Enfranchisement and Meaningful Inclusion of Diverse Populations in *All of Us*

01 June 2021

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Policy Director
All of Us Research Program

National Institutes of Health

Program Overview | Diversity at Scale

Diversity of Resources: Deliver a national resource of deep **clinical, environmental, lifestyle, & genetic data** from one million participants who are consented & engaged to provide data on an ongoing, longitudinal basis

Diversity of Participants: Reflect the broad diversity of the U.S.—**all ages, races/ ethnicities, gender, SES, geographies, & health status**—and over-recruit those historically underrepresented in biomedical research

Diversity of Researchers: Build the tools & capabilities that make it accessible to the public and easy for researchers—**from citizen and community scientists to scientists from premier university labs**—to make discoveries using *All of Us*

Commitment to Participant Partnership

Build a Culture of Participant-Centered Design

Incentivize Focus on UBR Communities

Develop Specific Plans for Population Engagement

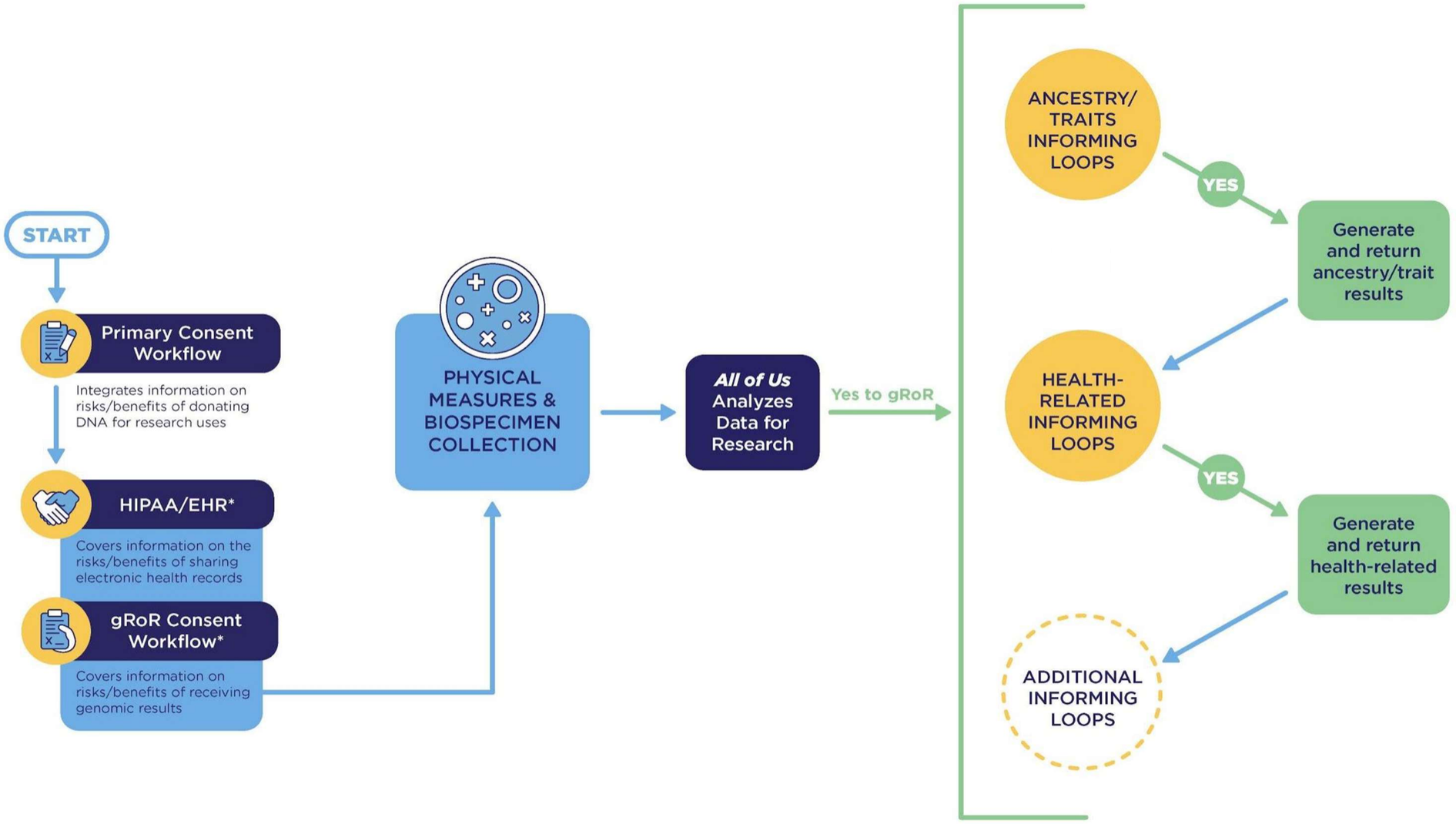
Grow a Network of National and Local Community Partners

