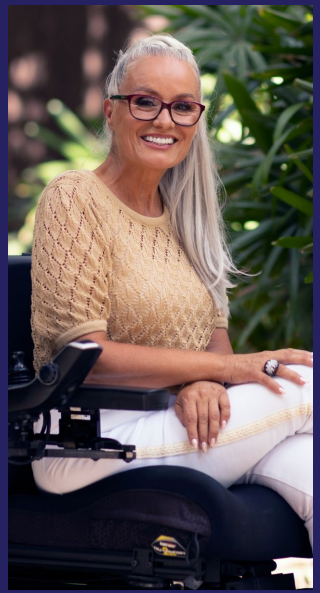
All of Us Research Program: Key Updates Including New Data Release

September 12, 2024

Josh Denny, M.D., M.S.
Chief Executive Officer

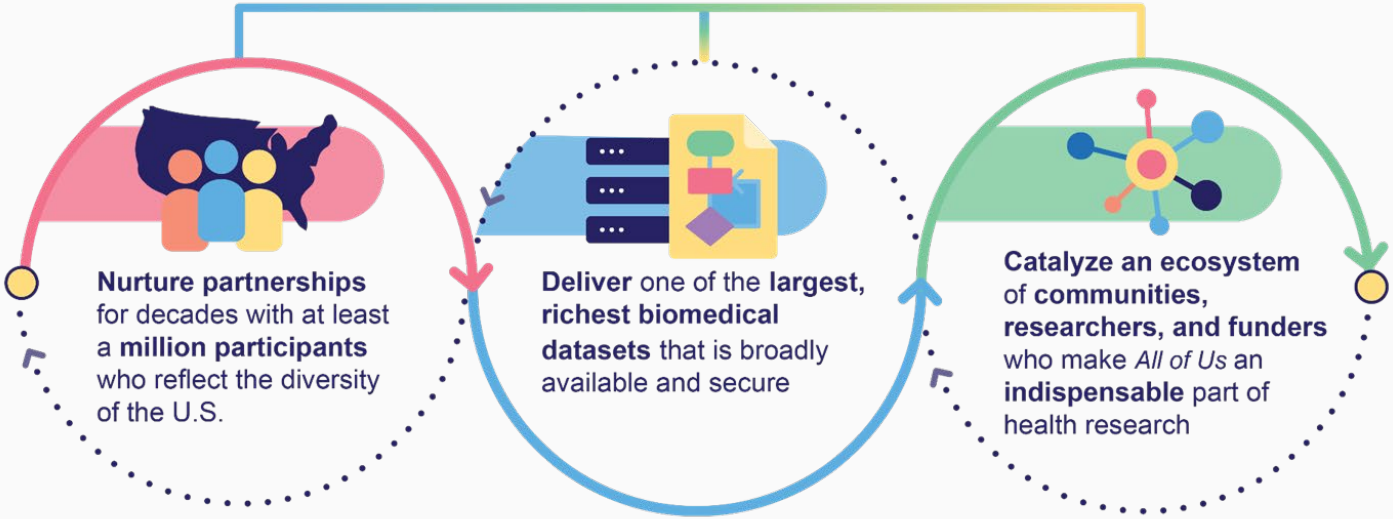
@AllofUsCEO






The *All of Us* Research Program Mission

Accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us



Made possible by a team that maintains a culture built around the program's core values

Timeline of the *All of Us* Research Program

2015
PMI announced in State of the Union address

2016
5,000 participants enrolled in pilot study (content testing)

2017
First participant enrolled

2018
National launch; 27,800+ core participants

2019
Public Data Browser launched

2020
Researcher Workbench launched; COVID Serology Study

2021
Start of genotyping and whole genome sequencing

2022
98k genomes available for researchers; start of returning health-related DNA results; 500k+ participants enrolled

2023
NPH Launches; ~245k genomes released, Fitbit, and survey data

2024
Initial test of pediatric cohort; 364k+ DNA results returned
830k+ participants
12k+ researchers

2015 | 2016 | 2017 | 2018 | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 Onward

Status of *All of Us* Participants

Participant Enrollment

832,000+
Participants

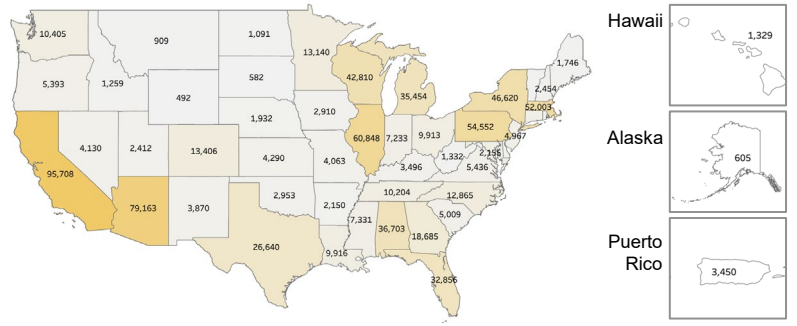
452,000+
Electronic Health Records

566,000+
Participants who have completed initial steps of the program

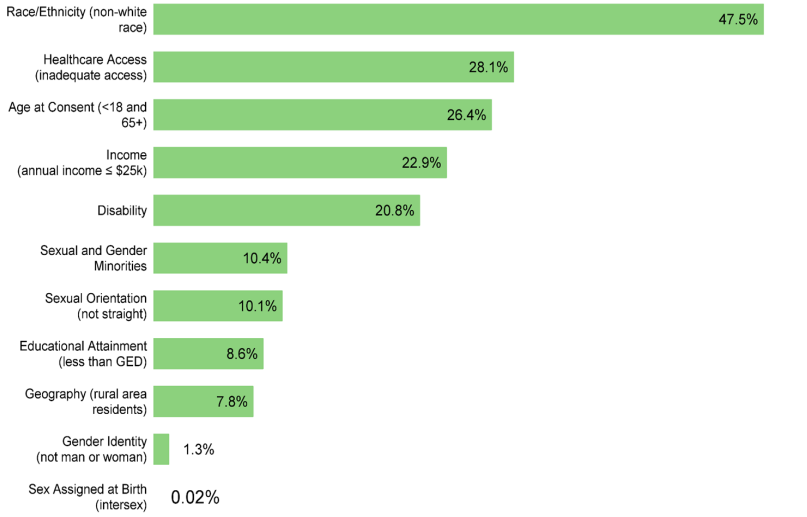
586,000+
Biosamples

Numbers as of August 24, 2024

Map of Participants



UBR Category



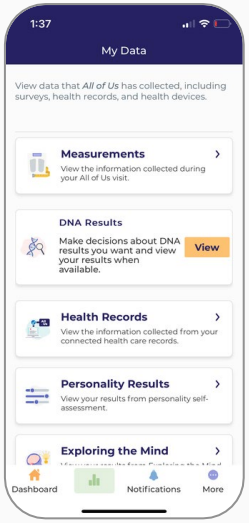
Data Collected and Return of Value to *All of Us* Participants

