The Precision Medicine Initiative®
Cohort Program

Kathy Hudson, PhD
NIH Deputy Director for Science, Outreach and Policy

October 27, 2015
The Challenges ...

- Many diseases lack effective prevention strategies, diagnostics, or treatments
  - Options fail to consider key differences among individuals: genes, lifestyle, environment
- Participants in biomedical research often treated as “subjects,” not partners
- Research findings take too long to be implemented into clinical practice
<table>
<thead>
<tr>
<th></th>
<th>Ten Years Ago</th>
<th>Now – 2014 (most recent data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of sequencing a human genome</td>
<td>$22,000,000</td>
<td>$1000 - $5000</td>
</tr>
<tr>
<td>Amount of Time to Sequence a Human Genome</td>
<td>2 years</td>
<td>&lt;1 day</td>
</tr>
<tr>
<td>Number of smart phones in the United States</td>
<td>1 million (&lt;2%)</td>
<td>160 million (58%)</td>
</tr>
<tr>
<td>EHR Adoption (% hospitals)</td>
<td>20-30%</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Computing Power</td>
<td>n</td>
<td>n x 16</td>
</tr>
</tbody>
</table>
PMI® Core Values

PMI®: A Small Drop that Affects the Whole Enterprise
PMI® Cohort Program Background

**Working Group Charge:** develop a vision for the PMI Cohort Program (PMI-CP) and advise on the design of a longitudinal national research cohort of ≥1 million volunteers

- Leverage existing cohorts, start from scratch, or hybrid?
- How to capture the rich diversity in the U.S. population?
- What data types should be included?
- What policies need to be in place for maximal benefit?
Advisory Committee to the NIH Director
Precision Medicine Initiative® Working Group

Co-Chairs:
Richard Lifton, MD, PhD, Yale University School of Medicine, New Haven, CT
Bray Patrick-Lake, MFS, Duke University, Durham, NC
Kathy Hudson, PhD, National Institutes of Health, Bethesda, MD

Members:

• Esteban Gonzalez Burchard, MD, MPH
  University of California, San Francisco

• Tony Coles, MD, MPH
  Yumanity Therapeutics, Cambridge, MA

• Rory Collins, FMedSci
  University of Oxford, UK

• Andrew Conrad, PhD
  Google X, Mountain View, CA

• Josh Denny, MD
  Vanderbilt University, Nashville, TN

• Susan Desmond-Hellmann, MD, MPH
  Gates Foundation, Seattle, WA

• Eric Dishman
  Intel, Santa Clara, CA

• Kathy Giusti, MBA
  Multiple Myeloma Res Foundation, Norwalk, CT

• Sekar Kathiresan, MD
  Harvard Medical School, Boston, MA

• Sachin Kheterpal, MD, MBA
  University of Michigan Medical School, Ann Arbor

• Shiriki Kumanyika, PhD, MPH
  U Penn Perelman School of Medicine, Philadelphia

• Spero M. Manson, PhD
  University of Colorado, Denver

• P. Pearl O’Rourke, MD
  Partners Health Care System, Inc., Boston, MA

• Richard Platt, MD, MSc
  Harvard Pilgrim Health Care Institute, Boston, MA

• Jay Shendure, MD, PhD
  University of Washington, Seattle

• Sue Siegel
  GE Ventures & Healthymagination, Menlo Park, CA
Inputs

- **Workshops**
  - Unique Scientific Opportunities for the National Research Cohort (April 28-29, NIH, Bethesda, MD)
  - Digital Health Data in a Million-Person Precision Medicine Initiative (May 28-29, Vanderbilt University, Nashville, TN)
  - Participant Engagement and Health Equity (July 1-2, NIH, Bethesda, MD)
  - Mobile and Personal Technologies in Precision Medicine (July 27-28, Intel Corp., Santa Clara, CA)

- **Requests for Information**
  - Building the cohort
  - Strategies to address community engagement and health disparities

- **FNIH Survey of public perceptions of precision medicine cohort**
- **White House Privacy and Trust Principles**
Scientific Opportunities in the PMI®-CP

- Develop quantitative estimates of risk for a range of diseases by integrating environmental exposures, genetic factors and gene-environment interactions
- Identify the causes of individual variation in response to commonly used therapeutics (pharmacogenomics)
- Discover biological markers that signal increased or decreased risk of developing common diseases
- Use mobile health (mHealth) technologies to correlate activity, physiological measures and environmental exposures with health outcomes
- Develop new disease classifications and relationships
- Empower study participants with data and information to improve their own health
- Create a platform to enable trials of targeted therapies
Assembling the PMI® Cohort

- One million or more volunteers
  - Broadly reflect the diversity of the U.S. (all ages, health statuses, areas)
  - Strong focus on underrepresented groups

- Longitudinal cohort, with continuing interactions, recontactable for secondary studies
  - Collect EHR data, provide biospecimen, survey, and complete a baseline exam

- Two methods of recruitment
  - Direct volunteers
    - Anyone can sign up
  - Healthcare provider organizations (incl. FQHCs)
    - Consider diversity of HPO participants, robustness of EHR, participant follow-up
Benefits of Approach

