The Precision Medicine Initiative Cohort Program – Building a Research Foundation for 21st Century Medicine

Precision Medicine Initiative (PMI) Working Group Report to the Advisory Committee to the Director

September 17, 2015

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"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

Mission of the Precision Medicine Initiative

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.

PMI Proposed Support: FY16

Agency	$ Million
NIH • *Cancer* • *Cohort*	$200 *$70* *$130*
FDA	$10
ONC	$5
TOTAL	**$215**

PMI Working Group of the Advisory Committee to the NIH Director (ACD)

- 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
Working Group On Building A Research Cohort For Precision Medicine

Co-Chairs:

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Kathy Hudson, PhD, National Institutes of Health

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  University of Washington, Seattle
- **Sue Siegel**
  GE Ventures & Healthymagination, Menlo Park, CA

Inputs

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

Why?

- Discover new biomarkers predictive of individual risk of future disease for many common diseases
- Understand individual variation in response to therapies
- Study populations reflecting diversity of the US population
- Accelerate research across many areas of health and disease
- Participant engagement and ongoing contact allows follow-up studies to advance understanding of disease mechanisms and targeted clinical trials.

Why now?

	Ten Years Ago	Now – 2014 (most recent data)
Cost of sequencing a human genome	$22,000,000	$1,000 - $5,000
Amount of Time to Sequence a Human Genome	2 years	<1 day
Number of smart phones in the United States	1 million (<2%)	160 million (58%)
EHR Adoption (% hospitals)	20-30%	>90%
Computing Power	n	n x 16 Deep Learning

Scientific Opportunities in the PMI-CP

- Discover new biomarkers predictive of future disease risk
- Discover determinants of individual variation in response to therapeutics
- Determine quantitative risk estimates in the population by integrating environmental exposures, genetic factors, and gene-environment interactions
- Integrate mHealth and sensor technologies
- Determine clinical impact of loss-of-function mutations on clinical outcome
- Discover new classifications and relationships among diseases
- Enable targeted clinical trials of subjects with rich clinical data
- Make ‘big data’ broadly available to investigators

Estimated disease incidences and prevalences in one million people

Disease	Expected prevalent cases	Incident cases	
		5 years	10 years
Type 2 Diabetes	135,658	40,411	123,196
Congestive heart failure	73,723	21,315	40,322
Asthma	62,149	17,292	44,036
COPD	48,728	15,396	33,584
Myocardial infarction	39,273	14,981	27,112
Epilepsy	33,426	4,161	11,248
Breast cancer (female)	20,470	12,068	21,382
Stroke	16,016	8,969	15,598
Lupus	14,659	3,283	6,738
Dementia	13,373	7,028	9,656
ADHD	13,039	7,213	13,582
Colorectal cancer	9,407	3,745	6,844

Assembling the PMI Cohort

- **One million or more volunteers:**
  - Be recontactable
  - Collect EHR data, provide biospecimen, survey, and complete a baseline exam
- Longitudinal cohort, with continuing interactions, recontactable for secondary studies
- Two methods of recruitment
  - Direct volunteers
    - Anyone can sign up
  - Healthcare provider organizations (incl. FQHCs)
    - Consider HPO diversity, robustness of EHR, patient follow-up

Assembling the PMI Cohort

Broadly reflect the diversity of the U.S.

- Groups that are underrepresented
- All states of health and disease
- All areas of the U.S.
- All life-stages
- Special policy considerations
  - enrolling 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