- Consent and Electronic Health Records
- Participant Surveys
- Physical Measurements
- Biosamples
- Mobile/Wearable Tech

Return of Value for Participants

Participants may receive:

- ***Genetic information***
- Survey data (comparative)
- EHR and claims data
- Ongoing study updates
- Aggregate results
- Scientific findings
- Opportunities to be contacted for other research opportunities



Delivering Clinically Impactful Individual Health Results

Hereditary Disease Risk

124k *All of Us* participants have viewed this report, which looks for genetic variants in 59 genes associated with serious health conditions, including:

- Breast cancer
- Ovarian cancer
- Uterine cancer
- Colorectal cancer
- Prostate cancer
- Melanoma
- Brain cancer
- Pancreatic cancer
- Stomach cancer
- Familial hypercholesterolemia
- Cardiomyopathies
- Arrhythmias
- Arteriopathies
- Neurofibromatosis type 2

~3% (>3,300 to date) of participants who receive their hereditary disease risk report will have **a potentially life-changing genetic variant.**

Medicine and Your DNA

117k *All of Us* participants have viewed this report, which analyzes seven genes that can affect how bodies process medicine and impacts which medication or what dosage you take. This report includes 50+ different medicines that may be impacted by your genetics, including:

- Citalopram (Celexa®)
- Clopidogrel (Plavix®)
- Escitalopram (Lexapro®)
- Sertraline (Zoloft®)
- Lidocaine
- Glimepiride (Amaryl®)
- Sulfamethoxazole/ trimethoprim (Bactrim®)
- Simvastatin (Zocor®)
- Amitriptyline (Elavil®)

~90% (>106,000) of participants who received this report have **a result that could impact how their body processes a medication within this report.**

Retrospective research using *All of Us* data suggests that ~20% of participants will be exposed to a drug with an actionable pharmacogenetic result.

Numbers as of August 2024

Data Tiered Access Levels Enable Discovery

Available to Anyone

PUBLIC TIER

Public resources include:

- **Data Snapshots**: Aggregated, public-facing overviews of participant characteristics and data types
- **Data Browser**: Interactive preview into the *All of Us* dataset through public-facing aggregate data
  - Currently includes participant-provided survey responses, physical measurements, data from EHRs and wearables, and genomic data
- **Survey Explorer**: Details the questions included in each of the surveys
- **Research Projects Directory**: Descriptions of each research project within the Researcher Workbench

Available to Registered Researchers

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


Electronic Health Records


Physical Measurements

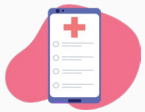

Wearables

Data have been processed to protect participant privacy

CONTROLLED TIER

Registered researchers with amended institutional agreements can access all of the data in the Registered Tier plus additional and expanded data types, including genomic data, real dates of health events, ICD codes, granular demographic data, and more.

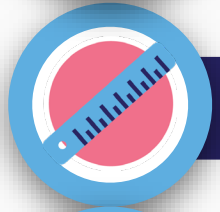

Genomics


Health and Lifestyle surveys

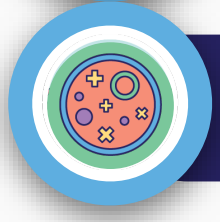
Data Currently in the *All of Us* Researcher Workbench

Participant Surveys
1,958,520+ Surveys Completed

Electronic Health Records
287,000+ EHRs



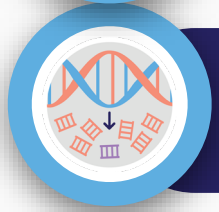
Physical Measurements
337,500+ Physical Measures



Biospecimens
14,000,000+ Aliquots (DNA, RNA, serum, plasma, cfDNA, RNA, urine)

Mobile/Wearable Tech
15,600+ Fitbit Records

Assays
1,500,000+ Structural Variants



Omics
312,900+ Genotyping Arrays
245,350+ Whole Genome Sequences
1,000+ Long-Read Sequences

The *All of Us* Researcher Workbench contains the one of the **largest sets of whole genome sequences widely available for research.**

The whole genome sequence dataset includes variation at more than **1 billion** locations, which is nearly **one-third** of the entire human genome

All of Us Research Program's Commitment to Researcher Diversity

(as of August 26, 2024)

