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The Precision Medicine Nation

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The Precision Medicine Initiative (PMI) has stirred much hope (and some hype) since its announcement in 2015. The ambitious initiative proposes to accelerate exponentially the adoption of precision medicine, an approach to healthcare that tailors disease diagnosis, treatment, and prevention to individual variability in genes, environment, and lifestyle. It aims to achieve this by creating a cohort of volunteers for precision medicine research, accelerating biomedical research innovation, and adopting policies geared towards patients' empowerment. The hope is that this combination “will usher in a new and more effective era of American healthcare.”¹ As strategies to implement the PMI are formulated, critical consideration of the initiative's ethical and sociopolitical dimensions is needed. Drawing on scholarship of nationalism and democracy, we discuss the PMI's construction of what we term “genomic citizenship,” the possible normative obligations arising therefrom, and the ethical, legal, and social challenges that will ensue. Naturally, some of the issues are neither new nor unique to the PMI. Also, as the PMI is a work-in-progress and the final details are not yet known, conclusive appraisal would be premature. However, a discussion of the existing and emerging issues can facilitate the development of policies, structures, and procedures that can maximize the ability of the PMI to produce equitable and socially sensitive outcomes. This is all the more so given that the PMI's laudable goals and deep commitment to public engagement—even if difficult to accomplish—should serve as a model for other programs invested in precision medicine research. Thus, although we focus here on the PMI as the largest and best known of the efforts to provide an evidence base for precision medicine, the analysis is equally applicable to other population-based, precision medicine research programs.

Constructing Genomic Citizenship

The connection between science—especially genetics—and citizenship has long been discussed in the social sciences literature. The inception, and especially the completion in 2003, of the Human Genome Project, which mapped the human genome, was pivotal in creating this connection. As scholars have observed, it has markedly advanced genetic

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testing in clinical and research settings; led to the rise of social movements based on the notion of “genetic identity”; mobilized networks of individuals with genetic conditions to promote therapeutic genetic research and interest-based policy agendas; and significantly, increased the expectation that individuals take responsibility for genetic testing, self-surveillance, and subsequent healthcare if found to be at risk.²

However, there are three ways in which the PMI may represent a “constitutional moment”³ in the understanding of the relationship between citizens and the state in the genomic era. First, the PMI's aims—to create a cohort of one million or more Americans that reflects the U.S.'s racial and ethnic diversity⁴ (making it the largest national biobank in the world) and to provide data access and analysis services to the broadest community of users to date—reflect the considerable societal role envisioned for genomic research.

Second, the PMI's planned scope, which would include governmental facilitation, budgetary allocation, collaboration with the private sector, and especially partnership with participants, far exceeds that of other national biobank initiatives. Unlike the sporadic, often post-factum, public engagement that has characterized other large genomic initiatives,⁵ the PMI uniquely promises an *ongoing*, “highly interactive, and proactive public participation model,” where “[p]articipants will be the primary source of many research observations, co-designers of studies, mediators of access to their healthcare data, contributors to overall data quality control, donors of data from mobile and wearable devices, and recipients of their own as well as aggregate data and analysis results.”⁶ This model would encompass a broad range of stakeholders (including researchers, cohort-participants, and multidisciplinary professionals) who would provide input and feedback on the cohort's design, planning and implementation.⁷ In addition, cohort participants of racially and ethnically diverse groups would serve on the PMI's governance and oversight committees and be involved in the development and application of policies and activities, including coordination of PMI operations. As the PMI Work Group described it, the initiative “seeks true partnership between participants and researchers,” and the cohort “should strive to be an exemplar in this [effort].”⁸ This participatory plan is significant: it extends to genomic settings the democratic vision, and emerging expectation, of individuals as active citizens (rather than obedient subjects).⁹

