Commentary: Two Threats to Precision Medicine Equity

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In January 2015, President Barack Obama unveiled the "Precision Medicine Initiative," a nationwide research effort to help bring an effective, preventive, and therapeutic approach to medicine. The purpose of the initiative is to bring a precise understanding of the genetic and environmental determinants of disease into clinical settings across the United States.[1] The announcement was coupled with $216 million provided in the President's proposed budget for a million-person national research cohort including public and private partnerships with academic medical centers, researchers, foundations, privacy experts, medical ethicists, and medical product innovators. The Initiative promises to expand the use of precision medicine in cancer research and modernize regulatory approval processes for genome sequencing technologies. In response, Congress passed the 21st Century Cures Act in December 2016, authorizing a total of $1.5 billion over 10 years for the program.[2] Although the Precision Medicine Initiative heralds great promise for the future of disease treatment and eradication, its implementation and development must be carefully guided to ensure that the millions of federal dollars expended will be spent equitably. This commentary discusses two key threats to the Precision Medicine Initiative's ability to proceed in a manner consistent with the United States Constitutional requirement that the federal government shall not "deny to any person . . . the equal protection of the laws."[3] In short, this commentary sounds two cautionary notes, in order to advance precision medicine equity. First, achieving precision medicine equity will require scientists and clinicians to fulfill their intellectual, moral, and indeed legal duty to work against abusive uses of precision medicine science to advance distorted views of racial group variation.

Introduction

First, achieving precision medicine equity will require scientists and clinicians to fulfill their intellectual, moral, and indeed legal duty to work against abusive uses of precision medicine science to advance distorted views of racial group variation. The prospect of using patients' genetic information to better predict and prevent disease could easily travel down the slippery slope toward eugenics – the immoral and deadly pseudo-science that gave racist and nationalist ideologies what Troy Duster called a "halo of legitimacy"[4] during the first half of the 20th century. While precision medicine and eugenics may not seem similar, the two movements share commonalities. Both hold that a new understanding of genetics will result not only in remarkable improvements in human health, but also in the betterment of society overall.[5] Both target ways to distinguish "a given patient from other patients" and propose to do so "on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics…" [6] Both movements emerged amidst rapidly developing technological and analytical advancements that could accelerate the speed and expand the scope of their influence beyond our ethical and legal capacity to accommodate plans to "revolutionize" health care as we know it.[7] And both movements are located contextually amidst a disturbing surge in the social acceptance of prejudice, xenophobic,

Precision medicine scientists must decisively denounce and distinguish this Initiative from the pseudo-science of eugenics – the immoral and deadly pseudo-science that gave racist and nationalist ideologies what Troy Duster called a "halo of legitimacy" during the first half of the 20th century.[4] Second, to combat the social threat to precision medicine, scientists must incorporate a comprehensive, ecological understanding of the fundamental social and environmental determinants of health outcomes in all research. Only then will the Precision Medicine Initiative live up to its potential to improve and indeed transform health care delivery for all patients, regardless of race, color, or national origin. *Ethn Dis:* 2019; 29(Suppl 3):629-640; doi:10.18865/ed.29.S3.629

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and White supremacist ideology in the United States, and worldwide.[8]

During the early 20th Century "[r]acism . . . provided the theoretical framework for eugenic thinking. In return, eugenics provided twisted versions of science and public health justifications for White supremacists to advocate that forced sterilization, anti-miscegenation laws, and state-sponsored segregation would advance the 'health of the race.'"[9] White Americans had for more than two centuries developed an understanding of the races as biologically distinct groups marked by inherited attributes of inferiority and superiority."[10] Eugenics, named from the Greek word meaning "well-born," is "the study of self-directed human heredity and breeding [that] promise[s] to raise the general welfare by reproducing better individuals"[9] Arthur Caplan famously recounts the deadly cruelty that eugenicists visited upon Jews during the Holocaust,[11] and Dorothy Roberts[10] poignantly traces the movement's cruel inspiration that institutionalized White supremacy in Racial Integrity Laws,[12] enacted across the United States to protect whiteness from race-mixing. Eugenics provided the biological justification for viciously legalized sterilization of the poor and mentally ill,[13] and intellectually fueled the discriminatory doctrines that instituted the Post-Reconstruction, segregated social order in America that persists today.