12,475+ Registered Researchers

865+ Organizations 44 HBCUs and 73 HSIs

610+ Publications using *All of Us* data

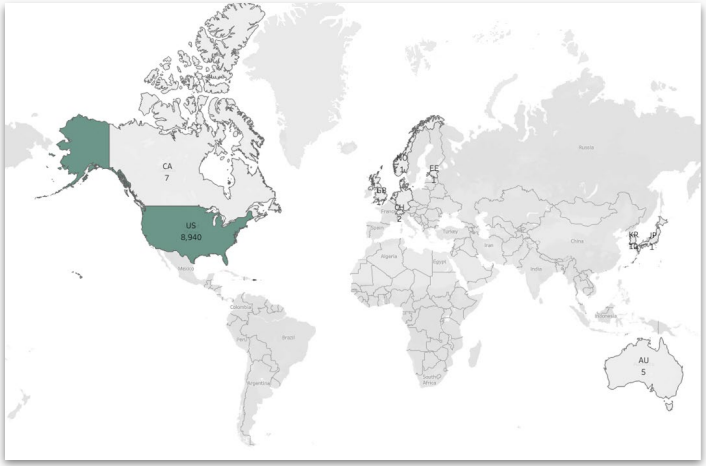
135+ International Institutions

12,390+ Workspaces Created

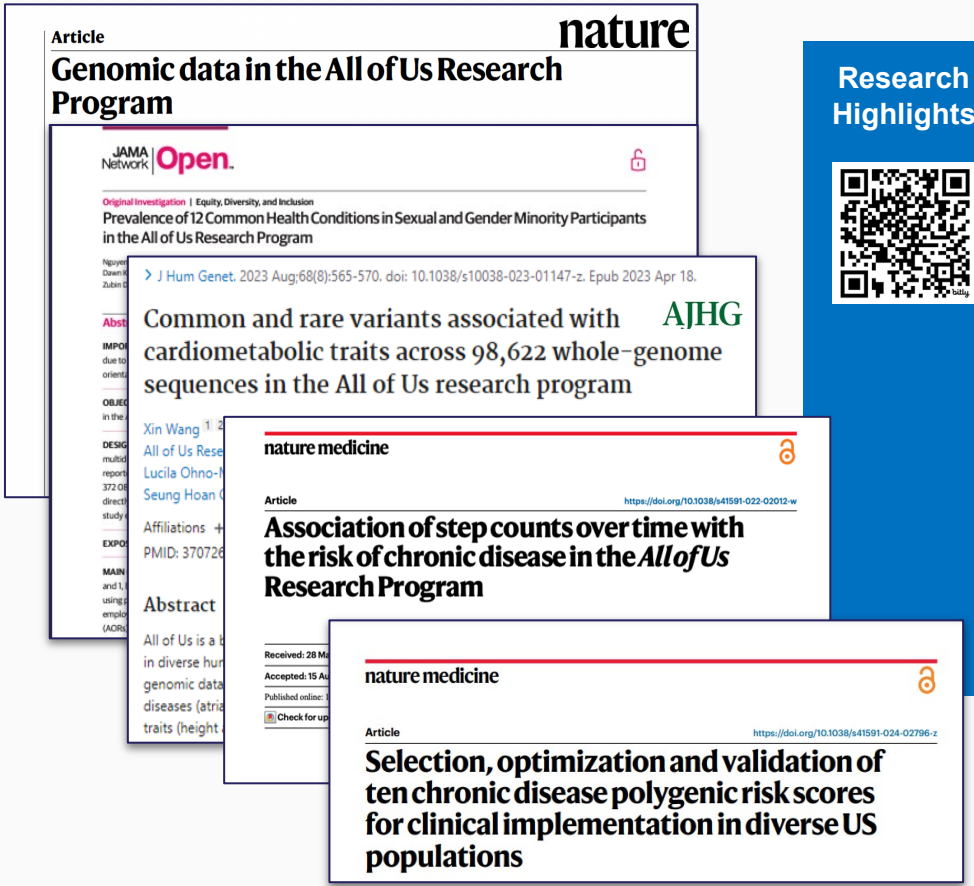
Baylor's UBR Faculty Summit

Over 78% of our researchers are underrepresented in the biomedical workforce, including more than 34% who are underrepresented by race and ethnicity (non-White and non-Asian researchers).

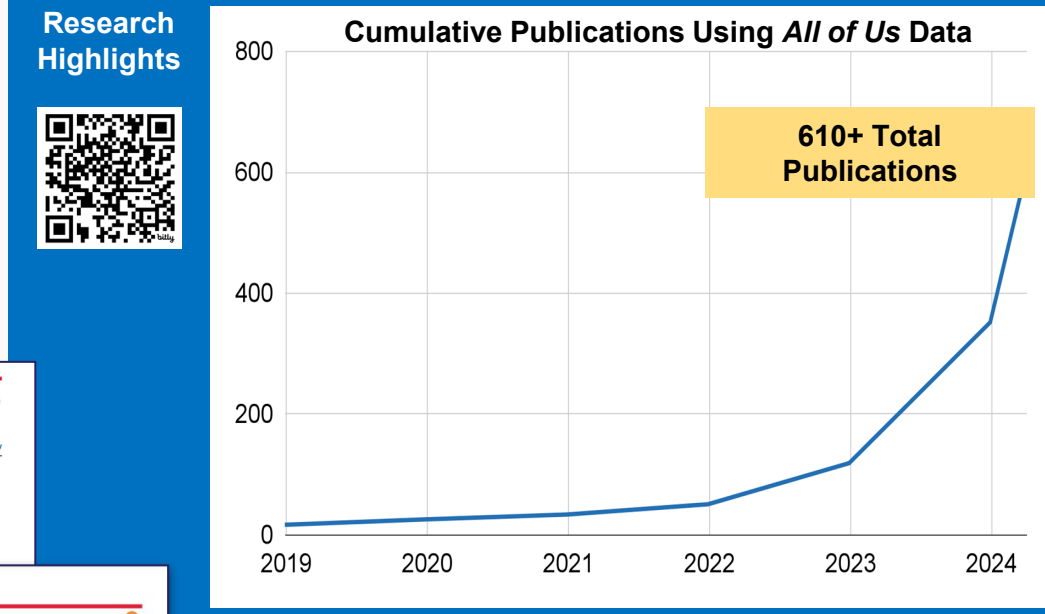
***All of Us* is open to national and international researchers at academic, not-for-profit, commercial, and health care institutions.**



The Exponential Growth of *All of Us*-Enabled Discoveries



Research Highlights



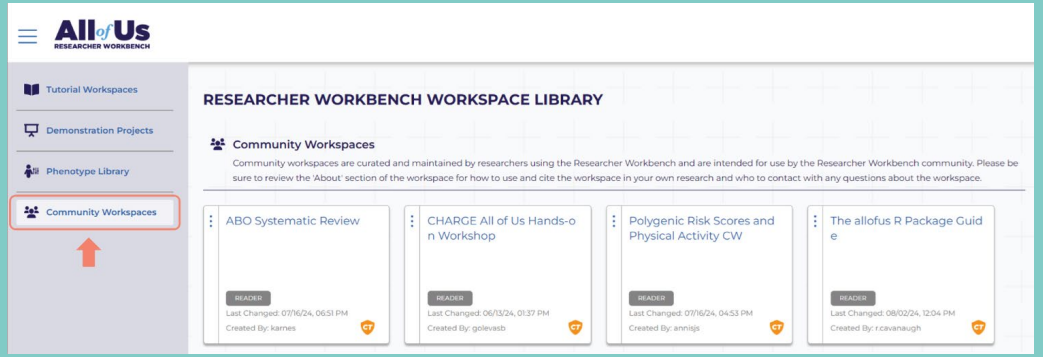
Researcher Workbench Supports Powerful Analyses and Collaboration

