Translating Precision Medicine into Global Impact

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of US



(on behalf of)
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Chief Medical and Scientific Officer

NASEM Workshop - Precision Medicine: Promoting Knowledge Exchange & Collaboration Between Kuwait and the United States – October 16, 2025











Factors of Risk in the Development of Coronary Heart Disease— Six-Year Follow-up Experience

The Framingham Study

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AND JOSEPH STOKES, III, M.D.
Framingham, Massachusetts

Increasingly reliable estimates of the prevalence and incidence of coronary heart disease (CHD) emphasize the importance of this disease as a contemporary health hazard. Cardiovascular disease is

Since it has been established that coronary atherosclerosis is present for many years prior to the development of symptomatic CHD, it seems evident that efforts at prevention must begin many years before the

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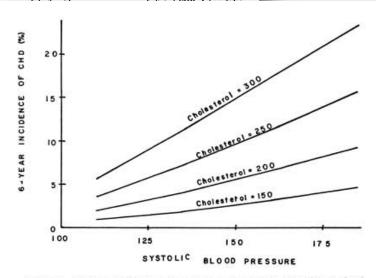


FIGURE 2. Six-year incidence of coronary heart disease according to level of systolic blood pressure at specified serum cholesterol levels (men 45 to 62 years). For explanation, see legends for Figure 1.

77th Anniversary Framingham Heart Study

Enrolled 5,209 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 Opportunity for Large Cohort Studies and Public Health

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

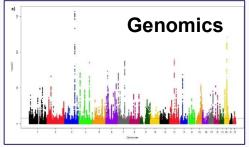
From 1950 - 1996: Heart disease mortality fell 56%, stroke rates fell by 70%

