PREFACE: PRECISION MEDICINE APPROACHES TO HEALTH DISPARITIES RESEARCH

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INTRODUCTION

The publication of this supplement on precision medicine and health disparities marks the 5th year since President Barack Obama announced the Precision Medicine Initiative during his state of the union address in January 2015.[1] The goal of the investment in efforts to personalize medical treatment was to enrich and refine, yet not replace, current staples of medicine and population health such as prevention, screening, diagnosis and treatment. [1] The potential to enable "…the provision of the right drug at the right dose to the right patient"[1, p.795] represented great hope and promise for transforming medical care, for precision medicine is much more than genomic medicine.[2] Because the effects of genetic associations on leading causes of death and leading causes of health disparities (eg, obesity and cardiovascular disease) are small relative to behavioral and social factors,[3] the principles of individualization, personalization and precision have been applied to other areas such as precision lifestyle medicine[4] and precision public health.[5] At five years old, precision medicine's vocabulary, thought process, creativity, and ability to engage with other fields, disciplines and areas of expertise are critical for its continued development and application to health disparity populations[6] and population health equity. Health disparities research evolved in a similar fashion when it emerged 20 years ago. Research on health disparities has moved from the detection and documentation of genetic, biological and individual-level beliefs and health

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behaviors to focus more on research that generates evidence on the dissemination, adoption, and implementation of strategies for reducing *and* eliminating health disparities.[7-9]

It is no accident that one of the first series of research articles dedicated to discussing the intersection of precision medicine and health disparities is being published in this journal. *Ethnicity & Disease* has been on the cutting edge of scholarship defining and discussing precision medicine and its implications for minority health and health disparities because the journal has been a critical venue for debating and refining the measurement of race, ethnicity, racism, discrimination and their implications for health and health disparities since its inception.[10-16] The journal has continued to publish works critiquing the use of race and ethnicity in biomedical research,[17] discussing how genomic medicine can be used to achieve health equity,[12,18] refining the use of polygenic risk scores in health disparities research,[19] and cautioning how direct-to-consumer genetic testing and pharmacogenomics may adversely affect health disparity populations.[20] Recently, the journal also published a supplement on the role that law and policy can play in utilizing genomics and precision medicine to reduce health disparities and advance health equity.[21] This supplement also includes critical insights into the effects that racism can play in shaping the potential that precision medicine has for achieving health equity,[22] and offers additional critique of the use of racial categories in precision medicine research.[23]

OVERVIEW OF THIS SUPPLEMENT ON PRECISION MEDICINE APPROACHES TO HEALTH DISPARITIES RESEARCH

This supplement on precision medicine approaches to health disparities research includes a dozen articles from researchers affiliated with the National Institute on Minority Health and Health Disparities (NIMHD) Transdisciplinary Collaborative Centers for Health Disparities Research Focused on Precision Medicine (PM TCCs). The supplement opens with a Foreword by Rajapaske, Sayre, and Perez-Stable from NIMHD. Rajapaske and colleagues briefly discuss the context that led to the funding of the PM TCCs, and argue that it is important to balance the potential promise of the precision medicine initiative with the recognition that it is unclear whether precision medicine may help to reduce health disparities. The question Rajapaske and colleagues raise is not one of the relevance of scientific rigor or scholarly acumen, but that of the importance of the structural and systemic context that shape the lives of Americans as critical determinants of how beneficial precision medicine may be to minority health and health disparities.[6]

