

Precision Medicine Initiative: Implications to Public Health

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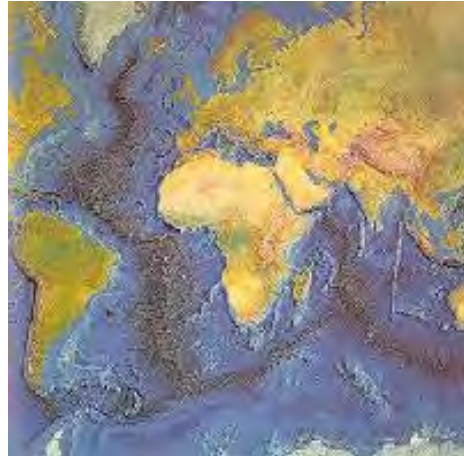
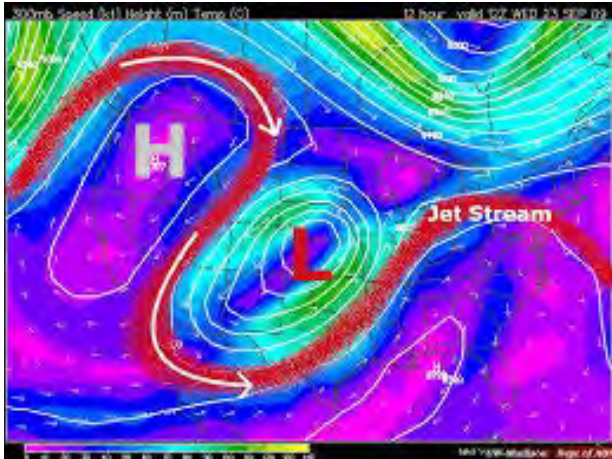


Research Methods in a Data Poor Environment

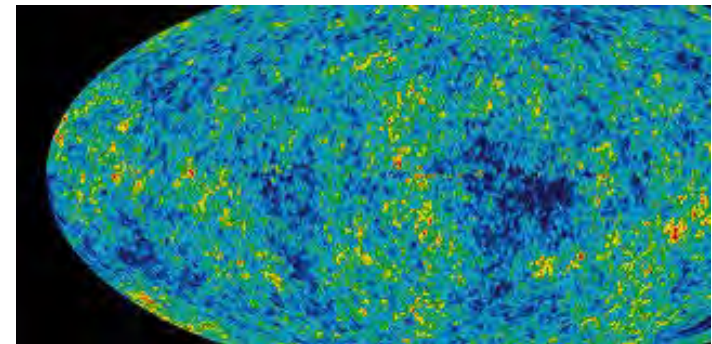
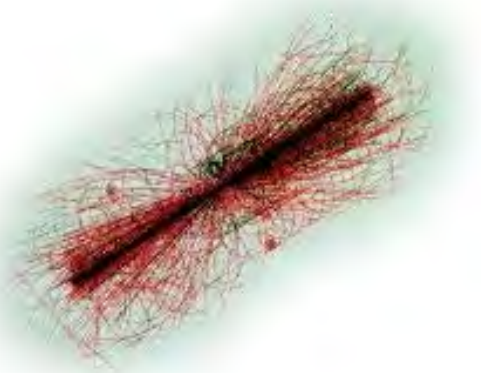
- Priority is on prospective design and data collection
- Limited data collection opportunities
- Predominately cross-sectional or minimally longitudinal designs
- Unable to assess or control myriad confounds
- Control confounds via randomization



Research Methods in a Data Rich Environment

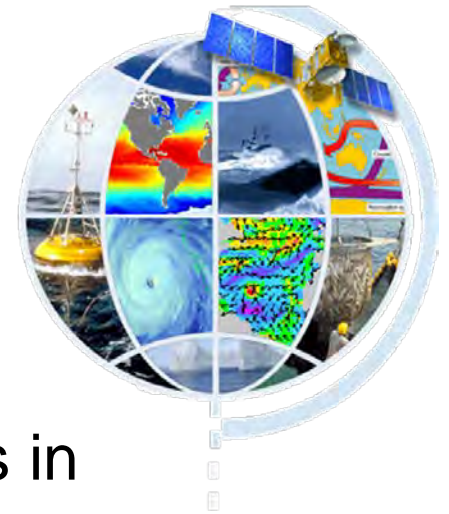


- Temporally Dense
- Computational
- Predictive



A Brief History of a Data Rich Science: Meteorology

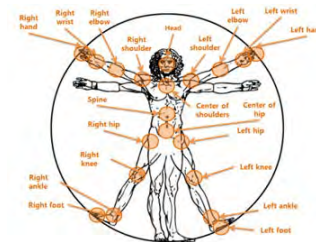
- Local, limited measurement
- Leverage communications technologies (telegraph) to connect data across sites
- Set standards for data integration
- Continued leveraging of technical advances in measurement and communication
- *Result: Rich, integrated data computationally modeled to explain and predict phenomena*



Is it possible for health research to become a data rich science?

