Responsibility in the age of precision genomics

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What is normal, anyway?

Genetically speaking, that's precisely the question that the Obama administration's Precision Medicine Initiative (PMI) seeks to answer. In recruiting and collecting comprehensive genetic, medical, behavioral, and lifestyle data from one million Americans, the scientific and medical communities will be better able to understand what constitutes normal genetic variation within the population, and in turn, what amount of variation causes or contributes to disease or disease risk.[1] Using this data, researchers could potentially create tailored approaches for intervention and treatment of an incredible range of diseases.

The PMI has a secondary aim: to increase the representation of previously underrepresented populations in research – primarily African Americans and Hispanics/Latinos. Inclusion of these groups in research has been a challenge for decades, with lack of access, distrust in the medical and research systems, and institutionalized racism all playing exclusionary roles. More broadly, outside of the government initiative, the promise of precision medicine ultimately seeks to alleviate disparities by finding and addressing supposed genetic differences, and empowering people with information to take responsibility for their health. This empowerment, while perhaps well intentioned, can misplace the burden of genetic responsibility for various outcomes, fostering blame and stigma. Furthermore, it may be used as an excuse to neglect social determinants of health.

Some social scientists now consider us to be in a "post-genomic" age, where promises of the genomic era have failed to materialize,[2] gene-environment interactions remain undefined, and issues around the role of data on race and ancestry remain contested.[3] Research is already starting to move in the direction of epigenetics, the modulation of the three-dimensional structure of DNA by molecular mechanisms - a seemingly promising avenue for translation[4] into both public health and individualized interventions. Additionally, genetic risk is highly dependent on penetrance, which is expressed as the percentage of those

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who have the gene who actually develop the disease. Concerns over responsibility may heighten as we begin to better understand both the plasticity of the epigenome and the level of penetrance of various genetic mutations. A useful set of paradigms came up in our discussion of responsibility: either "[clinicians/researchers] change us," "we change ourselves," or "the government changes the environment." Each of these options places the responsibility in the hands of a different party.

Matters of personal health and reproductive decision-making prompt questions of personal responsibility. Most Western countries like the United States and United Kingdom allow a high degree of reproductive liberty and parental autonomy; however, this could change in the context of the PMI and increased genetic information. Although this may not change from a legal standpoint, existing attitudes towards people with identifiable and potentially harmful genetic mutations -- which may pose harm to themselves or their future children -- may exacerbate stigma towards difficult reproductive decisions. Knowingly risking the transmission of harmful mutations to offspring, and when and if this should be considered irresponsible, remain to be addressed.[5] There has already been a push for increased access to assisted reproductive technologies and for increased societal acceptance of adoption with a normalization of non-nuclear family structures.[6] Society is going to have to weigh the relative importance of "genetic prudence" against personal autonomy, both in the historical context of eugenics and the present context of biological citizenship and responsibility.

Genes and genetic data, along with topics such as neuroimaging and HIV, have often been viewed as "exceptional" in comparison to other medical challenges and information - but the realm of such exceptionalism is limited. While each person is indeed genetically unique, such "exceptionalism" of individual genetic information is often invoked due to its potential for far-reaching impact and relevance for family members, both in a positive and negative sense. Other medical information - weight, blood panels, liver function tests don't have such direct bearing on others. As precise as the PMI intends to be, impact extraneous to the individual is unavoidable, and fears of discrimination and stigma abound.

Multiple studies, as well as a recent meta-analysis published in the BMJ, have found that genetic information does little, if anything to alter health related behavior.[7] This has been similarly shown with regards to other medical information such as cholesterol levels or lung damage from smoking, but the supposed "exceptionalism" of genetic information seems to carry little weight in this realm. We are left to wonder: how will ideas around "empowerment" play out in landscape of sensationalism and address this indifference?

The PMI aims for precision, down to the level of individual variation. But due to the inherent nature of genes and inheritance, precision, or at least "precision confidentiality" is hard to implement. Regardless of how precise we are with our molecular techniques; unintended consequences will result. While seeking to be precise, the PMI may not really "hitting the nail on the head" in terms of causality and disease risk. We've all seen those bull's-eye representations of precision and accuracy. Imagine for a moment that the target is health disparities, and the rings represent different contributing factors. Decades of research show that genetics isn't at the center of what causes these disparities; rather, it is income, poverty, and health care access.[8] Why are we throwing all of our darts (or dollars) so precisely, but not accurately? Medical research ought to ensure that taxpayer dollars being equitably distributed among the population.

There has been a recent push for many of our bioethical frameworks to shift to a more communitarian, public health-oriented approach;[9] but how to implement such a framework in the context of precision medicine and the PMI remains a salient question, given that public health is not precision-obsessed, but

rather looks to maximize outcomes. As the PMI moves forward under the new administration, bioethical scholarship and social science research remains imperative to answering these questions.

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