



## Review Article

# Role of genomics in eliminating health disparities

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## Abstract

The Texas Center for Health Disparities, a National Institute on Minority Health and Health Disparities Center of Excellence, presents an annual conference to discuss prevention, awareness education, and ongoing research about health disparities both in Texas and among the national population. The 2014 Annual Texas Conference on Health Disparities brought together experts in research, patient care, and community outreach on the “Role of Genomics in Eliminating Health Disparities.” Rapid advances in genomics and pharmacogenomics are leading the field of medicine to use genetics and genetic risk to build personalized or individualized medicine strategies. We are at a critical juncture of ensuring such rapid advances benefit diverse populations. Relatively few forums have been organized around the theme of the role of genomics in eliminating health disparities. The conference consisted of three sessions addressing “Gene-Environment Interactions and Health Disparities,” “Personalized Medicine and Elimination of Health Disparities,” and “Ethics and Public Policy in the Genomic Era.” This article summarizes the basic science, clinical correlates, and public health data presented by the speakers.

**Keywords:** Ethnicity, genomics, health disparities, socioeconomic status, race

## INTRODUCTION

A disproportionate burden of disease incidence, prevalence, morbidity, and mortality is shared by certain populations within the United States despite continued efforts by research scientists and the public health community to reconcile this issue. Although some notable improvements have been made in the recent past, large barriers to equitable health persist. Indeed, the largest gaps in health exist among underserved

groups characterized by race/ethnicity, socioeconomic status (SES), geographic location, gender, disability, and age. In a recent report on health disparities and inequalities by the Center for Disease Control and Prevention, 29 different health topics were assessed which covered a wide range of diseases, behavioral risk factors, environmental exposures, social determinants, and healthcare access. Their findings

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showed that health disparities related to race and ethnicity were found across all health topics examined.<sup>[1]</sup> A lower SES is also a major predictor of disparate health risk regardless of demographic factors. For example, African-American (AA) and non-Hispanic white men with 12 or fewer years of education have cancer mortality rates that are nearly 3 times greater than their college educated counterparts.<sup>[2]</sup> Race and ethnicity and SES, however, are only a small part of a much larger diverse group of interrelated factors that contribute to unequal health status in the United States. Since completion of the Human Genome Project, there has been an explosion of studies linking specific genetic variations to common human diseases. By extension, evidence suggests underlying genetic factors also contribute to an increased risk of disease susceptibility, progression, and mortality among specific segments of the United States population.<sup>[3]</sup>

Understanding how genetic variation influences the health and well-being of at risk communities is critically important in eliminating health disparities in the United States. The role of genomics in health disparities, however, is a profoundly complex issue and was the focus of the 9<sup>th</sup> Annual Texas Conference on Health Disparities on May 29 and 30, 2014. The conference was hosted by the Texas Center for Health Disparities in partnership with the University of North Texas Health Science Center (UNTHSC), the National Institute on Minority Health and Health Disparities (NIMHD), and the Institute of Applied Genetics. Nearly 400 students, scientists, clinicians, public health policy leaders, and patient advocates attended the 2-day event of seminars that focused on the current status, future, and challenges facing the genomics community in health disparity research. All three sessions showcased a complement of experts from some of the country's leading genomic centers. Although the talks covered a wide range of topics, each included a unique perspective on genomics research and how it relates to eliminating health disparities. Most importantly, the panel discussions at the end of each session captured the essence of the conference; it provided an open forum that allowed a diverse group of professionals to connect and engage in productive dialogue about ideas and best practices for addressing health disparities in genomics research.

Dr. Elaine Mardis, Co-Director of the Genome Institute at Washington University, commenced the conference with her keynote address focusing on the rapidly changing landscape of genomics and the unique challenges facing the research community associated with this new era of biology. The overarching theme of Dr. Mardis' talk, however, was technology. The past decade has witnessed significant advances in technology used to sequence DNA largely due to the overwhelming success of the Human Genome Project.