Dawn of a Data Rich Behavioral Science

- Ecological Momentary Assessment (EMA) methods improved and delivered on cell phones
- Capture of “digital breadcrumbs” from daily interactions with technology
 - Social media
 - Call data records
 - Consumer sensors
- Sensors that can passively and continuously monitor health risk behaviors in context
 - Physical activity sensors
 - Smoking sensors
 - Sun exposure sensors
 - Environmental exposure sensors
 - Dietary intake sensors (sort of)
- Applications of computational modeling and new statistical modeling approaches that provide the analytic capabilities for intensive longitudinal (temporally dense) data.





“And that’s why we’re here today. Because something called precision medicine ... gives us one of the greatest opportunities for new medical breakthroughs that we have ever seen.”

President Barack Obama
January 30, 2015



The NEW ENGLAND JOURNAL of MEDICINE

Perspective

January 30, 2015

A New Initiative on Precision Medicine

Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

“Tonight, I’m launching a new Precision Medicine

Initiative to bring us closer to curing diseases like cancer and diabetes — and to give all of us access to the personalized information we need to keep ourselves and our families healthier.”

— President Barack Obama, State of the Union Address, January 20, 2015

The proposed initiative has two main components: a near-term focus on cancers and a longer-term aim to generate knowledge applicable to the whole range of health and disease. Both components are now within our reach because of advances in basic research, including molecular biology, genomics, and bioinformatics. Furthermore, the initiative

www.nih.gov/precisionmedicine

Public Health Less than Enthusiastic about Precision Medicine

Public Health in the Precision-Medicine Era

Ronald Bayer, Ph.D., and Sandro Galea, M.D., Dr.P.H.

That clinical medicine has contributed enormously to our ability to treat and cure sick people is beyond contention. But whether and to what extent medical care has transformed mor-

bidity and mortality patterns at a population level and what contribution, if any, it has made to the well-being and life expectancy of the least-advantaged people have been matters of conten-

tion for more than a century. This debate has taken on renewed importance as the scientific leadership at the National Institutes of Health (NIH), National Academy of Medicine, and U.S.

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Seven Questions for Personalized Medicine

VIEWPOINT

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Personalized or precision medicine maintains that medical care and public health will be radically transformed by prevention and treatment programs more closely targeted to the individual patient. These interventions will be developed by sequencing more genomes, creating bigger biobanks, and linking biological information to health data in electronic medical records (EMRs) or obtained by monitoring technologies. Yet the assumptions underpinning personalized medicine have largely escaped questioning. In this Viewpoint, we seek to stimulate a more balanced debate by posing 7 questions for the advocates of personalized medicine.

Does the Human Genome Contribute to Disease Risk Prediction?

Personalized medicine builds on the Human Genome Project, which was forecasted to revolutionize disease risk prediction, with projected relative risks as high as 6 for gene variants linked to specific diseases. However, the relative risks for the vast majority of gene variants

are offered enhanced screening and preemptive surgery. In the 25 years since *BRCA1/2* was discovered, breast cancer mortality in the United States has declined by nearly one-third; however, little of this decline stems from the discovery of *BRCA1/2*. Moreover, *BRCA1/2* is a unique story because the gene variants account for such a substantial amount of the variance in outcome for a limited number of patients.

In CF, 2 drugs (ivacaftor and lumacaftor) have recently been developed based on the CF transmembrane conductance regulator gene (*CFTR*), but they are useful only in patients with specific *CFTR* mutations, in whom they increase, singly or in combination, maximum forced expiratory volume (FEV) by 5% to 10% and improve weight gain.⁴ However, since the discovery of this gene in the 1980s, CF survival has improved substantially as a result of strict adherence to clinical management guidelines originating in pulmonary physiology and infectious diseases, but not genomics.

Although well-deserved recognition has accompa-

“We worry that an unstinting focus on precision medicine... is a mistake — and a distraction from the goal of producing a healthier population.”

Bayer and Galea, NEJM, 2015

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

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Keywords

Precision medicine, Tailored interventions, Personalized medicine, Mobile health, Health informatics, Pharmacogenetics, Cohort studies, Behavioral risk factors, Environmental risk factors

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 re-

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

- **more than genes, drugs, and disease**
- reasonable hypothesis that subgroups characterized by their behavioral and environmental exposures may respond differentially to treatments
- advances beyond self-report of behavioral and environmental factors (e.g., technologies)
- participant engagement underpinnings in science of motivation and learning

Precision Public Health for the Era of Precision Medicine



Muin J. Khoury, MD, PhD,^{1,2} Michael F. Iademarco, MD, MPH,^{1,3} William T. Riley, PhD²

The Precision Medicine Initiative¹ promises a new healthcare era. A proposed 1 million-person cohort could create a deeper understanding of disease causation. Improvements in quality of sequencing, reduction in price, and advances in “omic” fields and biotechnology promise a new era, variably labeled personalized or precision medicine. Although genomics is one driver of precision health care, other factors may be as important (e.g., health information technology).

