Progress in Cardiovascular Diseases 62 (2019) 50–54

Contents lists available at ScienceDirect

Progress in Cardiovascular Diseases

journal homepage: www.onlinepcd.com

The Role of Government in Precision Medicine, Precision Public Health and the Intersection With Healthy Living☆

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ARTICLE INFO

Article history:
5 December 2018
5 December 2018

Keywords:
Precision medicine
Population health
Public health
Policy
Government

ABSTRACT

This paper focuses on the significant role of government in promoting precision medicine and public health and the potential intersection with healthy living (HL) and population health. Recent research has highlighted the interplay between genes, environments and different exposures individuals and populations experience over a lifetime. These interactions between longitudinal behaviors, epigenetics, and expression of the human genome have the potential to transform health and well-being, even within a single generation. Precision medicine can elucidate these longitudinal interactions with a granularity that has not been previously possible across the exposome. Understanding the interactions between genes, epigenetics, proteins, metabolites, and the exposome may inform more evidence-based, effective policy, system, and environmental change to optimize individual and population health. Government has an important role in helping to fund primary research in precision medicine and precision public health, as well as creating and enforcing standards related to food systems, air quality, and access to health care, defining and optimizing measures of health care quality and safety, and ensuring data privacy standards and protections, interoperability, and integration with surveillance systems. Government partnership and collaboration with the non-profit and private sectors can optimize precision medicine and precision public health for the benefit of the United States and global population.

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Abbreviations and Acronyms: AHA, American Heart Association; AoURP, All of Us Research Program; CRF, Cardiorespiratory fitness; HL, Healthy living; NIH, National Institutes of Health; PA, Physical activity; UK, United Kingdom; US, United States.

☆ Statement of Conflict of Interest: see page 54.

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https://doi.org/10.1016/j.pcad.2018.12.002
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Genes have a significant role in human development and health.[1] However, increasingly, researchers are understanding that transcription or expression of the genetic code is influenced by surrounding environments and the conditions in which people live.[2] For example, adverse child events, chronic exposure to poor air quality, lack of access to healthy foods, physical inactivity, lack of housing, and traumatic or chronic stress are associated with biological changes that potentially affect individual health and the development of chronic diseases later in life.[3–5] These external influences may change gene expression even within a generation,[3,6] although the debate about the causal nature of these individual relationships remains and warrants further research. Further understanding of the interplay between genes, epigenetics, proteins, metabolites, and the environment, including life experiences, may allow for evidence-based policy development, including system and environment change that can transform health and well-being. For example, understanding the impact of physical fitness or access to healthy foods on genetic expression may inform and help prioritize the integration of cardiorespiratory fitness (CRF) assessment, tailored physical activity (PA), and healthy food prescription within the health care system or worksite health promotion. Precision medicine and precision public health can also inform surveillance and prevention, screening, diagnosis, treatment, and ideally help to prevent and cure conditions, including chronic diseases, such as cardiovascular diseases and cancer.[7]

Government investment is pivotal in facilitating the primary research behind precision medicine to maximize its impact.[8] Governments can provide funding and technological infrastructure, establish data standards, ensure interoperability, provide access to care as a public payer, integrate with national, state, and local surveillance systems, promote privacy protection, and identify quality outcomes. Public, non-profit, and private partnership will optimize the impact and scale of the precision medicine and precision public health enterprise.

The announcement of the Precision Medicine Initiative in January 2015 galvanized interest in precision medicine, and funding in 2016 for the All of Us Research Program (allofus.nih.gov) further strengthened the attention for precision medicine "to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us." Concurrent with the initial announcement of the Precision Medicine Initiative by President Barack Obama, National Institutes of Health (NIH) director, Dr. Francis Collins and former NIH and National Cancer Institute director, Dr. Harold Varmus, outlined potential gaps that precision medicine can fill, including refinement in disease surveillance and monitoring, drug resistance, genomic heterogeneity of disease, and drug interactions.[9]

While precision medicine has focused on the integration of information on an individual level to develop a deeper understanding of conditions of interest and their treatment, integration of large and rich environmental data sources can be achieved for population level assessment. Precision public health has a broader definition and scope according to the Bill and Melinda Gates Foundation wherein "the use of data to guide interventions that benefit populations more efficiently is a strategy we call precision public health. It requires robust primary surveillance data, rapid application of sophisticated analytics to track the geographical distribution of disease, and the capacity to act on such information."[10]

Different levels of government have various contributions to precision medicine and precision public health with the aim of creating and maintaining systems and environments that equitably improve both individual and population health.

