Delivering on Our Promise: DNA Results for *All of Us* Participants and What It Means for Healthcare Providers





February 15, 2023

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All of Us Research Program



National Institutes of Health



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.

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

Large Cohort Studies Have Transformed Disease Treatment

Framingham and other cohorts have taught us much about heart disease...

...and cardiovascular deaths have decreased



Precision Medicine is Expanding, but Genomic Studies Are Not Diverse

There is a lack of diversity in genome-wide association studies.





... and many other impacts

Dissecting Individualized Health is Bigger than Genomics, Surveys, and EHRs



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

All of Us Research Program Core Values

Participation is **open** to all.

Participants reflect the rich **diversity** of the U.S.

Participants are partners.

Participants have **access** to their information.

Data will be accessed **broadly** for research purposes.

Security and privacy will be of highest importance.

Trust will be earned through transparency.

The program will be a catalyst for **positive change** in research.

All of Us Consortium Members (as of August 2022)



All of Us Community and Provider Partner Network (as of August 2022)



Enrolled 596K+ Participants With Continued Growth



Numbers current as of February 10, 2023

Participant Diversity





Over 80% of *All of Us* participants are underrepresented in biomedical research

Numbers current as of February 10, 2023

Data Collected from All of Us Participants





2:35 🗢 🔳 Search Connect Provider Your electronic health records are an important source of > information. They could help researchers make new discoveries. Connect to your provider or health plan (ex: Medicare) with the All of Us Research Program. **Frequently Asked Questions** PROVIDERS / HEALTH PLANS / DEVICES 2> Johns Hopkins Medicine Vanderbilt Lab Results 23 > GLUCOSE 93 211 🛙 07/19/22 07/19/22 HEMOGLOBIN 16.1 8 07/19/22 07/19/22 6 Medications Famotidine 10 MG Oral Tablet 5 > Cyclobenzaprine hydrochloride 5 MG Oral Tablet Glucosamine Sulfate 6 Allergies 1> Conditions Other affections of shoulder region, not elsewhere c... 7> ÷ My Data Settings

Returning Value for Participants

research opportunities

Engagement is key: we leverage engagement studios, surveys, and involvement of participants throughout all levels of *All of Us* leadership.

Participants may receive: Genetic information Survey data (comparative) • EHR and claims data Ongoing study updates Aggregate results Scientific findings ٠ Opportunities to be contacted for other



All of Us Genetics Return Strategy

Engagement



Genetic ancestry and traits

Hereditary Disease Risk Report



7 regions (21 subregions) and 4 traits

- Sub-Saharan Africa
- Europe
- Oceania
- Southern Asia

- Eastern and northern Asia
- The Middle East and North Africa
- The Americas

- Ear wax
- Bitter taste perception
- Cilantro preference
- Lactose intolerance

59 genes (SNVs + indels)

- Breast cancer
- Ovarian cancer
- Uterine cancer
- Colorectal cancer
- Prostate cancer

- Melanoma
- Brain cancer
- Pancreatic cancer
- Stomach cancer

- Familial Hypercholesterolemia
- Cardiomyopathies
- Arrhythmias
- Arteriopathies

Medicine and your DNA Report



7 genes

- CYP2C19
- DPYD • G6PD

- SLCO1B1
- NUDT15

- TPMT
- UGT1A1

Health information

Genetic Ancestry and Traits (as of February 10, 2023)

DNA Results ٠ You'll see all of your DNA results here when they're ready. See options for your DNA results Genetic ancestry and trait results 5 results Genetic ancestry View Results Genetic ancestry can be very interesting, but you may also learn information you didn't expect. learn more Bitter taste perception Learn what your genes can tell Cilantro preference Your genes play a role in wheth Earwax type Flaky or sticky? Earwax type is Lactose intolerance our genes have a say in how v

- **Over 182,000 participants sent notifications so far** (email, push, and SMS based on participant preference) to choose if they want to receive results
- The Americas 50% ~ The Americas 100% Such as North, Central, and South America The Middle East and 50% ~ North Africa Northern Africa 10% Such as Morocco, Algeria, and Egypt The Middle East 40% Such as the Arabian Peninsula and Egypt Western Asia and the Caucasus 50% Such as Turkey, Iran, Syria, Irag, and the Caucasus See Other Ancestry Groups Tested
- 72% complete genetic ancestry and traits informing loop choice (130k)
- 99% of those that view any result view any of the 4 trait results (129k)
- 98% of those that view any result viewed their genetic ancestry results (128k)

