HHS Public Access

Author manuscript

Am J Addict. Author manuscript; available in PMC 2018 August 01.

Published in final edited form as:

Am J Addict. 2017 August ; 26(5): 486–493. doi:10.1111/ajad.12495.

(Invited Review) Genetic Research on Alcohol Use Outcomes in African American Populations: A Review of the Literature, Associated Challenges, and Implications

Danielle M. Dick, PhD[1,2,3], **Peter Barr, PhD**[1,2], **Mignonne Guy, PhD**[2], **Aashir Nasim, PhD**[2], and **Denise Scott, PhD**[4]

[1]Department of Psychology, Virginia Commonwealth University, Richmond, Virginia

[2]Department of African American Studies, Virginia Commonwealth University, Richmond, Virginia

[3]Department of Human and Molecular Genetics, Virginia Commonwealth University, Richmond, Virginia

[4]Department of Pediatrics and Human Genetics and Alcohol Research Center, Howard University College of Medicine, Washington, District of Columbia

Abstract

Background and Objectives—There have been remarkable advances in understanding genetic influences on complex traits; however, individuals of African descent have been underrepresented in genetic research.

Methods—We review the limitations of existing genetic research on alcohol phenotypes in African Americans (AA) including both twin and gene identification studies, possible reasons for underrepresentation of AAs in genetic research, the implications of the lack of racially diverse samples, and special considerations regarding conducting genetic research in AA populations.

Results—There is a marked absence of large-scale AA twin studies so little is known about the genetic epidemiology of alcohol use and problems among AAs. Individuals of African descent have also been underrepresented in gene identification efforts; however, there have been recent efforts to enhance representation. It remains unknown the extent to which genetic variants associated with alcohol use outcomes in individuals of European and African descent will be shared. Efforts to increase representation must be accompanied by careful attention to the ethical, legal, and social implications of genetic research. This is particularly true for AAs due to the history of abuse by the biomedical community and the persistent racial discrimination targeting this population.

Conclusions and Scientific Significance—Lack of representation in genetic studies limits our understanding of the etiological factors that contribute to substance use and psychiatric outcomes in populations of African descent and has the potential to further perpetuate health

Address correspondence to Dick, Department of Psychology, Virginia Commonwealth University, 816 West Franklin Street, P.O. Box 842509, Richmond, VA 23284-2509. ddick@vcu.edu.

Declarations of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

disparities. Involving individuals of diverse ancestry in discussions about genetic research will be critical to ensure that all populations benefit equally from genetic advances.

INTRODUCTION

Our understanding of the contribution of genetic factors to psychiatric and behavioral outcomes has advanced dramatically in recent years.[1,2] Genetic epidemiological studies have enabled us to understand how genetic and environmental influences operate across development to influence pathways of risk, and statistical and molecular genetic studies are making progress in identifying the specific genes involved.[3–5] However, a major limitation of these advances is that African Americans (AAs) have been underrepresented in much of the genetic research examining complex psychiatric outcomes. This is true of twin studies[4,6,7] and gene identification studies, including candidate gene studies,[5,8,9] linkage studies,[10–12] and genome-wide association studies.[4,13–15] Lack of representation in genetic studies limits our understanding of the etiological factors that contribute to substance use and psychiatric outcomes in AAs and, with growing emphasis on precision medicine,[16] has the potential to further perpetuate health disparities. In this paper we discuss the limitations of existing genetic research on alcohol phenotypes in AAs and why it is important to conduct genetic research across diverse populations. We review possible reasons for underrepresentation of AAs in genetic research, the implications of the lack of racially diverse samples, and special considerations regarding conducting genetic research in AA populations. Some of the concerns reviewed here are applicable more broadly to underrepresented groups, while other considerations pertain to AA populations specifically. In general, most non-white populations have been underrepresented in genetic research.

OVERVIEW OF EXTANT GENETIC RESEARCH ON ALCOHOL USE OUTCOMES IN AFRICAN AMERICAN POPULATIONS

Genetic Epidemiology

The most common approach used to examine the extent to which genetic and environmental influences are important for a trait of interest is the twin methodology.[17] Twin studies involve comparing the similarity between monozygotic twins, who share all of their genetic variation, and dizygotic twins, who share on average half of their genetic variation, to estimate the relative importance of genetic and environmental influences. In traditional twin studies, genetic material (ie, DNA) is not collected, and no specific genotypes are measured; rather, the relative importance of genetic and environmental effects is estimated statistically based on the twin correlations. This means that the heritability estimate, which represents the proportion of the variance in the trait due to genetic influences, along with the estimates for the relative importance of environmental influences, are specific to the population being studied.

In a recent meta-analysis of twin (and adoption) studies, the heritability of alcohol use disorders was estimated to be between 47% and 54%,[18] with the remaining variance attributable to environmental factors. However, this compilation of the extant literature underscores how the body of studies used to examine the heritability of alcohol problems

overwhelmingly consists of homogeneous samples of European ancestry. Twin and adoption studies examining alcohol-related phenotypes have generally used samples from national populations with relatively little diversity (such as those in Sweden and Finland) or have focused exclusively on non- Hispanic, European American (EA) twins even in countries with greater racial diversity (such as in the United States).[18] Of the samples included in the meta-analysis, only the Vietnam Era Twin Registry included twins not of European descent. Potential differences in the importance of genetic and environmental influences across individuals of differing racial backgrounds was not even discussed in this meta-analytic compilation of the literature. The meta-analysis is representative of the broader historical problem of a lack of racial diversity in twin registries, especially in the United States and Europe. For example, the Virginia Twin Registry (now part of the Mid-Atlantic Twin Registry or MATR) and the National Academy of Sciences-National Research Council (NAS-NRC) Twin Registry originally limited participation to “Caucasian” and “White” twins, respectively.