The quantitative advances since the first published draft of the human genome are staggering: The financial cost to generate an entire human genome sequence has decreased by several orders of magnitude and the time to generate a human genome now only takes days and weeks as opposed to months and years. Massively-Parallel, Next-Generation Sequencing (NGS) platforms, such as the Ion Torrent Personal Genome Machine and Illumina Hi-Seq, are technologies that have made considerable contributions to our understanding of human genetic variation. A prime example is the success of the 1000 Genomes Project and the ENCODE Project which have produced enormous amount of genetic data that are freely accessible on public databases. For example, 4.9 terrabases of DNA sequence was generated in the initial phase of the 1000 Genomes Project using NGS technology.<sup>[4]</sup> The most recent release from the 1000 Genomes Project is a list of more than 79 million genetic variant sites which is based on data obtained from 2535 individuals from 26 different world populations. The impetus for such large scale genomics research is to ultimately elucidate the relationship between genome function and human biology and disease. Leading the field in genotype to phenotype analysis associated with human pathologies is cancer genomics. Large research consortiums like The Cancer Genome Atlas aim to translate insights from oncogenome sequencing and analysis into improving diagnosis, treatment, and prevention of cancer. However, linking an individual's oncogenome data to clinically actionable therapeutics is a tremendous operational challenge. The massive amount of data generated with genomic sequencing demands powerful computational and bioinformatic tools. To meet this demand, the Genome Institute at Washington University has developed the Database of Canonical Cancer Mutations (DoCM) and the Drug Gene Interaction database (DGIdb). These web-based tools are part of an analysis pipeline that combines highly curated oncogenomic information and known gene-drug interactions in an integrated approach. The goal is to use DoCM and DGIdb as part of a computational strategy to make personalized cancer treatment, e.g., genome-driven immunotherapy, a commonplace reality. Undoubtedly, genomics has the potential to transform medical care for all human pathologies, not just genetic diseases, which is evidenced by the emergence of the subdiscipline pharmacogenomics. However, given the major advances in sequencing technology and computational analysis capabilities, there still remain questions about how genetic variability affects human diseases among populations differently.

A major emphasis during the 9<sup>th</sup> Annual Texas Conference on Health Disparities was the critical need for the genomics research community to address the complex factors

underlying health disparities. The three sessions of the conference aimed to cover these topics and included: Gene-Environment Interactions and Health Disparities, Personalized Medicine and Elimination of Health Disparities, and Ethics and Public Policy in the Genomics Era.

## GENE-ENVIRONMENT INTERACTIONS AND HEALTH DISPARITIES

Dr. Christopher Amos from the Dartmouth-Hitchcock Medical Center spoke about the genetic and environmental effects in health disparities and posed the question “Why Are African-Americans at a higher risk for cancers?” The cancer incidence rates in AA men are higher than Caucasian men; both have higher cancer incidence rates than AA and Caucasian women.<sup>[4]</sup> Furthermore, the type of cancer can result in a higher death rate for AA when compared to Caucasians.<sup>[5]</sup> Furthermore the cancer burden is predicted to increase by 45% from 2010 to 2030 driven by cancer diagnosed in minorities and older adults.<sup>[6]</sup> Although overall cancer rates have decreased, health disparities among ethnic minorities have been persistent.<sup>[7]</sup> Furthermore, 68% of Americans are unaware of healthcare disparities in the quality of healthcare delivered to different racial and ethnic groups according to recent polls. In the words of Dr. Samuel Broder, former director of the National Cancer Institute, “Poverty is a carcinogen.” Economic issues for AA include lower incomes for both men and women compared to their white counterparts. SES is related to health disparities. Contributing factors to health disparities as a result of SES are negative experiences, environmental exposure, discrimination, chronic stressors, and lack of social support and health behaviors such as smoking.