> "The Negro problem is part of the greater problem of heredity. When eugenics seeks to eliminate the unfit and establish the fit it has for its purpose not the betterment of physical types merely, but the establishment of those types of greatest value to progressive civilization . . . Those who seek to maintain the White race in its purity within the United States are working in harmony with the ideals of eugenics. Asiatic exclusion and Negro repatriation are expressions of the eugenic ideal." – Earnest Sevier Cox [9, p138]

The possibility of incorporating information encoded in the human genome to address threats to human health could easily appeal to perverse notions of selective reproductive breeding. Moreover, the notion of biological hierarchies could extend to tolerate, if not justify legalized social and economic racial hegemony. Minority populations share a deep concern[14,15] that precision medicine's basis in genome science may be misused to resurrect the backwards and hateful assertions of racialized science.[10] Since the 1970's, the White power movement[16] in America has consolidated an escalating campaign of terror that sadly continues to claim adherents among geneticists today.[8,17,18] I call this the threat of scientific racism.

Second, if precision medicine science fails to fully incorporate knowledge of the ecological influences of structural discrimination and prejudice on the epigenetic and ecological outcomes shared among many minority populations, the genetic revolution may indeed exacerbate the disproportionate adverse health effects that racial and ethnic minority groups experience.[19] I call this the threat of social racism.

I discuss these two threats, beginning by illustrating the impact that indifference to the threat of scientific racism could have. Following this section, the threat of social racism is explored in light of the evidence precision medicine seems yet unable to incorporate. The conclusion offers some preliminary recommendations.

Scientific Racism Threat

In 2002, the Institute of Medicine published a landmark consensus report, *Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care*, which reviewed the empirical literature, considering more than 600, peer-reviewed studies and identifying dramatic and troubling health disparities across a broad variety of diseases and illnesses. It concluded that in America, racial and ethnic minorities tend to receive a lower quality of health care than non-minorities, even when access-related factors, such as patients' insurance status and income, are controlled.[20] In the wake of *Unequal Treatment*, the Center for Health Equity Research and Promotion describes researchers engaged in identifying the causes of observed disparities as well as interventions to eradicate them, as second and third "generation"[21] researchers, respectively, and precision medicine and genomics could contribute to these efforts. However, a group of geneticists have assailed the work of all generations of disparities researchers as unscientific,[22]

asserting that the field is driven by an ideological commitment to political correctness rather than rational fact.[23] These critics represent a scientific threat to the potential of precision medicine. They, like eugenicists, resort to scientifically unsupported and plainly degrading explanations of observed differences among racial populations in ways that amount to positing genetic inferiority of minority populations.[24,25] This form of racialized medicine could profoundly distort precision medicine research first by causing a dangerous re-focus on assertions of biological differences among human population groups that simply do not exist,[26] drawing attention away from productive second and third generation research needed to eradicate health disparities among underrepresented populations,[27] and second by suppressing policy solutions that might improve and lengthen lives. I will discuss these two aspects of the scientific racism threat in turn.