New tools added this year

RStudio®

SAS

Community workspaces for sharing analyses



Visit https://allof-us.org/3YMkIbC or scan the QR code to learn more

"All by All" Analyses Uncovering ~500 Billion Gene-Phenotype Associations
Results in Workbench; Public Website Coming in November

Phenotypes with number of participants > 200 per group

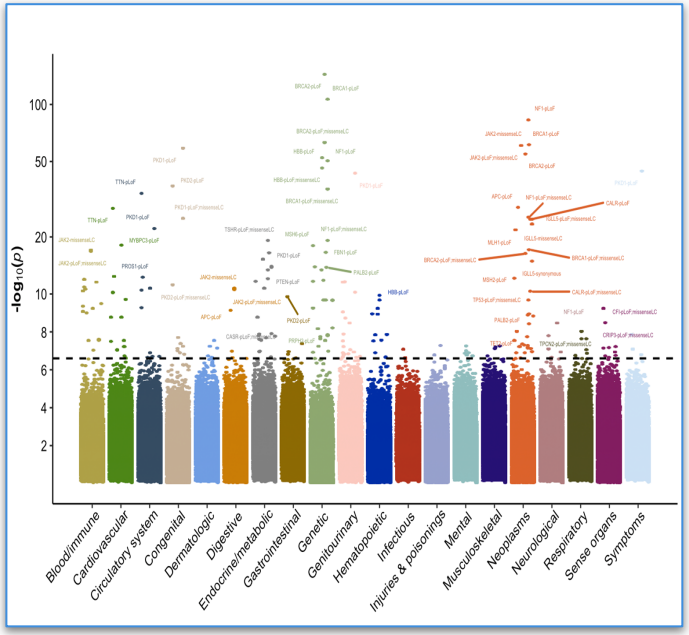
All by All: Common and rare variant association testing in 250,000 whole genomes across diverse ancestry groups

Genetic ancestry group	Num. individuals	Num. variants
AFR	56,913	383,702,267
AMR	45,035	334,390,971
EAS	5,706	122,729,124
EUR	133,581	628,935,579
MID	942	41,842,694
SAS	3,217	83,584,317
Total	245,394	1,116,593,592

Category	AFR	AMR	EAS	EUR	MID	SAS
Lab measurements	12	12	12	12	12	12
Random phenotypes	30	30	30	30	30	30
mcc2 phecode	573	477	45	1000	1	20
mcc2 phecodeX	869	776	80	1361	0	42
r drug	758	715	357	857	42	288
pfhh survey	20	17	0	78	0	0
physical measurements	10	10	10	10	10	10
Total: 8,688	2,272	2,037	534	3,348	95	402

2 versions of phecode
- Linked to EHRs

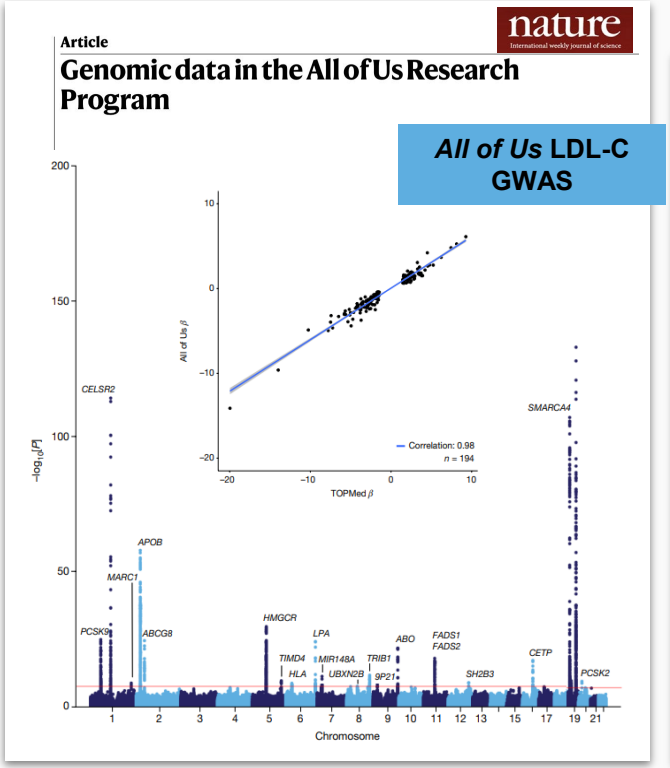
Lab values including: Cholesterol, Triglycerides Glucose, Hemoglobin



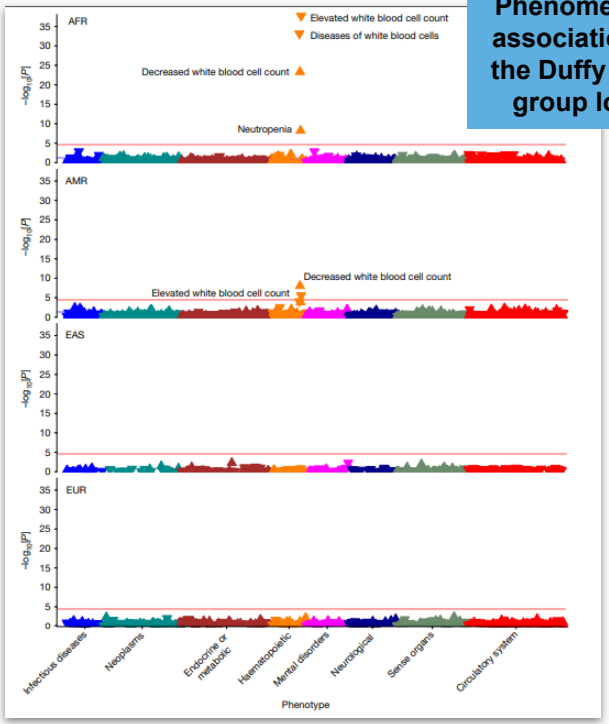
Associations across > 5K phecodes

Courtesy Konrad Karczewski, Broad Institute

Using a Diverse Dataset to Discover Novel Genomic Variants



***All of Us* LDL-C GWAS**



Phenome-wide associations of the Duffy blood group locus

>1 billion genetic variants
>275 million previously unreported genetic variants

Tested for replications of 3,724 genetic variants associated with 117 diseases:

AFR	AMR	EAS	EUR	SAS
18/25 replicated	13/13 replicated	7/15 replicated	1,064/1,421 replicated	1/1 replicated
72%	100%	46.6%	74.9%	100%

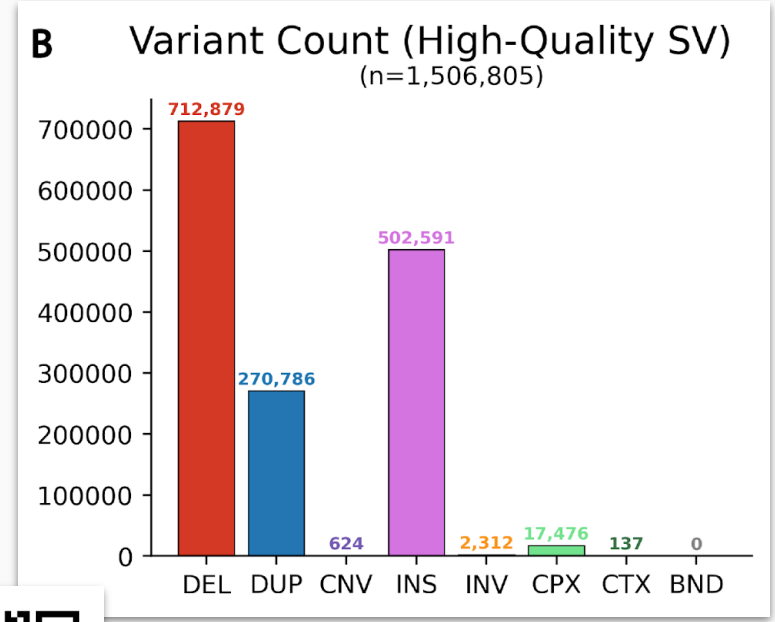
Kozlov, et al. (2024) *Nature*

Pioneering Genomic Research: Over 1.5 Million Structural Variants Ready for Discovery

All of Us greatly expanded the structural variant (SV) data available in the Researcher Workbench's Controlled Tier this summer.

Now, there are **more than 1.5 million SVs from nearly 98,000 participants with linked phenotype information**. This makes *All of Us* one of the largest and most widely available catalogs of SV data.

This release represents a huge step toward our goal of expanding the breadth and depth of genomic data: https://allof-us.org/SVData.



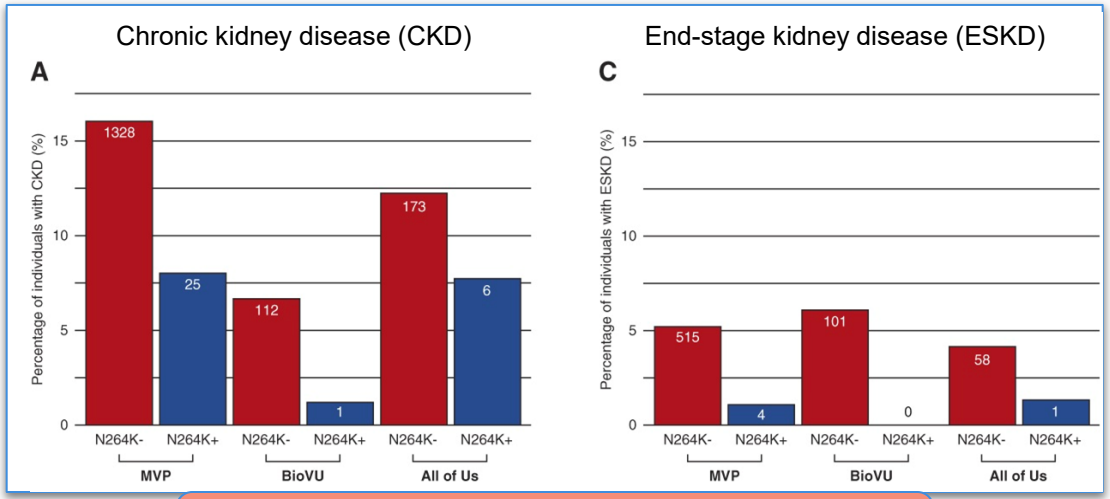
Using Large, Diverse Datasets to Understand Disease Risk of *APOL1* Variants

Variants in the *APOL1* gene are associated with end stage kidney disease (ESKD) in people of African ancestry

70% of excess ESKD risk in African Americans is thought to be related to *APOL1*

Significance:

- *All of Us* data from v5 with 98k WGS (v7 has 245k WGS — almost 2.5x increase!)
- Potential drug target for treating *APOL1* ESKD



***APOL1* p.N264K is associated with a lower risk of CKD and ESKD**

Read the Research Highlight

Hung *et al.* (2023). *Journal of the American Society of Nephrology : JASN*

All of Us Ancillary Studies

Increasing complexity

Nutrition for Precision Health

Exploring the Mind

COVID Serology Study

Embedded studies

Recontact of participants for custom surveys, wearables, etc

Biospecimen use to generate new data

Core *All of Us* participant data
Broad Data use through the Researcher Workbench

Ancillary studies:

1. **Address important scientific questions** and deliver insights into health and disease.
2. **Expand the *All of Us* dataset** by adding new data and/or engaging unique participant communities.
3. **Enable research across boundaries** with novel analyses of lifestyle, environmental, and biologic data.