Genetic factors may also explain increased cancer rates in AA. Problems with genetic studies in this area include a lack of participants in studies which may have resulted from a distrust of science due to past abuses and access to tertiary care centers which perform most studies.<sup>[8]</sup> Studies that have been performed implicate AGHPD1 on 15q25.1 as a risk factor in nonsmokers and CHRNA1 on 2q31.1 as a risk variant that is more common in Europeans.<sup>[1]</sup> Additionally, it has been demonstrated that recombination processes vary between Africans and Caucasians.<sup>[8]</sup> Hinch *et al.* built a recombination map in over 29,000 AA between Caucasian and African descent alleles, identified positions that were enriched for crossover derived from African background and identified a single nucleotide polymorphism (SNP) in the PRDM9 gene that identifies an allele that recognizes a different sequence in Africans versus Caucasians.<sup>[8]</sup> The conclusion of Dr. Amos is that AA males have a higher risk for developing many cancers than other ethnicities, and while SES may

account for part of the increased risk, it does not explain all of it. Genetic variation also plays a contributing factor, but biological determinants still may play an unrecognized role in the disparity of cancer in AA and Caucasians.

Dr. Tesfaye Mersha, from the University of Cincinnati, spoke about the role of genomics and environment in childhood asthma in AA. According to the National Heart, Lung, and Blood Institute, Asthma is a chronic disease that inflames and narrows the airways. Genetic and environmental factors contribute to the development of asthma and the heritability estimates are up to 79%. Environmental factors include air quality and stress, SES, health maintenance behaviors, and genetic factors. Children with one asthmatic parent are 3–6 times more likely to develop asthma and children with two asthmatic parents are 10 times more likely to develop asthma than normal. Asthma prevalence differs based on race, with AA having the highest and Caucasians the lowest.<sup>[9]</sup> The disparity among gender also exists; males have a higher prevalence of asthma at a younger ages, typically under the age of 15, however over the age of 15 females tend to have a higher prevalence.<sup>[10,11]</sup> Fifty-two candidate genes were identified using patient information of over 7000 individuals living in or near the greater Cincinnati area from the Greater Cincinnati Pediatric Clinic Repository. Six SNPs were significantly associated with childhood asthma in AA and five were associated in childhood asthma in Caucasians and two SNPs in IL4 were identified as associated with asthma in both,<sup>[12]</sup> indicating that the asthma associated SNPs are, to an extent, segregated based on ancestry. The lung function in terms of forced expiratory volume decreases as a percentage of African ancestry increases.<sup>[13]</sup> Both the associated genetic and physiological aspects of ancestry are important because the patient may misclassify themselves when reporting racial ancestry.<sup>[13]</sup> Furthermore, admixed populations are important because genetics is based on a European reference SNP panel. If a disease is identified in a European population, the genetic effects of that disease are diluted in people across other continents.<sup>[14]</sup> This is important because one of the challenges in asthma etiology is that genetics is based on a European reference SNP panel. Additional challenges are the heterogeneous nature of asthma and the subjective nature of phenotyping. Dr. Mersha concluded that difference in asthma prevalence could be genetic, environmental or both and that needs to be a dissection of nongenetic factors which correlate with ancestry in addition to population-specific reference panels. Data mining should also be used for integration across domains to include the genetics, gene expression, and epigenetics.

Dr. Ranajit Chakraborty, from UNTHSC, spoke of unresolved issues and a possible paradigm regarding gene-environment