The Distractive Threat of Scientific Racism

Many who attribute the problem of health disparities to genetic variations among the races define "race" as a group that is ancestrally connected to one of five population groups based on their primary continent of origin, a theory first advanced by racial topologist Johann Blumenbach in 1795. These are people who believe one's genes determine one's race. Hence, I call them "genetic deterministsm." Citing a human population genetic study as exemplary of many that confirm these categorizations, genetic determinists report "[t]he results are the same irrespective of the type of genetic markers employed, be they classical systems, restriction fragment length polymorphisms (RFLPs), microsatellites, or single nucleotide polymorphisms (SNPs)" These studies, they say, consistently find populations clustered into five groups: "The African branch [including] three sub-Saharan populations, . . . the Caucasian branch [which] included Northern Europeans and Northern Italians; the Pacific Islander branch [including] Melanesians, New Guineans and Australians; the East Asian branch including Chinese, Japanese and Cambodians; and the Native American branch [which] included Mayans from Mexico and the Surui and Karitiana from the Amazon basin."[27] While acknowledging that these categorizations have been blurred by migratory patterns, genetic determinists place fundamental importance on these findings,[28] which they interpret to have a profound impact on racial health disparities between Black and White Americans. Despite the fact that these researchers "categorize Africans as those with primary ancestry in sub-Saharan Africa; [including] African Americans and Afro-Caribbeans. . . [and] Caucasians [as] those with ancestry in Europe and West Asia, including the Indian subcontinent and Middle East,"[28] they believe they have found meaningful pathways to ascribe genetic variations that exist among ancestral population groups to self-identified racial groups in the United States.

To connect modern American racial groups to the population studies that focus on human evolution, genetic determinists assert that endogamous mating patterns have persisted from prehistoric times to the most recent US census: "[A]dmixture between races has occurred over many centuries. Nonetheless, during the same period of time, as well as currently, mating patterns are far from random. The tendency toward endogamy is reflected within the 2010 Census, which allowed individuals to report themselves to be of a single race or of mixed race – 69.1% of subjects reported being of one race, while 2.4% reported being of more than one race.[29] These figures, genetic determinists say, highlight the strong deviation from random mating in the United States. They explain that "gene flow from non-Caucasians into the US Caucasian population has been modest."[23] This surprising line of reasoning leads to the conclusion that despite "modestly" higher rates of admixture among Blacks and Asians, African Americans largely reflect African origins from a genetic perspective and Whites remain largely and genetically Caucasian.

Dr. Esteban Gonzalez Burchard is among the genetic determinists who conclude that recent genetic studies of population substructure have produced clusters of genetic information that can be used to identify an individual's self-described geographic ancestry. As is common among this group of researchers, Burchard quickly extrapolates from what is known about genetic differentiation for the few diseases where scientists have identified specific variations, to assert the promise of solving much more complex

and uncertain connections between other diseases that occur disparately among American racial groups. Burchard writes, "there are at least 15 million genetic polymorphisms and an undefined subgroup of these that underlie variation in normal disease traits. . . . [One] need change only a single base pair to cause many well-known inherited diseases such as sickle cell . . . or increase risk of common disorders such as Alzheimer's."[30]

Dr. Satel is another researcher whose work exemplifies the mistake common to genetic determinists, who similarly fail to appreciate that genomic variations are neither as common nor as deterministic as they suppose. Thus, this group misunderstands the context in which these variations can be important. Satel infamously proclaimed, "I am a racially profiling doctor," and asserted that "the .1 percent of human genetic variation [by race] is a medically meaningful fact" and "[n]ot surprisingly, many human genetic variations tend to cluster by racial groups…[31] Satel has worked for years with a group of physicians interested in the genetic association between dopamine transporter protein (DAT1) alleles and cocaine-induced paranoia; Satel and her group appear to have had a special interest in identifying racial differences in gene coding for DAT1, focusing their study on comparisons of Black and White patient samples.[32] This effort seems to have been largely fruitless,[33] but Satel's research orientation poses a grave threat to the efficacy and integrity of the Precision Medicine Initiative. Satel's views can lead to a false understanding of the true causes of racial and ethnic health disparities, distracting from generating effective interventions to eradicate inequities, and therefore ultimately serving to widen rather than narrow inequity in population health outcomes.

Dr. Satel flatly and incorrectly claims the problem of racial and ethnic health disparities is a "myth,"[24] turning an epidemiological phenomenon into a "civil rights problem" by ignoring confounding variables. She sees racial disparities such as the fact that White women more frequently suffer osteoporosis, while Black women suffer greater numbers of uterine fibroid tumors, as evidence of biological or genetic differences. [24] This view precludes Satel and health providers who share her medical myopia from taking a comprehensive approach to improving patient health outcomes, dismissing the social determinants that have been shown to have a substantial impact on health outcomes, entirely from the provider's concern.[34] This perspective robs underrepresented minority communities of the opportunity for precision medicine to be precisely tailored to reflect the environmental, social, and clinical determinants that affect their health, and prompts providers and researchers to reach for and privilege plainly incorrect explanations for disease disparities.