- Large and diverse
  - Less costly and less difficult than representative sample (which is rarely achievable)
  - 1M or more = lots of smaller but well-powered samples
  - Able to generate estimates of effect/association based on comparison between groups
- Support focus on underserved and underrepresented populations
- Prospectively understand resistance to & development of diseases
- Complement (not duplicate) existing disease-specific cohorts
## Initial Core Data Set

- Centrally collected and stored in a Coordinating Center
- Align with other data sets when possible
- Leverage existing data standards and common data models when possible

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Data Provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self report measures</td>
<td>Diet, substance use, self-report of disease and symptoms (e.g., cognitive or mood assessment)</td>
</tr>
<tr>
<td>Baseline health exam</td>
<td>Vitals (e.g., pulse, blood pressure, height, weight), medical history, physical exam</td>
</tr>
<tr>
<td>Structured clinical data (EHR)</td>
<td>ICD and CPT codes, medication history, select laboratory results, vitals, encounter records</td>
</tr>
<tr>
<td>Biospecimens</td>
<td>Blood sample</td>
</tr>
<tr>
<td>mHealth data</td>
<td>Passively-collected data (e.g., location, movement, social connections) from smartphones, wearable sensor data (activity, hours and quality of sleep, time sedentary).</td>
</tr>
</tbody>
</table>
Information Flow In

Direct Volunteers

Self-report Measures
- mHealth Data
- Consent
- EHR Data
- Baseline Exam
- Biological Samples

HPO Volunteers

12
Biospecimen Collections

- PMI-CP would collect biospecimens
  - Anticipate what future uses may be
  - Collect initially from everyone and at subsequent intervals
  - Start with blood, but should accommodate samples for exposure studies, metabolites, microbiome, etc.
- Quickly establish a central PMI-CP biobank
- CLIA-compliant specimen collection and testing where possible
## Possible data sources for the PMI® Cohort

<table>
<thead>
<tr>
<th>Data Source</th>
<th>Example Data Provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self report measures</td>
<td>Diet, substance use, self-report of disease and symptoms (e.g., cognitive or mood assessment)</td>
</tr>
<tr>
<td>Structured clinical data (EHR)</td>
<td>ICD and CPD codes, medication history, laboratory results, vitals, encounter records</td>
</tr>
<tr>
<td>Unstructured clinical data (EHR)</td>
<td>Narrative documents, images, EKG and EEG waveform data</td>
</tr>
<tr>
<td>Biospecimens</td>
<td>Blood sample, microbiome, nail and hair for environmental exposures over time</td>
</tr>
<tr>
<td>mHealth and sensor data</td>
<td>Passively-collected data (e.g., location, movement, social connections), wearable sensor data (activity, calories expended, hours and quality of sleep, time sedentary).</td>
</tr>
<tr>
<td>Healthcare claims data</td>
<td>Billing codes as received by public and private payors, outpatient pharmacy dispensing</td>
</tr>
<tr>
<td>Geospatial and environmental data</td>
<td>Weather, air quality, environmental pollutant levels, food deserts, walkability, population density, climate change</td>
</tr>
<tr>
<td>Other data</td>
<td>Social networking e.g., Twitter feeds, over-the-counter medication purchases</td>
</tr>
</tbody>
</table>
Information Flow Out

Volunteers → Data → Public → Results

Data

Researchers

15
Return of results and data

- Participants may receive, depending on their preferences:
  - Individual data
  - Individual health information
  - Ongoing study updates
  - Aggregated results
Policy for the PMI®-CP

- Policy needs for PMI-CP:
  - Single Institutional Review Board (IRB)
  - Privacy and security
    - Standards for data security
    - Safeguards against unintended data release
    - Penalties for unauthorized re-identification
  - Share results and provide access to data
    - Clarify CLIA and HIPAA
- Special policy considerations about enrollment/retention of:
  - children
  - decisionally impaired
  - participants who become incarcerated
Proposed Revisions to the Common Rule

- Require single institutional review board (IRB)
- Streamline consent
- Reduce the IRB process
- Require consent for biospecimen research
- Permit broad consent for biospecimen research
PMI®-CP Governance

- Governance structure
  - PMI-CP director
  - Independent Advisory Board
  - Executive Committee
  - Steering Committee with five subcommittees
    - Return of results and information
    - Data
    - Biobanking
    - Resource Access
    - Security

- Maintain interagency coordination
Participant Engagement in PMI®-CP

- Participant substantially represented at all junctures
  - Governance, incl. Return of Results, Data, Resource Access, Biobanking, Security
  - Design of cohort
  - Conduct of research
    - IRB
  - Dissemination of results
  - Evaluation of program
  - Build a strong foundation of trust

- Core requirement for participating entities
- Focus of launch phase
Implementation

You are here

Communications/Outreach/Engagement
- Web portal

PMI Staff Governance
- Protocol
  - IRB

Exams Biobank

Direct volunteer enrollment

Government HPO enrollment

Non-gov’t HPO enrollment

Coordinating Center

Lab stuff (SNPs, etc.)
Thank you!