23 NIH Institutes, Centers and Offices are involved in 9 completed, ongoing, and proposed ancillary studies.

Largest Precision Nutrition Research Effort of its Kind

Nutrition for Precision Health

Module 1: The Usual Diet Study

Examine baseline diet and physiological responses to meal challenges

Module 2: The Provided Diet Study

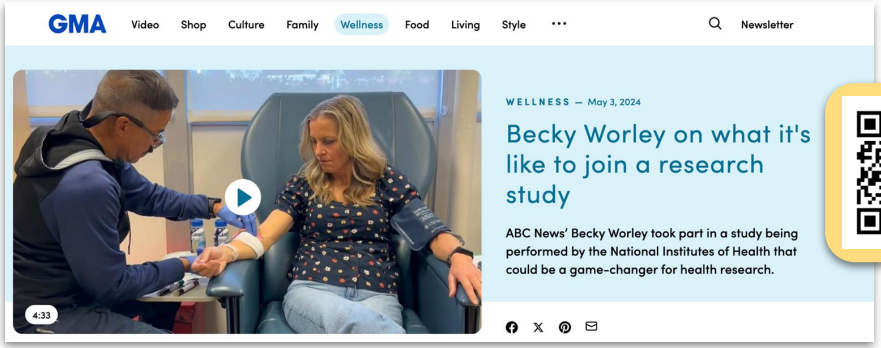
Examine responses to 3 short-term intervention diets in free-living controlled feeding studies

Module 3: The Live-in Diet Study

Examine responses to 3 short-term intervention diets in domiciled controlled feeding studies

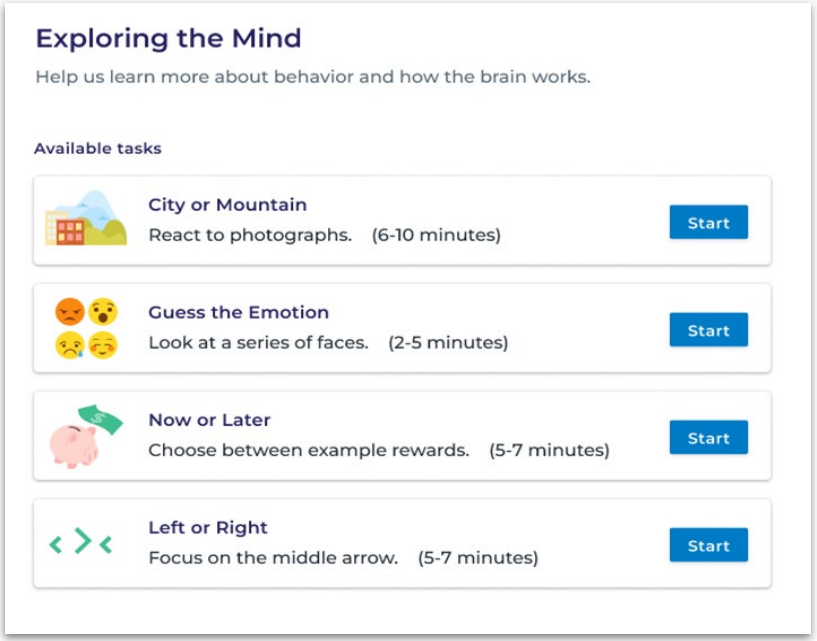
Researching how nutrition can be tailored to each person's **genes**, **culture**, and **environment** to **improve health**

Involving at least **8,000 *All of Us* participants**



Watch the Video

All of Us x NIMH: Cognitive Leaps with 10x More Data from 50K Minds in 6 Months



All of Us collected 10x more task completions in ~6 months than the Many Brains project collected in >10 years.

Over 73,000 participants have completed tasks and their responses overlap with other biomedical data types in *All of Us*:

- 94% have provided physical measurements
- 93% donated biospecimens
- 89% completed both mental health and well-being surveys
- 60% have EHR data

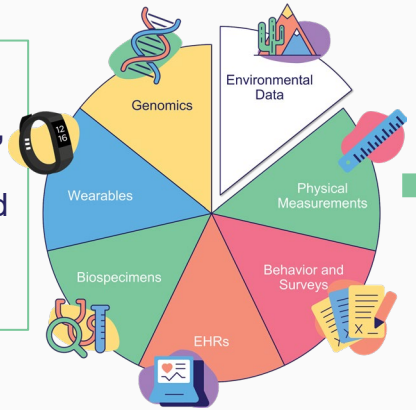
Exposome Ancillary Study on Environmental Health Launched in July

National Institute of Environmental Health Sciences (NIEHS) and *All of Us* launched a new ancillary study to assess **environmental exposures** and their interactions with genomic and behavioral health factors. Initial investigation is for participants with Type 2 diabetes (incident since joining *All of Us*). These data will become available to all approved *All of Us* researchers.

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

Samples selected for multi-omics overlap, including 86% UBR and 62% UBR R/E

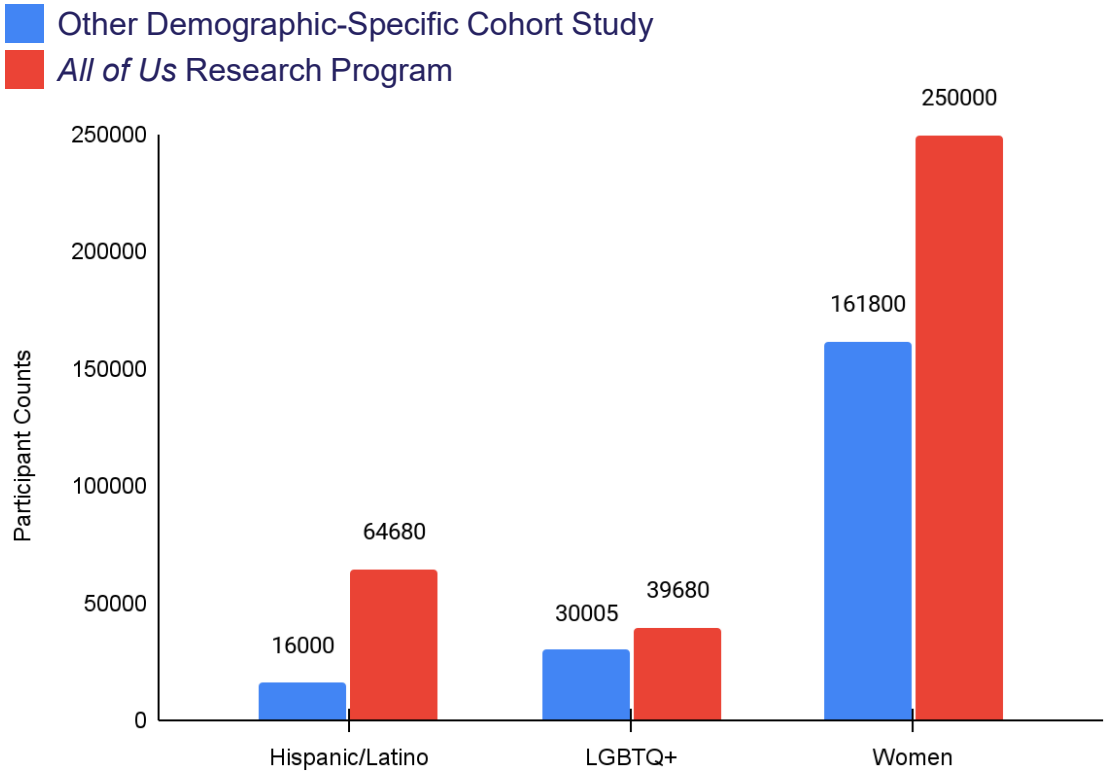
Data on **environmental, pharmaceutical, dietary, and endogenous metabolites** will be added to existing *All of Us* data in 2026.