Since 1990, heart disease mortality has continued to fall by 22%



Understanding Enabling Individualized Health Requires Multimodal Data Over Time

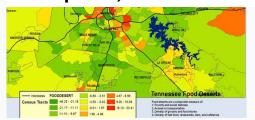


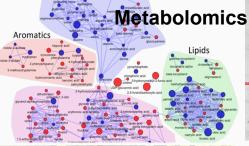


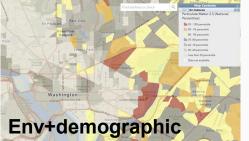


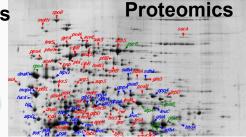


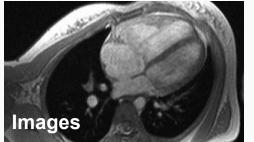
Geospatial, food deserts



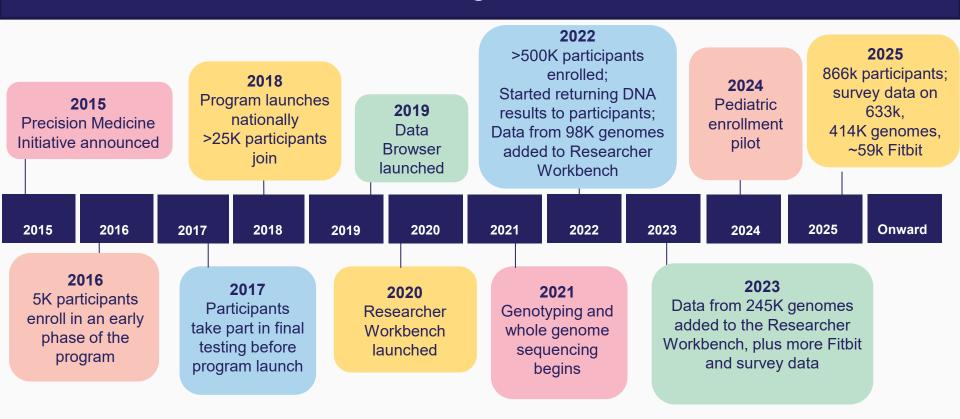






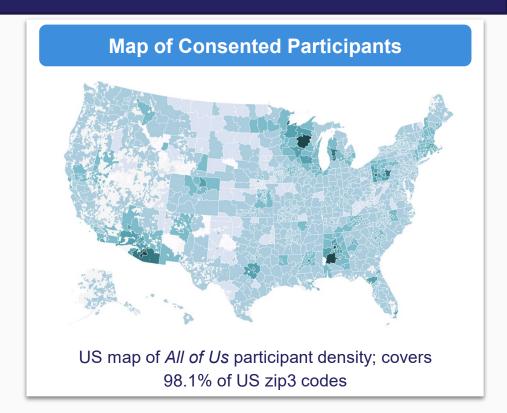


Timeline of the All of Us Research Program



Enrolled 867K+ Participants With Continued Growth

Participant Enrollment 472,000+ 867,000+ Electronic **Participants** Health Records 596,000+ 610,000+ Participants who Biosamples have completed initial steps of the program



The *All of Us* Research Program: Accelerating Health Research and Medical Breakthroughs, Enabling Individualized Prevention, Treatment, and Care for All

What Goes in...



Data from **867,000+** Participants from all 50 states including:

602,000+ Biosamples

467,000+ EHRs

1,958,500+ Survey Responses



Gets Combined & Curated...









Data Refinements



Cloud-based Platform

For harmonization, participant privacy, and quality

Leading to New Research...

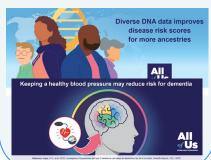
From **16,000+**Registered
Researchers
from **1,120+**

Organizations





750+Publications using *All of Us*Data, such as:



And Valuable Health Information Returned to Participants



700,000+ Individual DNA Results Returned to **228,000+** Participants, including:

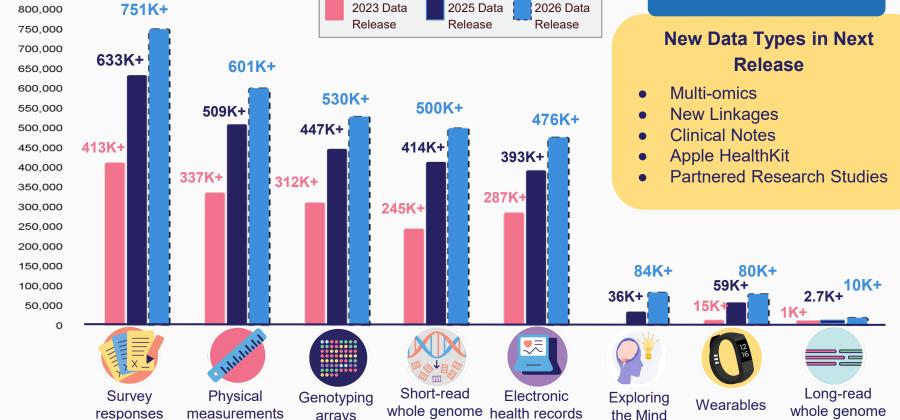
3,900+ (~3%) with variants in the ACMG 59 genes

108,000+ (100%) with PGx variants impacting at least one of 50+ medicines

Major New Data Releases Every 1 to 2 Years



Data Browser







whole genome health records sequences

whole genome sequences

Data Tiered Access Levels Enable Discovery



Available to Anyone



Available to Registered Researchers

PUBLIC TIER

- Data Snapshots: Aggregated overviews of participant characteristics and data types
- Data Browser: Aggregated All of Us data including survey responses, physical measurements, data from electronic health records (EHRs) and wearables, and genomic data
- Research Projects Directory: Descriptions of each research project within the Researcher Workbench

RESEARCHER WORKBENCH

REGISTERED TIER

Registered researchers can access in-depth data and a variety of research tools to conduct a wide range of studies.



Surveys



EHRs



Physical Measurements



Wearables

CONTROLLED TIER

Registered researchers with additional agreements can access the Registered Tier data plus additional and expanded data types.





