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ORIGINAL CONTRIBUTION

Targeting Representation: Interpreting Calls for Diversity in Precision Medicine Research

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Scientists have identified a “diversity gap” in genetic samples and health data, which have been drawn predominantly from individuals of European ancestry, as posing an existential threat to the promise of precision medicine. Inadequate inclusion as articulated by scientists, policymakers, and ethicists has prompted large-scale initiatives aimed at recruiting populations historically underrepresented in biomedical research. Despite explicit calls to increase diversity, the meaning of diversity – which dimensions matter for what outcomes and why – remain strikingly imprecise. Drawing on our document review and qualitative data from observations and interviews of funders and research teams involved in five precision medicine research (PMR) projects, we note that calls for increasing diversity often focus on “representation” as the goal of recruitment. The language of representation is used flexibly to refer to two objectives: achieving sufficient genetic variation across populations and including historically disenfranchised groups in research. We argue that these dual understandings of representation are more than rhetorical slippage, but rather allow for the contemporary collection of samples and data from marginalized populations to stand in as correcting historical exclusion of social groups towards addressing health inequity. We trace the unresolved historical debates over how and to what extent researchers should procure diversity in PMR and how they contributed to ongoing uncertainty about what axes of diversity matter and why. We argue that ambiguity in the meaning of representation at the outset of a study contributes to a lack of clear conceptualization of diversity downstream throughout subsequent phases of the study.

INTRODUCTION

It has been widely accepted that genomics has a diversity problem. Samples from individuals of European ancestry continue to make up over 80% of data sets [1,2]. Scientists warn that this skew limits their ability to make generalizable inferences about the relationships between

genes, behaviors, environmental exposures, and disease risks, and threatens the equitable translation of precision medicine research (PMR) for broad public health benefit [3,4]. Moreover, the promises of PMR are increasingly debated in the context of broader societal questions and social movements, such as the rise of the Black Lives Matter movement in the US in the wake of the death of

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Abbreviations: GWAS, genome-wide association studies; NHGRI, National Human Genome Research Institute; NIH, National Institutes of Health; PI, Principal Investigator; PMR, Precision Medicine Research; RFA, Request for Application.

Keywords: diversity, precision medicine research, bioethics

Michael Brown in Ferguson, Missouri in 2014 and the murder of George Floyd in Minneapolis, Minnesota in 2020. These developments, as well as the disparate health impacts of COVID-19 along racial, ethnic, and socioeconomic lines, have ushered in a new moment where the need to confront health inequities is a widely recognized imperative. As an intervention, public funding agencies have recently issued calls for research that target the recruitment of populations that are underrepresented in PMR.

Yet the focus on “representation” as a means for filling the diversity gap is far from straightforward. The meaning of representation in PMR is elusive. It is used variously to refer to, on the one hand, the ability to interrogate global genetic variation and on the other, the inclusion of historically marginalized groups in genetic research. The first focuses on the technical challenge in genetic epidemiology of identifying associations between genetic variants and disease risks and conditions, both within and between populations. Geneticists have recently underscored the importance of a diversity of population samples, both to foster the robust identification of common gene-disease associations that are shared by many patients and to help distinguish benign from pathogenic rarer variants that may vary with population background [5,6]. When searching for genetic contributions to rare genetic disorders, large sample sizes are necessary to capture enough instances of a rare event. This increases the importance of powering studies with sufficient numbers of samples from individuals of diverse genetic ancestry [2,7].

Researchers have begun to cite evidence that representative genetic discovery could inform measurements of disease risk, responses to drug treatments, and further understanding of the biological mechanisms of specific diseases, which have the potential to lead to improved health outcomes [1,8]. This goal of representation as a technical challenge for procuring missing global genetic variation suggests the need for implicit or explicit statistical or numeric criteria for *how much diversity* a genetics database or study ought to have (or, at the very least, which sorts of population backgrounds should be targeted for sampling). Yet, in the calls for greater diversity, the language of representation is used to refer to a second meaning: the inclusion of social groups that suffer from a disproportionate burden of disease [3,9-11]. Whereas the definition of representation for the purposes of genetic discovery is focused on statistical power (the ability to identify meaningful differences between groups), the latter is focused on “rhetorical power” and the goal of representing the social body.