Government frameworks

Federal

The All of Us Research Program

The All of Us Research Program (AoURP) is a longitudinal cohort study that aims to recruit at least 1,000,000 people living in the United States (US) and will evaluate behavioral, environmental, and biological exposures over at least 10 years. The study launched in May 2018, and as of October 2018 has recruited more than 100,000 participants, with more than 60,000 of those having completed biospecimen gathering, physical examinations, and electronic health record donation. The AoURP prioritizes enrolling populations traditionally underrepresented in biomedical research through $130 million in support from the NIH with an additional $70 million in support from the National Cancer Institute for cancer genomics.

The AoURP is one implementation of the Precision Medicine Initiative announced under President Obama in 2016, which emerged from a blue-ribbon working group process involving scientists, patients, physicians, ethicists, and government officials. This process makes the AoURP framework unique compared to similar efforts in both public and private spaces: it is both defined by its construction as a *public-access study* and by the *core values* established by the working group.

The AoURP's construction as a cohort study contains many framework elements of similar efforts such as a biobank, sequencing, electronic health records collection, and more. However, rather than being governed by a private entity or even a research institution, it is coordinated by program staff at NIH, and uses contracts rather than research grants to distribute funding. The study is overseen by a central, single Independent Review Board and is governed by a "core" protocol with site-specific amendments to account for local variation and customization. Additional protocols govern marketing and content, engagement, and novel technical pilots (such as Sync4Science, which facilitates health records donation for enrollees via the internet).

The AoURP Data and Research Center, administered jointly by Vanderbilt University, the Broad Institute, and Verily, receives data from all awardees, and manages it in a private cloud installation. This private cloud removes most risks associated with secondary and tertiary distribution (ranging from "laptop left on bus" to "data theft" to simple peer-to-peer sharing via Dropbox) while still allowing for robust use of data by many researchers. Indeed, the AoURP will make data liberally available to both traditional researchers and non-traditional researchers, including the participants themselves. The data flow to the Data Resource Center from a variety of enrollment methods, including in-person at large health provider organizations, smaller federally qualified health centers, Veterans Affairs' facilities, as well as digitally through mobile devices, tablets, and computers (with biospecimens gathered at Walgreens and other locations on-demand).

Importantly, the public nature of the AoURP study is backed by the core principles articulated by its Working Group.[11] These principles hang on the wall in the AoURP offices and are invoked during multi-stakeholder discussions:

- Participation is open to all.
- Participants reflect the rich diversity of the US
- Participants are partners.
- Trust will be earned through transparency.
- Participants have access to their information.
- Data will be accessed broadly for research purposes.
- Security and privacy will be of highest importance.
- The program will be a catalyst for positive change in research.

When combined with the rigorous federal oversight, these principles represent an evolution of existing frameworks from many government studies to one that is oriented to the public and participants, as much as it is to the research community. The AoURP creates a study that is also different from a privately governed study focused on revenue, profit, or private value creation with industry partners. All researchers, including those from industry, are welcome in full transparency, and the knowledge must be shared back with those whose data led to its creation.

Other federal and international programs

The Million Veteran Program[12] (n = 616,269 through October 2017)[13] is an ongoing, large-scale cohort that began formal planning in 2009 and enrollment in 2011 with funding from the Veterans Affairs Office of Research and Development. The Million Veteran Program uses a broadly similar approach to gathering large volumes of data from individuals with computationally-heavy synthesis across domains of exposure as the AoURP, but with an additional emphasis on exposures and conditions that disproportionately affect veterans, such as Gulf War illness or post-traumatic stress disorder.

Outside of the US, the United Kingdom's (UK) Biobank[14] (n = 503,325) China Kadoorie Biobank[15] (n = 512,891), and Danish National Biobank[16] (n = 5,700,000) are community-based examples of other large data collection efforts. While some large health systems are pursuing precision medicine initiatives with largely private funding, core funding for all of these large precision medicine cohorts includes, at least in part, large national government investments, which demonstrates the commitment that some national governments are making toward precision medicine.

