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ACMG STATEMENT

Clinical, technical, and environmental biases influencing equitable access to clinical genetics/genomics testing: A points to consider statement of the American College of Medical Genetics and Genomics (ACMG)

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Introduction

Bias within medicine, when unaddressed or not mitigated, has the potential to negatively affect health equity. As genetic testing becomes increasingly endorsed by the medical community and available to the public, a working group formed by members of the Social, Ethical and Legal Issues and Diversity, Equity and Inclusion committees of the American College of Medical Genetics and Genomics (ACMG) developed this document in an effort to address current factors in which bias can occur in clinical genetic testing and within the medical genetics profession, with the goal of fostering awareness and identifying strategies to reduce bias and improve health equity.

Without addressing the implicit bias involved in the development, implementation, and access to genetic testing, this technology may contribute to further health inequity among underserved and historically excluded populations and the continued systemic discrimination against such groups.[1] Health inequities or gaps in medical care because of bias are considered "unnecessary, avoidable, unfair, and unjust."[2]

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Disadvantaged groups experience poorer survival rates along with heavier disease burdens.[3-5] Many individuals may experience compounded discrimination if they are part of more than 1 historically excluded or underserved population (Table 1).

To improve the outcomes of these populations, we, as members of the medical genetics community, must acknowledge and address the effects of bias that inevitably exists within our field. Because bias is a pervasive part of the human condition and cannot be avoided, it is not our intention to remove bias altogether but to address specific and institutional biases to reduce the negative effects of those. We categorized the bias in genetic testing to be addressed into 3 main areas: environmental, clinical, and technical. Although each of these are intersecting and interdependent, the categorization provides a structure for how to tackle each bias and a framework for continually addressing them. These are by no means the only areas of bias; they merely represent the perceived priorities for this working group.

We acknowledge that the discussion of these topics is made more complex by the nuances of language. Terminology and its appropriateness evolve with time and understanding. Conflicting or contrary definitions may exist simultaneously, and at the time of writing, many leaders within the medical and human genetics societies have established working groups to develop standardized definitions for some of the terms that follow. For now, in Table 1, we have provided definitions of common terms that are important in the discussion of addressing unjust biases in genetic testing and used throughout the points to consider statement.

Environmental Factors

As widespread use of genetic testing increases, it is the responsibility of the medical community to ensure its equitable use across socioeconomic and cultural spectrums.

Mistrust in the medical field is a common concern based on historical and ongoing injustices, affecting the use of health care and, ultimately, health across underrepresented minorities (URMs) and their communities.[23] There are multiple historical events leading to this mistrust, including instances in which genetic samples were collected, analyzed, and shared without consent from the individuals involved in the studies. One example is the research project by Arizona State University from the 1990s that used samples from the Havasupai tribe considered to be sacred, shared them with other universities without consent, and provided little to no information about the findings to the study participants.[24] Continued mistrust in genetic testing is reflected by reduced uptake of testing by individuals of URMs resulting in increased health disparities, decreased diagnostic rates, and poorer health outcomes.[25]

Concerns for social stigmatization or genetic discrimination occur for many individuals considering genetic testing, especially those belonging to URMs.[26-28] Reported emotional hardships include feelings of shame and discrimination as well as concerns about receiving pity.[25,29] For instance, factors contributing to the stigmatization can include confusion between identifying the carrier status of specific individuals and disease status for autosomal-recessive conditions, public misinformation about negative associations with specific diseases, negative social consequences (such as decrease in "marriageability"),[30] and effect on the individual's identity.[31,32] Although, some communities such as the Ashkenazi Jewish community have attempted to overcome the lack of cultural acceptance by developing a carrier screening tool (Dor Yeshorim)[30] without identifying specific individuals as heterozygotes, most communities do not have access to similar resources. In addition, concerns around the use of genetics as an additional way to stigmatize and discriminate against communities have been raised. The lesbian, gay, bisexual, transgender, queer/questioning, intersex, other (referring to other gender identities/sexual orientations) (LGBTQIA+) community has faced stigmatization because several studies sought a genetic etiology for homosexuality,[33] which then led to a biological means of discrimination against the LGBTQIA+ individuals. Recent studies on the genetic basis of gender dysphoria have not included members or opinions of the transgender and gender-diverse advocacy groups,[34] again raising concerns for discrimination; however, there is an ongoing initiative to include transgender and gender-diverse individuals as investigators in the research teams to move trans-associated genetic research forward in a morally responsible manner.[35]