Though twin registries have historically consisted largely of individuals of European descent, a limited number of twin studies have attempted to estimate heritability in AA twins for alcohol use phenotypes, including alcohol abuse and dependence, [11] age of first use,[19,20] and problem use.[20] The study on alcohol dependence comes from the Washington University Twin Study of Alcoholism which included approximately 50 AA twins with alcohol dependence diagnoses. The latter two studies focusing on AA twins come from the Missouri Adolescent Female Twin Study (MOAFTS) which included approximately 240 AA twins. This sample was limited to female twins only. These studies have found both differences and similarities across populations. Twin correlations among individuals diagnosed with alcohol abuse or dependence suggested stronger genetic influences for both male and female EA twins (and correspondingly a greater importance of the environment in AA individuals), though the sample size was too small to produce accurate estimates for AA twins.[11] Additive genetic factors contributed to age of first drink and problem alcohol use in both EA and AA twins.[20] Estimates of genetic variance were greater for age of first drink in EA twins (eg, heritability of 44% in EA twins, 26% in AA twins), while genetic variance was stronger for problem alcohol use in AA twins (eg, heritability of 21% in EA twins, 41% in AA twins), though these estimates did not differ significantly.[20] This is likely due to a lack of statistical power resulting from the small number of available AA twin pairs, which makes it impossible to precisely estimate genetic and environmental contributions to complex traits or test for differences across populations. The MOAFTS sample is the largest twin sample that has systematically studied alcohol use outcomes in AAs; however, because it is limited to female-only pairs it precludes studying how sex and race influence complex traits such as alcohol related behaviors.[19,20] Recent efforts are underway to increase participation of AAs and populations other than EAs in twin registries such as the MATR.[21] Additional efforts have focused on creating AA specific twin registries, such as the Carolina African American Twin Study of Aging.[22] Much work remains to improve the diversity of twin registries.

Failure to include racially and ethnically diverse samples in twin studies is problematic because twin estimates of the importance of genetic and environmental influences are necessarily specific to the population under study. Individuals belonging to socially-

subordinated groups are disproportionately exposed to a variety of environmental stressors, including higher rates of poverty, lower socioeconomic status, and decreased employment opportunities, in comparison to socially-dominant groups.[23–25] For example, a survey of children in the 100 largest metropolitan areas in the United States reported that 76% of AA children lived under worse circumstances with respect to neighborhood poverty than the worst off EAs in those areas.[26] Twin studies have robustly demonstrated that the importance of genetic and environmental influences can vary as a function of the environment,[27–29] and the profound differences that exist in environments experienced by AAs suggests that the degree to which genetic and environmental influences impact substance use may vary in AA populations, just as the rates of alcohol use vary in AA populations.[30] In other words, the etiological pathways that influence risk for complex behavioral outcomes could vary across groups. Ignoring the heterogeneity within and across populations and assuming a "one size fits all" developmental model based largely on research conducted in EAs is unlikely to accurately represent the etiological factors operating in AAs and/or populations other than EAs. With the limited number of AA twins available for study it remains unknown to what extent genetic and environmental factors are important in impacting alcohol use milestones and outcomes in AAs. One could imagine that the disproportionate burden of environmental stressors experienced by AAs in our society could lead to a difference in the relative importance of the environment, as compared to genetic predispositions, in impacting substance use outcomes.

Measured Genotypic Studies

Whereas genetic epidemiological studies aim to characterize the relative importance of genetic and environmental influences on outcomes, measured genotypic studies have the goal of understanding the risk associated with specific genetic variants. Candidate gene studies examine the association between a particular measured genotype that is selected a priori based on some theoretical rationale for why a particular gene would be associated with the trait of interest. Commonly investigated genes for alcohol use outcomes (and often other psychiatric outcomes) include genes involved in the dopamine system (eg, *DRD2*), serotonin system (eg, *SLC6A4*), and alcohol metabolism (eg, *ALDH2*), among others.[8,31–33] Reviews of existing research show that like twin studies, candidate gene research is often lacking in sufficient numbers of AA participants. Much of the work has focused on European and Asian populations.[5,9] Samples included in a meta-analysis of the Taq1A polymorphism, studied extensively with respect to *DRD2* but now known to be located in neighboring gene *ANKK1*, and alcohol dependence included no AA participants.[33] Similarly, of the samples included in a meta-analysis of the 5-HTTLPR serotonin transporter gene polymorphism and alcohol dependence, [32] only two of the 17 studies included AAs.

An extension of the candidate gene approach tests whether the importance of a particular candidate gene varies across environmental conditions.[34–36] Some of these studies have tested whether these specific gene-environment interaction (GxE) effects differ in EAs and AAs. For example, studies have found that the protective effects of *ADH1B* variants against different alcohol phenotypes are reduced in risky environments, such as involvement with peers that drink[37] or exposure to childhood adversity,[38] in EAs but not AAs. Other GxE research has been conducted within available AA populations, for example one study found

that genetic variants related to the stress-response are protective against the effect of childhood trauma on suicidal behavior in substance dependent respondents. [39] However, systematic study of particular genes and environments that interact in hypothesized directions among AAs has not been a widespread area of study. Additionally, the small sample sizes of AAs in these analyses have limited the ability to detect significant interactions, if they exist. Closer collaborations between scientists who work in genetics and scientists who study cultural and environmental influences that impact substance use in AAs could lead to more hypothesis-driven research in this area.

In contrast to candidate gene studies, genome-wide association studies (GWAS) scan the entire genome for single nucleotide polymorphisms (SNPs) that are associated with a given trait in a more data driven, a theoretical approach. They have become a preferred tool in gene identification studies since they do not require a priori knowledge of the underlying biology of the outcome of interest. Search results from the NHGRI-EBI Catalog of published genome-wide association studies yield 26 GWAS studies focusing on alcohol-related phenotypes published since 2009. Of the 26 published GWAS studies, only four studies contained samples of AA respondents.