State

State governments can be important partners in the precision medicine and public health enterprise by facilitating interaction with the research community and the private sector, integrating with the Medicaid program, improving individual and population health surveillance systems that are administered at the state level, improving clinic-community linkages, creating better intersection between public health and the health care system, with special attention to meeting the needs of vulnerable, diverse populations. States can address the environment and cultural support systems that transform vulnerable communities such as improved transportation infrastructure, affordable housing, economic revitalization, support of pre-K-12 and higher education, water, sewage systems, ensuring public safety, and emergency response systems.

Local governments

Local governments meet people where they live and spend their time. Local governments provide fundamental services that protect the population including upstream social determinants of health like education, housing, public transportation, safe streets, fire, police, and emergency medical system protection, water, sewer, and sanitation. Local governments can translate precision medicine research into policy that improves population health like increased tobacco taxes, comprehensive smoke-free air laws, restaurant menu labeling, and clinic to community linkages with social service programs. Local governments extend precision medicine findings to the communities where people live and ideally thrive.

Non-profit sector commitment to precision medicine and public health

Non-profit organizations like the American Heart Association (AHA) catalyze a commitment to health and well-being through precision medicine at the local, state, national, and international levels. Specifically, the AHA has established an Institute for Precision Cardiovascular Medicine (Institute). Fig 1 depicts the five impact strategies of the Institute: to be a convener, provide transformational grants, enable date discoverability and access, act as the critical translational agent, and boost research by providing key services and tools. One strategy enables data discoverability and access through technology with the Precision Medicine Platform in partnership with Amazon Web Services.[17] This platform helps researchers access and analyze data using the power of cloud computing. The Institute is also training the next generation of precision medicine and public health researchers through its grant portfolio in data science, artificial intelligence, and machine learning that has already led to new tools and methods.

The British Heart Foundation is also engaged in data science efforts with the 2018 announcement for a new UK Cardiovascular Data Science Centre in partnership with Health Data Research UK. The Personalized Medicine Coalition represents innovators, scientists, patients, providers, and payers and promotes the understanding and adoption of personalized medicine concepts, services, and products to benefit patients and the health system.

Potential pitfalls

In 2011, the National Research Council report *Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease* foreshadowed the structure and key elements of the Precision Medicine Initiative.[18] For example, the knowledge network required to collect, integrate, and synthesize large volumes of data across different sources and populations requires an Information Commons that would integrate endogenous (e.g. genome, transcriptome, proteome, metabolome, lipidome, and epigenome) and exogenous (e.g. exposome) data.[19] Building such an Information Commons will be an important part of the Precision Medicine Initiative. Implementing precision medicine and public health systems requires addressing both sociopolitical and technical issues.[20] Skeptics have questioned the value of precision medicine compared with other treatment models, including preventive medicine,[21] given probabilistic principles that underlie treatment of any condition, inherent randomness between exposure-outcome relationships,[22] and limited demonstration of large effects in common conditions. Others have identified the potential paradox for precision medicine to increase uncertainty given the pursuit of more granular phenotyping leading to smaller sample sizes and potentially greater variance,[23] though this argument is less persuasive when considering precision public health.

If precision medicine and precision public health will contribute to a vibrant future improving individual and population health, then they must have an explicit emphasis on diversity and inclusion, improving equity. Most importantly, precision medicine and public health initiatives need to develop trust in vulnerable populations where there is a historically-motivated, legitimate mistrust in providing personal data to a research enterprise.

Policy levers for the role of government in precision medicine and public health

Appropriations

Appropriations at all levels of government are needed to fund primary research for precision medicine and precision public health and