Who is being represented in these two related but distinct goals is not synonymous. In the first, the diversity gap refers to missing genetic ancestry, whereas in the sec-

ond, the gap refers to the exclusion of the broad spectrum of dimensions of lived experience and social dimensions that bear on health, including but not limited to race and ethnicity, that contribute to health inequity. Achieving representation, then, becomes multiple goals that revolve around *what* dimensions of diversity or categories of populations are required for biomedical research to be seen as scientifically and socially legitimate.

In this paper, we draw on our empirical study of how diversity is conceptualized and operationalized in five federally funded PMR projects that are part of three large scale research consortia. To examine the meaning of “representation” for achieving goals of inclusion and the scientific and political strategies for targeting diversity, we reviewed the scientific literature that describes the evolution of national initiatives to support PMR and conducted document review of 18 Requests for Applications (RFAs) issued by the National Institutes of Health (NIH) from 2015-2018, 125 in-depth interviews from a purposive sampling of funders, principal investigators (PIs), and research team members, and over 465 hours of observations of study and consortia activities, including working group calls and in-person or virtual meetings.

Using our empirical data, we explore various categories and competing approaches towards achieving diversity. We begin by tracing some of the recent history around different dimensions of and benchmarks for diversity in genetic biobanks and genomics research. Then we follow these through the shift to large scale, publicly funded PMR consortia. We argue that dual meanings of representation as (1) a solution to the technical problem of capturing genetic variation, and (2) fulfilling the ethical imperative to include marginalized social groups, are often conflated so that goals of diversity and their operationalization are left uncertain. Representation, defined as a method for sampling diverse populations to correct existing data biases, should not be equated with fulfilling goals of redressing inequities that have led to the historical lack of participation of groups in biomedical research. Furthermore, we argue that while attention has focused on population-based genetic biases as defined by genetic ancestry, race, and ethnicity, other relevant axes of diversity have remained underexplored. Our findings highlight the limits of calls for increased diversity as a means to rectify long-standing health inequities. Indeed, we show conflation of the various meanings of representation, which may lead to the exacerbation of inequities in the genomics research ecosystem.

BIOETHICS HAS UNDERTHEORIZED GROUP HARM AND BENEFIT

Research on inclusion in clinical research has traced the development of NIH requirements for research partic-

ipation characteristics, expanding from women to racial and ethnic minorities [12-14]. Researchers and bioethicists have underscored the importance of addressing historical exclusion in participation in biomedical research and its relationship to health inequities [9,15-17]. Questions around how a study population “reflects” or “represents” the broader population remain unresolved, even as concerns about the potential negative consequences of failing to address diversity become more pronounced [4,7,18,19].

Bioethical frameworks for addressing the imperative for diversity and inclusion of groups in research in terms of health equity are anemic. There have been numerous critiques of the focus on individual autonomy in bioethics over the past two decades [20-22]. Bioethics has been firmly grounded in an assumption of autonomy that has emphasized individual agency as well as risk/benefit assessments to make informed decisions as a means of protecting individuals as health research participants [21,23]. In an influential article, bioethicists Emanuel, Wendler, and Grady [24] sought to move beyond individual informed consent as necessary, but not sufficient, for conducting ethical clinical research. In balancing research protections against equity, Emanuel and colleagues emphasized basing subject selection on the scientific rationales for the proposed research (p. 2704). While protecting individuals and communities [25] from exploitation in health research has remained a prevailing concern, this debate has evolved in the intervening decades. Adequate consent is not sufficient for addressing the fair selection of participants when the knowledge and interventions generated from research will not likely be accessible to communities that experience inequities to care and access to the most advanced therapies. Put simply, potential benefit from research is not equitably distributed. Renewed attention to the ethical principle of justice, especially through the lens of social justice, has reoriented bioethical discussions toward addressing disparities and understanding scientific and research efforts across fields through the lens of health equity [26-30]. In PMR, applying this framing has further raised questions around investment in genetic research, disparities among the populations that are represented, and ultimately who benefits from research.