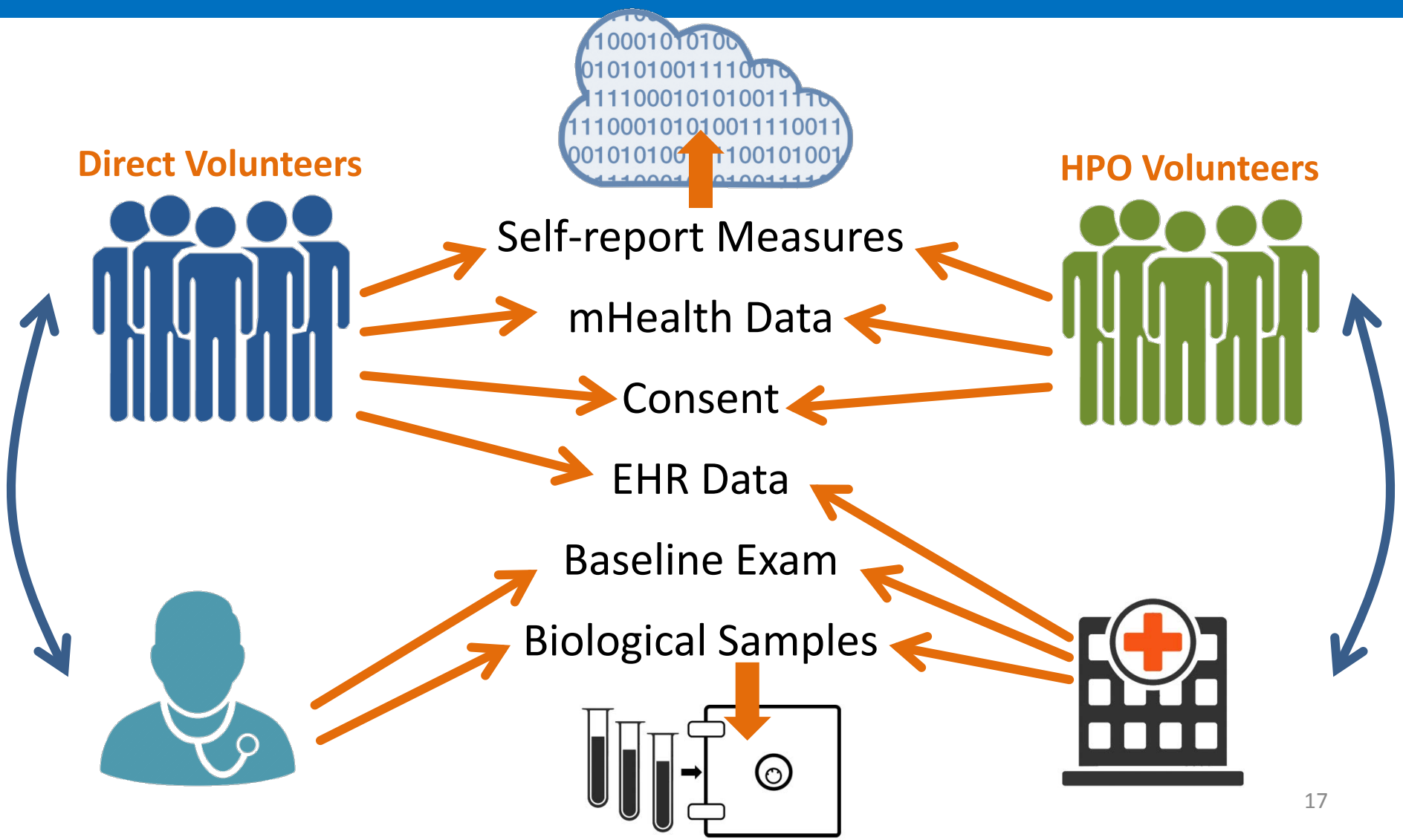
FNIH Survey of public opinion on a large US cohort study

