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Innovating for a Just and Equitable Future in Genomic and Precision Medicine Research

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From its inception, genomics has been a speculative endeavor, fixated on a far-off horizon that would deliver on the promise of targeted diagnostics and individualized therapeutics (Fortun 2008). More recently, the data-driven approach of precision medicine research furthers this trajectory by investigating individual differences in genes, environment, and lifestyle (Jooma et al. 2019). The substantial investment in genomic and precision medicine has begun to yield clinically useful interventions, yet questions about benefit and access create uncertainty about our ability to achieve equity goals. If the prediction by the National Human Genome Research Institute that "individuals from ancestrally diverse backgrounds will benefit equitably from advances in human genomics" by 2030 is to be taken seriously, ethical, legal and social implications (ELSI) research must engage with the meaning of equity and questions about whether and how genomic and precision medicine can achieve these goals in a geopolitical landscape characterized by extreme economic inequality and structural racism (Green et al. 2020, 690; Chancel and Piketty 2021; Yearby, Clark, and Figueroa 2022).

Transparency about scientific practice and the extensive data collection and triangulation necessary for genomic and precision medicine will be critical to the production of trustworthy science (Lee et al. 2019). Sampling bias resulting in research datasets comprised mostly of samples from individuals of European ancestry (Tsosie et al. 2021; Nooruddin et al. 2018; Popejoy and Fullerton 2016) means that peoples underrepresented in genomic research studies are more likely to receive non-informative or inaccurate genetic test results in the clinic (Landry and Rehm 2018; Chapman-Davis et al. 2021; Burke 2021; Manrai et al. 2016). Unequal access to genetic testing and interventions due to affordability, genetic literacy, and trust in the healthcare system have already undermined implementation of genomic applications (Khoury et al. 2022). Disparities and delays in access to genetic

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services for low income and minority patients in the U.S. are well documented (Chapman-Davis et al. 2021; Gene Hallford et al. 2020; Hoskins et al. 2018; Shields, Burke, and Levy 2008; Omorodion et al. 2022; Fraiman and Wojcik 2021; Wojcik et al. 2023). These barriers are likely to determine which Americans will be able to access and benefit from the substantial public investment in genomic and precision medicine and may undermine public trust in science (Reardon et al. 2023; Lee 2021; Lee et al. 2019).

Fully realizing the promise of equity will require investment in the study of sociopolitical, economic, legal, regulatory, and environmental factors that parallels the public investment in genomics (Lee 2021). Leveraging multi-disciplinary expertise and ELSI scholarship to address key questions should be paramount, including scholars and scholarship that can elucidate the roles of the built environment and health systems in facilitating or impeding equitable access, approaches for identifying and prioritizing the interests of communities, the creation of transparent public-private partnerships, and design of effective engagement to define the public good for genomic and precision medicine. This means centering the experiences of marginalized populations to create policies and practices that empower communities underrepresented in biomedical research to negotiate the terms of their research participation, ownership of their data, and the meaning of equitable benefit (Fox 2020; Tsosie et al. 2021).

This special issue of the *American Journal of Bioethics* comprises ELSI research focused on equity and inclusion of diverse publics in genomic and precision medicine research. Articles in this issue represent work presented at the 5th ELSI Congress: *Innovating for a Just and Equitable Future* held June 1-3, 2022, a biennial conference supported by the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH) and organized by the ELSI Congress 2022 Organizing Committee.[1] The committee selected the theme of advancing equity and justice in the context of ELSI research and solicited a call for presentations that resulted in a congress attended by approximately 600 participants. After the congress, we issued a separate call for papers devoted to the congress theme for this special issue and solicited all conference presenters to submit a proposal for an article. Proposals were selected by a guest editorial board[2] that included expertise and experience in bioethics, public health genetics, anthropology, law, philosophy, and health policy. The final papers were chosen for their capacity to catalyze questions about equity and justice in their engagement with public policy, participatory democracy, advocacy, and access to genomic and precision medicine.