Third, the PMI seemingly also extends to genomic settings the understanding of citizenship as a set of reciprocal relations between citizens and state. In exchange for participants' provision of their information (including access to electronic medical records; genetic, metabolic, and microbiomic makeups; and environmental and lifestyle data), participants are granted rights to make informed choices, to access their submitted data, and to have genomic findings returned to them.¹⁰ These rights are often portrayed as empowering. As stated by the PMI's crafters: “individuals want and deserve to know [their] results” to improve their own health.¹¹ But these rights can also generate an expectation for individuals to take measures of self- and familial surveillance (a dynamic that has already emerged with the rise of single-gene testing¹²), and possibly allow the PMI to claim for itself a role in the oversight of its citizens' lives. Indeed, as the PMI Working Group has suggested, “the PMI cohort can provide a platform for *formal investigations of whether and how* data are used by participants and ways to promote information use by individuals” [our emphasis]¹³. This is

significant not only because such centralized oversight is uncharacteristic of the U.S., but also because the PMI's use of next-generation sequencing and the scope of data to be collected may now extend individual responsibility beyond responding to the results of single-gene testing to monitoring the effects of multiple genes and to controlling one's environmental and lifestyle decisions.

Although these developments mirror legal and political dimensions of citizenship, the PMI's narrative establishes a third dimension of identity as a citizen. Because the initiative's success hinges on the formation of a cohort that is both large and reflective of the U.S.'s diversity—features that, to date, have been difficult to achieve—the establishment of public trust and sustained investment in the proposed genomic research agenda will be key.¹⁴ Unlike similar initiatives in other Western countries, the PMI will also need to overcome Americans' general skepticism of centralized government. The PMI has thus resorted to a strategy that, historically, has proven successful in mobilizing the masses: recruiting participants by appealing to national values and interests, while offering shared experiences and a collective identity as a *PMI nation*, embodied in Benedict Anderson's concept of “imagined community.”¹⁵ Indeed, the adoption of a new name for the PMI's cohort program—the “All of Us Research Program”—exemplifies this appeal.¹⁶

Following the credo that the U.S. is the “land of opportunity,” promotion of the PMI is framed around the tremendous health-related advances at stake and the possibilities for individuals to capitalize on these opportunities through participation in the cohort.¹⁷ The PMI's initial outreach materials plead for a “coordinated and sustained national effort”¹⁸ and urge participation in the name of boosting “American competitiveness and economy,” and sustaining the country's global leadership in biomedical research.¹⁹ The appeal interweaves recognition of existing health disparities among racial and ethnic minority groups with a call for altruism in genomic research and “shared responsibility for health knowledge,” while emphasizing the potential benefits to the health and wellbeing of individuals, families, communities, and the American population at large (p. 14, 40).

Aside from describing the cohort as a “*national* resource that will, over time, benefit the entire U.S. population [our emphasis]” (p. 25), the PMI highlights the “unprecedented opportunities” that a racially/ethnically and socio-economically diverse cohort will provide for examining and “understanding the interaction between the social and environmental milieu with an individual's biologic profile and genetic ancestry [that] can extend our understanding of disease pathology and extend the application of best practices in therapeutics to more diverse groups” (p. 26). On the more individual level, the cohort is described as an opportunity for participants “to use their health data in innovative ways for their own betterment” (p. 14). Indeed, the explicit and commendable goal of returning personal results and information to participants is that “all volunteers may have [the] opportunity to benefit from the science” (p. 43). Finally, the PMI offers volunteers a new communion—created by “correspondences recognizing goals met, anniversaries to joining, or birthdays (p. 42),”—and a new communal identity: implicitly, as powerful transformers of the currently deficient healthcare system, and explicitly, as recognized, valuable members of a racially and geographically diverse “PMI cohort family” (p. 42).

If the PMI is creating a new nation comprising “all of us,” what normative rights and obligations are conferred on the PMI's genomic citizens? Here, we consider three key issues: governance and participation, the demarcation of boundaries, and the social contract inherent to the PMI.

Governance and Participation

The “democratic turn” in science and technology values the informed and active participation of citizens.²⁰ This turn embraces contemporary preferences for deliberative democratic processes, which entail a plurality of viewpoints in decision-making processes and opportunities for public collective action. Deliberative democracy serves as a tool to increase governmental accountability and public trust. Given all this, citizens' informed participation holds strong normative force for the PMI.

On its face, the PMI takes seriously the value—and normative expectation—of informed citizen participation²¹: it requires explicit consent for enrollment in the cohort and envisions an ongoing and interactive partnership among stakeholders with the incentive that these will serve the public good. But the PMI, like other precision medicine research programs, is likely to encounter several challenges to achieving this goal. Studies have found that genomic knowledge in the general population is limited, especially among underserved communities and those with lower educational attainment, and that cultural differences may impact perspectives about genomic literacy and approaches to consent.²² It would thus be useful for the PMI to specify strategies for mitigating and accommodating cultural differences. Otherwise, the promise of a plurality of voices may wind up achieving only genetic rather than cultural variation—a key for precision medicine research but short of the spirit of a deliberative democracy.