Build Up FQHC Research Capacity as Valuable HPO Partners

Create Network of Direct Volunteer Partners

All of Us Community and Provider Partner Network

Participation | Granular Participant Controls



*Not required during initial consent experience, but MUST complete before proceeding to PM&B

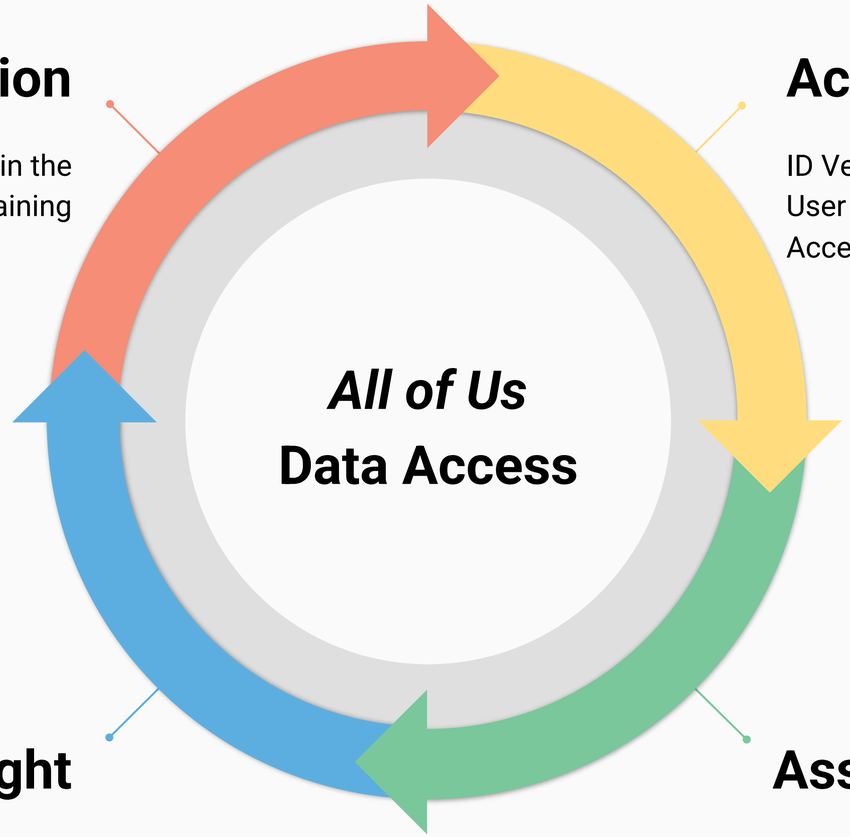
Data Access | Preventing Misuse, Building Trust

Education

Raising Awareness and Setting Expectations in the Responsible Conduct of Research Training

Accountability

ID Verification Mandatory compliance with the Data User Code of Conduct, Data Use Agreement, and Data Access and Use Policies