Both excitement and skepticism met the announcement.² Public health experts are concerned about the disproportionate emphasis on genes, drugs, and disease, while neglecting strategies to address social determinants of health. A prime concern for public health is promoting health, preventing disease, and reducing health dispar-

evidentiary foundation for use. The following are examples of priority areas.

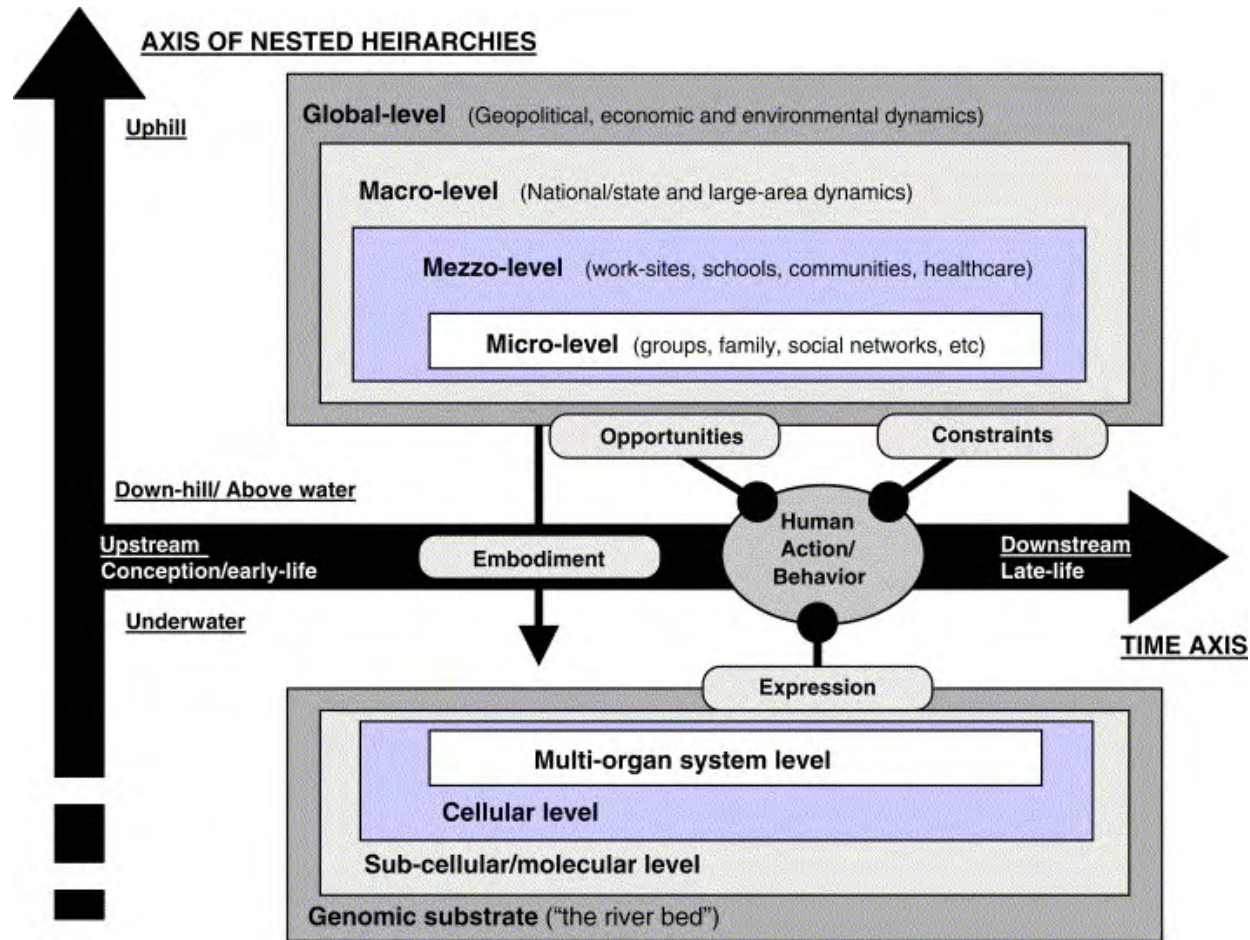
Role of Multidisciplinary Public Health Sciences