The arguments of genetic determinists obscure the hard work of parsing apart the true impact that genetic differences may have on population health,[35] and instead rest on a presumed understanding that "from both an objective and scientific (genetic and epidemiologic) perspective there is great validity in racial/ethnic self-categorizations, both from the research and public policy points of view."[23] The threat to precision medicine this view represents includes an oversimplification of diagnostic and therapeutic decisions that will be imprecise and inaccurate.[36] Even worse, the biologization of race threatens to mislead or exploit those most in need of medical interventions[37] to erase inequities that have produced racial health disparities that by one estimate, unnecessarily cost more than 84,000 lives each year.[38] However the most dangerous adherents to this school regard racial equality as "tripe." [39] This version of scientific racism has serious medical, legal, and policy implications. Dr. Satel's work provides ready fodder for the arguments of eugenicists and White supremacists with whom she, no doubt, does not identify ideologically. Nevertheless, Dr. Satel's scientific errors are useful to racists. For example, when she cites fatalism as an explanation for minorities' disinterest in medical treatment, ignoring egregious historical research abuses as well as persistent contemporary discrimination in medicine[40] that readily explains patient preferences, she dangerously diverts away from fashioning effective, evidence-based interventions to reduce disparities. When she cites "magical thinking" as a reason that minorities avoid cancer treatment while ignoring the simple fact that a majority of White as well as Black Americans believe in the devil,[41,42] she espouses the type of biased analysis that aligns squarely with the worst scientific racism, even if unintentionally.

In their preface to *Race:*

The Realities of Human Differences, Sarich and Miele argue:

> "We present what we believe is compelling evidence to support the propositions that race is a valid biological concept, and that human variations – that is, the differences among individuals and groups, whether in athletic competition, IQ tests, or the competition to lead a satisfying and successful life, however each individual or group may define it – reflect both genetic and environmental factors. On matters of social policy, we are both individualists. We oppose any governmentally sanctioned benefits or handicaps being applied *solely* on the basis of group membership. Rather, we argue for policies that help each individual do the best he or she can and wants to do. Both of us benefited from programs that foster and reward talent and performance, and we support making them open to anyone who is qualified – Period!" [43]

These authors' political objectives are as unabashed as their assertions about Africans' average cranial volume and related racial difference in intellectual ability are foolish. These biological assertions are affirmatively harmful to minority health. Dr. Satel appears to have fallen silent concerning health disparities in recent years. In the interim, some disparities have improved slightly but many have not,[44] and the danger presented by scientific racism persists. An analysis of its policy impact is illustrative.

The Policy Threat of Scientific Racism

Applying genetic determinists' view to a selected health disparity problem can demonstrate the practical import of their approach. The increase in the incidence of preterm birth presents an alarming public health problem in the United States. Preterm infants currently account for between 50% and 70% of all neonatal morbidity and mortality, and poor birth outcomes have been recognized as important predictors of adult disease and illness, particularly adult cardiovascular health for African Americans.[45] Most importantly for the purpose of this analysis, the disparate incidence of low birthweight babies between Blacks and Whites is well-documented. This case is therefore ideal for comparing the approaches of genetic and environmental determinists to analyze and address health inequity.