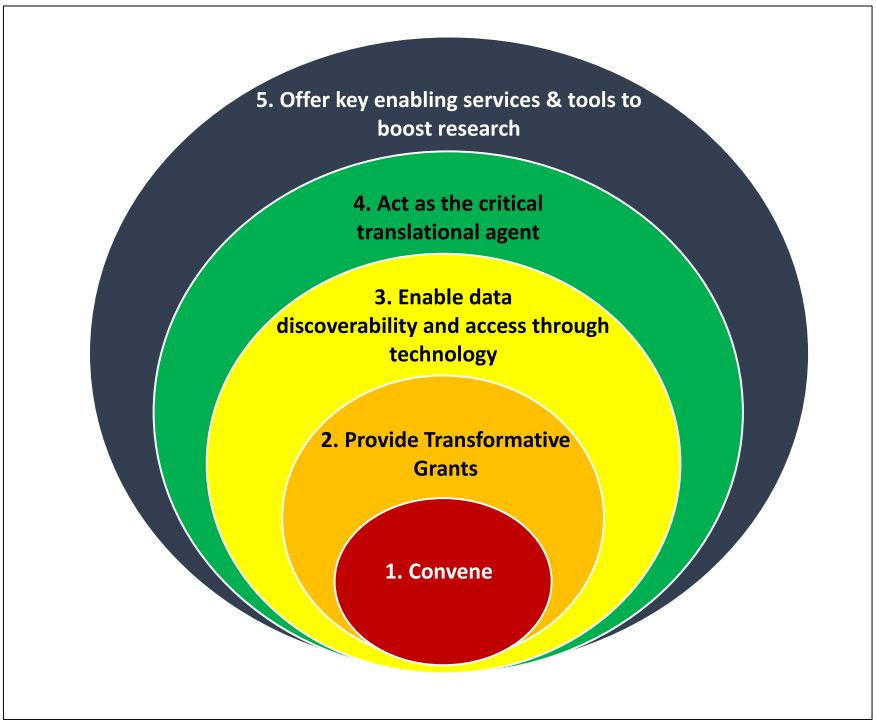

Fig 1. Five impact strategies for the American Heart Association Institute for Precision Cardiovascular Medicine.

their translation to clinical practice, quality initiatives, policy, systems and environmental change, and public health infrastructure. Governments can also amplify private sector investment in precision medicine and precision public health research and workforce development.[24] Federal investment in research includes the NIH, the Centers for Disease Control and Prevention for surveillance, public health infrastructure, and addressing chronic diseases and their associated risk factors, and the Agency for Healthcare Research and Quality for improving the safety and quality of the US health care system. Funding for state and local health departments maintains critical public health infrastructure and creates clinic-to-community linkages. Governments may also fund new technologies that employ and analyze data in an integrated and dynamic way to link precision medicine with public health, emphasizing upstream prevention efforts.[7]

Improving data quality and interoperability

Government agencies help set data quality standards, ensuring the precision and accuracy of research dissemination, effective clinical practice measures, and interoperability of electronic health records. Governments also work with non-profit organizations like the Joint Commission and the National Committee on Quality Assurance to assure clinicians and health care systems are implementing evidence-based guidelines and delivering recommended care with the right measures, transparency, and accountability.

Increasing access to care

As a public payer, governments provide primary access to quality and safe care. Medicare, Medicaid, the Children's Health Insurance Program, TRICARE, and the Veterans Affairs' health care program are key government payer examples. Especially during times of economic downturn, unemployment, and underemployment, government investment in health care increases access to quality, appropriate care.[25] This investment contributes to reducing health disparities. For example, the provision of universal health insurance coverage through Medicare since 1965 for older Americans combined with the supplemental income from Social Security, improved the economic well-being and reduced health disparities among Americans 65 years and older.[26] As a public payer, government has the leverage to integrate the findings of precision medicine research into optimal delivery systems of care.

Protecting patient safety and privacy

Through laws like the Health Insurance Portability and Accountability Act (HIPAA) and appropriate regulation, governments assure patient safety and health care data privacy. Preserving these patient protections will be essential for the integrity of the precision medicine and precision public health enterprise.

A vision for the future

Moving at the speed of trust through local communities and meeting people where they are will be as important to precision medicine and precision public health as any large change that affects people's and population's health and well-being. Continual digital innovation will be needed for sharing data equitably and securely, and innovative research combined with data science to drive new policies, prevention strategies, diagnostics and treatments for the right person at the right time for longer, healthier lives.

Conclusions

Governments have a central role to play in precision medicine and precision public health, helping to transform what is learned into evidence-based, equitable policy, system and environmental changes. Richer, more granular longitudinal data will be used for better decision making in medicine and public health to transform healthy living. A visionary future creates transparent, secure, and fair systems to equitably promote health, well-being, and better health care.

Statement of conflict of interest

Mark Huffman: MDH receives grant support from the World Heart Federation to serve as its senior program advisor for the Emerging Leaders program, which is supported by unrestricted educational grants from Boehringer Ingelheim and Novartis with previous support from AstraZeneca and Bupa. MDH also receives support from the American Heart Association, Verily, and AstraZeneca for work unrelated to this project. MDH also serves as associate editor for JAMA Cardiology for which he receives compensation from the American Medical Association.