Lack of representation of individuals of African descent in gene identification studies is problematic for reasons additional to the problems caused by under-representation of AAs in twin research. Since human populations originated in Africa, the genetic architecture of African populations is characterized by greater levels of genetic diversity than European populations.[40,41] Further, African populations are characterized by differences in allele frequencies and linkage disequilibrium (LD) patterns as compared to other non- African populations.[41–43] These factors contribute to the challenge of translating genetic findings from populations of European ancestry populations to populations of African descent. In particular, the greater genetic diversity in populations of African descent makes it more likely that there may be causal variants present in populations of African descent that would not be detected in populations of European descent. Differences in allele frequencies between populations mean that effects detected in populations of European descent will not necessarily have the same impact in populations of African descent. For example, if the causal variant is less common in populations of African descent, it may play less of a role in the genetic etiology of substance use outcomes in individuals with that ancestral background; conversely, there may be more common alleles that impact substance use outcomes in individuals of African descent that are not as common in populations of European descent, and therefore, would not be detected without explicit study of individuals of African ancestry. Finally, lower linkage disequilibrium also means that more genetic markers are needed to adequately cover genetic variation across the genome in populations of African descent for gene identification efforts. Thus, most standard genotyping platforms provide less thorough coverage of genetic variation among populations of African descent, thereby decreasing the likelihood of detecting relevant associated variants in this population.[41,43,44]

Results from the GWAS focused on alcohol use phenotypes across AA and EA populations have yielded mixed results. Two of the four GWAS containing diverse samples were unable to detect SNPs of genome-wide significance in either AA or EA populations, although the

top findings in EA and AA implicated different genes.[14,45] Beirut et al. found that none of the top SNPs from the EA and AA populations overlapped.[46] However, in further analyses of these samples Zuo et al.[15] found evidence that the gene KIAA0040 was associated with alcohol dependence in both EAs and AAs, using the replication across diverse samples to bolster evidence of a causal variant.[15] A more recent GWAS combined multiple samples containing individuals of AA and EA descent,[47] resulting in significantly enhanced power (n=16,087). Researchers were able to detect SNPs with genome wide-significance in both EA and AA populations. Top SNPs from both populations were then successfully replicated in independent samples. Results from this GWAS suggested population specific SNPs related to alcohol dependence (AD). However, although the individual SNPs differed across populations, many were located in similar risk loci for AD, such as SNPs in the *ADH* cluster responsible for alcohol metabolism.[47] These results support previous GWAS studies that suggested common biological pathways across ancestral populations,[15,48] though more work is still needed to understand the extent to which there are common biological and population-specific risks.

In summary, inadequate representation of AAs in genetic epidemiological studies and gene identification studies is problematic because findings from genetic studies in other populations may not directly translate to AAs. The reasons for potential differences in the importance of genetic factors are twofold. The differences in environmental conditions and stressors experienced by AAs as compared to EAs could impact the degree to which genetic and environmental influences are important in the etiology of alcohol use outcomes in AA populations. Secondly, because people of African descent have greater genetic diversity and differing allele frequencies based on ancestral history, failure to include African Americans in gene identification efforts could lead to important genetic variants being missed and/or the identified variants being less important in individuals of African descent. All of these factors underscore the need for adequate representation of AA populations in genetic research to ensure this group equally benefits from health advances related to genetic findings. The new initiative on precision medicine,[16] emphasizing the use of large-scale biologic databases including genetic information, makes it imperative that we ensure all populations are adequately represented in the research to ensure that all will benefit equally. It is critical to include representation across diverse populations as we build the research base that will support the precision medicine initiative. Although our understanding of the genetics of alcohol dependence remains in an early stage, with few replicated genetic variants currently identified, GWAS of other complex traits are beginning to account for nontrivial amounts of genetic variance (height= ~29%, schizophrenia=~7%).[49,50]

FACTORS THAT LIKELY CONTRIBUTE TO UNDERREPRESENTATION OF AFRICAN AMERICANS IN GENETIC RESEARCH

There are likely many factors contributing to underrepresentation of AA in genetic research. Within the general population, there are fewer AAs than EAs, making it more difficult to recruit the large numbers of individuals necessary for genetic research. Ancestral diversity significantly complicates genetic analyses,[51] providing impetus for scientists to maintain genetic homogeneity in their studies. In addition, because of the history of eugenics

associated with genetic research, recruiting and studying majority EA populations avoided the need to confront challenging issues raised by studying race and genetics.[52,53] Furthermore, the majority of GWAS conducted in the United States have used existing cohorts. These cohorts were mostly created before there was an increased effort to include minority populations in biomedical research and therefore, only included persons of a single ancestral background, which was usually that of the majority European descent population.[54]

There are also a number of other factors that may contribute to underrepresentation of AAs in genetic research, including cultural or racial stigma, mistrust of scientific research, concerns about discrimination, and confidentiality, perceptions of being used as "guinea pigs" by scientists, and lack of interest or perception that there is no perceived benefit from participation in genetic studies.[55–59] Participation in genetic studies of complex behavioral disorders such as alcohol use and related outcomes may be further hindered because of increased stigma surrounding psychiatric disorders in AA populations. For example, Schnittker and colleagues reported that AAs were less likely to accept genetic or familial influences as causative factors of psychiatric disorders.[60] While some apprehension about genetic research is shared across individuals of varying backgrounds,[61] AAs express greater concern about genetic research,[62,63] and are more likely to specifically express concern about the potential for racial discrimination than EAs.[61] In light of these concerns, it is perhaps unsurprising that a review of multiple studies that measured consent rates for genetic research participation found that AAs had significantly lower levels of consent.[58] Concerns are likely exacerbated in AAs due to the history of systematic and systemic oppression, racial discrimination, eugenics, and abuse by the biomedical community.[61]