Meanwhile, inadequate public competence with genomic concepts may negatively impact the quality of participation in multiple ways. First, the capability of potential participants to make informed decisions about enrollment and research choices may be compromised, with a concurrent risk that political, religious, and personal views (such as stigma about behavioral and psychiatric genetics) will prejudice decisions about participation, leading to the marginalization of vulnerable groups in genomic research.²³ Second, the knowledge gap among stakeholders, especially between researchers and cohort-participants, may reinforce a top-down model of engagement. That is, instead of the PMI generating two-way communication about the value and social acceptability of proposed genomic studies, scientific experts may control the agenda, framing of needs, and research decisions.²⁴

Although resorting to professional expertise in policy-making is common—indeed, it connotes progress in industrialized societies²⁵—such built-in dominance poses two concerns here, as in other biomedical research. One concern is that it will create a two-tiered class system within the initiative, violating democratic notions of human dignity and intrinsic worth: while researchers will retain their position as producers of knowledge, cohort participants will increasingly be objectified, viewed as disembodied datasets and means to an end. This concern is magnified for cohort participants whose consent to enroll or capability to engage in the PMI may be compromised (e.g., adolescents and persons deemed

incapable of consent, see below). Although some scientists might also be enrolled in the cohort, the odds of this are low, given that studies in other areas of medicine indicate a low rate of self-body donation (including blood) among physicians, even as they use such donations to advance their own research and encourage the public (but not their relatives!) to donate.²⁶ This concern could be partially addressed through a reciprocity requirement, that is: if the PMI required scientists and other data users to enroll in the cohort in exchange for access to (and possible benefit from) the data.

The built-in dominance of professional expertise within precision medicine research raises other equality-based concerns.²⁷ Unless the knowledge gap and the top-down model of engagement are tackled head on, public participants may be hesitant to express uneducated views, thus, in effect, ceding decisions about genomic studies to the scientists. Indeed, notwithstanding the success of initial efforts to elicit public stakeholders' input on the PMI (yielding over 200 comments),²⁸ it is important to note that neither the proportion of respondents from the general public nor the representativeness of the public respondents in these efforts and in subsequent formal, ongoing meetings is clear. This lack of representation could jeopardize the right of public participants to procedural and substantive equality in genomic policy-making,²⁹ including on the PMI's governance and oversight committees. That is, if guidelines do not require that public participants who serve on these committees have the numerical representation to contribute meaningfully to—and influence—the discussion, their roles may be primarily symbolic (as has occurred with some community members serving on Institutional Review Boards³⁰). Again, this may be especially pertinent for representatives from relatively disenfranchised groups such as people of color and Native Americans, whose cultural values and beliefs may be different than those of the majoritarian Caucasian public and scientists,³¹ and thus more likely to be overlooked if appropriate strategies to address cultural disagreements are not in place. To ensure substantive public participation, the PMI would need to develop extensive education programs for committee members, along with community governance mechanisms,³² conflict-resolution procedures that foster cross cultural and scientists/public dialogue, and perhaps selection of committee members by popular vote.³³ Even so, as discussed below, measures will be needed beyond the endorsement of deliberative processes in genomic decision-making to generate fairness in outcomes and equal access to the benefits.

Demarcating Boundaries

Although the PMI falls short of calling for mandatory participation, it advocates—at least in theory—the broadest possible enrollment of participants in the cohort. Beyond political appeals for voluntarism and mutual responsibility as civic virtues,³⁴ this approach is grounded in scientific rationales and considerations of distributive justice. That is, a categorical exclusion of certain groups would necessarily limit the scope of meaningful genomic findings that the PMI can produce, deprive those excluded from enjoying the benefits associated with genomic research, and potentially exacerbate existing health disparities if—as has often occurred in other cohort-based genomic studies—the excluded groups were to belong disproportionately to historically understudied populations. Accordingly, the PMI's stated plan to enroll participants across age, sex, race/ethnicity, and socioeconomic status is praiseworthy. Moreover, although the cohort is cast as a “national ...

cohort of one million or more Americans,”³⁵ neither U.S. citizenship nor verification of volunteers' legal status is required;³⁶ in this case the need for a racially/ethnically diverse genomic cohort for the nation's good has so far superseded contemporary debates about immigration.