Zachary A.F. Kistka,[46] a researcher studying the frequency and recurrence of preterm (and therefore) low-weight births between Black and White mothers, holds a genetic determinist view of health disparities. Recently, Kistka explained, "allele frequencies of functional gene variants differ between geographical isolates. This difference in functional gene variants would therefore be expected to be reflected [sic.] by race. Indeed a number of polymorphisms in inflammatory markers as a function of race or ethnicity have been identified in association with preterm labor." Kistka set out to test the strength of this asserted association by conducting a population-based cohort study in which he reviewed the Missouri Department of Health's maternally linked birth-death certificate database.[46] Kistka studied live singleton births from the cohort, focusing on the recurrence of preterm delivery in the same mother. His hypothesis was that genetic factors, independent of environmental ones, increase the risk for extreme preterm birth and its recurrence at a similar gestational age in Black mothers as compared with Whites. Indeed, Kistka did find that Black mothers had a higher relative risk rate of preterm and extreme preterm births than Whites (3.71 and 2.99, respectively). Moreover, while Black and White mothers both showed limited variation in the week of gestation for recurrent preterm birth, Black mothers were at increased risk for recurrent preterm birth and for Black multiparous mothers, recurrent preterm births occurred two weeks earlier than for Whites and were more likely to repeat during the same gestational week than Whites. Kistka and his research team reasoned that their "data suggest that the proposed genetic component of preterm birth may be a greater etiologic contributor than has previously been recognized because racial differences in preterm birth severity and recurrence persisted in [their study] cohort, even after adjusting for known medical and socioeconomic confounders."[46]

In contrast, biological anthropologist Christopher Kuzawa compared the incidence of low birthweight infants born to Blacks and Whites by reviewing evidence from existing studies to critically evaluate the evidence for developmental and epigen-

etic links between early life environments and adult disease disparities. Kuzawa's analysis was based on his "growing appreciation that environmental influences contribute to adult health disparities by influencing biological processes and responses across the life cycle."[45] Kuzawa aimed to evaluate the contribution of maternal stress as a biological pathway to cardiovascular health disparities between Black and White Americans. His study discussed the role of "developmental and epigenetic processes as underlying mechanisms" that contribute to racial disparities in heart disease. However, Kuzawa's definition of race differed from the Kistka's clinical classification:

> "[W]e choose to use the term 'race' because many of the social forces we discuss as underlying determinants of health disparities, such as discrimination, economic inequalities, or segregated neighborhoods represent the unique lived reality of race as a socially defined and *imposed* system in the US. . . . [W]e emphasize that we define race as a socially constructed category that has biological implications, rather than a genetically justified criteria for classifying human variation."[45]

Kuzawa and his team plainly asserted that low birthweight reflects both environmental and genetic factors but quickly concluded that genetic correlations did not fully explain the associations documented between birthweight and race. Moreover, Kuzawa began with the observation that "[t]he first line of evidence is the generally low heritability of birthweight," finding that studies based on twin registries generally report heritability between .2-.4, with national studies reporting estimates of .31 confirming this range. Kuzawa next reviewed studies of monozygotic twin pairs to observe the association between lower weight twins and their elevated risk for adverse changes that put them at risk for diabetes and hypertension later in life, finding that "genetic correlations do not fully account for the associations with adult disease risk." Finally, Kuzawa offered his support for the "developmental origins of health and disease" (DOHaD) model, which emphasizes the biological and developmental mechanisms that associate early life conditions such as malnutrition, stress, and maternal stress with modifications in the weight and condition of infants, later their risk of developing adult diseases, and hence the disparate outcomes that are seen between Blacks and Whites throughout the life cycle. Kuzawa concluded that, "[w]hereas group membership and continental race are poor predictors of genetic variation, these same categories are directly related to the social and structural manifestations of inequality that impact the development of responsive biological systems. A wealth of evidence now shows that the social and economic experiences of race have profound influence on adult health and beginning in childhood, can have effects that are both chronic and cumulative in their impact."