interactions. Disease class, such as autosomal dominant, autosomal recessive, X-linked, chromosomal abnormalities, chronic multifactorial, and congenital abnormalities affect a wide percentage of live births.<sup>[15]</sup> The view of a monogenic disorder where a mutation in a single gene is then inherited in a Mendelian fashion is the simplest manner in which genetics may play a role in disease.<sup>[16]</sup> A complex disorder model may have multiple genes with various mutations with a non-Mendelian inheritance pattern resulting in a variable risk for different families. This is important when attempting to identify the genotype in a complex disease. The paradigm of complex diseases is the genotype and the environment which results in the phenotype ( $G \times E = P$ ) with the genotype being the loci, alleles, and other genetic variants and the environment as the occupational and environmental agents, lifestyle, culture, SES, belief system, etc., In gene-environment interaction, an environmental agent may be dependent on the genotype of the individual exposed to the risk agent, whereas the genotypic susceptibility may vary depending on the individual's exposure to an environment agent. Moderators and mediators are two types of gene-environment interactions; moderator is an independent variable that affects the strength and/or direction of the association between another independent variable and an outcome variable whereas, a mediator is a variable that specifies how the association occurs between an independent variable and an outcome variable.<sup>[17]</sup> An example of a moderator is the association of pesticide exposure as a risk factor for Parkinson's disease (PD). Glutathione transferase (GSTP1-1), expressed in the blood-brain barrier, is known to influence response to neurotoxins.<sup>[18]</sup> Pesticide exposure risk of PD is moderated by two polymorphisms in GSTP1-1 resulting in nonsynonymous substitutions, which by themselves had no effect on PD, but the variants in the presence of pesticide exposure risk did moderate the risk of PD.<sup>[18]</sup>

Cells respond to radiation by altering expression of genes, some of which are EGF, PKC, EGR1, RPA, AT, and p53.<sup>[19,20]</sup> Cells with a nonfunctioning p53 will not be arrested in the cell cycle or enter apoptosis. This results in the accumulation of radiation-induced genetic damage. A single-locus model of genotype-dependent radiation-induced risk assumes a Mendelian inheritance model; the total is the aggregate of multiple factors dependent on the genotype, allele frequency, penetrance, predisposition risk, and radiosensitivity differential.<sup>[21]</sup> Three risk measurements are used to study the effects of presence of radiosensitivity and cancer predisposition genes: The ratio of risks under radiation exposure with or without the predisposing allele, the proportion of cancers as a result of radiosensitivity and the predisposing allele and the excess cancers due

to the presence of the radiosensitivity differential alone. The question of risk estimation was also brought forward weighing risks of radiation exposure from mammography versus the risk of breast cancer from those with the BRCA mutations conferring a predisposition onto the individual. The three risk measures were used to study the effects of the presence of radiosensitivity and cancer predisposition genes. The risk benefit analysis of mammography concluded that with increasing proportion of breast cancer detected, mammography is more beneficial; however it is important to note that this model is a single locus model, whereas cancer predisposition may be a result of more than one locus. The conclusions of Dr. Chakraborty is that evaluation of different forms of gene-environment interaction models and their distinctions in the context of risk estimation equations is a possible area for future research.

## PERSONALIZED MEDICINE AND ELIMINATION OF HEALTH DISPARITIES

The vision for future healthcare is to use genomic information in combination with medical history to personalize medical treatment. In his presentation, "The PREDICT program: Implementing prospective pharmacogenetics for inpatient and outpatient clinical care," Dr. Josh Denny, Vanderbilt University Medical Center (VUMC), discussed the role of electronic health records (EHR), genomic, and pharmacogenomic analyses in making the vision of personalized medicine a reality. EHR have many benefits over traditional paper records and in time will improve the quality of care for all patients. Indeed, health information technology (HIT) can help improve the healthcare of underserved communities and reduce health disparities.<sup>[22]</sup> However, EHR potential has not been fully realized despite a growing national HIT adoption rate. Vanderbilt established a unique biorepository which links more than 178,000 DNA samples with corresponding de-identified patient medical records. Vanderbilt's biobank, named BioVU, serves as a digital portal for researchers to search, record, and analyze phenotypic data, e.g., atrial fibrillation, Crohn's disease, and multiple sclerosis, that is derived from electronic medical records (EMRs). BioVU is also part of the EMR and Genomics network which provides genotype information that covers hundreds to thousands of SNPs with each de-identified DNA sample. As a resource for discovery, genome wide association studies (GWAS) are performed on the SNP genotype data in order to identify new associations with EMR-derived phenotypes. Using this approach, Denny *et al.* reported four SNPs in linkage disequilibrium at 9q22 near FOXE1 that are associated with hypothyroidism. One SNP, rs7850258, exhibited the strongest association with an odds ratio of 0.74 ( $P = 3.96 \times 10^{-9}$ ).<sup>[22]</sup> The results of