Genomic Health-Related Return of Results Now Available

Medicine and Your DNA

(Pharmacogenomics)

Hereditary Disease Risk (starting with ACMG59)

RESEARCH REGORAM	JANE DOE Specim DOB: January 1, 2000 Barcoc ID: 2 Collect Report r will need to confirm this result with a clinical test I	nen: Whole Blood ler: AOU 000 000 000 0002 ted: January 1, 2022 date: September 29, 2022 sefore using it in your care.	RESEARCH PROGRA	DOB: ID:	Spacimen: Berode Collected: Report date:	
	Your result: Something very important for your health was found in your <i>BRCA1</i> gene.		RESEAR		Medicine and your DNA	
What does this mean?	 If confirmed by a clinical DNA' that you are more likely to get than other people. It does not mean that you have It does not mean that you will of cancers. This result is important and sh 	test, this result means some types of cancers e some types of cancers. definitely get some types ould not be ignored.	Our genes al respond to n What is this information	ffect how we nedicine. kind of used for?	They do that in many different ways. Some genes help move medicines to the right part of the body. This test looked at a few of the genes in your DNA that can affect how medicines are used. The technical term for this kind of information is "pharmacogenetics." Doctors and pharmacists use this kind of information when they consider why medicines work differently for different	
IMPORTANTI Share this report with your doctor.	 This report comes from a ress a research result. Your doctor these results with a clinical DI them in your care. Do not change your medical is confirmed by your doctor. Results provided are from an device. An "investigational de is the subject of a clinical stud 	with program, so it is will need to confirm A test before using care before this result investigational wice" is a device that by.			people. But doctors and pharmacists don't make decisions based on just DNA. Some other important considerations can be age, weight, health, diet, and other medicines you are taking at the same time.	
Genome Center: BCM Laboratory Director: test	Hereditary Disease Risk Report	:: DNA and the risk for some diseases 1/12	Pharmacogenetic Genome Center: B Laboratory Direct	s: Medicine and your DN kroad institute of MIT and or: Heidi L. Rehm, PhD, F	Anarosed, CLIA #2202055652 1/ 13	

Participants can choose results they want

- Interpretation begins at Clinical Validation Laboratories
- All results supported by Genetic Counselors
- Started returning results on December 13
 - **16,991 participants** have been **notified** their report is ready to request
 - 6,705 participants have seen their results
 - Scaling each week to notify up to 155,000 eligible participants

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A Little Closer to Home: My Results

GENETICS AND MEDICINE Your genetic results		
Your Results: Gene CYP2C19 The <i>CYP2C19</i> gene is a "metabolizer" gene. These genes play a role in how quickly or slowly medicines are used, or metabolized, by the body.	Version *1/*8 What it means Intermediate Metabolizer An intermediate or likely int medicines at a slower rate t amount of time than expect	
Gene SLC01B1	Version *15/*15	GENETICS AND MEDICINE DNA and medicine

This table points out some medicines that may be affected by your genetic results.

If you are taking one of these medicines, talk with your doctor or pharmacist about whether ordering a clinical pharmacogenetic test is right for you.

These medicines MAY BE impacted by your genetics.

In some cases, pharmacogenetic information may help doctors and pharmacists choose medicines and doses.

Gene **CYP2C19**

- brivaracetam (Briviact[®])
- clobazam (Onfi*)
- clopidogrel (Plavix[®])

Gene SLCO1B1

simvastatin (Zocor[®])

The SLCO1B1 gene helps move some medicines out of the body when they are

these medicines from their body. This

body and cause muscle pain.

done working. People with changes in this gene may have a harder time removing

means those medicines may build up in the

What it means **Poor Function**

A "poor function" version of means some medicines may

Genomic Health-Related Return of Results Assets

All of Us has a variety of resources for participants and clinicians in English and Spanish about genomic health-related return of results

- Talking Points: Digital Health-Related Genetic Return of Result
- Fact Sheets
 - Clinical DNA Testing
 - DNA Results and Insurance
 - DNA Results and Your Family
 - Health-Related DNA Results from All of Us Research Program
 - Hereditary Disease Risk
 - Information for Clinicians Patient Health-Related DNA Results



(844) 842-2855 TTY dial 711 http://inallofus.org JoinAllofUs.org JoinAllofUs.org All of Us and the Aff of Us loss are resistend service marks of the US. Determinent of Haalth and Hamma Services.