An ongoing critique of genetic studies has focused on the lack of diversity of genetic ancestry in the databases that undergird such studies [1,3,31,32]. However, slippage between recognition of a diversity gap of global genetic variation and the need to address health inequities contributes to confusion over how the problem of missing genomic data should be understood. This stems in part from the inappropriate use of racial and ethnic categories in genomic research [33,34]. Social scientists and ethicists have raised concerns over the use of race

and ethnicity as social categories that are then mapped onto biological findings; meanwhile, requirements for diversity and inclusion have increased attention to these distinctions [35-37]. Yet it remains unclear whether and how procuring more samples of underrepresented genetic variation will mitigate health disparities for underrepresented social groups.

DEBATE OVER SAMPLING STRATEGIES FOR A DIVERSE NATIONAL COHORT

Current calls to increase diversity stem from concerns about Euro-centric biases in genomics research and are inextricably intertwined with the early debate about the appropriate role of population representation in genetic epidemiology. In 2004, then-director of the NIH National Human Genome Research Institute (NHGRI) Francis Collins published a prominent commentary in *Nature* calling for a nationwide longitudinal, prospective cohort investigation [38]. The proposed effort would complement related approaches that had been initiated in several other countries, including the UK, Iceland, Estonia, and Japan. Collins described the proposed effort as an appropriate successor to both the NHGRI-funded Human Genome Project and the International Haplotype Map (HapMap) Project, a multimillion-dollar project aimed at identifying common patterns of global human genetic variation to find genetic variants affecting health, disease, and responses to drugs and environmental factors [38,39]. The eventual success of the proposed gene-environment cohort study would be based on the degree to which it was able to adequately represent the population diversity of the United States. As Collins wrote:

...rigorous and unbiased conclusions about the causes of diseases and their population-wide impact will require a **representative population** to be monitored over time (a prospective cohort study). The time is right for the United States to consider such a project [38]. (emphasis added)

To achieve “a representative population,” Collins delineated “desirable characteristics” for the proposed cohort, including oversampling racial and ethnic minority groups (ie, recruiting in numbers greater than suggested by observed demographic proportions), as well as sampling a broad range of ages, genetic backgrounds, and environmental exposures. In this way, race and age came to stand in as the major axes of participant diversity.

Rationales for Creating a New Cohort

Collins’ proposal prompted considerable debate, including an alternate proposition penned by physician and nutrition scientist Walter Willett and colleagues. They wrote against Collins’ proposal, arguing that it would

be quicker and more efficient to invest in adding genetic analyses to existing epidemiological cohort studies rather than begin from scratch with a new national cohort study [40]. They noted that numerous large cohort studies were already underway, and while many of these focused on specific disease states such as cancer or heart disease, most had access to a wide array of additional phenotypes, banked biospecimens, and exposure data, making the repurposing of such cohorts for gene-environment research an effective way to proceed. They argued that in many cases combining data across multiple cohorts would be possible and could offer “even greater potential” when studying the interplay of environmental and genetic factors.

In the same issue of *Nature*, Francis Collins and his NHGRI colleague Teri Manolio penned a reply, acknowledging that while Willett et al.’s proposal had many merits, merely extending genetic analysis to existing population-based cohorts would not suffice [41]. Specifically, they identified three important core considerations in precision medicine research: data harmonization, emerging technologies, and population representation. Of the three rationales noted, the question about population representation and whether it was necessary to achieve the goals of precision medicine was central to this debate. Collins and Manolio noted that representative sampling was a “major concern driving the national cohort proposal.” For example, the age distribution represented by extant cohorts was remarkably skewed relative to proportions in the US population. The NHGRI authors also emphasized the importance of representing racial and ethnic diversity by emphasizing that “despite recent attempts to improve the representation of minorities and socioeconomically disadvantaged participants and newer cohorts, the proportions are still far below their representation in the US population” (p. 259). Collins and Manolio urged that both approaches, once feasible, should be pursued, writing, “we believe the real question is whether [the United States] can afford not to do both given the enormous and growing cost of healthcare for complex diseases” [41].

Willet et al., however, were more sanguine, arguing that such representative sampling was not essential to the task of identifying the ways that genes and environments contribute to disease risk. They went on to call out what they took as a related myth that population subgroups, be they racial, gender-based, or religious, must be represented *in proportion* to their prevalence in the general population. Instead, they wrote, “what is really needed is a subgroup large enough to examine the exposure and disease association within that subgroup” (p. 258): proportionality was not a condition of representation for the purposes of technical goals.

