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COMMENTARY

News from the NIH: potential contributions of the behavioral and social sciences to the precision medicine initiative

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At this year's State of the Union address, the President announced a new $215 million Precision Medicine Initiative in the 2016 budget that will pioneer a new model of patient-empowered research that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients [1, 2]. Concurrently, Directors of the National Institutes of Health and the National Cancer Institute, Drs. Francis Collins and Harold Varmus, respectively, published an article in the New England Journal of Medicine that describes two main components of this initiative, a near-term focus on cancer therapy and a longer-term effort to generate knowledge applicable to a wide range of health and disease [3]. This longer-term initiative seeks to generate a cohort of one million or more Americans to "enable better assessment of disease risk, understanding of disease mechanisms, and the prediction of optimal therapy for many more diseases, with the goal of expanding the benefits of precision medicine into myriad aspects of health and healthcare" [3].

Matching treatment to the unique biological, behavioral, or environmental characteristics of the individual is nothing new. Matching blood type for transfusions has been common practice for nearly a century [4]. The guidelines for the management of cholesterol have been based on individual patient factors for over a decade [5]. Tailored behavioral interventions have been evaluated for over two decades. Although early treatment matching studies were disappointing [6], tailored behavioral interventions, especially computerized tailored interventions, have generally been found more efficacious than untailored interventions [7, 8]. The concept of precision medicine is not new, but recent advances in genome sequencing, cohort study designs, health informatics, and mobile/wireless technologies make now an opportune time for a large precision medicine cohort initiative.

NIH PRECISION MEDICINE WORKSHOP

To initiate planning of a large precision medicine cohort that could fully leverage these advances in genomics, cohorts, informatics, and mobile/wireless technologies, the NIH hosted a workshop on February 11–12, 2015. This workshop was attended in person by approximately 80 invited participants and was watched by over 2000 via videocast. The full workshop report and reports of the various workgroups are available at http://www.nih.gov/precisionmedicine/workshop.htm. The following are brief synopses of the workgroup reports:

Cohorts–The NIH proposes a national cohort of at least one million Americans to provide detailed lifestyle, genomic, and clinical data of unprecedented scope. To build such a cohort in a timely manner, it may be necessary to build upon and collaborate with existing cohorts, while also recruiting new participants. By assembling existing cohorts in a large consortium of cohorts with a central infrastructure and expanding these cohorts with new members, NIH could harmonize data types, enhance data collection, achieve economies of scale, and provide a resource for addressing new scientific questions.

Participant engagement–The proposed large US cohort, while presenting numerous scientific possibilities, offers opportunities to transform traditional participant engagement practices and include participants as research partners throughout the initiative. Recent efforts like the Patients Centered Clinical Research Outcomes Network (PCORnet; http://www.pcornet.org/) provide direction for recruiting and engaging patients even with a complex array of policies, regulations, and laws pertaining to health research and participant protections.

Mobile technologies–Cell phones are ubiquitous, and smartphones are now owned by over half the population and growing rapidly. Combining the data available from cell phone technology with the data available from the rapid development of wireless, wearable sensors and with the digital traces that remain as people interact with the world (e.g., social media), these digital technologies now provide unprecedented methods to assess a range of physiological, behavioral, and environmental factors objectively and with minimal participant burden. These technologies also provide a potentially useful tool for participant engagement, providing regular feedback and incentives to maintain long-term engagement.

Electronic Health Records (EHRs)–Anchored by the clinical data recorded by healthcare providers, EHRs encompass not only the observations, disease diagnoses, treatments, and outcomes as documented by healthcare providers but also an increasingly broad range of self-reported health measures, records of communications, and novel forms of data such as health-related social networking. The utility of EHRs to generate scientifically valuable data as a byproduct of care delivery has been previously demonstrated for both discovery science and healthcare process improvement [9, 10].

Work remains in areas such as policy and data standards, and specialized software applications will need to be developed for EHR efforts to be successfully used in a large, diverse cohort. Critical initial steps will be to understand the potential motivations and goals of individual study participants and of organizations that produce and manage health data and to develop a business case that is mutually beneficial to all stakeholders in a large precision medicine cohort.

CONTRIBUTIONS OF THE BEHAVIORAL AND SOCIAL SCIENCES TO THE PRECISION MEDICINE INITIATIVE

The core question of any personalized or precision medicine effort is if there are subgroups of patients with a given disorder or disease who respond differentially to the available treatments. As noted earlier, this question is not new, but the growing capabilities of whole genome sequencing and the potential for targeted therapies for specific genetic variants has created considerable scientific focus on the identification of genetic subgroups who respond differentially to medical treatments. One of the most successful demonstrations of this precision medicine approach is the use of ivacaftor for patients with cystic fibrosis who have the G511D mutation [11]. In contrast, other rational, pharmacogenetically guided treatments, such as genotype-guided warfarin dosing, have failed to find positive results [12], further illustrating the need for rigorous clinical studies of these treatments.