this study demonstrate that EMR-linked genomic data can be used to identify risk alleles associated with the disease. However, from a pragmatic perspective it shows the potential value of using EMR-linked genomic analysis as a part of an informatics strategy to assist healthcare providers make accurate diagnoses. Equally important is the ability of clinicians to accurately prescribe medications to treat those diagnoses. It is well known that genetic variation contributes to variable drug response among the patient population.<sup>[23]</sup> Therefore, studying how gene variants modulate protein function, that is, pharmacogenomics, may improve treatment outcomes for patients and prevent adverse drug events (ADE). The Vanderbilt Electronic Systems for Pharmacogenomic Assessment uses data from BioVU and GWAS to determine whether responses to certain drugs can be predicted by EHR-linked genomic data. In personalized medicine, the value of pharmacogenomic analysis in predicting drug responses is two-fold: First, it is a great resource for determining the most effective dosing treatment for an individual prescribed medication. For example, the results of a warfarin study showed that using EHR-linked pharmacogenomic analysis improved dosing for European-Americans and African-Americans more than using the United States Food and Drug Administration (FDA) dosing recommendation or the International Warfarin Pharmacogenomics Consortium algorithm alone.<sup>[24]</sup> Second, the pharmacogenomic analysis is useful for identifying certain drugs a patient should avoid as was demonstrated in a clopidogrel study by Delaney *et al.*<sup>[25]</sup> Their study evaluated EHR-linked pharmacogenomic data of 693 patients prescribed the antiplatelet drug and showed that two SNPs, *CYP2C19\*2* (rs4244285) and *ABCB1* (rs1045642), were associated with recurrent cardiac events, HR 1.54 (95% confidence interval [CI]: 1.16–2.06,  $P = 0.003$ ) and hazard ratios 1.28 (95% CI: 1.04–1.57,  $P = 0.018$ ), respectively.<sup>[25]</sup> In a separate carbamazepine study, an HL\*3101 allele was found to be a population specific risk predictor for cutaneous adverse drug reactions, e.g., Stevens–Johnson syndrome, toxic epidermal necrolysis, and drug-induced hypersensitivity syndrome.<sup>[26]</sup> Together these studies illustrate how information from EHR-linked pharmacogenetic analysis could be translated into a proactive, actionable therapeutic strategy for improving pharmacological treatment and mitigating ADEs. Unfortunately, prospective genotyping is not commonly performed which, in terms of opportunity loss, has dire consequences. A retrospective study of 52,942 VUMC patients receiving one or more of 56 drugs with known gene–drug associations illustrates this point. The study found that six common medications, e.g. blood thinners and cholesterol lowering statins, accounted for 383 ADE over a 5-year period.<sup>[27]</sup> Disconcerting is the fact that the number of medications with known pharmacogenetic

effects has steadily grown since 2007 when the FDA first began including gene–drug effects in its labels. Therefore, the case of prospective genotyping for drug safety has never been stronger. Vanderbilt’s PREDICT project (Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment) is an example of translating proof of concept to real world implementation of pharmacogenomics. Given that many patients carry more than one pharmacogenetic variant, the “reactive” strategy has a higher testing and financial burden than the 1-time, preemptive multiplex genotyping strategy.<sup>[27]</sup> Interestingly, when grouped by race/ethnicity, 88% of individuals identified as European American (not Hispanic) and 96% of individuals identified as AA (not Hispanic) exhibited 1 or more risk alleles.<sup>[27]</sup> This finding further supports the position that HIT and, perhaps more importantly, genomics have the potential to improve patient care by personalizing medicine and help eliminate health disparities of underserved populations.

