatch 1977) – population geneticists proffer genetic ancestry estimation as a technical solution to the controversial use of racial and ethnic categories in research, yet downstream users may not always appreciate the distinction.

Epidemiologists' ambivalence toward ancestry and resistance to its wholesale replacement of race in their investigations remains a point of unresolved tension. While some population geneticists seek to avoid race altogether in their genetic research, epidemiologists and clinician-researchers work to make sense of ancestry in the context of race and ethnicity. Thus, normative recommendations regarding scientists' use of ancestry estimation (and race) (Bolnick et al. 2007; Lee et al. 2009; Shields et al. 2005) may be tailored to different groups of users by extending robust critiques of scientific validity to consider how disciplinary commitments relate to scientists' understandings of the benefits and harms of ancestry estimation.

Regardless of the validity of genetic ancestry as an organizing principle for disease research, the epistemic authority (Knorr-Cetina 1999) of population genetics, as a discipline far removed from the application and translation of disease research for public health or clinical benefit, may unintentionally focus researchers' attention on genetic causes of disease without sufficient regard for how such knowledge is best integrated with environmental, behavior, or structural epistemologies to enable tangible public health and health care interventions. Of course, population genetics need not be so narrow in its emphasis and there are examples of interdisciplinary research efforts that integrate these epistemologies (Burke and Press 2011; Jackson 2008; Worsham, Divine, and Kittles 2011). However, some informants suggest that there is a great distance from bench-to-barrio, as suggested by the frank statement, "I don't care about public health, I care about genetics" (Population geneticist, P04, 150:15). While it is doubtful that these remarks are representative of all population geneticists or clinician-researchers, this distance does call for paying closer attention to the disciplinary locations of those who generate knowledge deemed relevant for public health and medical benefit.

This study contributes to the limited body of literature concerned with use of ancestry estimation in biomedical research (Fujimura and Rajagopalan 2011; Fujimura et al. 2010; Fullwiley 2008; Montoya 2006; Nelson 2008; Tutton et al. 2008). While much of this literature richly describes how genetic ancestry estimation re-inscribes a biological understanding of race, this study provides a different perspective by demonstrating how different disciplinary understandings of race relate to the purposes to which scientists use ancestry estimation in disease research. From this perspective, we find that race remains an important part of the patient-clinician interaction and continues to frame epidemiologic inquiry. Yet, while the importance of race has driven clinician-researchers to adopt ancestry estimation as a research practice, it has had a somewhat opposite effect on epidemiologists who continue to question the analytic substitution of ancestry for race. This focus better connects the ethical and social implications of ancestry estimation to efforts to translate genetics research for broad medical and public health benefit.

This translational perspective also reframes another important entrenched belief. Re-inscribing biological meaning to our understanding of race has been described as an unintended consequence of genetics research that links racial categories to ancestry estimation (Caulfield et al. 2009; Duster 2005; Race Ethnicity and Genetics Working Group 2005). In contrast, we find this to be a very intentional process as evidenced by clinician-researchers' enthusiasm for ancestry estimation and epidemiologists' insistence of the enduring utility of racial categories. While public health practitioners and healthcare providers currently make decisions based on ascribed racial and ethnic identities, increasingly they are encountering genetic information framed by genetic ancestry (Giri et al. 2009; Lonjou et al. 2006; Payne 2008; Yang et al. 2011). Ultimately, paying attention to these disciplinary relationships highlights the challenge of reconciling the external embodiment of racial ascription with the internal embodiment of genetic ancestry (Tayo et al. 2011). This is where bioethics and qualitative research has an important role to play in helping scientists reflect on their own social and professional contexts and to ultimately enable scientists to develop practices that are both epistemologically satisfying and socially responsible (Egalite, Ozdemir, and Godard 2007).