In addition to social stigmatization, individuals also face discrimination through several avenues, including, but not limited to, employment, medical insurance, housing, and interactions with colleagues, peers, and medical institutions, a phenomenon that has been reported internationally.[36-38] Although legislation such as the Genetic Information Nondiscrimination Act (GINA) has been developed as a baseline to curb discrimination by health insurances and employers, there are evident limitations to GINA's protections, including small business exemptions and life, disability, or long-term care insurance, among others.[39]

Not only is insurance discrimination a concern for individuals considering genetic testing but also insurance coverage of genetic testing is a major issue because it is not standardized, is often not comprehensive, and often negatively affects URMs. Genetic testing is an integral part of clinical care and should be recognized by insurance as such. For instance, hereditary cancers have been a well-studied model of disease affected by the power of individual and familial genetic information, such that risk stratification, screening, preventive measures, and specific therapeutic options can reduce mortality and morbidity.[40] In addition, improvements in molecular and clinical diagnosis, disease prognosis, management, and therapeutic opportunities have been possible for a variety of conditions, including cardiomyopathies and arrhythmias.[41]

Table 1 Terminology and definitions

Term	Working Definition
Diversity (population)	Diversity refers to a nonhomogeneous group of people from a variety of different backgrounds or beliefs. Diversity focuses on increasing underrepresented populations. According to the National Institutes of Health, these populations include individuals from racial and ethnic groups that have historically been underrepresented (Blacks or African Americans, Hispanics or Latino-Americans, American Indians or Alaska Natives, Native Hawaiians, and other Pacific Islanders). In addition, it is recognized that underrepresentation can vary from setting to setting, individuals with disabilities (physical or mental impairment that substantially limits one or more major life activities as described by the Americans with Disabilities Act [ADA]), individuals from disadvantaged backgrounds, and women.[6]
Inclusion	Being included within a group or structure. More than simple diversity and quantitative representation, inclusion involves authentic and empowered participation, with a true sense of belonging and full access to opportunities.[7]
Bias	An inclination or preference, especially one that interferes with impartial judgment.[8]
Implicit bias	A form of bias that occurs automatically and unintentionally that informs and affects judgments, decisions, and behaviors.[8]
Discrimination	Treatment of an individual or group based on their actual or perceived membership in a social category, usually used to describe unjust or prejudicial treatment on the grounds of race, age, sex, gender, ability, socioeconomic class, immigration status, national origin, or religion.[7]
Genetic discrimination	The unjust or prejudicial treatment of an individual based on a genetic variant or diagnosis that causes or increases the risk of inherited disease. Most definitions only apply to individuals who are asymptomatic, because those presenting with a phenotype fall under disability discrimination frameworks.[9]
GINA	Genetic Information and Nondiscrimination Act (GINA), 2008, prohibits discriminatory use of a person's genetic information by their individual health insurers and employers with some exceptions, including individuals with symptoms of a genetic disorder or those working for employers with less than 15 employees; does not apply to other forms of insurance or those who receive health insurance through a variety of government agencies and the military.[10]
Stereotype	A set of cognitive generalizations (eg, beliefs, expectations) about the qualities and characteristics of the members of a group or social category. Stereotypes, such as schemas, simplify and expedite perceptions and judgments, but they are often exaggerated, negative rather than positive, and resistant to revision even when perceivers encounter individuals with qualities that are not congruent with the stereotype.[11]
Stigma	The co-occurrence of labeling, stereotyping, separation, status loss, and discrimination "Elements of labeling, stereotyping, separation, status loss, and discrimination co-occurring in a power situation that allows the components of stigma to unfold."[12]
Intersectionality	The acknowledgment that multiple power dynamics/"isms" are operating simultaneously—often in complex and compounding ways.[7]
Equity	An ethical concept based on fairness and justice.[13] Equity focuses on outcomes that are most appropriate for a given group, recognizing different challenges, needs, and histories. It is distinct from diversity and inclusion (described above). It is also not equality, or "same treatment," which does not take differing needs or disparate outcomes into account. Systemic equity involves a robust system and dynamic process consciously designed to create, support, and sustain social justice.[7]
Justice	Describes a future state in which the root causes (eg, racism, sexism, and class oppression) of inequity have been dismantled and barriers have been removed. It is an achievable goal that requires the sustained focus, investment, and energy of leaders and communities working together, holding each other accountable, to redesign our structures, policies, and practices to deliver the high quality and safest possible conditions that allow for everyone to reach their highest potential.[14]
Exploitation	Systematic transfer of the power of some persons or groups to others.[14] Exploitation enacts a structural relation between social groups. Social rules about what work is, who does what for whom, how work is compensated, and the social process by which the results of work are appropriated to operate or to enact relations of power and inequity.[15]
Social determinants of health	The conditions in which people are born and live and are shaped by the distribution of money, power, and resources and are mostly responsible for avoidable differences in health status.[16]
Race[a] self-described or assigned	A social and power construct not rooted in biology.[17]
Ethnicity[a] sometimes used interchangeably with race	Social characteristics people may have in common, such as language, religion, regional background, traditions, and culture not rooted in biology (eg, Latino-American).[16]