Information for Clinicians Health-Related DNA Results From the *All of Us* Research Program

All of Us participants who provide a blood or saliva sample can decide to get personalized DNA results for free.

All of Us offers the following health-related results:

- Medicine and Your DNA report (pharmacogenetics).
- Hereditary Disease Risk report

IMPORTANT: All of Us is a research program. The DNA results we provide are not authorized by the FDA for use in clinical decision-making. An FDA-authorized, clinical DNA test is needed to confirm our results before making changes to an individual's health care.

All of Us offers a free clinical DNA testing option through our partner, Color Health, to participants whose Hereditary Disease Risk report indicates an increased risk of disease. Participants may decide to get their clinical DNA test through another provider. All of Us will not pay for clinical tests through another provider.

All of Us will not offer a clinical DNA test to participants based on their Medicine and Your DNA results.

About All of Us Medicine and Your DNA Results

For this report, *All of Us* analyzes seven genes known to affect how the body processes medicine:

•	CYP2C19	•	SLCO1E	
	0.01/0		THE R A. LEWIS CO., NAMES	

1	DPYD	TPMT
ł	G6PD	UGT1A1

G6PD
 NUDT15

For each gene, the report will explain what kind of variant the participant has and what that means. The report also will include a table of medications that may be affected by their genetic results.

What is All of Us?

The All of Us Research Program is an ambitious effort to accelerate research and improve health by gathering health data from one million or more people living in the United States

We are creating the largest and most diverse health research database of its kind, including communities who have been historically underrepresented in biomedical research.

People from all walks of life can enroll and complete online surveys, provide samples, and connect their EHRs. By looking for patterns in this information, researchers may learn more about what affects people's health, leading to advances in precision medicine.

Researcher Data Access



All of Us Research Hub: Public Data Browser

Summary statistics of:

- EHR Data (Conditions, Drug Exposures, Lab & Measurements, Procedures)
- Genomic Variants
- Survey Questions (including COVID-19 surveys)
- Physical Measurements
- Open Access (no login required)

DataBrowser.ResearchAllofUs.org





Using Variant Search on the Data Browser



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

Researcher Workbench

- Cloud-based central resource
- Passport access model just create, describe your workspace, and get to work! No separate IRB approval needed.
- Currently open to US nonprofits ٠ and nonprofit/for-profit academic and healthcare organizations
- Working to expand to ٠ international and broader for-profit audiences as we speak



Data on the Researcher Workbench is Diverse and Longitudinal



All of Us Genomic Data Available to Researchers

Researcher Workbench's Controlled Tier Launched March 2022



ncludes 100M+ variants with ≥ 3 occurrences not seen in gnomAD 3.0



New release coming soon with >200k genomes!

anyone to analyze billions

of variants

ResearchAllofUs.org/Data-Tools/Workbench/

All of Us Will Enhance Diversity of Genomic Studies



All Global GWAS values from www.gwasdiversitymonitor.com. Values current as of February 17, 2022

Researcher Workbench Usage and Diversity (as of February 10, 2023)

Research on the Researcher Workbench





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



All of Us Data Includes Range of Diseases

Conditions	Domain	Participants	Conditions	Domain	Participants
Heart Disease	Heart	73,100	Depressive Disorder	Mental Health	67,380
Obesity	Endocrine	65,740	Bipolar Disorder	Mental Health	12,820
Type 1 Diabetes	Endocrine	5,620	Dementia	Mental Health	4,760
Type 2 Diabetes	Endocrine	45,360	Human Immunodeficiency	Infectious Disease	4,640
Any cancer	Cancer	42,080		Infectious Disease	58 000*
Asthma	Pulmonary	40,560		Ahuse	84.000
Chronic Obstructive Pulmonary Disorder	Pulmonary	19,740	Opioid Usage	Medication	155,000
Epilepsy	Neuro	7,440	Age-Related Macular	Eye	4,740
Stroke	Neuro	640		Hooring	30,400
Rheumatoid Arthritis	Autoimmune	6,980			4 960
Osteoarthritis	Autoimmune	81,980	*using combination of diagnosis code. lab test, and COVID survey an		

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



Explore the data available through the Data Browser, which provides interactive views of aggregate-level participant data. Learn about individual-level data access tiers and the Researcher Workbench tools.