The debate was left unresolved at the time because there was simply no budget to pursue the national cohort

investigation. Nevertheless, this debate reflects different ideas about what kinds of diversity are needed and standards for evaluating how much diversity is enough. Although the broad goal of “representative” data was never in question, the different approaches illuminate competing ideas about what diverse data ought to be able to do, and what and how much representation is needed to address the lack of diversity that was recognized early on as a challenge to the goals of precision medicine. Ultimately, the inauguration of President Barack Obama in 2008 and the initiation of a wider discussion about the importance of diversity and inclusion in many facets of public life pushed momentum towards the pursuit of both kinds of approaches. At the same time, public investment in genetic technologies and research increased as Collins moved from his role as leader of the NHGRI to leading the NIH in 2009.

Concerns over Equitable Benefit

In the same year that Collins moved to the helm of the NIH, investigators Anna Need and David Goldstein at Duke University examined the population background of samples for which genome-wide association studies (GWAS) had been reported and found that 96% of such studies had been conducted using samples from participants of European descent, suggesting just how remarkably non-representative most genomic research was from a population genetics standpoint [42]. These findings gained wider scientific attention when Bustamante and colleagues included them as part of a prominent call for renewed attention to diversity in genomic research. Both sets of authors expressed concern that important information about the role of genes in health would be overlooked by an overemphasis or exclusive focus on a single group. Need and Goldstein emphasized that “because researchers cannot know in advance which rare variants are geographically restricted if a resource is established only in Europeans and not others, it will be more difficult to interpret the significance of rare variants in other groups.” Framing the focus on diversity as a matter of benefit and equity, Bustamante et al. wrote,

Geneticists worldwide must investigate a much broader ensemble of populations, including racial and ethnic minorities. If we do not, a biased picture will emerge of which variants are important, and genomic medicine will largely benefit a privileged few [43].

In other words, the failure to include “a much broader ensemble of populations” could mean that those of non-European genetic ancestral background would fail to benefit from the expected fruits of PMR, potentially exacerbating troubling population health outcomes and disparities. It is important to note that the axis of repre-

• "Age"	• "Access to care"
• "Disabilities"	• "Ancestrally diverse populations"
• "Education"	• "Diverse cadre of volunteers"
• "Ethnic diversity"	• "Patients who come from racial or ethnic minority populations"
• "Gender identity"	• "Spectrum of clinical conditions and healthcare settings"
• "Geographic diversity"	• "Sufficient numbers of diverse populations and individuals"
• "Income"	• "Underrepresented in biomedical research"
• "Sex"	• "Underserved populations"
• "Sexual orientation"	• "The broad diversity of America"

Figure 1. Dimensions of diversity in PMR funding announcements, 2015-2018.

sensation that appeared to matter in these accounts was based on the understanding of genetic differences within and between populations, and not the fair representation of other demographic characteristics such as socioeconomic status that might reasonably be regarded as relevant to an investigation of the interplay of genes and environments in disease risk. As such, Bustamante and colleagues' framing of benefit was far narrower than the argument that Collins and Manolio had made, insofar as it focused on the implications of biased sampling for variant interpretation in genomic medicine.

During this time, as Need and Goldstein were making their arguments and in the period after the completion of the HapMap Project, a large number of genomic-based research initiatives began to be underwritten by the NHGRI and other NIH institutes, effectively enacting Willett and colleagues' proposal to bring together existing epidemiology cohort studies into one consolidated resource [44-46]. Then, in 2015, President Obama launched the Precision Medicine Initiative, which encompassed several ambitious goals, including the establishment of a national prospective cohort investigation in line with the vision that Collins had proposed in 2004. That vision is currently being enacted as part of the *All of Us* Research Program [47,48].

But we argue that the issue of multiple definitions of diversity and goals of representation have persisted, not just because both goals remained unfulfilled, but because they did not adequately take into account trenchant inequalities in health, science, and society. The questions of who ought to be represented in biomedical and PMR, how, and to what ends were never fully answered or addressed.

REPRESENTATION: WHAT KINDS OF DIVERSITY AND HOW MUCH?