(continued)

Table 1 Continued

Term	Working Definition
Ancestry[a]	A concept related to ethnicity and race yet distinct, ancestry refers to the genetic inheritance of variants from global ancestral populations.[18]
Genetic ancestry	The use of genome-wide genotyping and computation algorithms to predict geographic origins based on differences in the cumulative frequency of thousands of genetic variants.
Racial medicine (race-based medicine)	The system by which research characterizing race as an essential, biological variable, translates into clinical practice, leading to inequitable care.[19]
Classism	The systematic oppression of subordinated class groups, held in place by attitudes that rank people according to economic status, family lineage, job status, level of education, and other divisions.[7]
Telehealth	The use of electronic information and telecommunication technologies to support long-distance clinical health care, patient and professional health-related education, public health, and health administration. This definition encompasses telemedicine that refers more specifically to real-time remote clinical services requiring at minimum audio and video equipment.[20]
Accessibility	The possibility to identify health care needs, to seek and to obtain or use health care services, to reach the health care resources, and to be offered services appropriate to the needs for care.[21]
Equality in health care	Equal access to available care, use for equal need and equal quality of care for all.[2]
Cultural humility	"A lifelong commitment to self-evaluation and self-critique, for redressing the power imbalances in the patient-physician dynamic, and for developing mutually beneficial and nonpaternalistic clinical and advocacy partnerships with communities on behalf of individuals and defined populations."[22]

[a]Consistent and universally accepted definitions of race, ethnicity, and ancestry do not currently exist.[18] The authors recognize that current efforts are being made to standardize these definitions and may include changes from what is listed here.

The continuing decrease in sequencing technology costs allows for the simultaneous interrogation of hundreds to thousands of genetic targets, such as exome or genome sequencing. Accordingly, it has been shown that exome or genome sequencing are cost-effective testing strategies[42,43] and should now be considered as first- or second-tier tests in pediatric patients with one or more congenital anomalies, developmental delay, or intellectual disability;[44] individuals with cardiomyopathies and arrhythmias; and individuals with hereditary cancers.[41,45-47] Despite the overwhelming evidence of the clinical utility of next-generation sequencing in diagnosis and shortening the diagnostic odyssey and its support by all major clinical practice societies,[47-51] significant gaps in insurance coverage of genetic testing remain.[26] The lack of insurance coverage has been shown to negatively affect families of children with complex neurodevelopmental disorders by delaying diagnosis and access to appropriate care and management that may slow the progression of the disease.[52]