Several limitations also suggest cautious interpretation of these qualitative data. The most important is the possibility of response bias among informants who, given the stated intent of the study, provided what was perceived as socially or ethically acceptable responses. For instance, respondents may have interpreted questions pertaining to ancestry, race, and ethnicity as equating these three categories. It is possible that clinician-researchers' enthusiasm for ancestry estimation was simply a response to being interviewed about genetic ancestry or reflected a general enthusiasm for genomic medicine and the medical relevance of race (Bonham et al. 2009; Frank et al. 2010). We believe this is unlikely because migrant population geneticists often described how they had been recruited into clinical research collaboration to help educate clinician-researchers about genetic ancestry. Similarly, epidemiologists' ambivalence may also be questioned as a product of response bias, yet this cautious stance is consistent with epidemiologists' struggle to demarcate epidemiology as a discipline (Amsterdamska 2005).

The ASHG Statement on genetic ancestry testing points out not only the need for interdisciplinary perspectives to address the concerns that arise from commercial ancestry testing (Wagner 2010), but also a greater need for those using genetic ancestry in research to take heed of other disciplinary perspectives (Recommendation 4): "Scientists inferring genetic ancestry should consult or collaborate with scholars who have expertise in the historical, sociopolitical and cultural contexts needed to inform the processes and outcomes of their research and commercial efforts" (American Society of Human Genetics 2008). In order for these allied scholars to provide salient consultation, we suggest an additional need for bioethicists, especially those conducting empirical research that can guide the development of normative recommendations, to pay close attention to disciplinary differences in purpose and practice as they conduct research with science and scientists. Better understanding different disciplinary perspectives within communities of scientists—to identify exactly who is using technologies such as AIMS, GWAS, exome sequencing chips, etc., and why—will help us better locate putative sources of benefits and harms, and better target normative recommendations for maximum uptake and adherence.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

- Aldrich, MC. Genetic admixture in a lung cancer study of African Americans and Latinos. Berkeley: University of California; 2007. Ph.D. Dissertation
- Aldrich MC, Selvin S, Hansen HM, Barcellos LF, Wensch MR, Sison JD, Kelsey KT, Buffler PA, Quesenberry CP Jr, Seldin MF, Wiencke JK. CYP1A1/2 haplotypes and lung cancer and assessment of confounding by population stratification. *Cancer Research*. 2009; 69(6):2340–2348. [PubMed: 19276377]
- American Society of Human Genetics. Ancestry Testing Statement. 2008
- Amsterdamska, Olga. Demarcating Epidemiology. *Science, Technology, & Human Values*. 2005; 30(1):17–51.
