The Precision Medicine Initiative®
Cohort Program

Research as a Team Sport

NIH Collaboratory/PCORnet Grand Rounds
December 4, 2015

Josie Briggs, MD
PMI Interim Director

Joshua Denny, MD, MS
Associate Professor, Director, Center for Precision Medicine, Vanderbilt University

Bray Patrick-Lake, MFS
Director for Patient Engagement, Duke CTSA
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
What is Precision Medicine?

- Get the right treatment to the right patient at the right time:
  - more accurate diagnoses
  - more rational disease prevention strategies
  - better treatment selection
  - development of novel therapies
“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
To enable a new era of medicine through research, technology, and polices that empower patients, researchers, and providers to work together toward development of individualized treatments.
# Proposed FY16 Budget for PMI

<table>
<thead>
<tr>
<th>Agency</th>
<th>$ Million</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institutes of Health</td>
<td></td>
</tr>
<tr>
<td>• <em>PMI for Oncology</em></td>
<td>$200</td>
</tr>
<tr>
<td>• <em>PMI Cohort Program</em></td>
<td>$70</td>
</tr>
<tr>
<td>• $130</td>
<td></td>
</tr>
<tr>
<td>Food and Drug Administration</td>
<td>$10</td>
</tr>
<tr>
<td>Office of the National Coordinator for Health</td>
<td></td>
</tr>
<tr>
<td>Information Technology</td>
<td>$5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$215</td>
</tr>
<tr>
<td>Category</td>
<td>Ten Years Ago</td>
</tr>
<tr>
<td>----------------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Cost of sequencing a human genome</td>
<td>$22,000,000</td>
</tr>
<tr>
<td>Amount of Time to Sequence a Human Genome</td>
<td>2 years</td>
</tr>
<tr>
<td>Number of smart phones in the United States</td>
<td>1 million (&lt;2%)</td>
</tr>
<tr>
<td>EHR Adoption (% hospitals)</td>
<td>20-30%</td>
</tr>
<tr>
<td>Computing Power</td>
<td>n</td>
</tr>
<tr>
<td>Participant &amp; Patient Engagement</td>
<td>Expectations continually rising</td>
</tr>
</tbody>
</table>
PMI Core Values

1. Participation is open to interested individuals
2. Participants are partners in all phases of the cohort program
3. Participants have access to study information and data about themselves
4. Data can be accessed broadly for research purposes
5. Adherence to the PMI privacy principles and forthcoming security framework
6. PMI is a catalyst for progressive research programs and policies
**PMI Cohort Program Background**

**Working Group Charge**: develop a vision for the PMI Cohort Program 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
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
FNIH Survey of public opinion on a large US cohort study

- 79% agree cohort probably/definitely should be done
- 54% would probably/definitely participate in the cohort
- What motivates participation?
  - 82% interested in receiving results of study
  - 62% wish to help advance health research
- 71% said participants should be partners with researchers
Scientific Opportunities in the PMI Cohort Program

- 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
Statistical power of one million PMI cohort participants

- PMI Working Group: what is a cohort of 1 million powered to detect (exposure > outcome)?
  - Detect small risk factors (i.e., low odds ratios) for genetic and environmental exposures on a variety of health outcomes

<table>
<thead>
<tr>
<th></th>
<th>Disease case size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5000</td>
</tr>
<tr>
<td>Detectable OR for main effect (e.g., genetic study) at p&lt;10^{-7}</td>
<td>1.36</td>
</tr>
<tr>
<td>Detectable OR for interaction study (e.g., gene x environment) at p&lt;10^{-7}, 10% exposure</td>
<td>2.31</td>
</tr>
<tr>
<td>Estimated number of diseases in PMI Cohort Program exceeding each threshold</td>
<td>261</td>
</tr>
</tbody>
</table>
## Estimated disease incidences and prevalences in one million people

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estimated prevalent cases</th>
<th>Estimated incident cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5 years</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>135,658</td>
<td>40,411</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>73,723</td>
<td>21,315</td>
</tr>
<tr>
<td>Asthma</td>
<td>62,149</td>
<td>17,292</td>
</tr>
<tr>
<td>COPD</td>
<td>48,728</td>
<td>15,396</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>39,273</td>
<td>14,981</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>33,426</td>
<td>4,161</td>
</tr>
<tr>
<td>Breast cancer (female)</td>
<td>20,470</td>
<td>12,068</td>
</tr>
<tr>
<td>Stroke</td>
<td>16,016</td>
<td>8,969</td>
</tr>
<tr>
<td>Lupus</td>
<td>14,659</td>
<td>3,283</td>
</tr>
<tr>
<td>Dementia</td>
<td>13,373</td>
<td>7,028</td>
</tr>
<tr>
<td>ADHD</td>
<td>13,039</td>
<td>7,213</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>9,407</td>
<td>3,745</td>
</tr>
</tbody>
</table>
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)
  - Able to generate estimates of effect/association
  - Permits well-powered samples
- 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
- Biospecimens

HPO Volunteers

- 19
Biospecimen Collections

- PMI Cohort Program 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 Cohort Program 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 CPT 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

Public

Results

Data

Researchers

Test tubes with data.
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 Cohort Program

- Policy needs for PMI Cohort Program:
  - 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
“...I’m proud we have so many patients’ rights advocates with us here today. They’re not going to be on the sidelines. It’s not going to be an afterthought. They’ll help us design this initiative from the ground up, making sure that we harness new technologies and opportunities in a responsible way.”

President Barack Obama
January 30, 2015
How to Invite and Engage
Participant Engagement in the PMI Cohort Program

- 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
PMI Cohort Program Governance

- Governance structure
  - PMI Cohort Program Director
  - PMI Cohort Program Advisory Panel
  - Executive Committee
  - Steering Committee with five subcommittees
    - Return of results and information
    - Data
    - Biobanking
    - Resource Access
    - Security

- Maintain interagency coordination
Implementation

Direct volunteer enrollment

FQHC enrollment

Large HPO enrollment

Coordinating Center

Lab stuff (SNPs, etc.)
## PMI Cohort Program Funding Opportunities

<table>
<thead>
<tr>
<th>Title / Type</th>
<th>Year 1 $</th>
<th>Number of awards</th>
<th>Project Period</th>
<th>Application</th>
<th>Award</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct Volunteers Pilot Studies (OT)</td>
<td>TBD</td>
<td>1</td>
<td>1 yr</td>
<td>December 22, 2015</td>
<td>February 2016</td>
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<tr>
<td>Communication Support for the Precision Medicine Initiative Research Programs (OT)</td>
<td>TBD</td>
<td>1</td>
<td>2 yrs</td>
<td>December 22, 2015</td>
<td>February 2016</td>
</tr>
<tr>
<td>PMI Cohort Program Biobank (U24)</td>
<td>$15 M</td>
<td>1</td>
<td>5 yrs</td>
<td>February 4, 2016</td>
<td>June 2016</td>
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<tr>
<td>PMI Cohort Program Coordinating Center (U2C)</td>
<td>$21 M</td>
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<td>5 yrs</td>
<td>February 17, 2016</td>
<td>July 2016</td>
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<tr>
<td>PMI Cohort Program Healthcare Provider Organization Enrollment Centers (UG3/UH3)</td>
<td>$28 M</td>
<td>≤7</td>
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<td>February 17, 2016</td>
<td>July 2016</td>
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<tr>
<td>PMI Cohort Program Participant Technologies Center (U24)</td>
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<td>July 2016</td>
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</tbody>
</table>
Thank you!