People have different disease risk and variable drug response

- Healthy
- Drug beneficial
- Severe disease
- Drug toxic
- Disease risk, self-limited
- Drug beneficial, mild toxicity
- Atypical disease
- Drug does nothing
Framingham Heart Study

Enrolled 5209 men and women in 1948

Some Framingham early discoveries:
- 1960 – Cigarettes increase heart disease
- 1961 – cholesterol, blood pressure increase heart disease
- 1967 – exercise decreases risk of heart disease; obesity increases it
- 1970 – high blood pressure and atrial fibrillation cause stroke

The impact of Framingham (and similar cohorts) has been dramatic

https://www.cdc.gov/mmwr/preview/mmwrhtml/mm4830a1.htm
"I want the country that eliminated polio and mapped the human genome to lead a new era of medicine..."

- PRESIDENT BARACK OBAMA
State of the Union Address, Jan. 20, 2015

Finding solutions on a national scale: the All of Us Research Program

Funding:
$130M in FY2016
$230M in FY2017
21st Century Cures Act provides additional $1.45B over 10 years

Core goals for the All of Us Research Program

- 1 million or more
- Longitudinal, recontactable
- EHR data, biospecimens, baseline evaluations, and health surveys
- Focus on engagement
- Focus on diversity
- Network formed – July 2016

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

September 17, 2015

https://allofus.nih.gov/news-events-and-media/announcements/all-us-research-program-initial-protocol
**All of Us Research Program**

**Mission and Objectives**

1. Nurture relationships with **one million** or more participant partners, from all walks of life, for decades, reflecting the **broad diversity** of the U.S., especially those **underrepresented** in biomedical research.

2. Deliver the largest, **richest**, and most accessible biomedical **dataset** providing the **tools & capabilities** that make it easy for researchers, participants, and citizen scientists to make discoveries.

3. Catalyze a **robust ecosystem** of researchers and funders to use and support the rich, **longitudinal resource** of deep clinical, environmental, lifestyle, & genetic data.

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**Some of the All of Us research goals**

- Studying exposures and habits
  - Machine learning on Big Data
  - New biomarkers (and their interactions)
- Improving drug action
- Engaging diverse participants
  - New precision therapies & targeted clinical trials
  - Before ivacaftor
  - After ivacaftor
Why Diversity?

Popejoy & Fullerton, Nature 2016

PERSISTENT BIAS
Over the past several years, the proportion of participants in genome-wide association studies (GWAS) that are of Asian ancestry has increased. Groups of other ancestries continue to be very poorly represented.

4% GWAS represents >33% US population

Summary of the approach and protocol

Enroll, Consent, EHR sharing
Health Surveys
Baseline measurements
Biologic specimens
Smartphones & Wearables
Summary of our Version 1 Protocol

**Enroll, Consent & EHR**
- Recruit 18+ years old initially; plan to include children in next iteration
- eConsent or paper long-form
- EHRs collected periodically

**Surveys**
- Three initial participant provided information modules: The Basics, Overall Health, & Lifestyle
- More in development
- Linking to EHR data elements

**Physical Measurements**
- Blood pressure
- Heart rate
- Weight
- Height
- BMI
- Hip circumference
- Waist circumference

**Biosamples**
- Blood (or saliva, if blood draw is unsuccessful)
- Urine

Full protocol published at allofus.nih.gov. Planning for new releases every 2.5 to 3.5 years.

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Major building blocks of the program

**DATA AND RESEARCH CENTER (DRC)**
Big data capture, cleaning, curation, & sharing in secure Environment
Vanderbilt, Verily, Broad Institute

**BIOBANK**
Repository for processing, storing, & sharing biosamples (35+M vials)
Mayo Clinic

**PARTICIPANT CENTER**
Direct volunteer participant enrollment, digital engagement innovation, & consumer health technologies
Scripps Research Institute (with multiple partners)

**HEALTHCARE PROVIDER ORGS (HPOs)**
Clinical & scientific expertise network, enrollment & retention of participants
30+ regional med centers, FQHCs, VA, future awards to grow network

**COMMUNICATIONS & ENGAGEMENT**
Comms, marketing, & design expertise; Engagement Coordination & community partners network
Wondros, HCM, 19 community partner orgs, future awards to grow network
### Current Consortium Members

<table>
<thead>
<tr>
<th>Data and Research Center</th>
<th>Other Platform Development</th>
<th>Communication &amp; Engagement</th>
</tr>
</thead>
<tbody>
<tr>
<td>DV Network (Direct Volunteers)</td>
<td>HPO Network (Health Care Provider Organizations)</td>
<td>DV Network (Direct Volunteers)</td>
</tr>
<tr>
<td>RMHC</td>
<td>California Precision Medicine Consortium</td>
<td>New York City Precision Medicine Consortium</td>
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<td>Precion Medicine Consortium</td>
<td>Southern All Of Us Network</td>
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<td></td>
<td>UC San Diego/Scribz</td>
<td>Southeast Enrollment Center</td>
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<td></td>
<td>All of Us, Wisconsin</td>
<td>Precision Medicine Consortium</td>
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<tr>
<td></td>
<td>University of Arizona</td>
<td>University of Pittsburgh</td>
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<td></td>
<td>VA Medical Centers</td>
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</tbody>
</table>