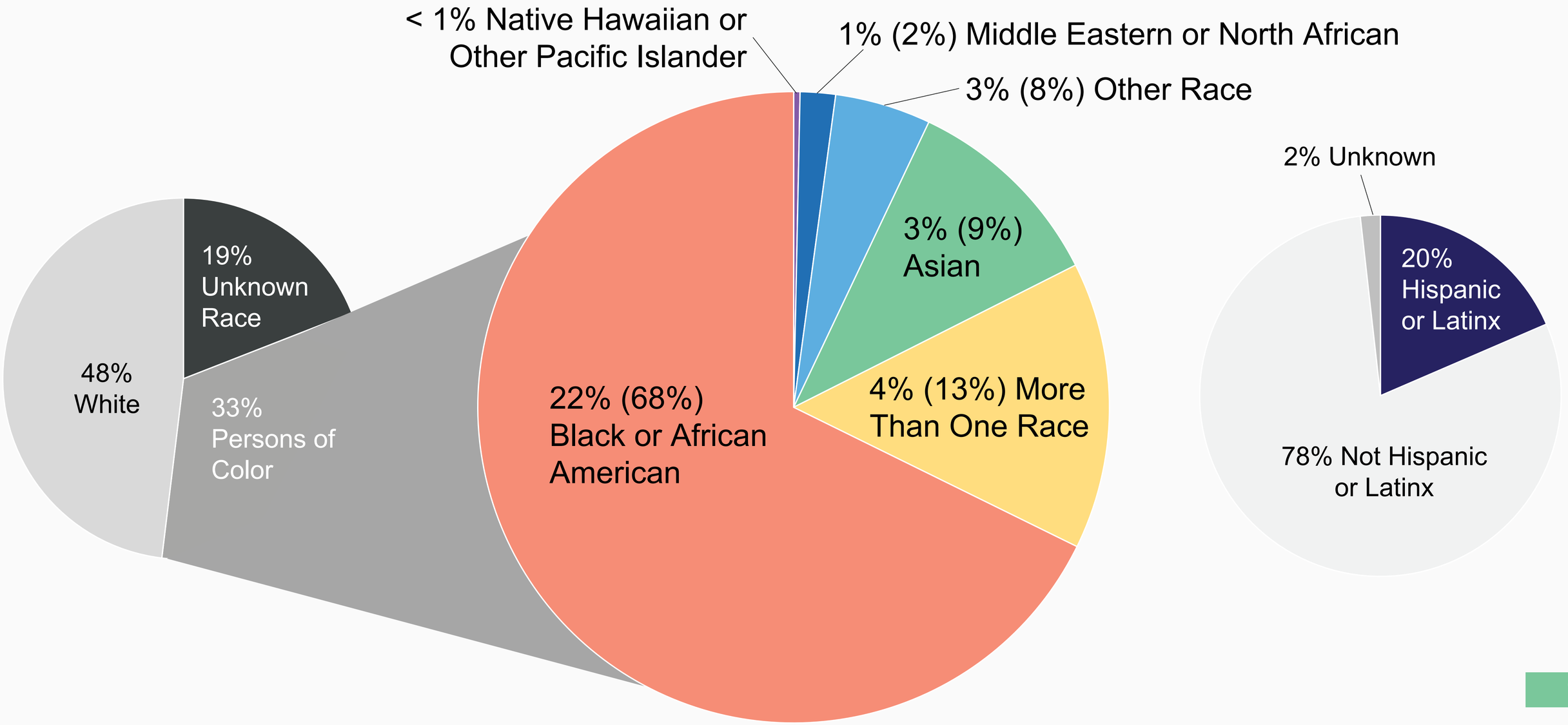
Oversight

Continual monitoring of curated data enclave by Data and Research Center; periodic audits and publicly-initiated reviews conducted by the Resource Access Board

Assistance

User-initiated reviews and assistance from the Resource Access Board available at any stage

All of Us Current Enrollment Numbers (As of May 28th)



RETENTION

Thank you!

AllofUs.nih.gov
joinAllofUs.org
ResearchAllofUs.org

katherine.blizinsky@nih.gov

NIH National Institutes of Health

extra slides

All of Us
RESEARCH PROGRAM

Background

NIH National Institutes of Health

Why do we even need an *All of Us* Research Program?

People/ Patients

- Patients may not be served well by treatments designed for the “average” patient. We hope in the future that *All of Us* will help advance precision medicine.
- Many people & populations have been left out of biomedical research, and thus, often left out of health care solutions.
- Health problems can take years to unravel and require much trial and error treatment.
- Patients may not have access to or make use of their own health data.