- Bamshad MJ, Wooding S, Watkins WS, Ostler CT, Batzer MA, Jorde LB. Human population genetic structure and inference of group membership. *American Journal of Human Genetics*. 2003; 72(3): 578–589. [PubMed: 12557124]
- Barnholtz-Sloan JS, McEvoy B, Shriver MD, Rebbeck TR. Ancestry estimation and correction for population stratification in molecular epidemiologic association studies. *Cancer Epidemiology, Biomarkers & Prevention*. 2008; 17(3):471–477.
- Bolnick DA, Fullwiley D, Duster T, Cooper RS, Fujimura JH, Kahn J, Kaufman JS, Marks J, Morning A, Nelson A, Ossorio P, Reardon J, Reverby SM, TallBear K. Genetics. The science and business of genetic ancestry testing. *Science*. 2007; 318(5849):399–400. [PubMed: 17947567]
- Bolnick, Deborah A. Individual Ancestry Inference and the Reification of Race as a Biological Phenomenon. In: Barbara, Koenig; Sandra, Soo-Jin Lee; Richardson, Sarah, editors. *Revisiting Race in a Genomic Age*. New Brunswick, New Jersey, and London: Rutgers University Press; 2008. p. 70-85.
- Bonham VL, Sellers SL, Gallagher TH, Frank D, Odunlami AO, Price EG, Cooper LA. Physicians' attitudes toward race, genetics, and clinical medicine. *Genetics in Medicine*. 2009; 11(4):279–286. [PubMed: 19265721]
- Bonham VL, Warshawer-Baker E, Collins FS. Race and ethnicity in the genome era: the complexity of the constructs. *The American Psychologist*. 2005; 60(1):9–15. [PubMed: 15641917]
- Bowker Geoffrey, C.; Star, Susan Leigh. *Sorting things out : classification and its consequences*. of Inside technology. Cambridge, Mass: MIT Press; 1999.
- Briscoe D, Stephens JC, O'Brien SJ. Linkage disequilibrium in admixed populations: applications in gene mapping. *Journal of Heredity*. 1994; 85(1):59–63. [PubMed: 8120361]
- Burke, W.; Edwards, K.; Goering, S.; Holland, S.; Trinidad, S. *Making Good on the Promise of Genetics: Justice in Translation*. New York: Oxford University Press; 2011.
- Burke, W.; Press, N. What outcomes? Whose benefits? In: Burke, W.; Edwards, K.; Goering, S.; Holland, S.; Trinidad, S., editors. *Making Good on the Promise of Genetics: Justice in Translation*. New York: Oxford University Press; 2011. p. 162-176.
- Burke W, Kuszler P, Starks H, Holland S, Press N. Translational genomics: seeking a shared vision of benefit. *American Journal of Bioethics*. 2008; 8(3):54–56. discussion W1–3. [PubMed: 18570105]
- Caulfield T, Fullerton SM, Ali-Khan SE, Arbour L, Burchard EG, Cooper RS, Hardy BJ, Harry S, Hyde-Lay R, Kahn J, Kittles R, Koenig BA, Lee SS, Malinowski M, Ravitsky V, Sankar P, Scherer SW, Seguin B, Shickle D, Suarez-Kurtz G, Daar AS. Race and ancestry in biomedical research: exploring the challenges. *Genome Medicine*. 2009; 1(1):8. [PubMed: 19348695]
- Chanock SJ, Manolio T, Boehnke M, Boerwinkle E, Hunter DJ, Thomas G, Hirschhorn JN, Abecasis G, Altshuler D, Bailey-Wilson JE, Brooks LD, Cardon LR, Daly M, Donnelly P, Fraumeni JF Jr, Freimer NB, Gerhard DS, Gunter C, Guttmacher AE, Guyer MS, Harris EL, Hoh J, Hoover R, Kong CA, Merikangas KR, Morton CC, Palmer LJ, Phimister EG, Rice JP, Roberts J, Rotimi C, Tucker MA, Vogan KJ, Wacholder S, Wijsman EM, Winn DM, Collins FS. Replicating genotype-phenotype associations. *Nature*. 2007; 447(7145):655–660. [PubMed: 17554299]