The unequal coverage of genetic testing by private and government insurers has in part facilitated the flourishing of direct-to-consumer testing laboratories, which offer low cost (out of pocket) testing that may not be comprehensive or clinically validated and whose results can lead to unwarranted anxiety or unsupported reassurance.[53] The lack of uniform genetic testing coverage has also led to a rise in corporate-sponsored genetic testing, which cannot provide subsidization for all genetic conditions nor replace clinical testing.[54] Privacy concerns are also raised by the amount and type of information shared with the pharmaceutical companies and the testing laboratories. Finally, several states, including California and Michigan with Project Baby Bear and Baby Deer, which cover rapid genome sequencing analysis in the pediatric/neonatal intensive care unit, supplement coverage for genetic testing. These models should be adopted more widely to provide more equitable and accessible genetic testing to all families.

Overall, the refractoriness from the medical insurance companies to recognize the guidelines on genetic testing from all major clinical practice societies in the United States and worldwide prevents the use of higher standard clinical grade tests, equitable access to care, timely diagnosis, appropriate management and therapy, and lower health care costs for societies.

Points to consider

- Members of the clinical genetics field should recognize the historical and current practices that have led to harm, medical mistrust, stigmatization, and unfair discrimination in individuals of marginalized groups and URMs.
- Respecting the autonomy, dignity, and traditional beliefs of individuals of a marginalized group or URM is vital to improve uptake of genetic testing while allowing genetic testing opt-out without judgment.
- Inclusion of members of marginalized groups and URMs in genetics research is essential to reduce bias and advance the field of genetics in a socially competent and just manner.
- Genetic testing should be recognized as an integral and indispensable clinical test, equally important as any other laboratory test, routinely ordered by clinicians and fully covered by insurance to guarantee equitable

access to care, timely diagnosis, and appropriate management and therapy.
- Genetic testing should be fully covered and adequately reimbursed as soon as any US nationally recognized medical and genetics societies, organizations, and alliances publish relevant clinical based–practice resources or guidelines recommending the use of genetic testing for a specific disease or disease spectrum.

Clinical Factors

Differences in the diversity of clinicians, access to genetic services, education of both health care professionals and patients, and complexities associated with unknown family history and/or genetic ancestry are clinical factors that contribute to inequities in genetic testing and result interpretation.

Clinicians who have a similar ethnic background of a patient share information in a more culturally appropriate manner and foster a more trusting clinician–patient relationship, which lead to improved health outcomes.[55] However, the US medical field does not reflect the diversity of the general population, with fewer individuals from certain racial and ethnic groups, fewer individuals with disabilities, and fewer women in leadership positions and medical school faculty.[56,57] Similarly, the field of medical genetics is not ethnically diverse, both at the clinician and resource levels. The majority (90%) of genetic counselors identify as White,[58] and only 3% of them identifying as Latinx, a much lower percentage than the general US Latinx population.[59] Just as few genetics professionals are bilingual, only a minority of patient resources are translated into preferred languages, such as Spanish,[60] thus placing non-English speaking patients at a greater disadvantage in receiving culturally appropriate care and in understanding their health care, likely leading to worse health outcomes. The National Human Genome Research Institute has called for diversifying the genetics workforce as a priority and has multiple initiatives underway to engage students, promote clinical and research opportunities for URMs, increase public genomic literacy, and expand leadership positions.[56] In addition, efforts to increase the diversity in the field of genetic counseling are underway, including recruitment and mentoring of minority students at the high school and undergraduate levels into genetic professions.[58] However, potential trainees from URMs face significant barriers that need to be addressed to truly diversify the pipeline and generate an inclusive field of genetics.[61]