Discussions about race and genetics are further complicated by confusion about how best to reconcile the concept of race as a social construct with the biological differences that are discussed in genetics across racial groups. Racial categories are clearly socially assigned and, in more recent history, socially-defined, as evidenced in part by the fact that they have changed over time.[64] Socially-defined racial categories do not necessarily reflect human genetic variation[65,66]; however, racial categories may be correlated with differences in ancestral history, which can lead to genetic variation across groups. Ancestral history derived from ancestry informative genetic markers (AIMs) provide a more biologically sound method of assessing human genetic variation and must be taken into account when conducting genetic research in order to draw accurate conclusions about the risk associated with any given variant. While this distinction is often clear to investigators in the field of genetics, it may not be as clear to those in other fields or in the broader population.[65] A failure to appreciate this difference has led to a concerning resurgence of the idea of race as a biological, rather than a social construct, in both social scientific literature[67] and popular science writing.[68] While advances in genetics have allowed us to identify markers that are differentially associated with geographic ancestry, these markers do not necessarily map onto current racial categories. [66] Many in both the social and biological sciences have spoken out against the idea of a biological basis for race,[66,69–72] as public misunderstanding about genetics could result in discrimination and eugenic practices.[53] Not only could these ideas reinforce implicit biases in the broader public, but they could also be used to advance racist ideologies.[69,71] Geneticists must take care to use accurate terminology when referring

to socially defined racial categories versus groups derived based on ancestral background so as to avoid perpetuating confusion and the potentially deleterious consequences that could result.

Finally, concern has been raised that attention to the role of genetics in contributing to health disparities could undermine research on the environmental contributions to health disparities, which are known to be significant.[73] AAs have been relegated to a unique social position that stems from a longstanding history of subjugation within the United States, frequently facing negative environmental conditions such as exposure to multiple forms of stress[24,25] and discrimination[76] across socioeconomic strata, and with many disproportionately burdened from residential segregation,[75] poor socioeconomic conditions, [77] and subsequent greater levels of incarceration[74] Understanding all factors that contribute to health disparities—both social conditions and genetics—is clearly a worthwhile pursuit. Genetic factors alone are unlikely to play a major role in accounting for racial health disparities[23,66] and, more importantly, health inequalities. However, as biologic data increasingly play a role in medicine, as per the precision medicine initiative, failure to include AAs and populations other than those of European descent could exacerbate health disparities in the future.

ETHICAL, SOCIAL, AND LEGAL CHALLENGES ASSOCIATED WITH GENETIC RESEARCH AND GENETIC TESTING

Several studies indicate that, when asked, AAs are interested in participating in genetic research[78,79] and there are clear benefits for advancing genomic science. For example, in a study of 353 African American, European American, and Hispanic individuals, racial/ethnic groups did not differ in their willingness to participate in psychiatric genetic research; more than 70% in each group stated they were willing to participate.[79] An exploratory study of factors associated with engagement in health-related genetic research among 212 African Americans found that 20% of participants had previously been involved in health-related research, and the majority of individuals who had not participated said they would be willing to provide family history and/or biological specimens for genetic research.[80] Of note, 89% of the participants who had not previously been involved in a health-related study who expressed a willingness to participate reported they “had never been asked.” [80]

Despite a willingness to participate, significant social issues for AAs remain to be addressed. Disparities in access, insensitive, and discriminatory programming, a lack of appreciation of environmental factors, and misuse of genetic databases are among the challenges.[81] In addition, issues related to the privacy and confidentiality of data; return of results and incidental findings to participants; data sharing and secondary use of samples; informed consent mechanisms; ownership of specimens; and benefit sharing (ie, the distribution of financial or other assets that result from the research) are of concern.[82] These concerns are increased as researchers engage in studies which include data sharing both nationally and internationally.[82] One study that assessed AA willingness to participate in genome-wide study that required the storage of genotypic and phenotypic data at NIH for distribution to qualified researchers found that fears included losing health insurance, being used as a

guinea pig, questions on how the information would be used, and who would have access to it. Factors that have been associated with an increased willingness to participate in genetic research include greater knowledge of genetics, an understanding of the benefits, risks, and utility of genetic research, higher levels of trust with providers, and a desire to contribute to the health of one's family and the larger community.[78,80]

The current era of next-generation sequencing deepens the need to investigate the ethical, legal, and social implications associated with genetic testing in AAs, alongside the efforts to encourage greater participation in genetic research. It is essential to balance the potential of new biomedical advances with the ethical and legal structures needed to ensure the protection of human participants involved in research projects.[83] This is especially true when working in communities in which there has been an historical misuse of scientific findings, policy implications that adversely affect the community,[84] a distrust of some research,[85] and concern of group harm.[86] The ethical, legal, and social implications surrounding the widely publicized invasion of privacy of Henrietta Lacks and her family as scientists developed the HeLa cell line, shared and sold the HeLa cells without compensation to the family, and published the HeLa genome on the internet, raised public concern, and distrust of genetic research.[87]

Studies have found that factors that facilitate participation in genetic research include respect of community, authentic collaboration, bidirectional education,[88,89] including community members in the recruitment process, transparency, and the potential for meaningful benefits.[88,89] As with medical research in general, establishing interpersonal trust between the researchers and the community is one of the major factors in engaging AAs. Effective strategies in establishing trust include collaboration with the community through a community advisory board and conducting community-based participatory action research.[90] It is recommended that future studies investigate the facilitators of engaging African Americans specifically alcohol genetic research since there may be unique factors associated with participation in genetic research on a disorder with an associated stigma.