The next three articles used qualitative methods to explore how historically marginalized health disparity populations thought about precision medicine and describe what they saw as the potential benefits and harms it may cause. Rosas and colleagues describe the findings of a focus group study that explored racial and ethnic differences in familiarity with precision medicine, enthusiasm about precision medicine, and concerns about precision medicine. While there was general enthusiasm for this novel research approach, Rosas and colleagues found significant racial and ethnic differences in concerns about how precision medicine may be used to promote health of their populations in Southern California. Specifically, Rosas and colleagues found that African Americans and American Indians expressed more and different concerns about precision medicine than Latino and Asian Americans, particularly in relation to past abuses in biomedical research. Next, Yeh and colleagues conducted focus groups with African Americans in Nashville, Tenn. and Hispanic Americans in Miami, Fla. to identify their perspectives on the likelihood that precision medicine would be equally beneficial for all Americans and if they felt it held particular promise for their ethnic group. Similar to Rosas and colleagues, Yeh and colleagues found that both groups generally thought there could be benefits of precision medicine for health for individualizing care and reducing medical uncertainty, but there was skepticism about whether either African Americans or Hispanics would benefit from precision medicine. Much like Rajapaske and colleagues, the concerns were rooted in the societal structural limitations that influenced access to, and quality of, care and that led to disparities in these determinants of health care. Yeh and colleagues also found that African Americans were particularly concerned that personal information – both genetic and non-genetic – could make them more vulnerable to racism and discrimination not only in health care but also in other aspects of their lives (eg, employment, insurance coverage). Nooruddin and colleagues analyzed data from African American adults who declined to participate in a cardiovascular pharmacogenomic research study. When contacted after they declined, participants indicated that they refused because of the amount of blood drawn, concerns about who may be able to access their genetic information, and mistrust of research. Interestingly, Nooruddin and colleagues found both gender and age effects among African Americans. For example, more African American men than African American women, and a larger percentage of older vs younger African Americans expressed concerns about who could access their genetic information.

Following the articles that explore perspectives on participation in precision medicine research, Johnson and colleagues examined the feasibility, acceptability and effectiveness of a participatory genomic testing educational intervention in a federally qualified health center in Chicago. The online educational modules on basic genetics, cardiovascular pharmacogenomics and personalized medicine and case-based discussions were well-received and were found to increase knowledge between the pretest and posttest. Hughes Halbert and colleagues examined the relationship between self-reported resilience and allostatic load among African American, Hispanic, and White male veterans undergoing prostate biopsy in a Veterans Affairs Medical Center in Charleston, S.C. They found that African American and Hispanic male veterans were more likely than White male veterans to report they were able to "bounce back," and that veterans with higher incomes and those who were married were more likely to report they were able to bounce back than those with lower incomes or those who were not married, respectively. In a second study of men with prostate cancer, Jefferson and colleagues used a retrospective cohort design to examine the rates of hypertension, diabetes, heart problems, stroke and high cholesterol among prostate cancer patients treated with radical prostatectomy in a medical center in the Southeastern United States. While neither race, stage at diagnosis, nor PSA level were associated with a cancer co-morbidity, men diagnosed with prostate cancer in the most recent four years were more than four times more likely to have a co-morbidity than those diagnosed five or more years ago.

The third section of the special issue includes four articles that describe formative research to inform strategies to conduct precision medicine research. First, Wang and colleagues describe the process, structure and lessons learned from efforts to use participatory approach to sharing data in the Caribbean that would help to reduce inequities in access to and utilization of health information systems. Second, Griffith and colleagues describe findings from focus groups that were designed to inform a precision lifestyle medicine intervention to promote weight control in middle-aged Latino men in South Florida. They found novel and actionable psychosocial factors that map onto motivational constructs that integrate age, gender and ethnic factors that may be useful as a foundation for a biopsychosocial approach to weight control for these men. Third, Clement and colleagues describe the process they will use to study the genetic variants that may partially explain why people in Trinidad and Tobago with type 2 diabetes may fail to respond favorably to treatment with metformin. Fourth, Basu, Faghmous and Doupe describe a structured tutorial that they developed to help medical and public health researchers more effectively apply machine-learning methods to conduct precision medicine research on health disparities. They use an example dataset with open-source statistical code in R to demonstrate how to apply common methods, interpret "black box" models and highlight the strengths and weaknesses of different learning approaches. And, in the final section of the issue, Jerome and colleagues present a "quasi-systematic" review of the response to atypical antipsychotics among Blacks being treated for schizophrenia. They found that genetic variation and other factors may influence systematic variation in outcomes by race in ways that can help tailor management of schizophrenia among Blacks treated with an atypical antipsychotic.