However, in practice, decisions made or avoided about enrollment strategies will unavoidably shape the cohort's composition in ways that may limit the access of particular subgroups and the exercise of their participatory rights. In particular, two main points are relevant. The first is that there is an inherent tension in the PMI's stipulated goal of advancing precision medicine research and its promise of addressing health disparities. Whereas the first indeed calls for a representative sample of the US population, the latter would be better served by creating a cohort that is overrepresented by “those who have greater disease burdens, groups that have been historically underrepresented, and populations with high levels of within-group genetic diversity.”³⁷ It will be critical for the PMI to resolve the balance between these two potentially conflicting goals.

Second, the PMI's approach to consent merits consideration. Debates about the gap between the ideal of consent as a “right” and its actual practice in genomic research are not new, nor are efforts to develop consent models that are more patient-friendly.³⁸ The PMI is clearly cognizant of these issues, though additional attention is needed to structural challenges around the *construct* of consent and the question of *whose* consent is sought to avert a cohort composition that reinforces non-egalitarian social structures. For example, as in other biomedical research settings, minors' consent is not required for enrollment in the cohort; this power is reserved for parents. Although this approach befits current laws and policies in the U.S., as well as clinical practice, re-thinking the role of minors, especially adolescents (ages > 13) in PMI-related decisions would be helpful.³⁹ Studies indicate that children desire greater engagement in genomic-related decisions, including participation in genomic research and return of results,⁴⁰ and significantly, that adolescents' knowledge of genetics is at least as good as adults⁴¹, and that they are as capable medical decision-makers as adults when given sufficient time and information upon which to reflect.⁴² Thus, parents' consent decisions may be challenged on the grounds that they ignore age and capability differences among minors, especially adolescents, that erode the justifiability of age-based distinctions in genomic decision-making.⁴³ It may, in addition, be detrimental to adolescents' interests, insofar as it deprives them of exercising their right not to know about their genomic makeup or to defer that decision until adulthood. Addressing this issue will require attention to mechanisms for encouraging adolescents' participation in the decision-making process, including resolution of parent-child disagreements.

Conversely, the PMI's apparent deferral⁴⁴ of engagement with the challenges of seeking meaningful consent among non-majoritarian groups other than Latinos and African Americans may endanger the cohort's inclusivity and reinforce these groups' marginalization. For example, while efforts to tailor consent processes to the needs of different racial/ethnic groups are gaining traction,⁴⁵ early development of information about the PMI in plain language or other modes of communication (e.g., Braille) is necessary to allow full inclusion of and informed participation from individuals requiring these accommodations. Crafting guidelines to address difficulties in conducting research with

prisoners is similarly necessary to ensure that those incarcerated are not excluded from the PMI nation. Indeed, it is unclear that revoking prisoners' genomic citizenship—especially cohort participants who become incarcerated after enrollment⁴⁶—would be normatively justified. Moreover, contrary to the small number of existing genomic studies with prisoners that have focused on genetic surveillance and proclivity for aggression,⁴⁷ and thus, play into public fear and increase prisoners' marginalization, ongoing genomic research with prisoners could provide insight about the impact of conditions of incarceration on epigenetic processes that contribute to the high rates of chronic diseases (such as diabetes) and psychiatric conditions among prisoners.⁴⁸ These conditions are costly to individuals, families, and the nation at large, and may be preventable.