John Wilbanks: JW through his position at Sage Bionetworks, is partially funded by the AllofUs Research Program mentioned in the article. He is also an advisor to Anonos, Digitalis Ventures, Medal, Precise.ly, and Wondros.

JH and LPW have no disclosures to report.

References

1. Timpson NJ, Greenwood CMT, Soranzo N, Lawson DJ, Richards JB. Genetic architecture: the shape of the genetic contribution to human traits and disease. Nat Rev Genet 2018;19:110-124.
2. Dupont C, Armant DR, Brenner CA. Epigenetics: definition, mechanisms and clinical perspective. Semin Reprod Med 2009;27:351-357.
3. Institute of Medicine. *Environmentally induced gene expression.* Washington, DC: The National Academies Press. 2001.
4. Sokolowsky A, Marquez E, Sheehy E, Barber C, Gerstenberger S. Health hazards in the home: an assessment of a southern Nevada community. J Community Health 2017;42:730-738.
5. Hughes K, Bellis MA, Hardcastle KA, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health 2017;2:e356-e366.
6. Choi JK, Kim SC. Environmental effects on gene expression phenotype have regional biases in the human genome. Genetics 2007;175:1607-1613.
7. Vaithinathan AG, Asokan V. Public health and precision medicine share a goal. J Evid Based Med 2017;10:76-80.
8. Whitsel LP. Government's role in promoting healthy living. Prog Cardiovasc Dis 2017;59:492-497.
9. Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med 2015;372:793-795.
10. Dowell S, Blazes D, Desmond-Hellmann S. Four steps to precision public health. Nature 2016;540.
11. National Institutes of Health. Precision medicine initiative: privacy and trust principles. Accessed online October 30, 2018 at, https://allofus.nih.gov/about/program-overview/precision-medicine-initiative-privacy-and-trust-principles November 2015. (1–4).
12. Gaziano JM, Concato J, Brophy M, et al. Million Veteran Program: a mega-biobank to study genetic influences on health and disease. J Clin Epidemiol 2016;70:214-223.
13. Million Veterans Program. Million veterans program insider newsletter. Winter 2017–18; January 2018. p. 1-8.
14. Allen N, Sudlow C, Downey P, et al. Current status and what it means for epidemiology. Health Policy Technol 2012;1:123-126.
15. Chen Z, Chen J, Collins R, et al. China Kadoorie Biobank collaborative group. China Kadoorie Biobank of 0.5 million people: survey methods, baseline characteristics and long-term follow-up. Int J Epidemiol 2011;40:1652-1666.
16. Information about the Danish National Biobank. February 2018:1-7.
17. Kass-Hout TA, Stevens LM, Hall JL. American Heart Association precision medicine platform. Circulation 2018;137:647-649.
18. Committee on a Framework for Development of a New Taxonomy of Disease, National Research Council. *Toward precision medicine: building a knowledge network for biomedical research and a new taxonomy of disease*. January 2017:1-143.
19. Rappaport SM. Implications of the exposome for exposure science. J Expo Sci Environ Epidemiol 2011;21:5-9.
20. Antman EM, Loscalzo J. Precision medicine in cardiology. Nat Rev Cardiol 2016;13:591-602.
21. Psaty BM, Dekkers OM, Cooper RS. Comparison of 2 treatment models: precision medicine and preventive medicine. JAMA 2018;320:751-752.
22. Smith GD. Epidemiology, epigenetics and the 'Gloomy Prospect': embracing randomness in population health research and practice. Int J Epidemiol 2011;40:537-562.
23. Kimmelman J, Tannock I. The paradox of precision medicine. Nat Rev Clin Oncol 2018;15:341-342.
24. Sussex J, Feng Y, Mestre-Ferrandiz J, et al. Quantifying the economic impact of government and charity funding of medical research on private research and development funding in the United Kingdom. BMC Med 2016;14:32.
25. Marshall M, Bindman AB. The role of government in health care reform in the United States and England. JAMA Intern Med 2016;176:9-10.
26. Arno PS, House JS, Viola D, Schechter C. Social security and mortality: the role of income support policies and population health in the United States. J Public Health Policy 2011;32:234-250.