Not only is there a lack of diversity in the field of genetics but there are also currently too few licensed medical geneticists and genetic counselors in the United States (and likely worldwide) to accommodate current and projected increased volumes of somatic, germline, and carrier screening testing.[62,63] Although access to timely genetic services is difficult everywhere, individuals living in rural areas, or in communities not otherwise served by academic medical centers, are most likely to face more barriers accessing genetics professionals, including lengthy appointment wait times or long travel distances to see a clinician.[64,65] Telehealth genetic services are one potential way to address such barriers but are not always available because of technological, reimbursement, and license restrictions and/or may not be acceptable, particularly, if not accompanied by translation in the patient's preferred language or related culturally competent care, or adapted to an individual's disability.[66] Another solution to current workforce shortages is greater reliance on primary care providers (PCPs);[65,67] however, few PCPs have the training or confidence to identify patients in need of genetic services or to order genetic tests without the assistance of a genetics professional.[67,68] Multiple studies have shown that URMs are less likely to be referred for genetic services or offered genetic testing.[68-72] Specifically, recent survey data of breast oncologists show African American women, who have a higher morbidity and mortality from breast cancer than White women, are less likely to be referred for genetic testing.[40] Thus, not being offered genetic services when appropriate leads to adverse health outcomes (eg, affecting preventative care or therapeutic management). These and related considerations suggest that underrepresented and underserved communities face significant barriers to genetic service access with the potential to perpetuate health disparities.

Lack of comprehensive genetics education for PCPs and patients, as well as specialist genetic training for recognition of syndromes and conditions in patients of non-European ancestry, are another important source of bias in clinical genetic testing. Core topics in inherited disease risk and genetic test ordering and interpretation are only briefly covered in most medical school curricula, and additional clinical exposure to genetics is attained for only 25% of medical students.[62] Once practicing, there is little to no relevant continuing education courses or accessible genetics training resources for PCPs.[67,68] These educational deficiencies, when combined with the generally low public understanding of genetics, especially among URM groups,[70] likely contribute to the referral disparities noted above. Increasing medical student and physician education to guarantee appropriate genetics referral and recognizing implicit bias in referral practices must be addressed to ensure that racial disparities are not further exacerbated.[40,70] The 2022 Association of Professors of Human and Medical Genetics consensus-based update of the core competencies for undergraduate medical education in genetics and genomics reflect the need to address those deficiencies at the medical school level.[73]

Within medical genetics itself, additional gaps in genetic education may contribute to the bias in genetic testing ordering and/or interpretation. For example, most genetic textbooks and resources lack phenotypic descriptions and clinical images of dysmorphology syndromes in individuals of non-Northern European ancestry.[74,75] Thus, syndromes in

these populations can be more difficult to recognize and lead to a delay in diagnosis. To address some of these issues, there have been efforts to increase studies of genetic syndromes in diverse populations,[75,76] and resources such as a free electronic atlas of syndromes in diverse populations has been launched;[74,77] however, these resources are not necessarily continuously updated.

In addition to the access to care and educational disparities noted above, another significant potential contributor to biases in clinical genetic testing involves the ways in which both patients and clinicians understand and interpret the relevance of family health history and personal genetic ancestry in the context of ordering the appropriate genetic test. Family health history is currently the most readily accessible genomic predictor of complex disease risk and can also provide important clues to the presence of inherited disease risks in families.[78,79] Accordingly, accurate assessment of family health history is often an important part of the pretest genetic counseling encounter and is frequently pertinent to subsequent genetic result interpretation as well. Yet, evidence suggests that disparities exist regarding knowledge and reporting of family health history among different ethnic groups, with URM patients generally reporting lower levels of family history knowledge than their White counterparts.[80-82] These, and related sociocultural differences in family health communication and awareness,[83-85] may interfere with the identification and counseling of underrepresented but still at-risk, patients.