Additionally, the PMI's focus on a traditional, Western construct of informed consent may unjustly prioritize personal autonomy over other constructs of decision-making—a particular challenge for a study that seeks engagement of diverse groups. Thus, for instance, the emphasis on individuals as loci of decision-making may exclude members of cultural groups that hold collective perspectives of genomics and prefer community-based deliberation, especially when, as with Native American nations, such groups also hold political power.⁴⁹ The conventional focus on individual autonomy as sine qua non of informed consent may have detrimental impact on pediatric participants, whose autonomy is inherently entangled with that of other family members. Indeed, as a study of adolescents' involvement in whole exome sequencing suggests, enhancing their agency—specifically asking them questions, exploring their opinions, etc.—rather than expecting that they have decisional autonomy—may be more appropriate for addressing their needs.⁵⁰ Similarly, the use of a relational understanding of autonomy, rather than a view of isolated decision-makers, would facilitate the involvement of persons determined to be legally incompetent in research-related decisions. This would require precision medicine research programs to move beyond an automatic expectation of a substitute consent by a legally authorized third party (a legally and normatively fraught issue on its own⁵¹) to ensure that formal procedures exist for assent and for creating environments that encourage participants to raise questions and voice their feelings, regardless of their presumed decision-making capacity. Involvement of this type would be more conducive to the recruitment—and possibly, long-term retention—of cohort participants who are cycling in and out of conditions that compromise their decision-making capacity, such as psychiatric crisis.⁵² It would also increase the likelihood of cohorts having sufficient statistical power to identify genetic and gene-environment effects on disease risk or response to medication in such populations. Importantly, such involvement would better reflect the normative, equality-based values of inclusion, empowerment, and recognition of human agency in genomic decisions.

Re-examining these potentially exclusionary practices is important. As the sad history of gender equality in nation-building attests,⁵³ groups whose interests are consigned lesser importance during the establishment phase are likely to remain second-class citizens later on. In the PMI context, unless addressed head-on, these practices would also undermine normative claims about public duty to enroll in the cohort. Indeed, contrary to the promise of improving the health of individuals, communities, and the nation, these practices tend to allocate participatory genomic citizenship to sociopolitical elites (white, abled, literate, majoritarian adults) and further mark marginalized groups as unworthy of public investment.

The PMI's Social Contract

In a society premised on respect for liberty and reciprocity (inherent to modern moral and political theory of the social contract), the question of what citizens are to gain in exchange for their personal and genomic data requires consideration of three issues: risks, benefits, and responsibilities.

Risks

Participation in the PMI cohort poses some risks. The obvious ones involve data security, re-identification, and privacy protection, which the crafters of the PMI will strive to tame. This effort is critical. As new predictive genomic tests are developed, genome-based discrimination might extend beyond disability and life insurance to other civil arenas not currently protected under the Genetic Information Non-Discrimination Act, such as housing⁵⁴ and child custody disputes.⁵⁵ Intra-family conflicts about the scope and meaning of genomic privacy (e.g., between parents and adolescents) will also need management.⁵⁶ However, achieving an adequate level of privacy protection will be challenging. Privacy regulations in the US are fragmented; they include complex, sometimes conflicting, federal and state policies⁵⁷; and, in any case, they focus on protecting individuals and families from state (and other external) intrusion but not on privacy concerns within families.

There are, however, other less obvious but equally real risks. When healthy cohort participants are enrolled for life-long medical surveillance that may turn them into patients (or “patients-in-waiting”⁵⁸) as secondary findings are returned to them, there is a chance that participants will conflate research and clinical care. This increases the risk that cohort participants will overestimate the medical benefits they may receive from research participation (the “therapeutic misconception”).⁵⁹ Beyond ethical concerns, such conflation may have clinical implications: as found in a study of Latinos enrolled in genetic research,⁶⁰ cohort participants who incorrectly believe that they are being medically monitored may forgo needed clinical checkups. How to implement the PMI's commendable undertaking of returning results while protecting participants from these potential “side-effects” should be the focus of careful consideration.

Another risk concerns the impact of cohort participation on non-consenting relatives (an issue in genomic research generally) who might unwillingly learn about their genomic proclivities and who might subsequently experience stigma and discrimination associated with genetic conditions. The psychosocial responses of cohort participants (and relatives) to secondary findings is yet another concern. A few studies suggest that serious adverse psychological reactions to the return of genetic findings are uncommon, although certain subgroups (e.g., those with increased risk for depression⁶¹) may experience more distress than others; longitudinal studies on these effects are lacking.⁶² How the PMI will filter, monitor, and support such participants and their relatives is unclear. The workforce required to alleviate such stresses, especially genetic counselors, is desperately understaffed and underfunded.⁶³ Worse: studies indicate that health professionals, including genetic counselors, often lack the necessary skills and time to communicate genomic information to various age and sociocultural groups, and that they can hold negative attitudes towards

stigmatized populations (e.g., persons with psychiatric conditions) that may interfere with the development of trust within the professional/client relationship.⁶⁴