An individual’s health and risk of disease are greatly influenced by the genes, lifestyles, and environments shared with its family members. Therefore, family health history (FHH) is an essential component of personalized medicine. In her talk, “FHH Risk Assessment in the Contest of Health Disparities” Dr. RYANNE WU, Duke University, discussed using FHH for risk stratification as part of a healthcare strategy. The initial phase of planning, developing, and implementing a personalized healthcare plan is to identify a patient’s health risk status. The use of guidelines based on FHH risk stratification is beneficial because it allows healthcare providers (providers) to tailor a personalized care plan that maximizes benefits over risks. For instance, patients with a familial risk for cancer would greatly benefit from prevention and risk management counseling. For example, women with a greater than population risk for breast cancer may be counseled to undergo genetic counseling and alternate magnetic resonance imagings (MRIs), with mammograms every 6 months. Whereas women with <20% risk for breast cancer may be counseled to undergo less intensive and less frequent tests. In this scenario, the FHH risk stratified based guidelines are designed to increase the likelihood of early detection for at risk women but also to decrease the likelihood of unnecessary invasive procedures for women with no familial risk. Despite its benefits and importance as a component of personalized healthcare, FHH risk stratification is not commonly performed. Reason being there is generally a lack of knowledge, in different respects, by patients and providers. Often patients do not have a complete or accurate understanding of their family’s health history due to a lack of communication with family members and/or a lack of appreciation for the importance of FHH. As a consequence, providers are challenged with making risk assessments based on limited and/or incorrect

information. For example, a patient may mistakenly report a relative dying from brain cancer because of not knowing the importance of distinguishing between the original (lung) and metastatic (brain) sites of their relative's disease. However, even when patients are adequately informed, providers find difficulty in translating FHH into appropriate, actionable risk stratified care management plans. In a recent study, Primary Care Provider's (PCP) clinical assessment of appropriate risk management for patients was compared to an informatics tool (MeTree) which uses well recognized clinical guideline-based recommendations. Overall, PCPs underestimated risk 77.5% ( $n = 38/49$ ) mostly in regards to the need for genetic counseling and early colonoscopy and overestimated 22.4% ( $n = 11/49$ ) the need for breast MRI, chemoprophylaxis, and ovarian cancer screening.<sup>[28]</sup> These findings demonstrate the disconcerting reality of inaccurate FHH risk assessment; average risk patients may be subjected to unnecessary screening and referrals whereas, high risk patients may not receive adequate risk management and disease surveillance most appropriate for their health risk status. PCPs encounter several barriers that challenge their ability to fully utilize FHH risk stratification and implement an appropriate risk management strategy for their patients. Major contributing factors include operational constraints in the clinic, a lack of standardization of FHH collection procedures, and the complexity of current guidelines for risk stratification calculations. To address these issues, the Genomedical Connection developed the Genomic Medicine Model (GMM). The goal of GMM is to improve the quality of FHH utilization for risk stratification and risk management at the primary care level. The GMM development team included a diverse board of stakeholders which included genetic counselors, medical geneticists, cardiologists, oncologists, health behaviorists, and IT experts. Their guiding principles required GMM satisfy a comprehensive list of criteria which includes patient participation and multi-level decision support for providers. Given the complexity of FHH and risk stratification analysis, education is a key component of the GMMs design.