- Chubin DE. The conceptualization of scientific specialties. *The Sociological Quarterly*. 1976; 17:448–476. Autumn.
- Collins-Schramm HE, Kittles RA, Operatio DJ, Weber JL, Criswell LA, Cooper RS, Seldin MF. Markers that discriminate between European and African ancestry show limited variation within Africa. *Human Genetics*. 2002; 111(6):566–569. [PubMed: 12436248]
- Darvasi A, Shifman S. The beauty of admixture. *Nature Genetics*. 2005; 37(2):118–119. [PubMed: 15678141]
- Davis DS. The changing face of “misidentified paternity”. *Journal of Medicine and Philosophy*. 2007; 32(4):359–373. [PubMed: 17712708]
- Dean M, Stephens JC, Winkler C, Lomb DA, Ramsburg M, Boaze R, Stewart C, Charbonneau L, Goldman D, Albaugh BJ, et al. Polymorphic admixture typing in human ethnic populations. *American Journal of Human Genetics*. 1994; 55(4):788–808. [PubMed: 7942857]
- Duster T. Deep roots and tangled branches. *Chronicle of Higher Education*. 2006 B13.
- Duster T. Medicine. Race and reification in science. *Science*. 2005; 307(5712):1050–1051. [PubMed: 15718453]
- Egalite N, Ozdemir V, Godard B. Pharmacogenomics research involving racial classification: qualitative research findings on researchers’ views, perceptions and attitudes towards socioethical responsibilities. *Pharmacogenomics*. 2007; 8(9):1115–1126. [PubMed: 17924827]
- Frank D, Gallagher TH, Sellers SL, Cooper LA, Price EG, Odunlami AO, Bonham VL. Primary care physicians’ attitudes regarding race-based therapies. *Journal of General Internal Medicine*. 2010; 25(5):384–389. [PubMed: 20174973]
- Fujimura JH, Duster T, Rajagopalan R. Race, genetics, and disease: questions of evidence, matters of consequence. *Social Studies of Science*. 2008; 38(5):643–656. [PubMed: 19227816]
- Fujimura JH, Rajagopalan R. Different differences: the use of ‘genetic ancestry’ versus race in biomedical human genetic research. *Social Studies of Science*. 2011; 41(1):5–30. [PubMed: 21553638]
- Fujimura, Joan H.; Rajagopalan, Ramya; Ossorio, Pilar N.; Doksum, Kjell A. Race and ancestry: operationalizing populations in human genetic variation studies. In: Whitmarsh, Ian; Jones, David S., editors. *What’s the use of race?: modern governance and the biology of difference*. Cambridge, Mass: MIT Press; 2010. p. 170-183.
- Fullerton SM, Yu JH, Crouch J, Fryer-Edwards K, Burke W. Population description and its role in the interpretation of genetic association. *Human Genetics*. 2010; 127(5):563–572. [PubMed: 20157827]
- Fullwiley D. The biological construction of race: ‘admixture’ technology and the new genetic medicine. *Social Studies of Science*. 2008; 38(5):695–735. [PubMed: 19227818]
- Giri VN, Egleston B, Ruth K, Uzzo RG, Chen DY, Buyyounouski M, Raysor S, Hooker S, Torres JB, Ramike T, Mastalski K, Kim TY, Kittles R. Race, genetic West African ancestry, and prostate cancer prediction by prostatespecific antigen in prospectively screened high-risk men. *Cancer Prevention Research*. 2009; 2(3):244–250. [PubMed: 19240249]
- Glaser BG. The constant comparative method of qualitative analysis. *Social Problems*. 1965; 12(4): 436–445.
- Halder I, Shriver M, Thomas M, Fernandez JR, Frudakis T. A panel of ancestry informative markers for estimating individual biogeographical ancestry and admixture from four continents: utility and applications. *Human Mutation*. 2008; 29(5):648–658. [PubMed: 18286470]
- Hoggart CJ, Parra EJ, Shriver MD, Bonilla C, Kittles RA, Clayton DG, McKeigue PM. Control of confounding of genetic associations in stratified populations. *American Journal of Human Genetics*. 2003; 72(6):1492–1504. [PubMed: 12817591]
- Jackson FL. Ancestral links of Chesapeake Bay region African Americans to specific Bight of Bonny (West Africa) microethnic groups and increased frequency of aggressive breast cancer in both regions. *American Journal of Human Biology*. 2008; 20(2):165–173. [PubMed: 18205202]
- Kim H, Hysi PG, Pawlikowska L, Choudhry S, Gonzalez Burchard E, Kwok PY, Sidney S, McCulloch CE, Young WL. Population Stratification in a Case-Control Study of Brain Arteriovenous Malformation in Latinos. *Neuroepidemiology*. 2008; 31(4):224–228. [PubMed: 18841030]