Similarly, unknown or complicated personal genetic ancestry, particularly when captured by social proxies, such as racial and/or ethnic identity, can adversely affect genetic test selection and result interpretation. Few patients are fully aware of their genetic heritage and those who participate in direct-to-consumer testing are often surprised when their genetic ancestry is different from expected.[86] Although many genetics professionals regard consideration of a patient's genetic ancestry as at least somewhat important for clinical variant interpretation,[18] available evidence suggests both widespread use of racial/ethnic identity as a proxy for genetic ancestry[87] and marked heterogeneity of approaches to the collection of race, ethnicity, and/or ancestry data on clinical laboratory requisition forms.[88]

Points to consider

- Increasing medical student and physician education to guarantee appropriate genetics referral and recognizing implicit bias in referral practices must be addressed to ensure that social determinants of health and adverse health outcomes are not further exacerbated.
- Diversifying the genetics workforce must continue to be a priority with a goal of increasing the representation of individuals from underrepresented populations to reduce bias, provide care with cultural humility, and ensure equitable access to genetic testing.
- Genetics health professionals and other individuals interacting with patients in the context of potential risks of inherited disease should take account of differing family communication styles or cultural dynamics, which might affect understanding and reporting of family health history.
- Genetics professionals should, wherever possible, avoid the use of racial and ethnic categories as proxies for patient genetic ancestry.
- Education and resource materials should be written in different languages representing the US population makeup at an understandable literacy level.

Technical Aspects

At its core, genetic testing aims to identify variants associated with disease; however, multiple technical factors play a role in this process, particularly those pertaining to the interpretation of human variation in the context of genetically diverse populations. Various branches of clinical genetic and genomic testing are at different stages regarding strategies to mitigate the risk of inherent technical bias that may affect patient care. In this section, we provide examples that highlight successful instances and areas for improvement.

Genome-wide association studies (GWAS) were the first large-scale strategy to discover variants associated with complex diseases.[89] Approximately 80% of >800 million individuals in GWAS are described as being of "European" descent.[90-92] Although GWAS data have historically been considered as research data with limited clinical utility, their use for estimation of polygenic risk scores (PRS) has grown in recent years. PRS screening may be used to determine the risk of common complex diseases for individuals and their offspring, and although it is not widely clinically available now, there is an ongoing interest in increasing its utility. Use of GWAS data from European populations for PRS estimation would subsequently impose a bias in favor of individuals with similar ancestry, whereas limited benefit is expected for other populations with different genetic risk variants.[91,93] Moving toward diverse GWAS data is already past due and requires key elements including global capacity building and strategic funding.[90,94] These efforts would prevent certain populations from being excluded from databases and is a crucial step toward equity in genomics.

Another area in which bias may impose potential risks to patient care is clinical genome sequencing. Advances in sequencing technologies have pushed the genomics field toward an unprecedented availability of genomes.[95,96] The challenge of clinical genome sequencing lies in the interpretation of the hundreds and thousands of variants obtained within each test.[95] Current clinical guidelines recommend a scoring system for variant classification based on various factors including the rarity of variants among the databases of phenotypically normal populations and disease-specific large-scale sequencing projects.[97,98] Among such databases are the Database of Genomic Variants with compiled data

on structural variations from published studies and the Genome Aggregation Database (gnomAD) with a comprehensive list of variants from many genome/exome studies from various disease-specific and population genetic studies.[99,100] Similar to GWAS, there exists a concern that limited genome data from diverse biogeographical populations would negatively affect the correct interpretation of variants in individuals undergoing clinical genetic testing. Rare variants in gnomAD may be classified as variants of uncertain significance, whereas, in reality, they may be polymorphic variants in ancestries not sufficiently represented. This limitation may particularly explain the higher rate of variants of uncertain significance reported in non-European individuals tested for reasons such as hereditary cancer syndromes.[101,102] The most recent version of gnomAD noted the importance of ancestral diversity and included additional genomes from new populations. This approach has provided new data that could be applied to genetic testing and screening strategies.[103]

Although the efforts to integrate genetic ancestral diversity in GWAS and gnomAD are in progress, the generation of human reference pan-genomes is emerging as a solution for effective incorporation and use of biogeographically diverse genomic data. Numerous national and international projects have driven the availability and representation of diverse ancestries in genomic research.[104-109] The pan-genomes are collections of genomic sequences to be analyzed jointly or to be used as a reference, representing a more complete description of human genomic diversity.[110-112] Inclusive population analyses have successfully enhanced the discovery of previously unidentified genetic variants, including potentially disease-causing variants associated with changes in gene expression, which could be tied to GWAS data.[113]