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

By leveraging *All of Us* as a platform for this research, NIEHS was able to begin data collection <1 year after submitting their initial proposal and reduced the cost of this study by ~75%.

Inclusion in *All of Us* Compared to Other Community-Specific Cohorts



All of Us has unprecedented representation compared to other major studies including:

- Hispanic Community Health Study/Study of Latinos
- PRIDEnet
- Women's Health Initiative
- RURAL Cohort Study

Milestones of *All of Us* Consultation & Tribal Engagement

2017

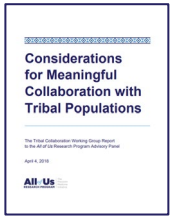
Dec 2017

All of Us Research Program Advisory Panel establishes **Tribal Collaboration Working Group (TCWG)**

2018

Aug 2018

TCWG releases "Considerations for Meaningful Collaboration with Tribal Populations" report


Considerations for Meaningful Collaboration with Tribal Populations

The Tribal Collaboration Working Group Report to the All of Us Research Program Advisory Panel

April 4, 2018

All of Us

2019

2019

All of Us hosts listening sessions and Tribal Consultation meetings across the country

2020

May 2020

Rapid-response Tribal Consultation convened to discuss the COVID-19 serology study

2021

March 2021

All of Us releases Tribal Consultation Final Report


All of Us Research Program Tribal Consultation Final Report

March 2021

All of Us Commitments to Tribal Nations

In This Report

2022

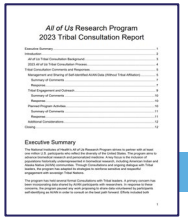
May 2022

Research Opportunity Announcement released by *All of Us* with an area of interest specific to engaging with Tribal Nations and Urban AI/AN Populations

2023

2023

Tribal Engagement partners awarded; *All of Us* releases consultation report on integrating AI/AN data into the program's data


All of Us Research Program 2023 Tribal Consultation Report

Executive Summary

Intentional and Thoughtful Outreach Driven by Foundational Commitments

Visit https://allof-us.org/TribalEngagement or scan the QR code to learn more

- We will **respect Tribal sovereignty** by engaging Tribal Nations to ensure that research using the program's biospecimens and data from Tribal members is done in a way that is respectful and transparent.
- **We will not recruit on Tribal lands** or **share information about participants' Tribal affiliation** without first getting approval from the Tribe.
- We will **support the development of educational materials** for researchers and participants, work with AI/AN researchers in partnership with AI/AN communities, and promote community-based participatory research.
- We will work to **ensure representation of AI/AN populations** throughout all aspects of program governance.

Indigenous-led Demonstration Projects for In-Depth First Look at AI/AN Data

All of Us awarded the American Indian Science and Engineering Society (AISES) to create and promote the "We Are All Scientists" campaign, focused on Indigenous workforce diversity.

Phenotypic/Survey Project

Purpose: To analyze and compare non-genomic data in comparison to the NHLBI Strong Heart Study

Genotypic Project

Purpose: To compare data to reference populations and associations with elevated disease risk and prevalence factors

Goal: To publish these findings, along with a marker paper describing the program's Tribal engagement and outreach efforts to date

Future Communications About AI/AN Data Update

To date, data from self-identified AI/AN participants has not been included in the data available to registered researchers or in the Public Data Browser.

Through the years, we have conducted an extensive series of Tribal consultations and engagement activities to work towards the inclusion of data from self-identified AI/AN participants in the *All of Us* Researcher Workbench.

When this time comes, communications about this data update will be shared through a comprehensive notification plan including:

- Advance notifications to NIH and HHS Tribal advisory groups and collaborators
- Message to AI/AN participants
- Updates to *All of Us* websites
- Information for investigators, including *All of Us*' new policy "Respectful Research Involving American Indian and Alaska Native Populations" and a research guide coming soon

Coming Soon: Incredible New Data on the Researcher Workbench

Total participants will increase from **413k to 633k (+53%)**

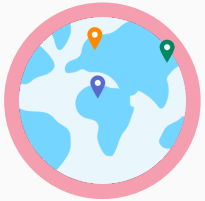
429,000+
With genotyping arrays
(+37%)

400,000+
With whole genome sequences (WGS)
(+63%)

2,700+
Long-Read Sequences
(+170%)

633,000+
With survey responses
(+53%)

59,000+
With Fitbit records
(+278%) 6.3 TB!