NIH's acknowledgment of the bias in genetic research, and biomedical research more broadly, has resulted in RFAs that identify target thresholds for enrolling historically underrepresented groups into PMR. Resonant of the earlier unresolved debate over how to pursue goals of representation, these new funding mechanisms supported genetic sampling and analysis of ongoing cohort studies in some cases; while in others, they seeded new cohorts. In practice, however, calls for diversity manifest in opaque ways. In what follows, we present findings from our analysis of funding announcements, showing the ambiguous ways that diversity is defined. Drawing on interviews with program officers and research team members, we then show how this ambiguity enables flexibility in interpretation and enactment.

FUNDER INTENT FOR CAPACIOUS DEFINITIONS OF DIVERSITY

Our analysis shows that there is a common understanding that recruiting sufficient numbers of diverse participants is necessary to make study results generalizable. This comes through most clearly in our document analysis where NIH RFAs refer to diversity broadly and often in vague and undefined ways (see Figure 1). For example, these funding announcements include language that alludes to the possibility of answering scientific questions across a "spectrum of clinical conditions and healthcare settings" and, at another point, to attaining "sufficient numbers of diverse populations and individuals" with which to perform analyses. These descriptions seem to indicate concerns with numerical representation. In this way, representation is defined in terms of statistical power

and of claims-making about differences across and within groups into which participants and data are categorized.

But when coupled with the imprecise ways in which “diversity” is defined and framed, the funding announcements leave open-ended the questions of how participants should be categorized and what proportions should come from diverse populations to enable the analyses and comparisons among categories. There are varied attempts at grappling with and qualifying diversity, with none presenting an especially clear picture of just what the concept means. In one case, a funding announcement explicitly defines it as “patients who come from racial or ethnic minority populations, underserved populations, or populations who experience poorer medical outcomes,” but then adds the new, different dimension of ancestry (presumably genetic ancestry) with phrases such as “ancestrally diverse populations.” Most funding announcements only obliquely engage with the concept of diversity, which was often referred to in imprecise and general terms. For example, one describes the aim of the consortium is to recruit a cohort that “reflects the broad diversity of America.” The diffuse language of the funding announcements leaves open the question of how to put into practice procuring enough diversity required to “reflect” the entire country and by what standard this would be assessed. Later in the same announcement, the concept of “broad diversity” is characterized with the far-reaching demographic categories of “race and ethnicity, sex, age, gender identity, sexual orientation, income, education, access to care, and disabilities, and geographic diversity.”

To discern the intentions behind how diversity was written into funding documents, we asked program officers of funding agencies that contributed to funding announcements to reflect on conceptions of diversity. In the case of the above-mentioned announcement that explicitly defined diversity as “patients who come from racial or ethnic minority populations, underserved populations, or populations who experience poorer medical outcomes,” a program officer described to us how the team tasked with writing the announcement selected these three axes by balancing “importance” and “clarity”:

It was somewhat of a judgment call in terms of which factors we felt were the most important and how many of them we could describe clearly enough that applicants could write to those criteria and reviewers could review them.

In their explanation, the first axis, “racial or ethnic minorities,” was included with the thought that “people are used to thinking about that” and would have a concrete sense of how to respond. The second, “underserved populations,” “got at factors beyond race or ethnicity” and so was intended to be more open-ended. However, the funders also understood that clarity of definition would be important, and so referred to the US Health

Resources and Services Administration (HRSA) designations of medically underserved geographic areas [49]. The last axis, “populations who experience poorer medical outcomes,” however, was provided as a means of allowing applicants flexibility in responding to the funding announcement. As the program officer told us, “that was really the only one that didn’t have a cut-and-dry definition” and it was, therefore, “decided to let the investigators make the case for that group in their applications.” In the process of writing funding announcements, diversity was thus taken up in ways that included, but moved beyond, what was recognized as common, standard definitions of “diversity.”

Further, they stressed that a desire for enhanced diversity “informed the entire RFA” and so was written into the document as more than a metric by which participant recruitment would be evaluated:

We obviously set [recruitment] thresholds... but we really wanted the grants to be able to address more than just check the box that we met the recruitment milestones. We wanted people to work diversity into their study design, into their results, into the dissemination.