### Community Engagement Partners – led by Dara Richardson-Heron

- American Academy of Family Physicians, Leawood, Kansas
- American Academy of HIV Medicine, Washington, D.C.
- American Association of Colleges of Nursing, Washington, D.C.
- American Medical Association, Chicago, Illinois
- Arab Community Center for Economic and Social Services, Dearborn, Michigan
- Asian & Pacific Islander American Health Forum, Oakland, California
- Association of Nurses in AIDS Care, Uniontown, Ohio
- Black Women's Health Imperative, Washington, D.C.
- Cobb Institute (W. Montague Cobb/National Medical Association Health Institute), Washington, D.C.
- Delta Research and Educational Foundation, Washington, D.C.
- FiftyForward, Nashville, Tennessee
- National Alliance for Hispanic Health, Washington, D.C.
- National Baptist Convention, Nashville, Tennessee
- National Hispanic Medical Association, Washington, D.C.
- National Minority Quality Forum, Washington, D.C.
- National Network of Libraries of Medicine, Bethesda, Maryland
- San Francisco General Hospital Foundation, San Francisco, California
- UnidosUS, Washington, D.C.
Enrollment - HPO/FQHC/Direct Volunteer
Current and Planned Locations

QTC/Liedos Purple
Quest Red
ESMI Olive
Walgreens Clinics Green
National Blood Collaborative Blue
HPOs/FQHCs Plus Sign

Key DRC Products for Data Ingestions, Curation, and Dissemination

Researcher Portal, Environments, and APIs
- FireCloud/Worbench
- Cohort Builder & Public resources
- Precomputed results

Participant Portal (PTSC)
- Registration
- Consent
- EHR (via S4S) (future)
- PPI

HPO and DV Staff Tools
- EHR Upload

Operational Dashboards
- Electronic Health Records (OMOP)
- Registrations over time
- Registrations by Recruitment Sites
- Participants by Phase

HealthPro Portal
- Physical Measurements
- Biobanking
- Work Queue

Centrally linked data
- Death index
- Claims & Rx Data
- Geospatial & Env.

Curated Data Repository (OMOP + VCF + others)
- Algorithms, Standards, Data Linkages, De-identification

Biobank RLIMS
Biobank MayoLINK
Sync 4 Science (S4S) – a technology to share health data

Intelligent Curation

AOU data gets smarter over time.

Leverage the “Web dividend” for Health.

Automatically captioned:
“Two pizzas sitting on top of a stove top oven”
AOU centralizes data to **enhance security** and **improve usefulness**

**Traditional Approach**
Bring data to researchers

**AoU Approach**
Bring researchers to the data

Building tools to facilitate research

A **RESEARCHER - COHORT FILTER TOOL**

B **RESEARCHER - PARTICIPANT REVIEW**

C **CC ACTIVATED DATA SHARING & PARTICIPANT ENGAGEMENT**
A key tenet of *All of Us*: participants will have access to their information.

3.5% of all tested had an actionable result.
86% were new diagnoses.
And... most people have a variant that would effect drug prescribing

Van Driest, CPT 2014

In beta testing now...

The future of health begins with you

All of us Research Program has a simple mission. We want to speed up health research breakthroughs. To do this, we’re asking one million people to help us find the way. In the coming weeks, share this with all of us.
May 31, 2017: Launched Beta phase

- Version 1 protocol tested & IRB approved
- Completed security plan/tests = Authority to Operate
- Completed end-to-end “dress rehearsals” nationally
- Enrollment website & participant portal up & running
- Call center & command center up & running
- Direct Volunteer capability & HPO network established
- New sites launched every 1-3 weeks
- Kicked off mobile exhibit, the All of Us Journey
- Announced Fitbit pilot with 10,000 individuals

>11,000 participants in beta phase (slow ramp up)
Goal: 1 million in ~4-5 years

All of Us timeline

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 2015</td>
<td>President’s State of the Union Address announcing PMI</td>
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<tr>
<td>September 2015</td>
<td>NIH Advisory Committee to the Director (ACD) PMI Working Group report</td>
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<tr>
<td>July 2016</td>
<td>Initial awards</td>
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<tr>
<td>May 2017</td>
<td>IRB &amp; FISMA security approvals</td>
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<tr>
<td>May 31, 2017</td>
<td>Beta testing begins with initial participants</td>
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<td></td>
<td>first set of participant provided information (PPI) surveys, baseline measures, biospecimen collections, EHR data</td>
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<tr>
<td>Now</td>
<td>&gt;11,600 people, first real EHR upload tested</td>
</tr>
<tr>
<td>Through 2018</td>
<td>Expand to national network, test &amp; revise protocol, EHR uploads, develop additional survey modules, plans for genomics &amp; pediatrics</td>
</tr>
<tr>
<td>Spring 2018</td>
<td>National launch</td>
</tr>
<tr>
<td>Late 2018 / Early 2019</td>
<td>Initial researcher site launch</td>
</tr>
<tr>
<td>Next 4-5 years</td>
<td>Enroll 1M+ volunteers</td>
</tr>
<tr>
<td>Next 10+ years</td>
<td>Platform releases growing the data, tools, focus areas</td>
</tr>
</tbody>
</table>
What personalizing medicine really means

57yo with DM2, FHx heart disease, ↑chol admitted for chest pain, has her first myocardial infarction

Recath, stent “Plavix x 1 year minimum. ASA life long.”

Cath, more stents

9th admission, 5th intervention, 9th stent

CYP2C19*2/*2 clopidogrel poor metabolizer

In-stent thrombosis, restent

In-stent thrombosis, restent

January

clopidogrel started

December

Switched to prasugrel

What personalizing medicine really means – 2

Cystic Fibrosis

[Images of people and landscape]
Questions?

- **NIH All of Us website:** [https://allofus.nih.gov](https://allofus.nih.gov)
- **Enrollment site:** JoinAllofUs.org
- **Follow us on social media:** @AllofUsResearch, #JoinAllofUs

Thank you