Though precision medicine focuses on individualized care, its success truly requires a population-based approach. To learn what interventions work for whom, data on each individual need to be compared with data from large, diverse numbers of people to identify population subgroups likely to respond differently to interventions. In addition, collecting information from large numbers of people is far more informative when diverse people are included from the underlying pop-

“providing the right intervention to the right population at the right time”

“use of information technology and data science in enhancing public health surveillance”

Multiple Levels of Influence



PMI: National Research Cohort

- Will comprise:
 - >1 million U.S. volunteers
 - Health Provider Organizations (HPOs)
 - Direct Volunteers
- Participants will:
 - Be centrally involved in design, implementation
 - Be able to donate biological samples, healthcare records, longitudinal self-report and sensor data
 - Receive regular feedback on the data they donate
- Will forge new model for scientific research that emphasizes:
 - Engaged participants
 - Open, responsible data sharing with privacy protections



A TRANSFORMATIONAL APPROACH TO PARTICIPATION

Participants in the PMI Cohort Program will be true partners—
not patients, not subjects—in the research process

Involved in every step of program development

- What data we collect
- What lab analyses we do
- What research is conducted
- How data gets returned



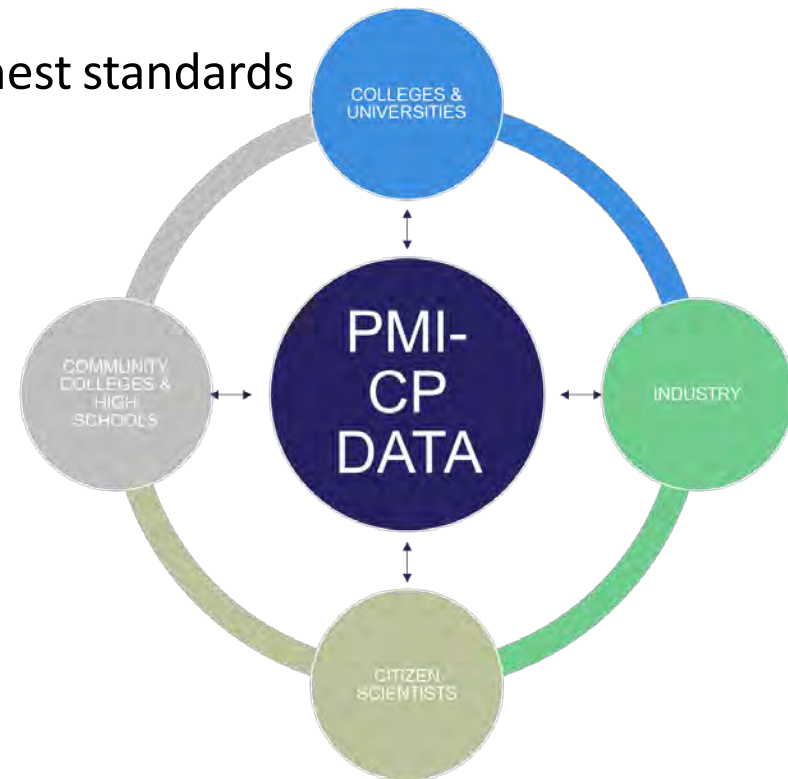
A TRANSFORMATIONAL APPROACH TO DIVERSITY

The cohort will reflect the rich diversity of America to produce meaningful health outcomes for subpopulations traditionally underrepresented in health research (across race/ethnicities, across socioeconomic status, across geographic areas).



A TRANSFORMATIONAL APPROACH TO DATA ACCESS

- Rapid data sharing both to researchers and participants
- Data collection will start small and will grow over time
- Privacy and security will adhere to the highest standards
- Will invest to level the playing field so diverse researchers can benefit





TWO METHODS OF ENGAGEMENT

Direct Volunteers



Healthcare Provider Organizations



PMI COHORT PROGRAM DATA

- The Program will start by collecting a limited set of standardized data from sources that will include:
 - Participant provided information
 - Electronic health records
 - Physical evaluation
 - Biospecimens (blood and urine samples)
 - Mobile/wearable technologies
 - Geospatial/environmental data
 - Data types will grow and evolve with the science, technology, and participant trust.
 - Tiered approach (not all data from all participants)
-



PROGRAM INFRASTRUCTURE

- Data and Research Support Center (DRC) –
Vanderbilt University Medical Center, with the Broad Institute and Verily
- Biobank – Mayo Clinic
- Participant Technologies Center (PTC) –
Scripps Research Institute, with Vibrent Health
- Healthcare Provider Organizations (HPOs)
 - Regional Medical Centers
 - Community Health Centers (e.g., Federally Qualified Health Centers)
 - VA Medical Centers

**In collaboration with
community and federal
partners, provider groups,
and others**



Patient Partnerships



EHRs



Technologies



Genomics



Data Science