All of Us Research Hub: Public Data Browser



FAQ

Summary statistics of:

- EHR Data (Conditions, Drug Exposures, Lab & Measurements, Procedures)
- Genomic Variants
- Survey Questions
- Physical Measurements
- Open Access (no login required)

Data Browser

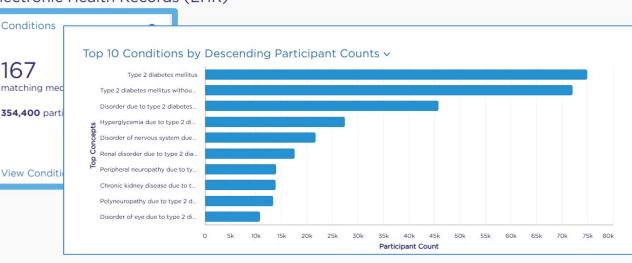


Search Across Data Types



Data includes 633,540 participants as of 10/1/2023.

Electronic Health Records (EHR)

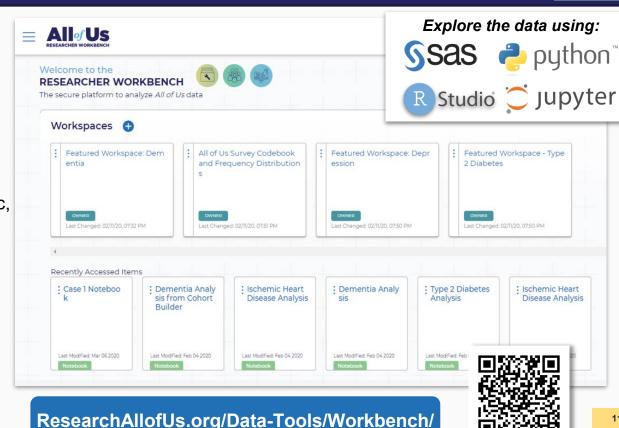


All of Us Researcher Workbench: Access to Row-Level Data for Analysis

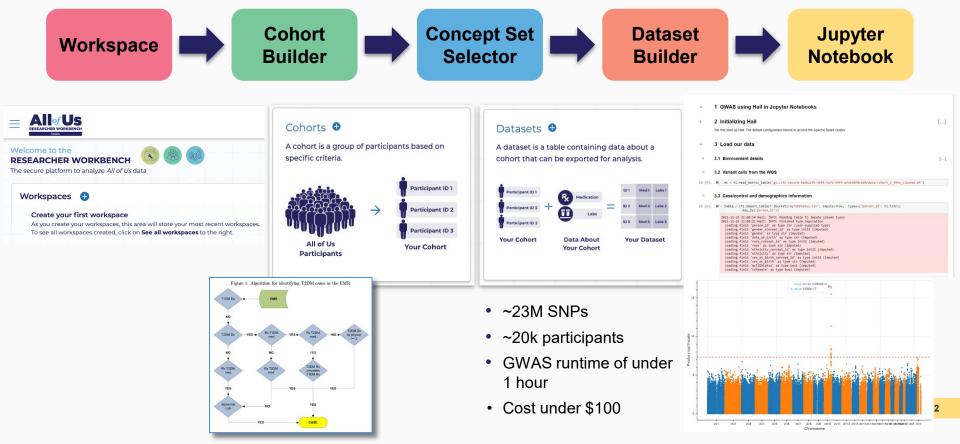


Researcher Workbench

- Cloud-based platform
- Graphical tools for creating cohorts and datasets
- Open to researchers at academic, not-for-profit, and health care institutions
- Passport access model with institutional agreements for all researchers
- No separate IRB approval needed



What Does It Look Like To Do an Analysis in *All of Us*? A Genome Wide Association Study (GWAS) of Type 2 Diabetes





Scientific and Clinical Impact of *All of Us*On Precision Medicine

All of Us Data Leads to Impactful Health Discoveries

New discoveries in rare disease, chronic conditions, ophthalmology, neurology, preventive medicine and more!