STEP

Before you can register, your institution must have a Data Use

and Registration Agreement in place with All of Us to ensure data security.

CREATE A RESEARCHER WORKBENCH ACCOUNT

STEP

3

Complete your researcher profile, sign the Terms of Service. and agree to the Privacy Policy.





Verify your identity using Login.gov. You may need to provide an SSN and a stateissued ID. Your institution may also require you to use an eRA Commons account. If so, contact vour institution directly. Read more about Login.gov.



COMPLETE ALL OF US RESEARCH TRAINING

The mandatory training provides education on conducting responsible and ethical research with data from All of Us participants. Please allow at least one hour to complete.



CODE OF CONDUCT

The Data User Code of Conduct is an agreement that outlines the program's expectations for researchers.

ResearchAllofUs.org/Data-Tools/ Workbench/

Individual Biospecimen and Participant Data (Available in the future)

Controlled Tier (Available Now) Narrative data, and m

Registered Tier (Available Now) Surveys, EHRs, Physical Measurements Exceeds HIPAA Safe Harbor Standards

> **Public Tier** (Available Now) Summary Statistics Aggregate Counts

What Kind of Research Can All of Us Support?

Example studies in All of Us

- Associations between diseases, medications, behaviors, SDOH, genomics
- Health disparities
- Historically underrepresented populations
- Genomics and PGx
- Drug target discovery
- Early disease detection
- Geospatial linkages (future)
- Insert your topic here

Modalities of research All of Us supports

- AI/ML
- Risk stratification
- Predictive analytics
- Phenotype algorithms & cohort development
- Novel method development
- Basic EHR investigations
- Validation of other studies

All of Us is not

- A representative US sample
- A study with uniform follow-up of all variables
- A resource for real-time outbreak surveillance

Recent Scientific Publications Utilizing All of Us

JOURNAL ARTICLE ACCEPTED MANUSCRIPT

Migraine among adults with atopic dermatitis: A cross-sectional study in the *All of Us* research program @

Ryan Fan, Audrey C Leasure, William Damsky, Jeffrey M Cohen 🕿

Clinical and Experimental Dermatology, llac004, https://doi.org/10.1093/ced/llac004

Published: 20 October 2022 Article history v

nature > nature medicine > articles > article

Article Open Access Published: 10 October 2022

Association of step counts over time with the risk of chronic disease in the *All of Us* Research Program

 Hiral Master, Jeffrey Annis, Shi Huang, Joshua A. Beckman, Francis Ratsimbazafy, Kayla Marginean,

 Publis
 Robert Carroll, Karthik Natarajan, Frank E. Harrell, Dan M. Roden, Paul Harris & Evan L. Brittain

 Ophtnatmol Sci. 2022 March ; 2(1): . doi:10.1016/j.xops.2021.100099.

Novel Association between Opioid Use and Increased Risk of Retinal Vein Occlusion Using the National Institutes of Health *All* of Us Research Program



Journal of the American Academy of Dermatology Available online 13 October 2022 In Press, Journal Pre-proof (?)



Racial and Ethnic Differences in Barriers to Care Among US Adults with Chronic Inflammatory Skin Diseases: A Cross-Sectional Study of the All of Us Research Program

G OPEN ACCESS 🖻 PEER-REVIEWED

RESEARCH ARTICLE

Ø PLOS ONE

An Overview of Cancer in the First 315,000 All of Us Participants

Briseis Aschebrook-Kilfoy 🔄, Paul Zakin, Andrew Craver, Sameep Shah, Muhammad G. Kibriya, Elizabeth Stepniak, Andrea Ramirez, Cheryl Clark, Elizabeth Cohn, Lucila Ohno-Machado, Mine Cicek, Eric Boerwinkle, Sheri D. Schully, [...],

On behalf of the All of Us Published: September 1,

ELSEVIER

Journal of Pain and Symptom Management Available online 9 September 2022 In Press, Corrected Proof (?)



Original Article

Predictors of Unrelieved Symptoms in All of Us Research Program Participants With Chronic Conditions

Caitlin Dreisbach PhD, RN $^{1,\,2},$ Susan Grayson BSN, RN $^{3},$ Katelyn Leggio MSN, RN $^{4},$ Alex Conway MS $^{3},$ Theresa Koleck PhD, RN $^{3},$ \thickapprox

All of Us Top 5 Publications of 2022 by Altmetric

Metrics as of December 22, 2022

In 2022, 100+ articles using All of Us data were published in peer-reviewed publications.