- 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

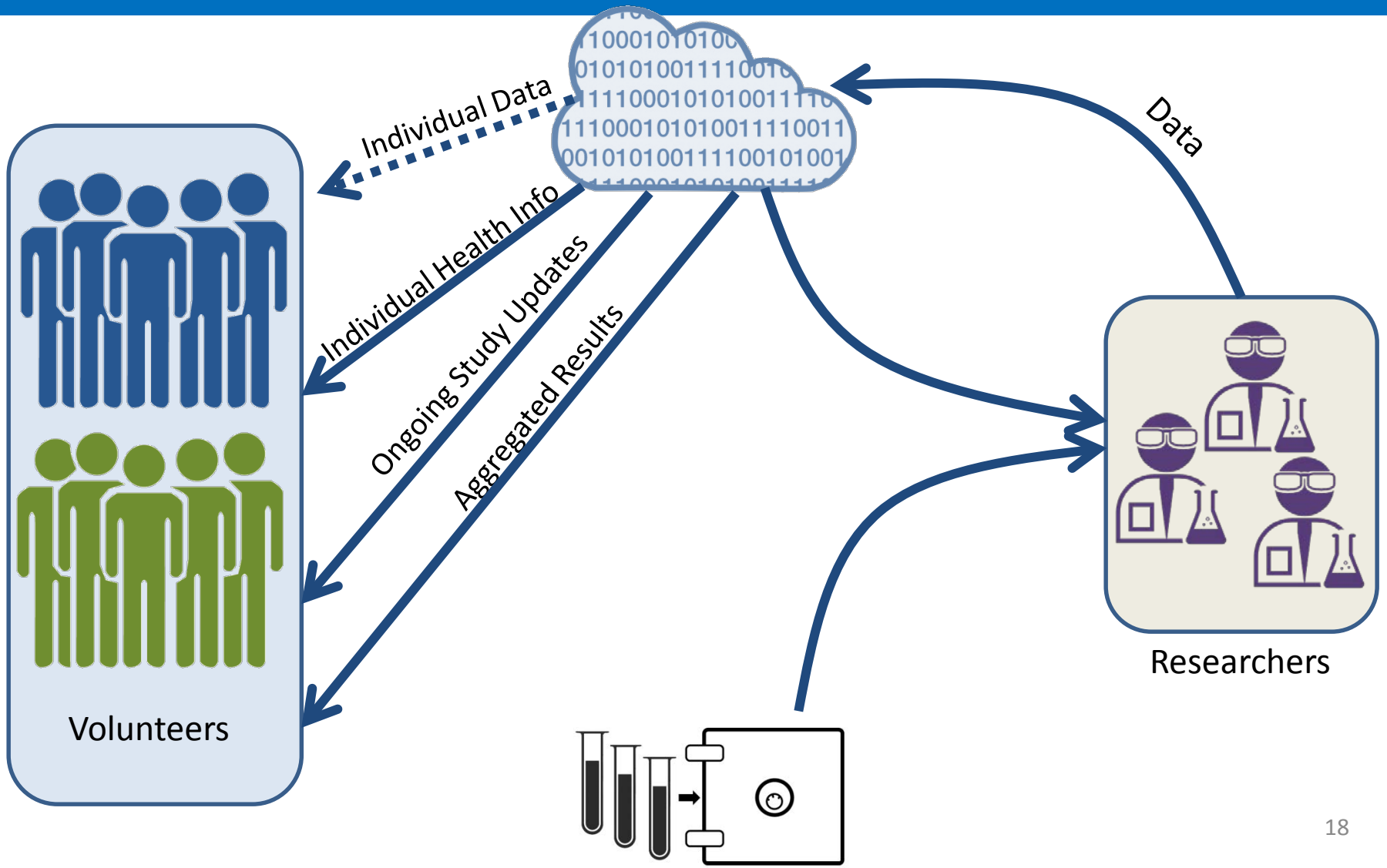
PMI-CP Focus on Engagement

- Highly interactive and proactive participant model
  - Participant representation in governance, design, conduct, dissemination, evaluation
  - Build a strong foundation of trust
- Participant engagement and communication activities should be centrally coordinated
- Consent is with PMI Cohort Program
  - Basic consent to be part of the cohort
  - Broad consent for secondary use
  - Consent is adaptable over time for new components
  - Future option to join supplementary/complementary studies
- Single IRB for PMI-CP
- Return of results and access to data
  - Aggregate results should be available to all participants
  - Individuals may set preferences for return information