Funders hoped research teams would not take the cursory approach of “check-box diversity” to fulfill recruitment goals stipulated in the RFAs. The intent of funders was to allow research teams to define the most salient dimensions of diversity for themselves and to implement its goals throughout the stages of the study lifecourse. And indeed, as we detail next, we found that without explicitly articulated definitions of diversity that could anchor recruitment, data collection, and data analysis practices, PMR investigators exercised a great deal of interpretive flexibility, reading multiple meanings of diversity from funding announcements and implementing widely varying ideas about which dimensions of diversity mattered and how much diversity was sufficient into their PMR studies.

INVESTIGATOR INTERPRETIVE FLEXIBILITY TO REVERT TO RACE AND ETHNICITY

Our interviews with PIs and research staff revealed a lack of consensus about what a representative sample should look like and what dimensions of diversity should matter. The result of open and seemingly agnostic perspectives in the RFAs on how representative samples should be recruited and what groups should be represented triggered for some a “reading between the lines” that recapitulated race and ethnicity as the primary axes of diversity. One study team PI explained:

The team was definitely under the impression that even

though there were three categories of diversity that were named in the RFA, that the review and then ultimately the ... decision about funding was going to be driven in large part by diversity with respect to underrepresented minority groups from a race and ethnicity perspective. Again, that was not in the RFA but the folks putting together the grant and who were really thinking about how we want to get funding for this, how we want to make this a fundable proposal assumed that they needed 60% of the participants to be from an underrepresented racial and minority group, or racial or ethnic minority group.

When asked about other dimensions of diversity, the PI underscored the focus as a “race/ethnicity thing...not as much the underserved.” But this often led to variable definitions of underserved being taken up in different research sites of the consortia. Furthermore, once funded, some study teams did attempt to identify and act on alternative dimensions of diversity. In one instance, an investigator described an experience at a scientific meeting during which they and others realized that study sites were operating with divergent understandings of the concept:

I asked this question, I said, “I don’t understand how we’re defining underserved.” There was a kind of awkward [silence]... So there was no answer. I thought, “Okay. Well, I just missed a memo or something.” Then, it turned out that nobody knew, and then it turned out that we sent a survey out. We asked all the sites, “How are you defining it?” and we got these weird mishmash answers and some non-answers.

Several of our interviews revealed how researchers intuited the goals of diversifying genomics research, which shaped responses to the funding announcements and did lead some to question the categories through which the concept of diversity was operationalized. In one instance, an investigator told us, “I knew one of the goals was to increase the diversity of samples in these biobanks,” but then questioned the appropriateness of using “social categories” as a lens through which to achieve that. Researchers recognized a tension between the perceived drive to diversify biobanks, which they regarded as “a biological... a genetic question,” and achieving that through what were read as social categories.

In sum, we found that negotiating which dimensions of difference PMR participants should represent, and what sorts of diversity count, is a critical process by which representation is rendered and occurs post-funding between individual sites and consortia. But notably, at the stage of research design, researchers, wishing to be competitive in the funding process, opted to give what they perceived funders wanted, rather than taking advantage of what funders thought was an open invitation to use the capacious definition of diversity in the RFAs to propose alternative, relevant dimensions of diversity that strayed

from race and ethnicity.

WHAT DOES REPRESENTATION MEAN?

We found that fundamental questions of what kinds of diversity matter and how much are left to individual studies and consortia to determine. As a result, definitions of and practices to achieve diverse representation in PMR studies varied widely. Investigators fell into common default categories centered on racial and ethnic diversity, or slipped between prioritizing certain underrepresented groups over others, to defining representation through proportionality.

Some investigators’ intuition that race and ethnicity were the most salient dimensions of diversity, despite the open-ended call by funders, seemed warranted. One program officer noted that if “we didn’t have a cohort from let’s say the Hispanic/Latino population, we would probably get questions as to why that wasn’t the case. Why didn’t we have a large omics sample size in Hispanic/Latinos?...We would have to be prepared to answer those questions from our leadership... from the top down.” As a result, they continued, when grant applicants propose new studies, “we tell them flat out that if it’s an all-white cohort, it’s not of high interest to us.”

For another investigator, given their concerns about not knowing the expected genetic variation in a population, one answer to the question of representation was to capture as wide a range of human genetic variation as possible:

How do we know when we’ve got enough diversity? I think it’s a really hard question to answer. I don’t think you can fully answer it with one analysis or even 10. There are lots of different ways to think about that problem. One way to think about it, is in terms of the representation of genetic variants and the amount of diversity you’re likely to see in a population. We’re just getting at a small piece of it, not seeing the question. If we look in a population database, to see if this variant is there, how much uncertainty is there around that absence?