Perhaps the most striking difference between the role that biological and environmental, as well as epigenetic,[47] factors play in Kuzawa's understanding of racial disparities and the role that biological factors serve in Kistka's conclusions, is evident in their recommendations. Kuzawa concluded his study by observing that the "emerging epigenetic model of health disparities points to social and economic change as key to addressing racial differences in disease burden and underscores the need to implement . . . interventions across the life-course." Kuzawa's list is long – improving access to adequate prenatal care and nutrition buffering stress to improve lactating, improving social support through maternity leave, and other far reaching solutions. In contrast, Kistka's discussion remarkably concludes with no hint of an intervention responding to his disparities findings.[48] Kistka and other genetic determinists suggest nothing to improve the health outcomes of minorities.[49]

Summary: The Scientific Racism Threat

I see six exemplary, though non-exhaustive, threats that scientific racism presents to the precision medicine movement. First, it perpetuates inaccurate notions of human populations. For example, researchers such as epidemiologist Nancy Krieger have definitively challenged the unscientific descriptions of artificial human groups that Kistka and other genetic determinists employ.[50] Krieger faults their use of the term "Caucasian," a factually and scientifically inaccurate term coined by 18th century racial topologist Johann Blumenbach, who

incorrectly assumed that Europeans were the original humans and human life emanated from the Caucasus region of Russia. Second, scientific racism advances the mistaken notion that phenotype is equivalent to genotype. In other words, the self-reported racial categories that genetic determinists rely upon are a function of observed traits that arise out of gene expression, rather than traits that are heritable because they are a function of gene frequency. Third, scientific racism overlooks the well-documented fact that 99.9% of humans are genetically identical and ignores the vast variability *within* people groups that is far greater than the variability among people groups.[51] Fourth, it confuses gene frequency with gene expression. The notion that genetic variability accounts for medically important difference in disease outcomes among racial and ethnic groups depends on the frequency of genetic variants or alleles underlying the susceptibility of diseases. While a rare set of mutations that have frequencies of less than 2% do show race-specific variance, the vast majority of diseases have complex mutations that cannot be superficially explained by genetic determinants. Fifth, scientific racism exhibits what researchers Dar-Nimrod and Heine describe as an essentialist bias.[52] They document that using the cognitive heuristics that simplistically organize people into stable, immutable, groups for whom behavior and physiology are merely the result of innate, biological potential, causes affirmative harms in perception and prejudice. However, it is the sixth and final critique that best explains why scientific racism is a dangerous threat. It redirects precious research and policy resources away from innovative interventions that might genuinely aid in eradicating health inequalities, giving false comfort that ideologically driven research has proved that real solutions are not needed. Thus, inaction is the deadliest threat of scientific racism.

Scientific racism inspires vigorous opposition to policies aimed at reducing disparities such as efforts to increase physician workforce diversity or even data collection that measures the relative health of racial and ethnic groups. Perhaps the most pernicious view of this group is their attack on the "assumption" that health gaps can be closed. Fundamentally, those who characterize health disparities as a "myth" distance themselves and other health providers from the responsibility to address health disparities by derisively calling those of us who believe that disparities are associated with structural racism "the disparity-equals-racism crowd."[53] These theorists pronounce, "questions about societal leveling: how to execute it; whether to pursue it at all and, if so, in which domains – are best left to politicians, voters, and social welfare policy experts." The circularity of this view – that social determinants do not cause disparities, but to the extent that they contribute to disparities they are not a scientific concern – leaves nothing for medical scientists or clinicians to do. This is, perhaps, the most tragic flaw and the most serious threat that scientific racism presents to the precision of precision medicine.

The Threat of Social Racism

A second threat to the precision of precision medicine is the possible exclusion of racism itself as an important determinant of health. David Williams et al define racism as "an organized social system in which the dominant racial group, based on an ideology of inferiority, categorizes and ranks people into social groups called "races" and uses its power to devalue, disempower, and differentially allocate valued societal resources and opportunities to groups defined as inferior."[54]

In order for precision medicine to realize its full potential at the population level, the design of studies and the topics of the clinical interventions that result from those studies must not only avoid reifying race as a genetic concept, but also understanding race as a reflection of the societal and individual identity constructions that impose social consequences on groups of people based on societal status. Researchers should follow the example set by historical epidemiologists, [55] sociologists, [56] philosophers, [57] and hosts of physicians[58] who have reasoned that racial disparities in health status and outcomes derive from interplay between complex social forces such as economic disadvantage, institutional and interpersonal discrimination, structural barriers to healthy life choices; unequal access to healthy food, education, work and housing environments; disparate access to water and sanitation; and, indeed, non-genetic transmission of biological differences among the races.