All five of these articles score in the top 5% of all research publications scored by Altmetric.



Research Program.



Master, H., Annis, J., Huang, S. et al. (2022) Nature Medicine Association of longitudinal activity measures and diabetes risk: an analysis from the

Association of step counts over time with the risk of chronic disease in the All of Us

NIH All of Us Research Program. Perry, A (2022) The Journal of Clinical Endocrinology & Metabolism



Revisiting the Latino Epidemiologic Paradox: an analysis of data from the All of Us **Research Program.** Montanez-Valverde R, et al. (2022) Journal of General Internal Medicine



Association of everyday discrimination with depressive symptoms and suicidal ideation during the COVID-19 pandemic in the All of Us Research Program. Lee Younga H, et al. (2022) JAMA Psychiatry



Wearable fitness tracker use in federally gualified health center patients: strategies to improve the health of all of us using digital health devices. Holko Michelle, et al. (2022) NPJ Digital Medicine (1) 53

AltMetric is an indicator of the volume and type of attention a research publication has received. The donut score reports identify how much and what type of attention a publication received



All of Us Discoveries: Physical Activity and Human Disease



Hiral Master, PT, PhD, MPH, CPH Senior Scientist at Vanderbilt University Medical Center



Evan Brittain, MD, MSc Associate Professor of Medicine, Division of Cardiovascular Medicine at Vanderbilt Translational and Clinical Cardiovascular Research Center



Analysis uses average of daily steps prior to diagnosis.

Effect size per 1000 steps, adjusted for age, sex, race



Adjusted for age, sex, race, CAD, cancer, BMI, systolic blood pressure, education level, smoking, alcohol use, and *monthly daily steps* (*time varying*)

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Sharing Discoveries: Comparing the Prevalence of Cardiovascular Disease across Diverse Populations



Olveen Carrasquillo, MD, MPH

Chief, Division of General Medicine at University of Miami

Principal Investigator for the *All of Us* Research Program at University of Miami



Raúl Montañez-Valverde, MD

Resident, Internal Medicine at Jackson Memorial Hospital at University of Miami

Revisiting the Latino Epidemiologic Paradox: an Analysis of Data from the All of Us Research Program

Raul Montanez-Valverde MD, Jacob McCauley PhD, Rosario Isasi JD MPH, Stephan Zuchner MD, PhD & Olveen Carrasquillo MD MPH [⊡] on behalf of the SouthEast Enrollment Center Investigators and the All of Us Research Program Demonstration Projects Subcommittee

Journal of General Internal Medicine (2022) Cite this article

Scientific Question Being Studied: Is there evidence of the Latino Epidemiological Paradox in cardiovascular outcomes for *All of Us* participants?

Findings: In contradiction to the paradox, Latinx participants in the *All of Us* dataset actually **have a higher, not lower, prevalence of CVD** than white participants and, in some cases, even black participants.

Mental Health Projects & All of Us

New Mental Health & Wellbeing Module

Goals:

- Encourage and enable research projects relevant to mental health through self-reported data
- Engage participants on topic of mental health in meaningful and innovative ways

Survey Content spans over 17 mental health-related domains, combining over 10 validated instruments:

- Domain: Depression, Anxiety, Trauma, Personality, General Well-being, Phobias
- Instrument: PHQ-9, GAD-7, UK Biobank, ACE Questionnaire

Planning **Return of Information** including relevant resources

Exploring the Mind Ancillary Study Pilot started December 2022





Research Funding Opportunities with *All of Us* in Partnership with 27 Other **NIH Institutes and Centers**



RFA-PM-23-001: R21 Enhancing the Use of the *All of Us* Research Program's Data



RFA-PM-23-002: R03 Small Grants to Enhance the Use of the *All of Us* Research Program's Data



OTA-23-002: All of Us Research Participant and Partner Services Center (PPSC)

All of Us Notices or ROAs Available

NOT-PM-23-002: Notice of Future Research Opportunity Announcement for All of Us Center for Linkage and Acquisition of Data (CLAD)

NOT-ES-23-003: Notice of Intent to Publish a Funding Opportunity Announcement for Reporting Back Environmental Health and Non-Genomic Research Results



Thank you to our 596,000+ participants!