Currently, genetic information about risk for alcohol use disorders is not clinically predictive[91]; however, the eventual translation of genetic testing into medical practice will depend on numerous factors, including clinicians' and researchers' abilities to properly engage patients of varied ancestral lineage in research to ensure the accuracy of applied tests for all populations. At least one study suggests that if there were a clinical genetic test for the susceptibility of alcohol dependence there would be a strong interest in testing among AAs.[92] However, even among AAs with access to health care, participation in currently available multiplex genetic susceptibility tests[93] is limited. This is problematic, as it is thought that the availability of these test results may encourage people to take advantage of more health-care services.

The majority of the recommendations and pathways for exploring decision-making criteria for return of results have focused on populations of European descent. However, evidence suggests that opinions about receiving results and participating in research differ among racial and ethnic groups.[94] Several factors such as level of control,[95] type of disease, and validity of the findings[96] could affect persons' interest in participating in studies. Also, the

management of individual research results and incidental findings could influence AAs' decisions to participate in genomic research. Further, privacy, confidentiality, and informed consent procedures (traditional, binary, or tiered) could affect research enrollment and data sharing decisions.[95]

The Genetic Information Nondiscrimination Act (GINA) was passed by the United States Congress to address the concerns of genetic discrimination and provide protection for genetic information.[97] This act forbids employers and health insurers from using genetic information to make decisions. This includes "information related to genetic services requested or received by an individual, such as counseling, testing, or education, as well as participation in clinical research that includes genetic services.[97,98] A recent study on GINA in a diverse population sample indicates that awareness of genetic nondiscrimination laws is low, while perceived importance of these types of laws is high. This indicates that there is a need for public education to raise awareness about protections provided through current genetic nondiscrimination laws.[99]

CONCLUSIONS AND FUTURE DIRECTIONS

Efforts to understand genetic influences on alcohol use outcomes in AAs clearly lag behind studies in populations of European descent. Virtually all twin studies have been conducted in European or European–American populations. The differing rates and patterns of alcohol use among AAs, coupled with significantly different environmental circumstances within AA populations, suggests that the genetic epidemiology of alcohol use outcomes is likely to vary in AAs. With no large scale twin studies in populations of African descent in existence, next to nothing is known about how genetic and environmental influences impact alcohol use outcomes across development specifically in AAs.

Gene identification efforts also have been focused largely in populations of European descent historically; however, there has been progress more recently in expanding study populations to include more individuals of African descent. This is particularly critical since there are different ancestral histories, resulting in different genetic architectures, among individuals of African descent. This means that different genetic variants may be associated with the same outcome in different populations. It remains unknown the extent to which specific genes and specific variants that are important in alcohol use outcomes in individuals of European descent will be shared among individuals of African descent.

Studies indicate that AAs largely support genomic science as long as there are adequate assurances of inclusion, and protections built into the research and service delivery systems. Increased representation of AA individuals must be accompanied by careful attention to the ethical, legal, and social implications of genetic research in underrepresented populations. The best way this can be accomplished is through interdisciplinary and collaborative work with persons of diverse ancestry.[81] There is an ongoing need to involve AAs in human genome policy and for AA participation in the oversight of human genome research.[81] This need is especially crucial in alcohol use disorder, a disease with associated stigma. More careful attention to the ethical, legal, and social implications of genetic research will allow for cultural and contextual strategies to overcome these issues, and also have the likely

added benefit of increasing AA participation in genetic studies. This will be critical for all populations to benefit equally from genetic advances, so as to not further enhance health disparities.

Acknowledgments

Support for this work was provided in part by K02 AA018755 and U10AA00801-26 from the National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD, to Danielle M. Dick.

References

1. Sullivan PF, Daly M, O'Donovan M. Genetic architectures of psychiatric disorders: The emerging picture and its implications. Nat Rev Genet. 2012; 13:537–551. [PubMed: 22777127]
2. Cross-Disorder Group of the Psychiatric Genomics C. Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. Nat Genet. 2013; 45:984–994. [PubMed: 23933821]
3. Dick DM. Developmental changes in genetic influences on alcohol use and dependence. Child Dev Perspect. 2011; 5:1–8.
4. Kendler K, Kalsi G, Holmans P, et al. Genomewide association analysis of symptoms of alcohol dependence in the molecular genetics of schizophrenia (MGS2) control sample. Alcohol Clin Exp Res. 2011; 35:963–975. [PubMed: 21314694]
5. Rietschel M, Treutlein J. The genetics of alcohol dependence. Ann NY Acad Sci. 2013; 1282:39–70. [PubMed: 23170934]
6. Meyers JL, Salvatore JE, Vuoksimaa E, et al. Genetic influences on alcohol use behaviors have diverging developmental trajectories: A prospective study among male and female twins. Alcohol Clin Exp Res. 2014; 38:2869–2877. [PubMed: 25421521]
7. Knopik V, Heath AC, Madden PA, et al. Genetic effects on alcohol dependence risk: Re-evaluating the importance of psychiatric and other heritable risk factors. Psychol Med. 2004; 34:1519–1530. [PubMed: 15724882]
8. Edenberg HJ. The genetics of alcohol metabolism: Role of alcohol dehydrogenase and aldehyde dehydrogenase variants. Alcohol Res Health. 2007; 30:5–13. [PubMed: 17718394]
9. Samochowiec J, Samochowiec A, Puls I, et al. Genetics of alcohol dependence: A review of clinical studies. Neuropsychobiology. 2014; 70:77–94. [PubMed: 25359488]
10. Foroud T, Edenberg HJ, Goate A, et al. Alcoholism susceptibility loci: Confirmation studies in a replicate sample and further mapping. Alcohol Clin Exp Res. 2000; 24:933–945. [PubMed: 10923994]
11. Prescott CA, Caldwell CB, Carey G, et al. The washington university twin study of alcoholism. Am J Med Genet B Neuropsychiatr Genet. 2005; 134B:48–55. [PubMed: 15704214]
12. Kuo PH, Gardner CO, Kendler KS, et al. The temporal relationship of the onsets of alcohol dependence and major depression: Using a genetically informative study design. Psychol Med. 2006; 36:1153–1162. [PubMed: 16734951]
13. Beirut L, Rice J, Goate A, et al. Common and specific factors in the familial transmission of substance dependence. Am J Med Genet. 2000; 96:459.
14. Edenberg H, Koller DL, Xuei X, et al. Genome-wide association study of alcohol dependence implicates a region on chromosome 11. Alcohol Clin Exp Res. 2010; 34:840–852. [PubMed: 20201924]
15. Zuo L, Gelernter J, Zhang C, et al. Genome-wide association study of alcohol dependence implicated KIAA0040 on chromosome 1q. Neuropsychopharmacology. 2012; 37:557–566. [PubMed: 21956439]
16. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015; 372:793–795. [PubMed: 25635347]
17. Plomin, R., DeFries, JC., McClearn, GE., et al. Behavioral Genetics. New York, NY: Worth Publishers; 2008.