## ETHICS AND PUBLIC POLICY IN THE GENOMIC ERA

Dr. Barbara Koenig, University of California San Francisco, addressed the topic of research targeted by race in translational genomics. A two-fold central dilemma was set forth: To what extent are health disparities the result of unequal distribution of resources, and thus a consequence of varied social and economic background? And, to what extent are variations in health outcomes the result of inherent characteristics on individuals? Research conducted since the completion of the Human Genome Project focus on the differences between

human genomes, despite the high level of homology between any two individuals. Disparities in translational genomics are a concern given the history of how race has been used. The concerns of research integrity, conflict of interest and harm as a result of the ethical, legal and social implications may be reducing the rate at which genomic research can be translated in outcome for improved health results. Unfortunately, the need to maintain interdisciplinary dialogue can result in an "irritative phase" between individuals can result in the questioning of their assumptions, methods, and application to their problem. After a review of genetic data, it was shown that people can usually be assigned to ancestry clusters that agree with their self-identified ethnicity. Dr. Collins of the National Institute of Health stated that there are no human races in the strict biological sense and that humans represent a continuum of diversity.<sup>[29]</sup> However, science has been used to justify theories of racial hierarchy. Although race is real it is not a thing, but a social relation. The United States Office of Management and Budget (OMB) uses racial categories that are not biological categories; the OMB directive 15 clearly states that "these classifications should not be interpreted as being scientific or anthropological in nature..." The use of race and genetics has a history of abuse in the United States; the United States Air Force Academy used the sickle-cell trait as a rationale to test individuals of African-American descent in order to prevent them from enrolling. Variations in the frequency of diseases can be delineated by ancestry, such as the prevalence of triple-negative breast cancer.<sup>[30]</sup>

What are the best practices in describing the human difference in genomics research? A recommendation by Dr. Koenig for discussion was the use of ancestry to describe genetic variation, the use of race when studying health statuses in societies characterized by racial hierarchies and ethnicity to refer to lifestyle, diet, values, etc., Furthermore, explanations of how categories of human difference were ascertained should be present in publications, and the conflation of biological and social categories should be avoided. Instead of avoiding the word "race" in genetics research the right question should be "Under what conditions should we use race?"

Dr. Jennifer Wagner, Albert Einstein College of Medicine, spoke about personal genetics in sports medicine and public health. The role of sports in public policy includes public health intervention and education opportunities, community development, and crime prevention. Over 45 million youth participate in organized sports, and 75% of United States families with school age children have at least participating in sports.<sup>[31]</sup> Federal legislation regarding the safety of participants in sports has included addressing education and awareness for cardiomyopathy and concussions.<sup>[31]</sup> States have also taken an active role

in enacting their own legislation regarding concussions in sports; sudden cardiac prevention acts were first adopted by Pennsylvania in 2012, with more states following their lead. Diversity in the players and ownership of sports is the context in which public policies will be implemented. The breakdown of players and owners based on their race, ethnicity and gender is important because it is the context in which public policies will be implemented.

Athletic ability has numerous phenotypic characteristics; strength, cardiovascular endurance, hemodynamic traits, anthropometry, body composition, metabolism, lipid, lipoprotein, and hemostatic factors. Influences of these phenotypes include sociocultural, economic and gestational exposures, and genetic factors such as epistasis and gene-environment interactions. Around 250 genetic variants have been implicated in sports performance.<sup>[32]</sup> One of the genetic factors is a variant in the ACTN3 gene, which is expressed in fast twitch muscle fibers; nonsense polymorphism R577X can result in three possible genotypes; RR, RX, or XX.<sup>[33]</sup> Presence of the XX genotype is skewed toward endurance Olympians, and RR is skewed toward the power Olympians.<sup>[33]</sup> Direct-to-consumer testing had been available to test DNA for sports-related genes, although some of the companies are no longer in business. One of the issues with these DTC testing is the lack of a standard in which results are given. This is an additional set of information in the world of the data-driven movement for personalized fitness which already utilizes certain food, nutritional supplements and sports enhancing substances, personal trainers, and fitness apps and devices. In the past racial segregation in sports persisted in the United States persisted until the mid-20<sup>th</sup> century with the justification that race conferred a natural advantage or disadvantage. With other policies still in effect to segregate individuals based on gender, age, experience, and weight for participation based on various characteristics begs the question will genotype segregation be part of the future? The applications for genetic technologies in sports are broad; it could be used to identify potential elite talent, risks of injury, as a way to verify sex or identity. However, there are several concerns over this testing for potential-talent including false advertising, child testing, psychosocial harms, genetic discrimination, and the addition of unnecessary burdens on the healthcare system and privacy concerns. Chronic traumatic brain injury, hypertrophic cardiomyopathy, and concussion risk screening are other examples of how genetics could be used to screen players for risk on the field. Dr. Wagner's conclusions are multifold. One is that disparities exist within sports and must be considered with the design and implementation of policy. Genetic information and preparticipation screening should be used to manage risk and not as guise for disqualification.