Recent changes in approaches to carrier screening demonstrate another example of efforts to address bias and inequity in genetic testing. Carrier screening aims to identify heterozygous healthy individuals who carry a risk of having a homozygote child affected with an autosomal-recessive condition. Carrier screening for cystic fibrosis (CF), recommended by ACMG, was initially limited to specific common variants in the CFTR gene.[114] Subsequent studies showed that as high as 30% of non-White CF patients may be homozygous for variants other than the ACMG-recommended list that would have been missed in a routine CF screening of their parents.[115] As a result, a revision by ACMG-recommended assessment of all the coding regions and splice junctions of the CFTR gene and reporting of pathogenic/likely pathogenic variants in all individuals,[116] with a current revision focusing on the expansion of CFTR variants recommended for carrier screening to allow for more equitable testing across races, ethnicities, and ancestries.[117] Carrier screening for other autosomal-recessive conditions has also been limited to panels for specific populations such as Ashkenazi Jewish and French Canadians.[118,119] However, studies in large populations have shown that variants known to be specific to one ancestry may be detected in an individual who is not aware or not willing to share their ancestry.[120] Moreover, a higher number of reproductive partners may come from multiancestral backgrounds, necessitating the use of more than 1 specific carrier screening panel. As a solution, ACMG has recently recommended offering a universal screening panel to all individuals seeking carrier screening regardless of their ancestry.[63,121]

As demonstrated, the outcomes of including biogeographically diverse individuals in genomic research and patient care are tangible and far-reaching. Universal carrier screening panels and reference pan-genomes are conscientious efforts to address health inequities. Such efforts would halt racial categorization as a means of diagnosis and treatment, which can show ineffectiveness within members of the same population.[122-124] The broader inclusion and translation of diverse human haplotypes into clinical research is an outstanding requirement for personalized medicine, not only to overcome technical interpretation and diagnostic challenges but also to achieve health care equity.

Points to consider

- Despite various efforts, the current population databases lack diversity and may not be of comparable clinical utility in all ancestral populations.
- Genomic research should be critically focused on the recruitment of individuals from ancestral populations underrepresented in current databases as well as on the formation of global consortia to share the genome data from different biogeographical regions.
- Pan-genome reference usage by clinical laboratories could facilitate the sharing and analysis of biogeographically diverse genomes and the assessment of genomic variants in the context of disease.
- When ancestral data are limited for patients seeking genetic testing, large ethnic-neutral panels should be offered to cover variants known to be common in different ancestral populations.

Conclusion

The application of genetics in medicine and the ever-developing knowledge about the human genome has already been impactful and has the potential to revolutionize clinical practice. The ACMG is a leader in the genetics field and brings attention to the increasingly important role of genetics in guiding health care decisions and management. As genetic testing is becoming more frequently used and accessible, it is our responsibility to bring awareness and address factors leading to bias and health inequity. Efforts should be made to be inclusive in genomic databases and study cohorts while respecting personal autonomy and cultural beliefs and traditions. Recruitment of more diverse individuals to provide genetic services tailored to the full spectrum of the patient population is a necessary focus of

our field to begin to overcome medical mistrust, address clinician bias, and provide more accessible and culturally competent care and research opportunities. This document is meant to provide a framework to support a positive and constructive dialogue among all stakeholders and lawmakers to continually address advances in genetic testing and their clinical application, with the goal of recognizing and reducing bias to ensure equitable care and avoid unfair discrimination.

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Conflict of Interest

C.J.Z.-M. is a director of a cytogenomics testing laboratory that offers cancer diagnostic testing. M.A. is a director of a molecular testing laboratory that offers carrier screening. K.B. is a genetic counselor of a molecular testing laboratory that offers carrier screening. F.Q.-R. is a director of a cytogenomics testing laboratory that offers cancer diagnostic testing. M.V. is a director of a molecular testing laboratory that offers carrier screening and sponsored panel testing. All other authors declare no conflicts of interest.

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