[1]The ELSI Congress was co-directed by Sandra Soo-Jin Lee and Mildred Cho, who convened an organizing committee that included Dounya Alami-Nassif (Columbia University), Paul Appelbaum (Columbia University), Jessica Blanchard (University of Oklahoma), Joy Boyer (NHGRI), Larry Brody (NHGRI), Shawneequa Callier (George Washington University), Mildred Cho (Stanford University), Deanne Dunbar Dolan (Stanford University), Gail Henderson (University of North Carolina), Steven Joffe (University of Pennsylvania), Angelica Johnson (Columbia University), Dave Kaufman (NHGRI), Gabriel Lázaro-Muñoz (Harvard Medical School), Sandra Soo-Jin Lee (Columbia University), Nicole Lockhart (NHGRI), Caroline Moore (Stanford University), Osagie Obasogie (UC Berkeley), Lisa Parker (University of Pittsburgh), Kayte Spector-Bagdady (University of Michigan), Rene Sterling (NHGRI), James Tabery (University of Utah), Wendy Uhlmann (University of Michigan), Emily Van Poetsch (Stanford University), Joe Vitti (Broad/Harvard/MIT), Alexis Walker (Columbia University), Joon-Ho Yu (University of Washington), and Rachel Yarmolinsky (Columbia University)

[2]The guest editorial board for this issue included: Jessica Blanchard, Shawneequa Callier, Mildred Cho, Deanne Dunbar Dolan, Gabriel Lázaro-Muñoz, Sandra Soo-Jin Lee, David Magnus, Kayte Spector-Bagdady, James Tabery, and Joon-Ho Yu

Authors in this special issue reflect multi-disciplinary, multi-institutional collaborations inside and outside of the U.S. They address a range of ELSI research that surfaces critical questions about equity for the future of genomics and precision medicine. From their vantage points in the varied sites of these research enterprises, the authors argue for the need to assess carefully what, who, and how patients, research participants, families, communities, and nation-states may benefit and the importance of addressing competing individual and collective interests in defining public good. In addition, several of these articles raise the question of what meaningful engagement with communities looks like or should be.

Several common themes emerge across these papers as they reflect upon important questions for realizing the promise of an equitable future for genomics and precision medicine. Halley and colleagues (this issue) illustrate the consequences for justice and an equitable distribution of the potential benefits of scientific innovation that follow the *de facto* reliance on advocacy for access to clinical care or research funding for rare diseases. A competitive, advocacy-based system disadvantages patients and families who face barriers to self-advocacy, such as those who have low health literacy, few financial resources, or are impacted by systemic racism (for a proposal to remove these barriers to participation in advocacy see Neeman 2023, this issue). Addressing a range of stakeholders across the research ecosystem, Halley and colleagues provide a palette of recommendations for moving toward equity goals (Halley et al., 2023). Bonkowski and Smith (this issue) highlight how industry partners in particular can divert or promote progress and offer more recommendations, including changes to industry data sharing and stewardship practices (Bonkowski and Smith 2023).

In their assessment of reproductive genetic carrier screening (RGCS) program design, Dive, Holmes, and Newson argue that providing genomic results beyond the scope of a program intended to inform reproductive decisions could lead to intensified consumption of healthcare resources—especially by those who can pay—which may divert resources away from individuals with higher *a priori* risk (this issue) (Dive, Holmes, and Newson 2023). They argue that a just approach to RGCS requires attention to the multi-faceted context of program implementation (including resource limitations and social context) and the balancing of individual preferences, utility in relation to the goals of screening, and potential health system and societal impacts. Garland-Thomson and Larson (this issue) argue for an even *more* limited scope as they consider the societal impact of the suggestion by Dive, Holmes, and Newson that social norms may promote the mistaken assumption that all genomic information is inherently valuable—an assumption that could “limit the imagination of individuals and couples making reproductive decisions” and assert the medical model of disability (Garland-Thomson and Larson 2023).