18. Verhulst B, Neale MC, Kendler KS. The heritability of alcohol use disorders: A meta-analysis of twin and adoption studies. Psychol Med. 2015; 45:1061–1072. [PubMed: 25171596]
19. Sartor CE, Agrawal A, Lynskey MT, et al. Common genetic influences on the timing of first use for alcohol, cigarettes, and cannabis in young African-American women. Drug Alcohol Depend. 2009; 102:49–55. [PubMed: 19261395]
20. Sartor CE, Nelson EC, Lynskey MT, et al. Are there differences between young African-American and European-American women in the relative influences of genetics versus environment on age at first drink and problem alcohol use? Alcohol Clin Exp Res. 2013; 37:1939–1946. [PubMed: 23763496]
21. Lilley EC, Silberg JL. The mid-Atlantic twin registry, revisited. Twin Res Hum Genet. 2013; 16:424–428. [PubMed: 23218199]
22. Whitfield KE. A registry of adult african american twins: The carolina african american twin study of aging. Twin Res Hum Genet. 2013; 16:476–480. [PubMed: 23088829]
23. Williams DR, Mohammed SA, Leavell J, et al. Race, socioeconomic status, and health: Complexities, ongoing challenges, and research opportunities. Ann NY Acad Sci. 2010; 1186:69–101. [PubMed: 20201869]
24. Sternthal MJ, Slopen N, Williams DR. Racial disparities in health. Du Bois Rev. 2011; 8:95–113.
25. Turner RJ, Avison WR. Status variations in stress exposure: Implications for the interpretation of research on race, socioeconomic status, and gender. J Health Soc Behav. 2003; 44:488–505. [PubMed: 15038145]
26. Acevedo-Garcia D, Osypuk TL, McArdle N, et al. Toward a policy-relevant analysis of geographic and racial/ethnic disparities in child health. Health Aff. 2008; 27:321–333.
27. Turkheimer EN, Haley A, Waldron M, et al. Socioeconomic status modifies heritability of IQ in young children. Psychol Sci. 2003; 14:623–628. [PubMed: 14629696]
28. Dick DM, Bernard M, Aliev F, et al. The role of socioregional factors in moderating genetic influences on early adolescent behavior problems and alcohol use. Alcohol Clin Exp Res. 2009; 33:1739–1748. [PubMed: 19624574]
29. Dick DM, Kendler KS. The impact of gene environment interaction on alcohol use disorders. Alcohol Res. 2012; 34:318–324. [PubMed: 23134047]
30. Grant BF. Prevalence and correlates of alcohol use and DSM-IV alcohol dependence in the United States: Results of the National Longitudinal Alcohol Epidemiologic Survey. J Stud Alcohol. 1997; 58:464–473. [PubMed: 9273910]
31. Dick DM, Foroud T. Candidate genes for alcohol dependence: A review of genetic evidence from human studies. Alcohol Clin Exp Res. 2003; 27:868–879. [PubMed: 12766633]
32. Feinn R, Nellissery M, Kranzler HR. Meta-Analysis of the association of a functional serotonin transporter promoter polymorphism with alcohol dependence. Am J Med Genet B (Neuropsych Genet). 2005; 133B:79–84.
33. Smith L, Watson M, Gates S, et al. Meta-analysis of the association of the Taq1A polymorphism with the risk of alcohol dependency: A HuGE gene-disease association review. Am J Epidemiol. 2008; 167:125–138. [PubMed: 17989061]
34. Rutter M, Moffitt TE, Caspi A. Gene-environment interplay and psychopathology: Multiple varieties but real effects. J Child Psychol Psychiatry. 2006; 47:226–261. [PubMed: 16492258]
35. Enoch MA. The influence of gene-environment interactions on the development of alcoholism and drug dependence. Curr Psychiatry Rep. 2012; 14:150–158. [PubMed: 22367454]
36. Dick DM, Agrawal A, Keller M, et al. Candidate gene-environment interaction research: Reflections and Recommendations. Perspect Psychol Sci. 2015; 10:37–59. [PubMed: 25620996]
37. Olfson E, Edenberg H, Nurnberger J, et al. An ADH1B variant and peer drinking in progression to adolescent drinking milestones: Evidence of a gene-by-environment interaction. Alcohol Clin Exp Res. 2014; 38:2541–2549. [PubMed: 25257461]
38. Sartor CE, Wang Z, Xu K, et al. The joint effects of ADH1B variants and childhood adversity on alcohol related phenotypes in african-American and european-American women and men. Alcohol Clin Exp Res. 2014; 38:2907–2914. [PubMed: 25410943]
39. Roy A, Hodgkinson CA, Deluca V, et al. Two HPA axis genes, CRHBP and FKBP5, interact with childhood trauma to increase the risk for suicidal behavior. J Psyciatr Res. 2012; 46:72–79.