Importantly, access to all these social determinants of health is affected by racism. Thus, understanding racism as both a direct and indirect mechanism producing disparate health outcomes in minority groups is crucial to developing an individualized understanding and clinical treatment of these patient populations.

Dr. Camara Jones[59] has defined three levels of racism that adversely affect health: internalized, interpersonal and systemic. Internalized racism is the incorporation of racist ideologies, beliefs or attitudes within a person's worldview.[60] Interpersonal racism refers to racist interactions among people. Systemic racism, also known as structural, cultural, societal, civilizational and institutionalized racism, refers to prejudiced institutions controlling access to material, informational and symbolic resources. The effects of each must be recognized and included in quality precision medicine.

A body of emerging literature has considered the aggregate impacts of racism on individual health. African Americans have disproportionately been exposed to environmental stimuli that may be sources of chronic and acute stress including perceived racism.[61] Experiences of racial discrimination and mental health outcomes are often affected by stress.[62] The biomarker measure, allostatic load, calculates the "wear and tear on the body" that accrues after repeated or chronic stress. Several studies have found evidence of the association between individually mediated racism and poor health. For example, African American mothers die at three to four times the rate of non-Hispanic White mothers while infants born to African American mothers die at twice the rate,[44] notwithstanding higher incomes and educational attainment than their White counterparts. Research suggests that African American women's lifetime exposure to interpersonal racial discrimination is associated with pregnancy outcomes.[63] Continuous exposure to racial discrimination is associated with cardiovascular responses that could harm pregnancy outcomes. An association has also been found between low-income, urban African American mothers' perception of exposure to unfair treatment and infant birthweight. The association between exposure to racism and very low birthweight is strongest among mothers who engage in high-risk behaviors, which may reflect the impact of institutional racism on health such as the disproportionate targeting of African Americans for alcohol and tobacco products.

Other emerging literature links structural racism to disproportionately adverse health outcomes for minority populations. Researchers have found that residential segregation highly correlates to poor health outcomes.[54] Several studies utilized internet search-based proxy of area racism by measuring area racism as a proportion of Google searches or tweets containing the "n-word." [64] One study found that areas characterized by a one standard deviation greater level of area racism were associated with an 8.2% or 30,000 increase in the all-cause Black mortality rate annually; even after controlling for White mortality rate, area racism was still significantly associated with all-cause Black mortality rate. The same proxy of area racism was utilized to measure the relationship between area racism and birth outcomes. After adjustment for maternal age, Census region, county-level measures of urbanicity, percent of Black population, education, and poverty, researchers found that each standard deviation increase in area racism was associated with relative increases of 5% in the prevalence of preterm birth and 5% in the prevalence of low birthweight among Blacks.

Genomic research must address racial inequality before biomarkers and stochastic modeling can be effective in producing and informing the promising therapeutic prospects of precision medicine and translating these breakthroughs into the clinical setting. Fortunately, precision medicine scientists have demonstrated cognizance of the historic discrimination by the scientific community and its threat to reliable and valid research. For instance, Giorgio Sirugo reported that by 2018, 78% of the individuals included in genome-wide association studies (GWAS) were of European ancestry, despite this demographic constituting only 15% of the global population. Asians represented another 10% of the individuals included in GWAS, while African and Hispanic populations comprised only 2% and 1%, respectively. Further still, nearly three-quarters of GWAS have been conducted in either European (52%) or Asian (21%) populations.[65] Landry et al explained the striking difference between the prevalence of diseases in underrepresented communities and the lack of studies be-