- Kittles RA, Chen W, Panguluri RK, Ahaghotu C, Jackson A, Adebamowo CA, Griffin R, Williams T, Ukoli F, Adams-Campbell L, Kwagyan J, Isaacs W, Freeman V, Dunston GM. CYP3A4-V and prostate cancer in African Americans: causal or confounding association because of population stratification? *Human Genetics*. 2002; 110(6):553–560. [PubMed: 12107441]
- Klein, Julie Thompson. *Interdisciplinarity: history, theory, and practice*. Detroit: Wayne State University Press; 1990.
- Klein, Julie Thompson. *Crossing boundaries : knowledge, disciplinarity, and interdisciplinarity. of Knowledge, disciplinarity and beyond*. Charlottesville, Va: University Press of Virginia; 1996.
- Knorr-Cetina, K. *Epistemic cultures : how the sciences make knowledge*. Cambridge, Mass: Harvard University Press; 1999.
- Lee C. Race” and “ethnicity” in biomedical research: How do scientists construct and explain differences in health? *Social Science and Medicine*. 2009; 68:1183–1190. [PubMed: 19185964]
- Lee SS, Bolnick DA, Duster T, Ossorio P, Tallbear K. Genetics. The illusive gold standard in genetic ancestry testing. *Science*. 2009; 325(5936):38–39. [PubMed: 19574373]
- Lonjou C, Thomas L, Borot N, Ledger N, Toma Cde, LeLouet H, Graf E, Schumacher M, Hovnanian A, Mockenhaupt M, Roujeau JC. A marker for Stevens-Johnson syndrome....: ethnicity matters. *Pharmacogenomics Journal*. 2006; 6(4):265–268. [PubMed: 16415921]
- Ma J, Amos CI. Theoretical formulation of principal components analysis to detect and correct for population stratification. *PLoS ONE*. 2010; 5(9)
- Maienschein J, Sunderland M, Ankeny RA, Robert JS. The ethos and ethics of translational research. *American Journal of Bioethics*. 2008; 8(3):43–51. [PubMed: 18570103]
- McCarthy MI, Abecasis GR, Cardon LR, Goldstein DB, Little J, Ioannidis JP, Hirschhorn JN. Genome-wide association studies for complex traits: consensus, uncertainty and challenges. *Nature Reviews Genetics*. 2008; 9(5):356–369.
- McKeigue PM. Prospects for admixture mapping of complex traits. *American Journal of Human Genetics*. 2005; 76(1):1–7. [PubMed: 15540159]
- Montoya, Michael J. *Chicano/Latino Studies Program*. Vol. 9. University of California: Irvine; 2006. Genetic Admixture: Diabetes and Mexican/a ethnicity: how inequity gets into and out of genetic science.
- Montoya, Michael J. *BIOETHNIC CONSCRIPTION: Genes, Race, and Mexicana/o Ethnicity in Diabetes Research*. *Cultural Anthropology*. 2007; 22(1):94–128.
- Nassir R, Kosoy R, Tian C, White PA, Butler LM, Silva G, Kittles R, Alarcon-Riquelme ME, Gregersen PK, Belmont JW, De La Vega FM, Seldin MF. An ancestry informative marker set for determining continental origin: validation and extension using human genome diversity panels. *BMC Genetics*. 2009; 10:39. [PubMed: 19630973]
- Nelson A. Bio science: genetic genealogy testing and the pursuit of African ancestry. *Soc Stud Sci*. 2008; 38(5):759–783. [PubMed: 19227820]
- Oudshoorn, Nelly; Pinch, TJ. *How users matter: the co-construction of users and technologies. of Inside technology*. Cambridge, Mass: MIT Press; 2003.
- Payne PW Jr. For Asians only? The perils of ancestry-based drug prescribing. *Journal of Law, Medicine & Ethics*. 2008; 36(3):585–588.
- Price AL, Patterson NJ, Plenge RM, Weinblatt ME, Shadick NA, Reich D. Principal components analysis corrects for stratification in genome-wide association studies. *Nature Genetics*. 2006; 38(8):904–909. [PubMed: 16862161]
- Price AL, Zaitlen NA, Reich D, Patterson N. New approaches to population stratification in genome-wide association studies. *Nature Reviews Genetics*. 2010; 11(7):459–463.
- Pritchard JK, Rosenberg NA. Use of unlinked genetic markers to detect population stratification in association studies. *American Journal of Human Genetics*. 1999; 65(1):220–228. [PubMed: 10364535]
- Pritchard JK, Stephens M, Rosenberg NA, Donnelly P. Association mapping in structured populations. *American Journal of Human Genetics*. 2000; 67(1):170–181. [PubMed: 10827107]
- Race Ethnicity and Genetics Working Group. The use of racial, ethnic, and ancestral categories in human genetics research. *American Journal of Human Genetics*. 2005; 77(4):519–532. [PubMed: 16175499]

