

This is an Accepted Manuscript of an article published by Taylor & Francis in The American journal of bioethics on 23/02/24, available at:

<https://www.tandfonline.com/doi/full/10.1080/15265161.2024.2303147>

From “Inclusion in What” to “Equity in What”: (Re)Thinking the Question of In/Equity in Precision Medicine and Health

The American Journal of Bioethics 2024, Vol. 24, no. 3, 89–91

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Precision medicine (PM) and genomics are increasingly scrutinized through the lens of health inequities. This is a welcome development for a field that, while concerned with health-related differences, has traditionally paid scarce attention to the question highlighted by Galasso (2024)—when do differences amount to inequalities or even inequities? Despite the growing attention to inequalities and inequities, however, the current debate often overlooks a crucial question at the heart of the problem: equity in what? (Sen 1992) Sen famously argued that because all theories of justice claim equality in some form, the fundamental issue for ethical assessment in the debate on inequality is: equality of what, or equity in what form (Sen 1992; Sen 2002). In this commentary, we draw on Sen and Nussbaum’s approach (Sen 1992; Nussbaum 2011), particularly as applied to health (Sen 2002; Marmot 2016), to expand on Galasso’s analysis. We argue for a more precise and consistent delineation of two distinct conceptualisations of equity: (1) in/equity in PM, encompassing differences in applicability, availability and inclusivity of PM, and (2) health in/equity, referring to avoidable, systemic and unfair disparities in health outcomes.

From “Inclusion” to “Inclusion in what?”

Galasso explores how concerns and expectations surrounding health inequities are conceptualized and addressed in two leading PM initiatives, the All of Us research programme and Genomics England. Both initiatives placed diversity and inclusion at the center of their efforts to promote equity. However, they disproportionately focused on upstream inclusion (i.e. removing barriers to participation in research), while “leaving aside” downstream inclusion (i.e. removing barriers to access PM outputs and benefits). Galasso’s distinction between upstream and downstream inclusion opens up questions about the operationalization of Equity, Diversity and Inclusion strategies, and the insufficient attention paid to structural disparities in access and quality of care. This imbalance, Galasso argues, “could result in a scenario in which diverse representation makes medical research robust and widely applicable, but not widely applied” (80), with the risk of exacerbating rather than reducing health inequities. Further, Galasso reveals how upstream

and down-stream inclusion are interconnected. Where much of the debate treats health benefits as following from inclusion in research, Galasso shows that the opposite is also true: when people do not trust that they will benefit, they will be less likely to take part in the first place. Our own research indicates that efforts to engage underrepresented groups are likely to be perceived as disingenuous when neglecting inclusion downstream, with the result of further entrenching mistrust and compromising even well-intended attempts at promoting diversity and inclusion upstream (Middleton et al. 2023). However, the strength of Galasso's framework (namely, the emphasis on "inclusion", as used by interviewees themselves) is also its main limitation, insofar as "inclusion" continues to stand in for "equity." Downstream inclusion encompasses, in Galasso's definition, access to both "PM outputs" and "benefits". Elsewhere, Galasso elaborates this as access to "the benefits deriving from precision medicine research, either therapies or other kinds of health interventions" (75). But while outputs (such as therapies or health interventions) are resources that can be accessed, benefits are outcomes that need to be realized. For everyone to achieve fair outcomes, everyone needs fair access to fair resources—fairness in the applicability, availability and accessibility of resources is usually referred to as equity in opportunity (Sen 1992; Sen 2002; Nussbaum 2011; Marmot 2016). However, as Galasso acknowledges, "opportunities...can[not] benefit those who cannot afford to harness them" (83). That is because not every-one has equal capabilities (capacity to act on PM insights, but also different susceptibility to disease due to genetic and environmental factors) to convert equal opportunities into equal outcomes (Sen 1992; Sen 2002; Nussbaum 2011; Marmot 2016). To be clear, Galasso would not appear to disagree with the importance of foregrounding capabilities. Our suggestion, though, is that for the construct of downstream inclusion to have meaningful purchase, its combination of inequity in opportunity, capability and outcome remains analytically imprecise. The result is that it is not always clear whether Galasso's conclusion that PM should focus on public health interventions rests on an ethical prioritization of the capability approach (opportunities alone risk being "superfluous"), or on an empirical assessment of the challenges underlying the opportunity approach (opportunities will always remain "out of reach").

From "Inclusion in what?" to "Equity in what?"

Galasso is not alone in substituting equity in one space (PM) with equity in another (health outcomes). Jooma and co-authors (Jooma et al. 2019), for example, define "health equity in the context of genomics" as comprising both underrepresentation in datasets, as well as accessibility and inclusivity of genomic health-care services. Yet, they fail to examine how health equity in the context of genomics relates to health equity more broadly. In other words, how PM that is both equitably applicable and applied might lead to a reduction in avoidable health disparities. The same slippage is repeated in public messages from various PM initiatives too, including the UK's lead-ing PM initiatives, Genomics England (Genomics England 2023) and Our Future Health (Our Future Health 2023), as well as in the implementation of the Genomic Medicine Service (NHS North West Genomic Medicine Service Alliance 2023). Such messages propose genomics as "a key

part of our armoury against inequities and inequalities in health” (NHS North West Genomic Medicine Service Alliance 2023) that can make “a huge difference, particularly to inequalities faced by black, Asian and minority ethnic groups” (NHS North West Genomic Medicine Service Alliance 2023). Representation upstream as well as equity of access and inclusivity downstream are key themes of such messages, but the extrapolation that PM could have a huge impact on health inequities still requires some contextualization. For most common diseases, interventions targeting genetic predisposition are unlikely to make a significant difference to health disparities. Even if PM could contribute new knowledge on the social determinants of health, this would have limited effect if directed through an increased focus on individualized medical intervention rather than public health and social policies of the kind envisioned by Galasso (Tabery 2023). Health equity, therefore, cannot be reduced to the equitable applicability and availability of PM. It does not follow, however, that equity in PM is unimportant, as Galasso sometimes seems to suggest when arguing for example that “inclusion in itself does not affect inequities” (74) or that fair PM outcomes “risk being superfluous” (83). First, genetics does affect health, and the impact of exposure to environmental risks can be modulated by genetic factors. Even if we only consider clinical genomics (as opposed to public health), access to and quality of healthcare are important to overall health outcomes. Finally, any system that deliberately disregards the generalizability of medical knowledge and fair distribution of healthcare resources would arguably violate deeply held principles of equity and justice, even if the impact on overall outcomes turned out to be marginal (Sen 2002; Nussbaum 2011). Often enough, the current debate confuses and conflates two distinct yet interrelated conceptualisations of equity: (1) equity in PM, and (2) equity in health outcomes. The first asks how equity would look in the context of PM, i.e. how to ensure PM is fairly applicable, available and accessible to all. The latter interrogates how PM would look in the context of health equity, i.e. if, and how, unbiased and accessible PM can contribute to reducing avoidable and systemic inequalities in health status. Both conversations are valid, valuable and, crucially, not mutually exclusive. But they are not the same. It is incumbent on the bioethics community to actively avoid confusing the two, including by failing to contextualize how equity in PM could lead to equity in overall health outcomes. Simply put, we should be clear about what we mean by in/equity, especially when engaging with those who are most likely to be affected by avoidable and unfair health disparities.

Disclosure Statement

No potential conflict of interest was reported by the author(s).

Funding

This research was funded by the Wellcome Trust [grant number: 220540/Z/20/A].

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