ing conducted to better understand these diseases. For example, Landry found no studies whatsoever in underrepresented groups for colorectal cancer and fewer than 5% of studies for breast cancer included patients from underrepresented groups.[66] Clearly this can mean that underrepresented groups are less likely to be able to find the causes of their diseases and reap the benefits of being able to detect and understand disease. Researchers will need to make concerted efforts to include minority populations in genomic studies as racial minorities are often reluctant to participate for multiple and complex reasons. Some of these relate to historic research abuses such as the Tuskegee syphilis experiment, now familiar to most.[67] But other reasons include lack of information[68] and lack of diversity among researchers who can engender trust in minority communities.[69] Efforts to address these disparities are hopeful. For example, the National Institutes of Health (NIH) has launched the "All of Us" program to collect health, genomic, and behavior data from one million Americans and to specifically oversample and build trust with communities that have been historically underrepresented in research.[2] At last report more than 100,000 participants have been enrolled. NIH has also awarded $18.9 million toward research that aims to accelerate the use of genome sequencing in clinical care, including efforts to ensure that the effectiveness of genomic medicine can be applied to all individuals and groups, including underserved populations, through the Clinical Sequencing Evidence-Generating Research (CSER2) Consortium. While these efforts to diversify the database and scientific workforce are important, they are not enough.

Recommendations

Precision medicine presents a promising opportunity for the future of health care; but if we are to truly advance the interests of health and health equity, we must ensure that precision medicine is *precise* and considers the environmental, as well as genetic, determinants of disease. In furtherance of this goal, policymakers should adopt the following recommendations:

1. First and Foremost, Unequivocally and Resoundingly Reject All Attempts to Biologize Race

The scientific community must engage in a concerted and consistent condemnation of all efforts and expressions that biologize the social construct of race.

2. Create Policies Ensuring the Inclusion of Social Determinants of Health in Research Funding

Racial disparities and health status and outcome are largely driven by social and environmental contexts such as economic opportunity, access to healthy food, education, and housing, structural barriers to healthy life choices, and non-genetic transmission of biological differences. Understanding the role these determinants play in producing disparate health outcomes for minorities is crucial to developing an individualized understanding and clinical treatment of these patient populations.

3. Increase Funding for Ecologic Development of Data Science Focusing on Epigenetic Heritability

Epigenomes are chemical compounds and proteins that influence gene expression without modifying the underlying DNA. Epigenetic change is heritable and may occur rapidly in response to environmental conditions and the experiences of parents. A greater understanding of epigenetic inheritance will enhance our knowledge of ways that the environment, including the social determinants of health, influence genetic expression and inform our decision to promote better health outcomes.

4. Recognize and Address Disparities in Genomic Medicine

Gross racial inequality in genomic research will continue to frustrate the efficacy and equity of precision medicine unless the scientific community makes concerted efforts to include currently underrepresented populations into future studies. This process necessarily requires establishing trust among underrepresented groups that have historically been excluded from and exploited by medical research and the recruitment of a diverse scientific workforce that can engender trust in these communities.

5. Increase Access to Precision Medicine Services

The opportunities and benefits provided by precision medicine

will be limited unless patients of all backgrounds have access to these services. Ensuring equitable access begins with the elimination of barriers to services such as a lack of insurance coverage and the inability to see relevant health professionals that produce existing health disparities.

6. Increase Education of Scientists and Communities

Scientists and clinicians must be trained to include social determinants, including individual, cultural, and structural racism measures in research funding. Enhanced funding for ecologic development of data science focusing on environmental as well as epigenetic heritability.

Conclusion

Without question, the Precision Medicine Initiative has enormous potential to advance the quality of health care and improve health outcomes for all. However, the two most important and influential steps that precision medicine scientists can and should take to protect precision medicine equity are first to denounce and distinguish this movement from the pseudo-science of eugenics, and second to incorporate a comprehensive, ecological understanding of the fundamental social and environmental determinants of health outcomes in all research. These steps will help to clear the way for scientists to accurately and equitably translate the science of genomic and precision medicine into the clinical setting. Only then will the Precision Medicine Initiative live up to its potential to improve and indeed transform health care delivery for all patients, regardless of race, color, or national origin.

Conflict of Interest

No conflicts of interest to report.

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