40. Gonder MK, Mortensen HM, Reed FA, et al. Whole-mtDNA genome sequence analysis of ancient African lineages. Mol Biol Evol. 2007; 24:757–768. [PubMed: 17194802]
41. Campbell MC, Tishkoff SA. African genetic diversity: Implications for human demographic history, modern human origins, and complex disease mapping. Annu Rev Genomics Hum Genet. 2008; 9:408–433.
42. Gabriel SB, Schaffner SF, Nguyen H, et al. The structure of haplotype blocks in the human genome. Science. 2002; 296:2225–2229. [PubMed: 12029063]
43. Rosenberg N, Huang L, Jewett EM, et al. Genome-wide association studies in diverse populations. Nat Rev Genet. 2010; 11:356–366. [PubMed: 20395969]
44. Huang L, Li Y, Singleton AB, et al. Genotype-imputation accuracy across worldwide human populations. Am J Hum Genet. 2009; 84:235–250. [PubMed: 19215730]
45. Kendler KS, Chen X, Dick D, et al. Recent advances in the genetic epidemiology and molecular genetics of substance use disorders. Nat Neurosci. 2012; 15:181–189. [PubMed: 22281715]
46. Bierut LJ, Agrawal A, Bucholz KK, et al. A genome-wide association study of alcohol dependence. Proc Natl Acad Sci USA. 2010; 107:5082–5087. [PubMed: 20202923]
47. Gelernter J, Kranzler HR, Sherva R, et al. Genome-wide association study of alcohol dependence: Significant findings in African- and European- Americans including novel risk loci. Mol Psychiatry. 2014; 19:41–49. [PubMed: 24166409]
48. Kos M, Yan J, Dick D, et al. Common biological networks underlie genetic risk for alcoholism in African- and European-American populations. Genes Brain Behav. 2013; 12:532–542. [PubMed: 23607416]
49. Ripke S, Neale BM, Corvin A, et al. Biological insights from 108 schizophrenia-associated genetic loci. Nature. 2014; 511:421. [PubMed: 25056061]
50. Wood AR, Esko T, Yang J, et al. Defining the role of common variation in the genomic and biological architecture of adult human height. Nat Genet. 2014; 46:1173–1186. [PubMed: 25282103]
51. Webb BT. Paper from this special review issue. Am Addict. In press.
52. Dikötter F. Race culture: Recent perspectives on the history of eugenics. Am Hist Rev. 1998; 103:467–478.
53. Phelan JC, Link BG, Feldman NM. The genomic revolution and beliefs about essential racial differences: A backdoor to eugenics? Am Sociol Rev. 2013; 78:167–191. [PubMed: 24855321]
54. Haga SB. Impact of limited population diversity of genome-wide association studies. Genet Med. 2010; 12:81–84. [PubMed: 20057316]
55. Royal C, Baffoe-Bonnie A, Kittles R, et al. Recruitment experience in the first phase of the African American Hereditary Prostate Cancer (AAHPC) study. Ann Epidemiol. 2000; 10:S68–S77. [PubMed: 11189095]
56. Hoyo C, Reid ML, Godley PA, et al. Barriers and strategies for sustained participation of African-American men in cohort studies. Ethn Dis. 2003; 13:470–476. [PubMed: 14632266]
57. Schulz A, Caldwell C, Foster S. What are they going to do with the information?" Latino/Latina and African American perspectives on the Human Genome Project. Health Educ Behav. 2003; 30:151–169. [PubMed: 12693521]
58. Sterling R, Henderson GE, Corbie-Smith G. Public willingness to participate in and public opinions about genetic variation research: A review of the literature. Am J Public Health. 2006; 96:1971–1978. [PubMed: 17018829]
59. Murphy E, Thompson A. An exploration of attitudes among black Americans toward psychiatric genetic research. Psychiatry. 2009; 72:177–194. [PubMed: 19614555]
60. Schnittker J, Freese J, Powell B. Nature, nurture, neither, nor: Black- White differences in beliefs about the causes and appropriate treatment of mental illness. Soc Forces. 2000; 78:1101–1132.
61. Bates BR, Lynch JA, Bevan JL, et al. Warranted concerns, warranted outlooks: A focus group study of public understandings of genetic research. Soc Sci Med. 2005; 60:331–334. [PubMed: 15522489]
62. LAF. Perceptions of genetic research as harmful to society: Differences among samples of African-Americans and European-Americans. Genet Test. 2002; 6:25–30. [PubMed: 12180073]