- Rebbbeck TR, Sankar P. Ethnicity, ancestry, and race in molecular epidemiologic research. *Cancer Epidemiology, Biomarkers & Prevention*. 2005; 14(11 Pt 1):2467–2471.
- Rosenberg NA, Pritchard JK, Weber JL, Cann HM, Kidd KK, Zhivotovsky LA, Feldman MW. Genetic structure of human populations. *Science*. 2002; 298(5602):2381–2385. [PubMed: 12493913]
- Royal CD, Novembre J, Fullerton SM, Goldstein DB, Long JC, Bamshad MJ, Clark AG. Inferring genetic ancestry: opportunities, challenges, and implications. *American Journal of Human Genetics*. 2010; 86(5):661–673. [PubMed: 20466090]
- Sankar P. Hasty generalizations. *New Genetics and Society*. 2006; 25(3):249–264.
- Sankar, Pamela. Moving beyond the two race mantra. In: Koenig, Barbara A.; Soo-Jin, Sandra Lee; Richardson, Sarah S., editors. *Revisiting race in a genomic age*. New Brunswick, NJ: Rutgers University Press; 2008. p. 271–284.
- Seldin MF. Admixture mapping as a tool in gene discovery. *Current Opinion in Genetics and Development*. 2007; 17(3):177–181. [PubMed: 17466511]
- Shields AE, Fortun M, Hammonds EM, King PA, Lerman C, Rapp R, Sullivan PF. The use of race variables in genetic studies of complex traits and the goal of reducing health disparities: a transdisciplinary perspective. *The American Psychologist*. 2005; 60(1):77–103. [PubMed: 15641924]
- Shriver MD, Kittles RA. Genetic ancestry and the search for personalized genetic histories. *Nature Reviews Genetics*. 2004; 5(8):611–618.
- Shriver MD, Parra EJ, Dios S, Bonilla C, Norton H, Jovel C, Pfaff C, Jones C, Massac A, Cameron N, Baron A, Jackson T, Argyropoulos G, Jin L, J.Hoggart C, McKeigue PM, Kittles RA. Skin pigmentation, biogeographical ancestry and admixture mapping. *Human Genetics*. 2003; 112(4): 387. [PubMed: 12579416]
- Shriver MD, Smith MW, Jin L, Marcini A, Akey JM, Deka R, Ferrell RE. Ethnic-affiliation estimation by use of population-specific DNA markers. *American Journal of Human Genetics*. 1997; 60(4): 957–964. [PubMed: 9106543]
- Smith MW, O'Brien SJ. Mapping by admixture linkage disequilibrium: advances, limitations and guidelines. *Nature Reviews Genetics*. 2005; 6(8):623–632.
- Tayo BO, Teil M, Tong L, Qin H, Khitrov G, Zhang W, Song Q, Gottesman O, Zhu X, Pereira AC, Cooper RS, Bottinger EP. Genetic background of patients from a university medical center in Manhattan: implications for personalized medicine. *PLoS ONE*. 2011; 6(5):e19166. [PubMed: 21573225]
- Tsai HJ, Choudhry S, Naqvi M, Rodriguez-Cintron W, Burchard EG, Ziv E. Comparison of three methods to estimate genetic ancestry and control for stratification in genetic association studies among admixed populations. *Human Genetics*. 2005; 118(3–4):424–433. [PubMed: 16208514]
- Tutton R, Smart A, Martin PA, Ashcroft R, Ellison GT. Genotyping the future: scientists' expectations about race/ ethnicity after BiDiL. *The Journal of Law, Medicine & Ethics*. 2008; 36(3):464–470.
- Wagner JK. Interpreting the implications of DNA ancestry tests. *Perspectives in Biology and Medicine*. 2010; 53(2):231–248. [PubMed: 20495260]
- Wang H, Haiman CA, Kolonel LN, Henderson BE, Wilkens LR, Marchand LLe, Stram DO. Self-reported ethnicity, genetic structure and the impact of population stratification in a multiethnic study. *Human Genetics*. 2010; 128(2):165–177. [PubMed: 20499252]
- Weiss KM, Long JC. Non-Darwinian estimation: my ancestors, my genes' ancestors. *Genome Research*. 2009; 19(5):703–710. [PubMed: 19411595]
- Worsham MJ, Divine G, Kittles RA. Race as a social construct in head and neck cancer outcomes. *Otolaryngology -- Head and Neck Surgery*. 2011; 144(3):381–389. [PubMed: 21493200]
- Yang BZ, Zhao H, Kranzler HR, Gelernter J. Practical population group assignment with selected informative markers: characteristics and properties of Bayesian clustering via STRUCTURE. *Genetic Epidemiology*. 2005; 28(4):302–312. [PubMed: 15782414]
- Yang JJ, Cheng C, Devidas M, Cao X, Fan Y, Campana D, Yang W, Neale G, Cox NJ, Scheet P, Borowitz MJ, Winick NJ, Martin PL, Willman CL, Bowman WP, Camitta BM, Carroll A, Reaman GH, Carroll WL, Loh M, Hunger SP, Pui CH, Evans WE, Relling MV. Ancestry and