The question of who is to benefit is central to Shozi and Thaldar’s discussion (this issue) of their deliberative public engagement study of heritable human genome editing (HGGE) (Thaldar et al., 2022). They challenge the Eurocentric orientation of ethical frameworks that center the individual and the concerns of the present, by drawing on an interpretation of the African philosophical concept of *Ubuntu*, an ethic that articulates moral duties to community members, present and future. They conclude that this ethic explains participants’ support for

entitling future generations to equal access to HHGE as a healthcare service and propose active government intervention in support of this aim (Shozi and Thaldar 2023). Afolabi and Sodeke and Nyamnjoh and Ewuoso (both this issue) extend the discussion by pointing to a plurality of facets of the *Ubuntu* philosophy and scholarly debate, which create the expectation that range of conclusions could follow region-specific, public discourses about HGGE (Afolabi and Sodeke 2023; Nyamnjoh and Ewuoso).

Public engagement is also a central concern for Conley and colleagues (this issue) who raise questions about the effectiveness of common approaches and their capacity to advance just and equitable governance of HGE research (Conley et al. 2023). Revealing gaps between theory and practice, the authors argue for the need to reconceptualize public engagement. Without such scrutiny, engagement, as a battle cry for inclusion, may recapitulate inequities when those with "means, motive, and opportunity" distort a more fulsome representation of public interests.

The *meaning* of inclusion is taken up by Ferryman (this issue), who builds on the framework of "bounded justice" (Creary 2021) to caution against anemic inclusionary processes. These are limited to recruitment efforts designed only to diversify precision medicine datasets and risk racializing study participants and using them for "diversity propaganda." Reflecting on the hypervisibility and invisibility of minoritized and marginalized populations in precision medicine research, Ferryman argues that efforts towards inclusion can be "performative" and "empty" because they fail to recognize "fundamental, even existential, exclusion" (Creary 2021:242). She argues that equitable genomics will require the integration of race theory into ELSI and bioethics research to confront racism, reflect upon how inclusion goals are enacted, and deliver less "bounded" inclusion interventions (Ferryman 2023). Fletcher (this issue) extends Ferryman's call by proposing that NHGRI initiatives focused on enhancing workforce diversity could, through its ELSI program, deliver a bioethics workforce that prioritizes racial justice and advances health equity (Fletcher 2023).

Together, these papers illustrate that if we do nothing to address equity in the policy realm, the "Matthew effect" (Merton 1968) of accumulated advantage will result in those with more resources and "the loudest" not only gaining greater access to the benefits of genomic research and precision medicine but laying claim to what counts as the public good. ELSI researchers and their institutions, funders, and other stakeholders share a responsibility for leveraging ELSI conceptual, empirical, and normative scholarship to bring knowledge, tools, and practices to bear on efforts to achieve an equitable future in which "everyone has a fair and just opportunity to attain their highest level of health" (CDC 2022).

Ongoing health inequities between population groups will not be resolved by the routine implementation of genomic and precision medicine; instead, there must be an *intentional* focus on definition and distribution of benefit (Jooma et al. 2019). This work will require more trusting relationships between scientists, scientific institutions, and the public. Trust can be built by including ELSI analysis and diversity, equity, and inclusion (DEI) commitments early in and throughout the production of scientific knowledge and scientific "common goods" (Reardon et al. 2023). Addressing power dynamics embedded in the infrastructure of the research enterprise will be critical to prevent further entrenchment

of inequities. Change will require “tilting the playing field and the while ecosystem” to instantiate shared power and decision-making relationships between researchers, research institutions, research participants, and communities (Shim et al. 2022; Shim et al. 2023). Charting a path towards a just and equitable future in genomic and precision medicine requires thoughtful and meaningful participation of diverse publics. Capitalizing on their rich tradition of interdisciplinarity, ELSI scholars can make a unique contribution by tackling the difficult moral and empirical questions about what it means to represent the fullness of “the public”, how their engagement should be facilitated, and how we should interpret and apply their recommendations to maximally enhance equity and justice.

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