Although a primary goal of the Precision Medicine Initiative is the identification of genetic variants that produce differential responses to medical treatments, the initiative also recognizes the importance of behavioral and environmental factors. As Drs. Collins and Varmus wrote, "The initiative will encourage and support the next generation of scientists to develop creative approaches for detecting, measuring, and analyzing a wide range of biomedical information–including molecular, genomic, cellular, clinical, behavioral, physiological, and environmental parameters" [3]. Behavioral and environmental factors contribute more to premature death than do genetic factors [13, 14], and it is a reasonable hypothesis that subgroups characterized by their behavioral and environmental exposures may respond differentially not only to behavioral and environmental interventions but also to biomedical interventions. Furthermore, except under conditions of high heritability of rare genetic variants, there are limits to the genetic prediction for complex chronic conditions without incorporating behavioral and environmental influences [15]. Research in gene–environment interactions [16] and epigenetics [17] provides scientific frameworks for incorporating behavioral and environmental risk factors to improve our understanding of how genetic variants predict treatment response. This work extends beyond the treatment of traditional biomedical diseases to the treatment of behavioral risk factors such as smoking in which genetic variants of nicotine dependence show promise in predicting response to smoking cessation treatments [18].

Until recently, most of these behavioral and environmental factors were assessed predominantly via retrospective self-report. Self-report, although subjective, is not inherently imprecise, and a number of recent efforts, such as the Patient Reported Outcomes Measurement Information System (PROMIS), have utilized modern psychometric theory to produce precise and efficient measures of common patient outcomes such as depression, pain, and physical functioning [19]. PROMIS, as well as consensus measure projects such as PhenX which have already been utilized in personalized medicine projects [20], provide a robust set of potential measures of behavioral and environmental factors as well as health outcomes that can be harmonized across existing cohorts. Items from item-banks such as PROMIS can be administered not only retrospectively but also prospectively using ecological momentary assessment (EMA) methods that sample the experiences of individuals intensively over time, based either on random prompts or in response to specific events, using smartphones and other portable devices [21]. In contrast to the relatively static nature of the genome, phenotypes, health outcomes, and behavioral and environmental influences on health are dynamic processes, and approaches such as EMA provide critical data on the patterns and variability of these phenomena over time.

The administration of EMA via smartphones is only a small part of the potential of cell phones and other wireless and wearable devices to assess behavioral and environmental factors as well as health outcomes in real time and in the context of participants' daily lives. As outlined by the precision medicine mobile technologies workgroup (http://www.nih.gov/precisionmedicine/whitepapers/Data-Collection-Mobile-Technologies.pdf), even basic cell phones provide the capability to send and receive data via voice and text messages, identify location, and provide estimates of social contact. Smartphones, now used by over 60 % of US adults, provide not only the computing platform for a range of apps but also internal sensors that can be used to capture physical movement, location, mode of transportation, sounds, images, social interactions, and some physiological parameters [22]. Smartphones also serve as an important conduit between wearable sensors such as accelerometers and heart rate monitors, and an emerging generation of specialized physiologic monitors for parameters such as blood glucose [23] and respiration [24]. Commercial wearable health sensors, including smartwatches, are now owned by an increasingly larger proportion of the population [25], and research grade sensors to measure behavioral and environmental exposures have developed at a rapid pace since the initial efforts of the Genes, Environment, and Health Initiative [26].

Beyond portable and wearable devices, behavioral and environmental factors as well as health outcomes can be estimated from the digital traces that individuals leave as they interact in their digital world [27]. Social media has been the primary source of these digital traces for research, but as the internet of things grows, the data from digital technologies in homes and cars will provide a rich and unobtrusive data source of activities and environments with minimal burden for project participants beyond agreeing to make these data accessible for research purposes.

One of the more exciting aspects of the Precision Medicine Initiative is the commitment to engage each of the over a million individuals in the cohort not as participants but as partners in the research effort. This effort is envisioned to place the participants at the center of this national cohort effort with control over their data, the ability to donate these data for research, and with input into how best to contribute to the initiative. For example, the Precision Medicine EHR workgroup envisioned a "Synch for Science" smartphone app that would use capabilities such as Blue Button functionality [28] to allow participants to donate their health data to the precision medicine initiative. Advances in technologies including the ability to communicate frequently and in real time with participants via their cell phones will play an important role in facilitating this level of engagement, but there are a number of behavioral and social sciences experiences and findings that predate these technologies that can assist in producing this level of engagement. Over nearly two decades of community-based participatory research (CBPR), much has been learned about how to effectively engage participants as partners in the research effort. [29] Fields such as behavioral economics have refined our understanding of how to facilitate motivation and engagement via often subtle changes in environmental structures and incentives [30]. Drawing from the empirical research in the behavioral and social sciences to optimize long-term engagement of a large national cohort will be an important contribution of these sciences to the Precision Medicine Initiative.

SUMMARY

The President's Precision Medicine Initiative, in his words, "will pioneer a new model of patient-powered research that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients" [2]. The behavioral and social sciences can contribute to the goals of this initiative in many ways. Recent advances in behavioral measurement methods and technologies can be used to better characterize health outcomes, including not only the presence or absence of disease but also the functional impacts of these conditions on participation in daily life. These measurement methods and technologies also can be used to assess behavioral and environmental influences on health at a level of precision and temporal granularity not previously possible. The Precision Medicine Initiative is much more than just "genes, drugs, and disease." It is a comprehensive effort to better understand which treatments work for which individuals under which conditions.

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