However, it is important to avoid genetic exceptionalism and overly paternalist policies.

Dr. Avni Santani, Children's Hospital of Philadelphia, presented on the challenges and opportunities in clinical genomics. The clinical applications of genetic testing include diagnostic testing, prenatal diagnosis, newborn screening, carrier screening, predictive testing, and pharmacogenetics. The benefits of this testing allows for better management and intervention of the disease and allows for early intervention. One example of a need for genetic testing provided was bilateral sensorineural hearing loss was illustrated as an example of a heterogeneous genetic disorder, over 100 genes are correlated with this type of hearing loss. The genetic testing could consist of sequencing for a single gene, a panel of genes, the whole exome, or the whole genome. The challenges in incorporating genomics into clinical medicine include the understanding, or lack thereof, of the human genome. There is an uncertainty of results which may arise from unknown variants, epistatic interactions, epigenetic inheritance, and other limits of biological insight. As previously discussed, there is an underrepresentation of ethnic groups in research. The use of genetic information can have multiple impacts on patients and their parents including the precipitation of more questions and the alleviation of guilt or blame.<sup>[34]</sup> The misuse of science to discriminate in the past in the form of eugenics in Europe and the United States is a reminder and the potential misuse of genomics in the future; the promise of genomic medicine today is provide information so people can have the ability to make decisions about their health, for the care of children and to ensure proper education. Ethical principles must stem from the precept of "do no harm"; protecting and defending the rights of the patient, avoiding harm, informed consent, and a decision process free of coaxing, as well as equitable treatment of patients. There is also the ethical question of what to do with incidental findings. Should a child and their parents be burdened if in the search to discover the cause of a disease results in the discovery of a risk factor for another disease? What if the risk factor is for an adult-onset disease? What if there is a treatment available, or what if there is no treatment available? What if an unexpected familial relationship is revealed? The ACMG recommended reporting incidental findings in clinical exome and genome sequencing in 56 genes associated with medically actionable conditions. This created controversy and the recommendation was revised to include and opt-out of incidental findings. To further address barriers regarding health disparities, international genomic collaborations have a key role in the future, especially with the study of underrepresented ethnic groups as well as demonstration of value of genomics testing for reimbursement. There needs to be proper patient engagement by the medical staff and

with genetic counselors if desired, education on genetics and genomics and improving access of genomics based healthcare through public policy and reimbursement by insurance companies.

## CONCLUSIONS

The three highly informative and interactive sessions in the conference provided an excellent platform for researchers, clinicians, and public health professionals to better understand the progress made in the past decades, the current scenario, and the future challenges to be faced, from different perspectives, in the fields of genomics and personalized medicine. The critical need for the genomics research community to address the complex factors underlying health disparities were emphasized in each of the three sessions. Many factors have been associated, either positively or negatively, with the disease/relapse predictions, but the complexity of the confounding variables associated with the primary factors is still quite large. It is important to comprehend that though very significant advances have been made in the field of genomics, we are still at the learning phase - trying to understand how to deal with affected individuals at a social level, trying to bridge the gaps causing disparities in access to care and treatment effectiveness, questioning the intricate complexities at the molecular level and/or taking advantage of the understanding to create new or better existing algorithms to enhance personalized therapies as cost effective and clinically efficacious alternatives.

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There are no conflicts of interest.

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