Benefits

A major expectation of precision medicine research is that the therapeutic benefits conferred on individuals, communities, and the nation will outweigh the risks. This is a key incentive for participation in the PMI and a prerequisite of the social contract, in which individuals' transfer of power to a civil state is premised on the latter's ability to realize and secure basic benefits, beginning with security. It is also reflective of a common expectation among research participants. For instance, a genetic epidemiology study of colon cancer risk factors found that most participants embraced a belief that their contributions to genomic efforts were part of a reciprocal exchange that would benefit their families and larger community.⁶⁵

However, revising—possibly even significantly reforming—existing infrastructures will be needed to accomplish this goal. Identification of genetic variants that affect disease risk or predict drug response within and across racial/ethnic and other minority populations requires sufficiently powered subgroups within cohorts.⁶⁶ Efforts to achieve these may be stymied by the potential limitations of the PMI's enrollment strategies (see above) and the challenges involved with the enrollment of minority racial and ethnic groups. Along with the lack of trust of many minority group members in the medical research system, the latter has traditionally focused on self-reported race/ethnicity rather than an objective determination of genetic ancestry, resulting in larger European-ancestry samples and significant difficulties in detecting clinically relevant genetic variation among non-European groups.⁶⁷ Significantly, even if members of racial and ethnic groups enroll in the cohort to increase the power of “their” respective group's racial/ethnic genomic analysis, challenges may arise. First, participants who volunteer to benefit “their” social group may also expect to retain some ownership of their genomic information and share the benefits of such research, although no such arrangements have been made by the PMI; and second, such enrollment may reconstruct group identities as a matter of genomic differences and reinforce “social divisiveness in the name of health equity.”⁶⁸ Early development by the PMI of a scheme to overcome these issues will be necessary to avoid the replication of historical racial/ethnic inequalities in healthcare and ensure just distribution of benefits arising from genomic knowledge.

The privatized American healthcare system will also limit medical benefits even among individuals of European ancestry. Even for the latter, who represent the overwhelming majority of participants in genomic studies,⁶⁹ access to and affordability of genetic services, including pharmacogenomic testing, typically depends on the policies of insurers.⁷⁰ Indeed, unlike other Western democracies,⁷¹ the U.S. does not view healthcare as a basic right nor the products of genomic research conducted in national biobanks as collective goods to be equally distributed to citizens through a central healthcare system.⁷² Rather, the PMI requests from cohort participants something closer to pure altruism: forfeiting property rights in their biological material without a plan to ensure that they and their families enjoy the benefits arising from genomic research. In the U.S. context, this proposition may backfire. With exorbitant prices for drugs, often unaffordable health insurance premiums,

and a regulatory system that seems designed to protect the interests of for-profit entities (e.g., pharmaceutical companies),⁷³ participants' innate altruism may succumb to a legitimate fear of commercial exploitation, resulting in a decision to forgo participation in the cohort.

Responsibilities

As occurred with the rise of single-gene testing,⁷⁴ it is possible that the availability of genomic data will induce individuals to take responsibility for expanded self-surveillance measures, from enrolling in the cohort and receiving updates about new genomic findings to making “healthier” environmental and lifestyle choices. Such responsibility—which the PMI has framed as part of its vision of participants' empowerment⁷⁵—fits the American emphasis on individualism and self-reliance, the democratic expectation that citizens bear responsibility for their society, and the PMI's call for shared responsibility for health knowledge. This emerging responsibility also finds initial (though partial) support in a focus-group study about return of secondary findings: laypersons believed that patients hold the responsibility to track genomic developments and re-contact clinicians for new findings.⁷⁶