633,000+
Racial and Ethnic Subcategories
(+53%)

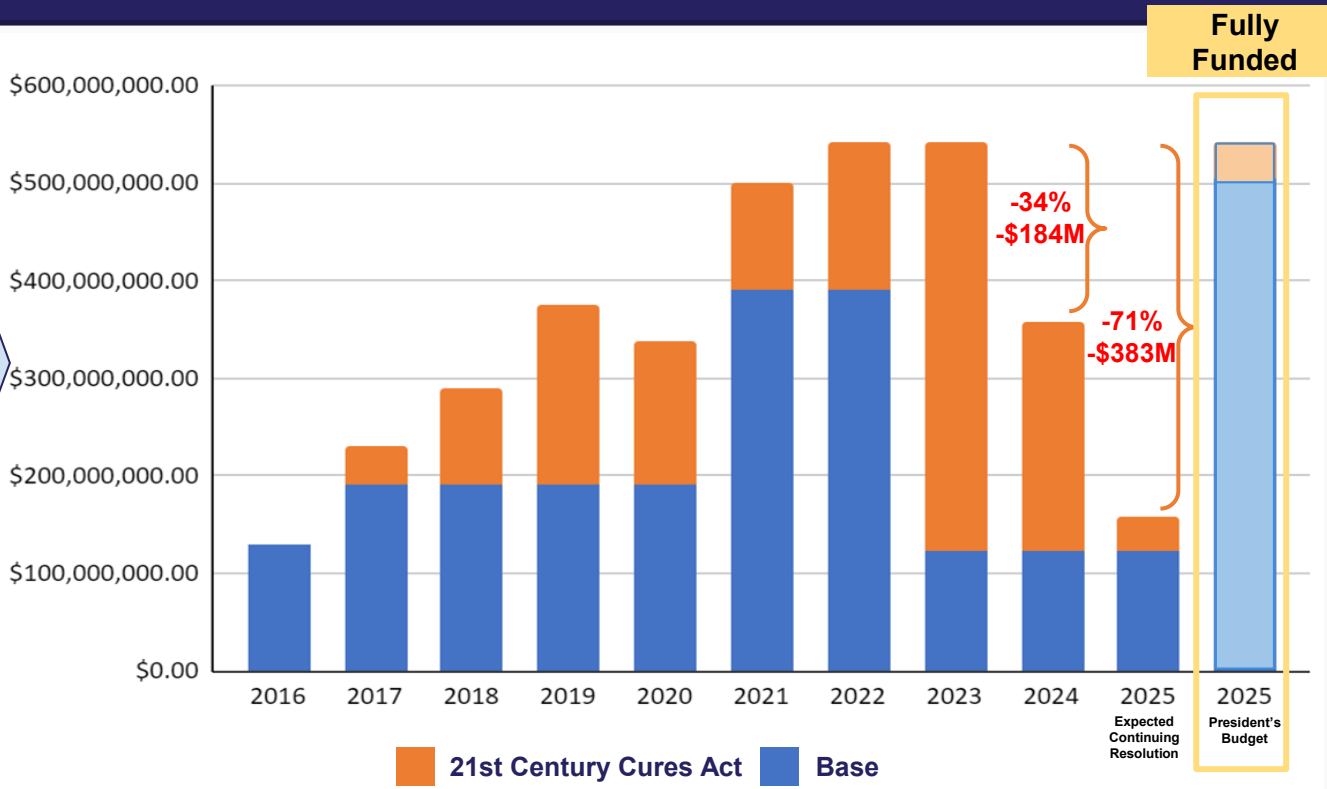
Self-Identified AI/AN Participant Data

Budget Background and FY25 Budget Requirements

FY25 President's Budget Request: $541M

Senate FY25 Labor-HHS bill **restored funding** for the program to the FY23 enacted level of $541M.

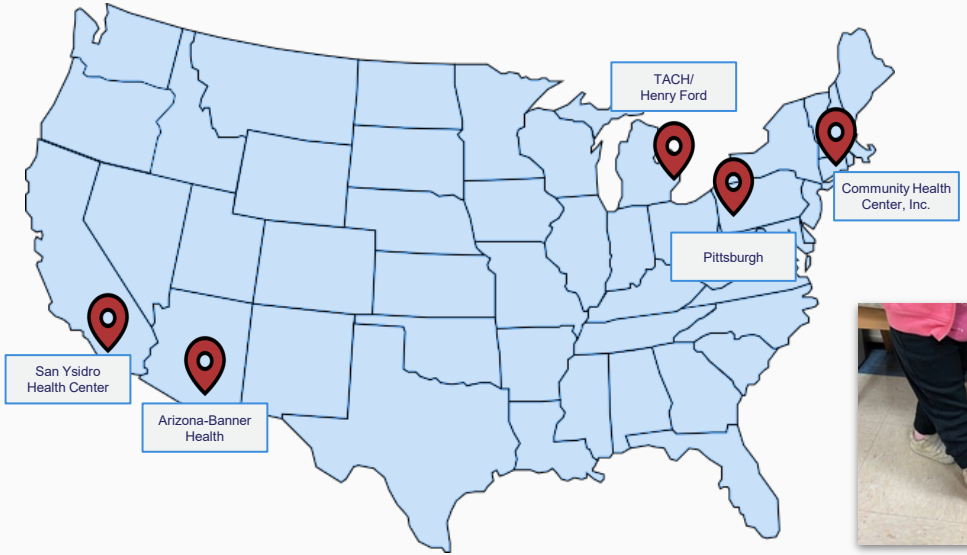
If the base allocation stays flat, when the Cures Act funding drops, **the program's budget will be cut an additional 56%.**



*During the Aug. 1st FY25 L-HHS markup, Subcommittee Chair Tammy Baldwin (D-WI) and Ranking Member Shelley Moore Capito (R-WV) strongly supported advancing precision medicine by restoring full funding to *All of Us*.

Pediatrics: Limited Launch Now; Ready to Expand when Funding Permits

Now Enrolling Ages 0-4 at Five Clinical Sites



"Data from children and parents will allow researchers to elucidate the biological, social, and environmental influences that impact our health over time."

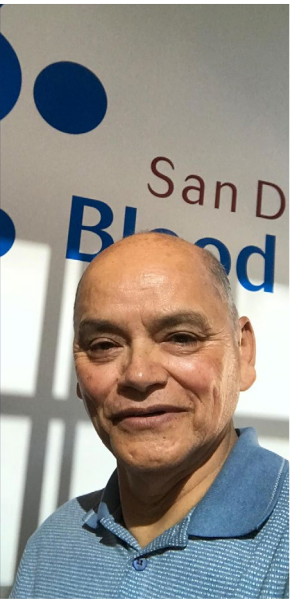
Read the Press Release

All of Us

AllofUs.NIH.gov

JoinAllofUs.org

ResearchAllofUs.org



Thank you!

@AllofUsResearch
@AllofUsCEO
#JoinAllofUs

Thank you to our 832,000+ participants!