Another researcher expanded on the focus on genetic variation to also include the concept of proportionality: “If a data set is unbiased, then you would not expect to see more white people of European ancestry than you would as a percentage of the population from which those samples are drawn.” They went on to underscore the objective to ensure “the diversity that’s present in whatever entity you’re talking about, reflect the same proportion that you see in the general population.

However, when asked to specify the categories or sub-groups in which representation, proportional or not, ought to be achieved, research team members equivocated or jumped from speaking about global genetic varia-

tion to percentages of racial and/or ethnic populations as defined by the US Census to a more general discussion of health disparities. Some described representation as a broad goal of diversity but emphasized that more narrowly defined aims sometimes took priority, such as to “cover various gaps” in terms of specific diseases or traits. Others challenged the notion of representativeness or proportionality: several investigators suggested that “there is no right balance. There is no right representation. We have a long way to go” to correct current biases in data; some suggested that to do so, researchers should recruit exclusively non-white underrepresented participants. One study PI preferred to use the word “*reflect*,” in lieu of “represent,” citing the failures of other national cohorts that attempted proportionally representative samples:

... it’s probably one of the things we spent the most time discussing...how we would sample...the National Children’s Study which had recently been killed at that point, had tried to be a representative sample and NHANES [National Health and Nutrition Examination Survey] tries to be a representative sample of the United States.

Instead, this PI argued, a commitment to “reflect” rather than represent meant “to project, actually, towards the future of the United States.... We would rather shoot towards the projected racial/ethnic diversity of the United States in the future rather than where we were today or in the past.”

Here the analogy of aiming at “where the puck is going, and not where it has been,” affirms a commitment to recognizing that the US will soon be a majority non-white population. However, perhaps not surprisingly, answers to the question of what that would mean in practice to achieve representation – either in terms of the present or future – were difficult to pin down and would change depending on context and the disciplinary background of research team members. Often, the specifics of assessing representation were left as a vague and undefined aspiration. All of this perpetuated ongoing ambiguity about the overall goal for diversity and which standards should be applied to studies to determine if they were contributing meaningful diversity to enable future work.

CONCLUSION

Our research suggests that diversity is conceptualized and operationalized in PMR, and biomedical research more broadly, through a sociopolitical process in which values, interests and practices bear on what counts as the most salient dimensions of diversity, how the problem of underrepresentation is understood, and what strategies must be pursued to remedy the problem. “Representative” has a specific statistical definition and thus suggests a clear set of criteria in the context of biomed-

ical research. However, “representative” has a different meaning when used rhetorically to refer to the inclusion of dimensions of diversity beyond genetics that contribute to health disparities. Indeed, our data suggest a shift from the more exacting demands of demonstrating representation to opaque, diffuse approaches to diversity or a conflation of these. Such diffuseness, in some cases, had downstream consequences for research and the questions that can be answered.

Representation, as a goal of increasing diversity in PMR, has focused primarily on addressing the now well-established underrepresentation of non-White (ie, individuals of presumed non-European ancestry) populations in genome-wide association studies. Yet, while some genomic researchers’ attention has focused largely on population genetic biases which might be addressed by attending to genetic ancestry as a sampling criterion, a wide range of other relevant axes of diversity have remained under-interrogated or haphazardly pursued. Instead, representation has given way to diffuse goals of *reflecting* diversity in which non-specific inclusion justifies a laundry list of differences to count as progress, while sidestepping technical standards for statistical power that would enable detection of differences in health outcomes within or between populations.

All of this has led to downstream consequences of putting off fundamental questions of what kinds of diversity matter; how much is necessary and for what purpose? By deferring answers to the fundamental question of what diversity is for, the goal of “representation” in PMR is assessed flexibly, elusively in ways that risk rendering the concept of diversity meaningless and without accountability. How inclusion is defined by large-scale PMR initiatives will bear directly on public trust in research. Obtaining a “representative” sample must address the uncertainty of how to correct data biases in confronting ongoing inequities in research and directly answering the long overdue question of what is diversity for.

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