PRECISION MEDICINE AND HEALTH EQUITY: A WAY FORWARD

Precision medicine has garnered considerable excitement, attention, resources and hope about its potential to transform medicine, health care and to improve population health,[1,24] but cautions about the potential for precision medicine to increase medical uncertainty for patients and providers[25,26] and to exacerbate health disparities are noteworthy.[4,24,27,28] The sheer volume of articles that discuss and try to refine distinctions among race, ethnicity and ancestry in *Ethnicity & Disease* and elsewhere[29,30] highlights an important point made by LaVeist in this journal 25 years ago: we need to continue to study race but do a better job.[10]

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While much in the field of medicine, health disparities, genetics, genomics and related fields have improved and evolved over the last quarter century, LaVeist points out that, "Only when we move beyond race as a proxy and directly measure those concepts believed to be measured by race will we make truly important advances in describing the true nature of racial variation in health."[10,p.26] This remains an issue that still plagues health research today. Bonham, Green and Perez-Stable[29,31] have highlighted some of the pragmatic and conceptual challenges that are particularly relevant as biomedical research continues to struggle to study race but do a better job.[10] The heterogeneity among the ways that race, ethnicity and ancestry data are ascertained, categorized and applied to genomic and other health research severely limits efforts to achieve health equity and eliminate health disparities in the United States. Also, the fact that most large and national datasets continue to lack data that reflect the multidimensional nature of a person's identity, cumulative experience and exposure to racism and other social determinants of health continues to limit efforts to advance research on health equity.[29,32] As several scholars have noted, there remains a need to use Office of Management and Budget categories in biomedical research, particularly to monitor the inclusion of racial and ethnic groups that have historically been underrepresented in research,[23] yet there also is a need to push scholars to continue to refine how they use race and ethnic categories in health research.[33-35] Surely, there is a need to create guidelines and standards for how and when race, ethnicity, and ancestry data are collected and utilized to draw inferences about minority health and health disparities.[6]

CONCLUSION

Particularly as the new NIMHD definition of health disparities becomes more widely used and adopted,[6] it will be critical to continue to push for greater conceptual clarity and precision, rather than hoping that methodological and technological innovation can overcome imprecision and lack of hypothesis-driven science. As several of the articles from the PM TCC illustrate, it is not enough to consider one socially meaningful demographic category at a time; the intersection of attributes, characteristics, behaviors, biology and other factors that influence and represent proxies for risk and protective factors that map onto mechanisms that influence health are critical to consider together, not only one at a time.[6,11,36,37] Several of the articles included in this supplement also illustrate how these concerns reinforce fears of repeating unethical medical research on African Americans, Native Americans, Hispanic-Latinos and Asian Americans.[38,39] While often researchers lament working in the shadow of the Tuskegee Study of Untreated Syphilis in the Negro Male and other instances of unethical research, it is important for researchers to grapple with the reality that the concerns of health disparity populations also are the result of incidents that have occurred well after the historic Belmont Report set standards for human research protections in 1979.[40] Inasmuch as researchers may not want to deal with the notion that they are viewed as untrustworthy, several articles in this issue highlight the heterogeneity among perceptions of trust among health disparity populations. For groups with a history of experiencing racism, discrimination or exclusion, even those that are not defined by race and ethnicity,[41] concerns about the trustworthiness of health professionals, medical care, health research and institutions that deliver health services abound.[42-45] Fritz and Holton[46, p.32] caution that "we should only trust the truly trustworthy," because when trust is violated or diminished, the reaction is often not simply one of disappointment but a sense of betrayal. Placing trust in people and systems that are not trustworthy can be profoundly harmful.[46]

In sum, in this early stage of precision medicine efforts to address health disparities, this PM TCC supplement represents a critical early step in research to utilize precision medicine to improve minority health and achieve health equity. Researchers must continue to tackle the technical issues that impede the mechanics of genomic analysis and other foundations of precision medicine and related fields. But perhaps more importantly, it is critical that we, as a field, do not lose sight of the reality that much of the work that is fundamental to improving the health of the United States will come with being precise in the conceptualization of variables, measures, hypotheses and findings to improve population health and achieve health equity.

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