Integration of Results from All of Us Data into Clinical Care

09/03/2025

Mass General Brigham Launches Genetic Test Developed in Collaboration with Broad Clinical Labs to Predict Risk Across Eight Cardiovascular Conditions

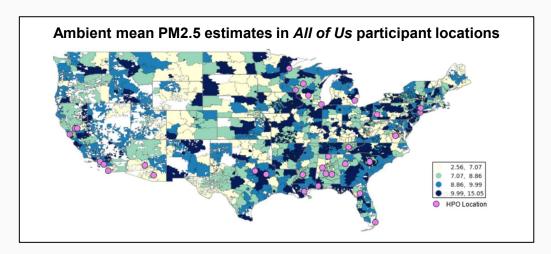
- Developed on genotypic and clinical data from 236,393 All of Us participants
- Integrated publicly available polygenic risk scores for each of eight conditions to develop a single, integrated score for each condition
- Validated in participants from the Mass General Brigham Biobank
- Clinician-ordered test is now available through Broad Clinical Labs/Mass General Brigham

Routine Integration of the Exposome and Genomics is Essential for Achieving Precision Medicine

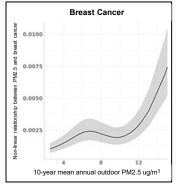
Integrating the genome and exposome for precision health in Kuwait Hamad Ali, Barrak Alahmad, Faisal H. Al-Refaei, Ahmad Abou Tayoun, Hilal A. Lashuel, Salman Al Sabah & Fahd Al-Mulla

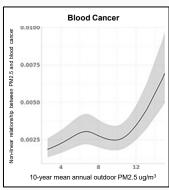
- Environmental conditions of Kuwait (extreme heat, air quality) make it an ideal system to test gene-environment interactions
- The simultaneous collection of exposure data along with genomics and wearables will enable deeper analyses at the outset of any new cohorts
- Strong data governance and privacy principles should be baked into cohort infrastructure

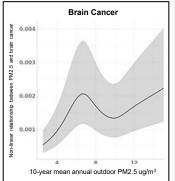
All of Us Discoveries: Air Quality and Cancer Risk

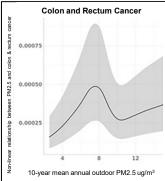


PM2.5 exposure was associated with increased odds for several cancers, including breast, blood, brain, and colon and rectum cancers.

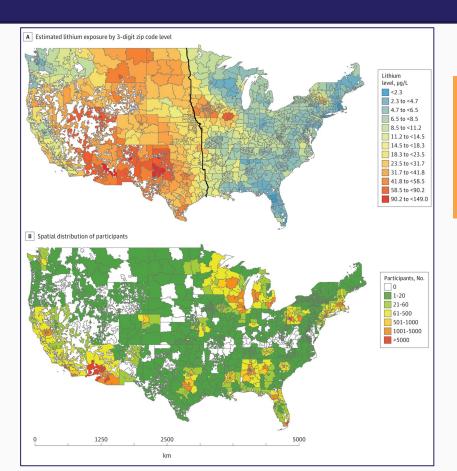








All of Us Discoveries: Lithium Groundwater and Cancer Risk





Original Investigation | Environmental Health

February 20, 2025

Cancer Risk and Estimated Lithium Exposure in Drinking Groundwater in the US

Jiajun Luo, PhD, MPH^{1,2}; Liang Zheng, MD, PhD³; Zhihao Jin, MPH⁴; <u>et al</u>

» Author Affiliations | Article Information

JAMA Netw Open. 2025;8(2):e2460854. doi:10.1001/jamanetworkopen.2024.60854

A study of more than 25,000 *All of Us* participants found that **higher lithium exposure** in drinking water was related to **lower incidence of cancer.**

New Insights into the Impact of Exposomics and Environmental Health

Goal: Assess **environmental exposures** and their interactions with genomic and behavioral health factors (study in collaboration with NIH NIEHS).

This study will perform untargeted metabolomics on >5,600 diverse participant samples to measure environmental exposures.

All samples analyzed by the end of April 2025.

Data on environmental, pharmaceutical, dietary, and endogenous metabolites will be added to existing *All of Us* data in 2026

Raw and annotated data will be available to researchers.



New research on environment, gene, and behavior interactions will drive discovery across health conditions.

Identifying needed resources for researchers.

Initial investigation focuses on participants with Type 2 diabetes (incident since joining *All of Us*) but provides a model for future studies to follow adding more metabolomics data.