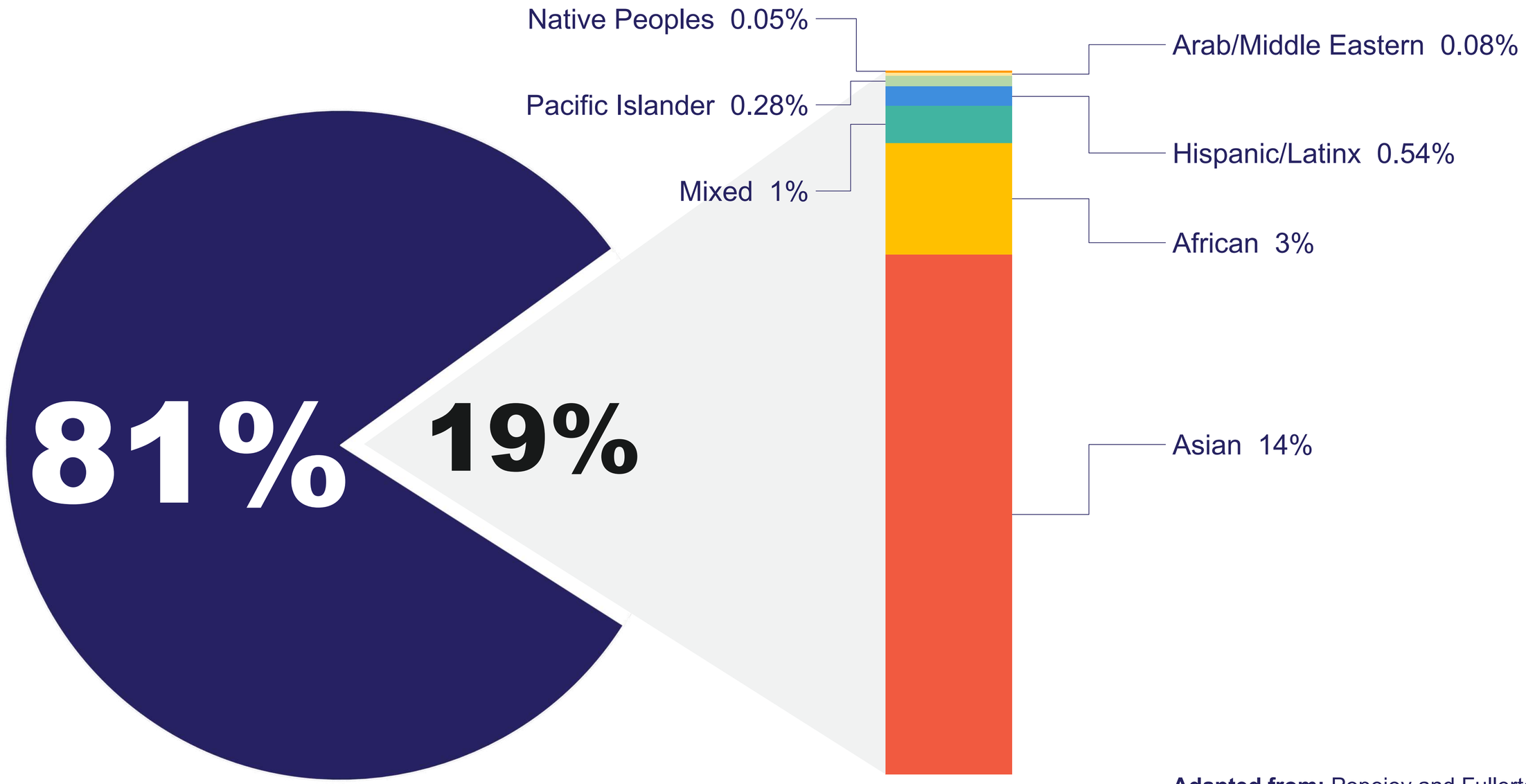
Professional Providers

- Precision medicine research is still in the early days, so providers do not have enough information available to provide precision care for many conditions.
- Developing individualized approaches to care often requires overtime.
- It can be difficult to coordinate care between many different providers, especially with medical records and key data scattered in different silos.

Biomedical Researchers

- Researchers spend a lot of time and resources creating new IT systems, databases, and analytic tools.
- They also face enormous costs & time just to recruit participants.
- Data collection is often not standardized, and data can be siloed and difficult to integrate.
- A single lab’s resources may not be sufficient to answer the research questions that matter.