Whether the empowerment envisioned by the PMI will materialize is unknown at this point. As studies suggest, empowerment in precision medicine projects to date has been somewhat illusory, as more, not less, power has been conferred on medical professionals.⁷⁷ We hope that the PMI will find ways to overcome this challenge and make its vision of empowerment a reality. Still, there is a need to acknowledge that the cohort's life-long surveillance under the PMI is a double-edged sword. Such surveillance increases the probability that individuals—and communities⁷⁸—with ill health increasingly will be blamed for making bad lifestyle choices (including mere refusal to enroll in the cohort), while structural issues that constrain their ability to make positive choices (e.g., poverty, pollution, health illiteracy, inadequate housing) are ignored. Indeed, as a recent study found, some precision medicine proponents expect that individuals who do not act on their genomic findings will be penalized for making bad lifestyle choices, e.g., by paying more for healthcare.⁷⁹ Mothers from disenfranchised groups may be particularly vulnerable to this dynamic. Studies indicate that women are commonly entrusted with the responsibility to guard their family's genetic health, and that they are more likely to participate in genomic research.⁸⁰ However, as has occurred in other biomedical research,⁸¹ there is a concern that political and numerical power of male researchers may lead to gender bias and decisions about genomic research that differentially comport with men's interests.

Beyond Solidarity

For the PMI to implement its exemplary goals of addressing health disparities, the discourse of a collective good and public engagement may be useful as a strategy for cohort enrollment.⁸² Yet, existing political and structural conditions in the U.S. could forestall a just distribution of rights and obligations as required under optimal notions of the social contract. As the precision medicine nation moves from theory to practice, the initiative must go beyond the (potentially fraught) promise of social solidarity in healthcare to establish

adequate policies that ensure representative inclusion criteria and equal distribution of rights and responsibilities. Informed participation across sociocultural groups is key for a substantive discussion about which genomic research best serves the public good, versus merely benefitting (medically and financially) the social and political elites. Measures are needed to avoid the replication of sociopolitical structures that reinforce disparities across age, sex, health status, and race/ethnicity and that promote the “haves” at the expense of the “have-nots.”

Because no other national biobank has stipulated a vision of partnership with citizens as strongly as the PMI, the U.S. has the opportunity to lead the way. This is a laudable – though daunting – task. Although a comprehensive list of suggestions for accomplishing this is beyond the scope of this essay, we offer just two examples of strategies to address some of the concerns raised above. First, since broad representation in the cohort is key to its success, interviews and surveys with cohort participants and, significantly, cohort decliners – will be invaluable for understanding the rationales for and against enrollment and allowing adjustment of the PMI's approaches to recruitment. The creation of a component of the PMI that addresses ethical, legal and social issues associated with the initiative, similar to the ELSI program that was created as part of the Human Genome Project, would facilitate relevant work. Such an entity could also be entrusted with developing required guidelines and “best practices.” For instance, experience indicates that commercial use of biological tissues creates discomfort among potential genetic research participants, and may lead to a drop in public trust and willingness to enroll in biobanks.⁸³ Eliminating such collaborations is unlikely (and undesirable). However, assuming that the existence of such attitudes is confirmed among potential PMI participants, the PMI could adopt policies that embed greater reciprocity, e.g., requiring that companies provide cohort participants and their families preferential access to pharmacologic products (resembling blood transfusion and organ donation policies, whereby donors and their families receive priority status if they need transfusions or transplants⁸⁴). Such a requirement may incentivize vulnerable groups to enroll in the PMI, and also serve as a first step in mitigating health disparities.

Second, consideration of innovative ways for “equalizing” the power imbalance among researchers and participants should be a priority for the PMI. For instance, the PMI could require that researchers who request access to the cohort's data—whether they are academics, independent researchers, or from for-profit companies—be enrolled in the cohort. This measure is unlikely to alleviate concerns about access to benefits, for example, but it will increase the sense of equality among participants and investigators. In addition, the PMI could grant the cohort the power to elect its own representatives to the PMI's governance bodies. This could be done on a rotational basis, perhaps while allocating seats to certain marginalized groups (as exists in some judicial systems).⁸⁵ Another possibility is for the PMI to require that decisions about which studies to pursue (and how they should be pursued) be made in consultation with representatives of those who are most likely to be affected. Native Americans who hold a community-based approach and other racial/ethnic minorities may be the most relevant groups for such engagement. But it should not stop there. Thus, for instance, engaging people with a variety of disabilities in the PMI would be critical, given their prevalence in the US population (estimated at 22% of adults⁸⁶) and possible stakes in the initiative's success. Ultimately, the key to dealing with the challenges

of the PMI will be to address barriers to full participation proactively, with the priority they deserve. That is the surest route to assuring the success and longevity of this ambitious initiative.

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