Polyexposure Score (PXS)

- Composite score combining exposures across the lifespan
- Captures broad cumulative effects of modifiable factors on health
- Highlights interactions among exposures rather than any single risk
- Prioritizes intervenable exposures; those that can be prevented or treat
- Examples: Occupational hazards, lifestyle risks, stressors



Adding New Data Types to *All of Us*: Partnered Research Studies

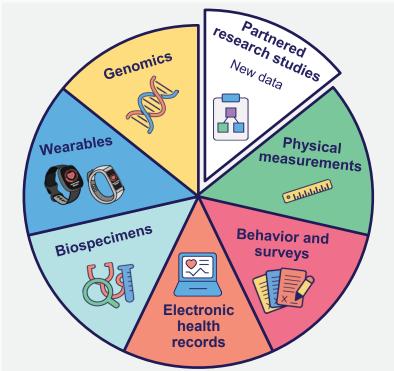
Partnered Research Studies are Important Drivers of Discovery

These partnered research initiatives allow researchers to leverage the program's resources to drive discovery by collecting and adding new data to the *All of Us* dataset.

- Partnered research studies align with the program's core values
- These studies support new data collection or generation and return additional value to participants
- New data will be made available through the Workbench
- Partnered research studies are externally funded

The program is building its capacity to support partnered research studies by partnering first with NIH Institutes, Centers, and Offices. In the future, researchers outside of NIH will be able to propose studies.

allof-us.org/PartneredResearchStudies



Incorporating partnered research study and core data will help researchers address complex questions about how genomic, environmental, and social interactions influence human health.

Current Partnered Research Studies: Enabled by *All of Us* for NIH Institutes & Centers

Platform Enables Fast Access to Research-Ready Participants



World's largest study of precision nutrition!

Exploring how personalized diets can improve health and prevent chronic diseases through the study of diet and physiological responses in at least 8,000 people.

National News Spotlights

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SUNDAY
MORNING





Watch the Vide



Eyes On Health

Eyes are the window to the body, and we will capture ocular images from 5,000 *All of Us* participants to enhance research on cardiovascular, neurological, and behavioral health.

Data Collected and Released

Color Fundus Photo



Optical Coherence Tomography



Optical Coherence Tomography
Angiography





Studying influences of environmental exposures on Type 2 Diabetes

Investigating how genetics and environmental factors influence type 2 diabetes in 5,600 *All of Us* participants, one of the most costly and prevalent chronic health conditions in the country.



Understanding connections between health factors and behavior

Exploring the mind of 36,000 *All of Us* participants through four game-like cognitive tasks, supporting researchers in making connections between cognitive function, health factors and behavior.



Working Together

Working Together to Accelerate Research and Global Health Impact



Opportunities for Global Exposome and Human Health Research

- Align to **shared standards** and **data models** (phenotypes, exposures, exposome)
- Set up a federated node or trusted research environment for cross cohort analysis
- Define **priority themes** e.g, heat, air quality, occupational exposures
- Share methods and tools
- Build talent and capacity
- Convene the community

Opportunities for International Collaboration



Closing the Data Gap in Global Genomics, Medicine & Population Health (D2)

April 27-30, 2026 | Herrenhausen Palace, Hannover, Germany Geoffrey S. Ginsburg, Michèle Ramsay, Lyndon Mitnaul and Naomi Allen

Scholarship Deadline: Jan. 6, 2026 | Short Talk Abstract Deadline: Jan. 6, 2026 | Poster Abstract Deadline: Apr. 6, 2026 | Early Registration Deadline: Feb. 26, 2026

Join the Researcher Workbench

Strengthen US-European scientific relationships:

- Data harmonization & common data models
- Standards development
- Joint research projects



230+ International
Data Access
Agreements Signed

Leverage All of Us Data to Advance Bold, Innovative Research:

Discovery and Validation Opportunities

https://bit.ly/43EjQa5

Sample Language:

About the All of Us Research Program

The All of Us Research Program is a historic effort to gather data and biospecimens from at least 1 million people living in the United States, with the goal of accelerating research and medical breakthroughs and enabling individualized prevention, treatment, and care.



SanD









AllofUs.NIH.gov









@AllofUsResearch #JoinAllofUs









Thank you to our 870,000+ participants!