pharmacogenomics of relapse in acute lymphoblastic leukemia. *Nature Genetics*. 2011; 43(3):237–241. [PubMed: 21297632]

Yang N, Li H, Criswell LA, Gregersen PK, Alarcon-Riquelme ME, Kittles R, Shigeta R, Silva G, Patel PI, Belmont JW, Seldin MF. Examination of ancestry and ethnic affiliation using highly informative diallelic DNA markers: application to diverse and admixed populations and implications for clinical epidemiology and forensic medicine. *Human Genetics*. 2005; 118(3–4): 382–392. [PubMed: 16193326]

Ziv E, Burchard EG. Human population structure and genetic association studies. *Pharmacogenomics*. 2003; 4(4):431–441. [PubMed: 12831322]

Table 1**Key Informant Characteristics**

Self-identified discipline	Position	Education	Gender
Population genetics	Assistant Professor	PhD	Male
Population genetics	Postdoctoral fellow	PhD	Female
Population genetics	Postdoctoral fellow	PhD	Male
Population genetics	Assistant Professor	PhD	Female
Population genetics	Postdoctoral fellow	PhD	Female
Population genetics	Assistant Professor	PhD	Male
Clinical-researcher, pediatrics	Professor	MD, PhD	Male
Clinician-researcher, pulmonology	Associate Professor	MD, MPH	Male
Clinician-researcher, dermatology	Assistant Professor	MD	Male
Clinician-researcher, pediatrics	Assistant Professor	MD, PhD	Male
Clinician-researcher, orthodontics	Assistant Professor	DDS, PhD	Female
Clinician-researcher, psychiatry	Professor	MD, PhD	Male
Clinician-researcher, ophthalmology	Assistant Professor	MD, PhD	Male
Genetic epidemiology	Doctoral candidate	MS, PhD	Male
Genetic epidemiology, epidemiology	Assistant Professor	PhD, MPH	Female
Epidemiology, genetic epidemiology	NIH Senior investigator	MD, PhD	Female
Genetic epidemiology	Assistant Professor	PhD	Female
Epidemiology, genetic epidemiology	Postdoctoral fellow	PhD	Female
Epidemiology	Professor	PhD	Male
Epidemiology	Professor	PhD, MPH, FAHA	Female
Epidemiology	Research Professor	MD, MSc	Male

Table 2

Summary of Major Findings

Participants who use ancestry estimation in genetic epidemiology studies self-identified as population geneticists, epidemiologists, or clinician-researchers.
Participants viewed ancestry as a way to “move beyond” race but this often meant “moving beyond” the controversies associated with using race in genetics.
Population geneticists shared their expertise in genetic ancestry, especially with clinician-researchers; and preferred to use ancestry over race in genetic research.
Clinician-researchers relied on population geneticists, expressed the greatest enthusiasm for ancestry estimation, and yet often equated genetic ancestry with race/ethnicity.
Epidemiologists expressed ambivalence about practices involving ancestry estimation; some preferred race and ethnicity to genetic ancestry in genetic epidemiology studies.