63. Tambor ES, Bernhardt BA, Rodgers J, et al. Mapping the human genome: An assessment of media coverage and public reaction. Genet Med. 2002; 4:31–36. [PubMed: 11839956]
64. Lee SM. Racial classifications in the US census: 1890–1990. Ethn Racial Stud. 1993; 16:75–94.
65. Batai K, Kittles RA. Race, genetic ancestry, and health. Race Soc Probl. 2013; 5:81–87.
66. Fujimura JH, Bolnick DA, Rajagopalan R, et al. Clines without classes: How to make sense of human variation. Sociol Theor. 2014; 32:208–227.
67. Shiao JL, Bode T, Beyer A, et al. The genomic challenge to the social construction of race. Sociol Theor. 2012; 30:67–88.
68. Wade, N. Race and Human History. New York: Penguin Group; 2014. A troublesome inheritance: Genes.
69. HoSang DM. On racial spectulation and racial science: A response to Shiao et al. Sociol Theor. 2014; 32:228–243.
70. Morning A. Does genomics challenge the social construction of race? Sociol Theor. 2014; 32:189–207.
71. Cohen PN. How troubling is our inheritance? A review of genetics and race in the social sciences. Ann Am Acad Pol Soc Sci. 2015; 661:65–84.
72. Coop G, Eisen MB, Nielsen R, et al. Letters: A troublesome inheritance. N Y Times. Aug 8.2014
73. Sankar P, Cho MK, Condit CM, et al. Genetic research and health disparities. JAMA. 2004; 291:2985–2989. [PubMed: 15213210]
74. Schnittker J, Massoglia M, Uggen C. Incarceration and the health of the African American community. Du Bois Rev. 2011; 8:133–141.
75. Williams DR, Collins C. Racial residential segregation: A fundamental cause of racial disparities in health. Public Health Rep. 2001; 116:404–416. [PubMed: 12042604]
76. Williams DR, Mohammed SA. Discrimination and racial disparities in health: Evidence and needed research. J Behav Med. 2009; 32:20–47. [PubMed: 19030981]
77. Williams DR, Sternthal MJ. Understanding racial-ethnic disparities in health: Sociological contributions. J Health Soc Behav. 2010:S15–S27. [PubMed: 20943580]
78. Walker ER, Nelson CR, Antoine-LaVigne D, et al. Research participants' opinions on genetic research and reasons for participation: A Jackson Heart Study focus group analysis. Ethn Dis. 2014; 24:290–297. [PubMed: 25065069]
79. Murphy EJ, Wickramaratne P, Weissman MM. Racial and ethnic differences in willingness to participate in psychiatric genetic research. Psychiatr Genet. 2009; 19:186–194. [PubMed: 19593860]
80. Millon, Underwood, Buseh, A., Kelber, S., et al. Enhancing the participation of African Americans in health-related genetic research: Findings of a collaborative academic and community-based research study. Nurs Res Pract. 2013; 2013:749563. [PubMed: 24369499]
81. Walton LM. Human genomics: Challenges for African Americans and policy implications for direct social work practice. Soc Work Public Health. 2011; 26:366–379. [PubMed: 21707346]
82. Virani AH, Longstaff H. Ethical consideration in biobanks: How a public health ethics perspective sheds new light on old controversies. J Genet Couns. 2015; 24:428–432. [PubMed: 25348083]
83. Hayden EC. Informed consent: A broken contract. Nature. 2012; 486:312–314. [PubMed: 22722173]
84. Snell CL, Guyot J. Balancing environmental and genetic factors for alcoholism in the black community: Implications for social work practice. Soc Work Public Health. 2011; 26:431–443. [PubMed: 21707351]
85. Corbie-Smith G, Thomas SB, St George DM. Distrust, race, and research. Arch Intern Med. 2002; 162:2458–2463. [PubMed: 12437405]
86. Henderson GE, Juengst ET, King NMP, MM, et al. What research ethics should learn from genomics and society research: Lessons from the ELSI Congress of 2011. Law Med Ethics. 2012; 40:1008–1024.
87. Callier S, Husain R, Simpson R. Genomic data-sharing: What will be our legacy? Front Genet. 2014; 5:34. [PubMed: 24634673]

88. Buseh AG, Stevens PE, Million-Underwood A, et al. Community leaders' perspectives on engaging African Americans in biobanks and other human genetics initiatives. J Community Genet. 2013; 4:483–494. [PubMed: 23813337]

89. Ochs-Balcom HM, Jandorf L, Wang Y, et al. "It takes a village": Multilevel approaches to recruit African Americans and their families for genetic research. J Community Genet. 2015; 6:39–45. [PubMed: 25112899]

90. Dancy BL, Wilber J, Talashek M, et al. Community-based research: Barriers to recruitment of african americans. Nurs Outlook. 2004; 52:234–240. [PubMed: 15499312]

91. Yan J, Aliev F, Webb BT, et al. Using genetic information from candidate gene and genome wide association studies in risk prediction for alcohol dependence. Addict Biol. 2013; 18:708–721.

92. Scott DM, Nwulia E, Kwagyan J, et al. Genetic testing for the susceptibility to alcohol dependence: Interest and concerns in an African American population. Genet Test Mol Biomarkers. 2014; 18:538–545. [PubMed: 24926856]

93. Hensley AS, McBride CM, Reid RJ, et al. Participation in genetic testing research varies by social group. Public Health Genom. 2011; 14:85–93.

94. Yu JH, Crouch J, Jamal SM, et al. Attitudes of African Americans toward return of results from exome and whole genome sequencing. Am J Med Genet A. 2013; 161A:1064–1072. [PubMed: 23610051]

95. McGuire AL, Oliver JM, Slashinski MJ, et al. To share or not to share: A randomized trial of consent for data sharing in genome research. Genet Med. 2011; 13:948–955. [PubMed: 21785360]

96. Wolf SM, Crock BN, Van Ness B, et al. Managing incidential findings and research results in genomic research involving biobanks and archived data sets. Genet Med. 2012; 14:361–384. [PubMed: 22436882]

97. Genetic Information Nondiscrimination Act of 2008, 881. 2008.

98. DHHS. GINA, The Genetic Informaiton Act of 2008, Information for Researchers and Health Care Professionals. Department of Health and Human Services (HHS); 2009.

99. Parkman AA, Foland J, Anderson B, et al. Public awareness of genetic nondiscrimination laws in four states and perceived importance of life insurance protections. J Genet Couns. 2015; 24:512–521. [PubMed: 25242499]