Information Flow In



Information Flow Out



Possible data sources for the PMI Cohort

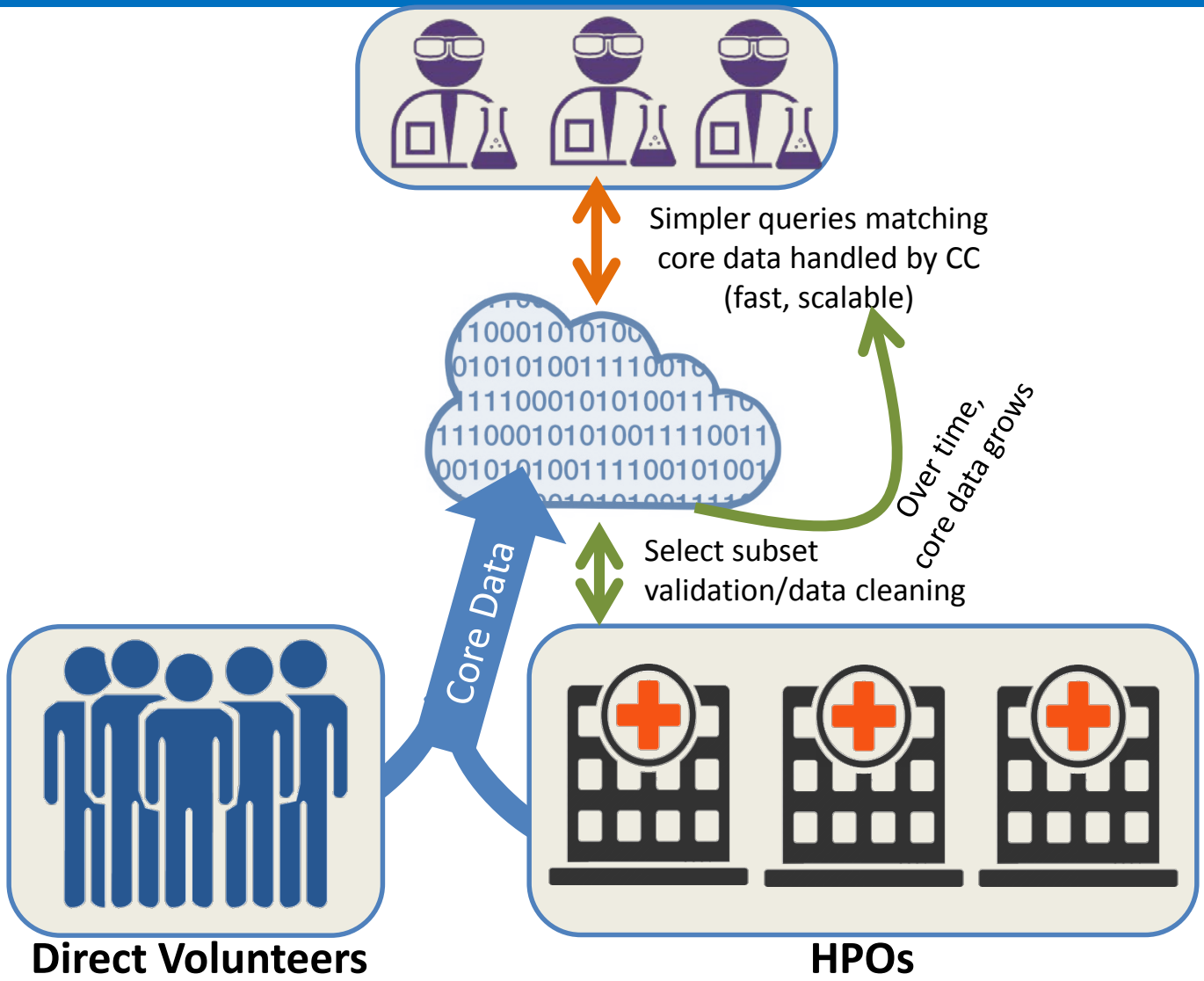
Data Source	Example Data Provided
Self report measures	Diet, substance use, self-report of disease and symptoms (e.g., cognitive or mood assessment
Structured clinical data (EHR)	ICD and CPD codes, medication history, laboratory results, vitals, encounter records
Unstructured clinical data (EHR)	Narrative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

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

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

Data Flow Between Coordinating Center (CC) and Participant Sites



Biospecimen Collections

- PMI-CP would collect new biospecimens
  - Anticipate what future uses may be
  - Collect initially from everyone and at subsequent intervals as determined by use cases
  - Start with blood, but should accommodate samples for exposure studies, metabolites, microbiome, etc.
- Quickly establish a central PMI-CP biobank
- Maintain CLIA-compliance in specimen collection and testing where possible

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
    - Support broad consent in Common Rule NPRM
    - Clarify CLIA and HIPAA
- Special considerations for certain populations

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

Next Steps

Principles:

- Utilize innovative ways to implement the cohort
- Stay flexible, nimble, cutting edge

Priorities:

- Act quickly to bring in a PMI Director & to “staff up”
- Quickly build infrastructure to support enrollment
  - Communications & engagement
  - Single IRB and consent
  - Data storage & acquisition infrastructure
  - Biobank
- Begin enrollment ASAP

Thank you!

- Working Group Members
- Workshop participants and RFI respondents
- NIH workshop planning teams
- Workshop hosts Vanderbilt and Intel
- Gwynne Jenkins and NIH Staff