Persistent Racial and Ethnic Bias in GWA Studies



Adapted from: Popejoy and Fullerton, Nature, 2016

Minorities make up

38%

of the US population.

Minority populations to rise to over

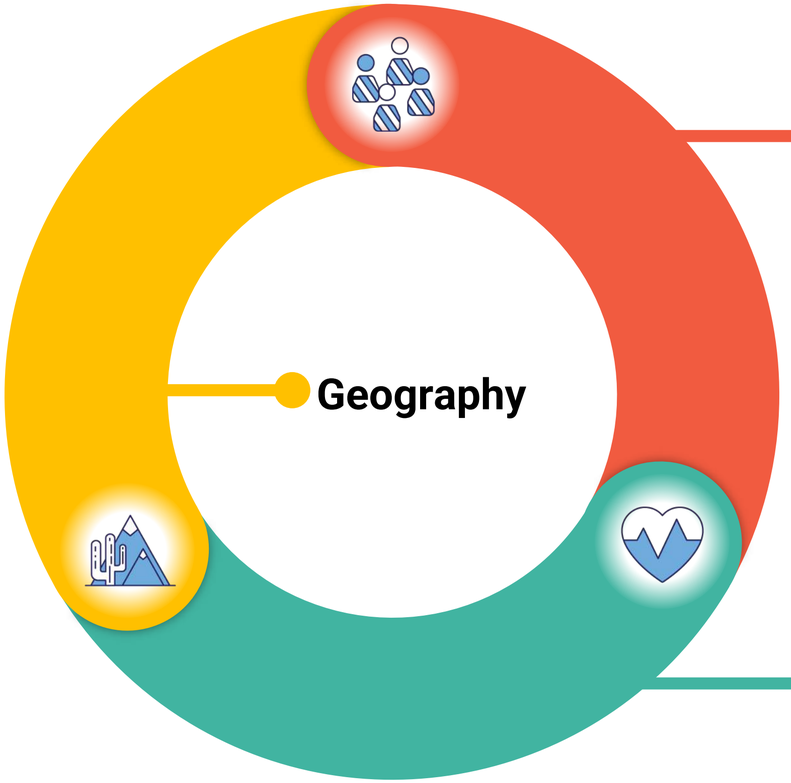
56%

of overall population.

Minority enrollment in clinical trials

<10%

underrepresentation in biomedical research includes dimensions of...



All of Us Mission

Nurture relationships
with one million or more participant partners, from all walks of life, for decades

Deliver the largest, richest biomedical resource ever,
making it as easy, safe, and free to use as possible

Our Mission

To accelerate health research, enabling individualized care for all of us.

Catalyze the robust ecosystem
of researchers and funders hungry to use and support it

Build and maintain a strong *All of Us* Team
capable of achieving the program's mission

All of Us Core Values

- Participation is open to **all**
- Participants reflect the rich **diversity** of the United States
- Participants are **partners**
- **Transparency** earns trust
- Participants have **access** to their information
- Data are **broadly accessible** for research purposes
- Security and privacy are of **highest importance**
- The program will be a **catalyst for positive change** in research

How will *All of Us* lead to discoveries?

Participants Share Data
Participants share health data online. This data includes health surveys and electronic health records. Participants also may be asked to share physical measurements and blood and urine samples. We also want to know if you will want information about your DNA.

Data Is Protected
Personal information, like your name, address, and other things that easily identify participants will be removed from all data. Samples—also without any names on them—are stored in a secure biobank.

Researchers Study Data
Approved researchers use the data to conduct studies. By finding patterns in the data, they may learn more about what affects people's health.

Participants Get Information
Participants will get information back about the data they provide, which may help them learn more about their health.

Researchers Share Discoveries
Research may help in many ways. It may help find the best ways for people to stay healthy. It may also help create better tests and find the treatments that will work best for different people.

All of Us is catalyzing innovation in the research enterprise

For participants

- Empowering people from all walks of life to engage and help shape the future of research.
- Committed to responsibly returning information to participants.
- Developed a network of community partners to serve as “a trusted person I can talk to.”
- Creating a network of non-traditional partners for biomedical research, starting with Federally Qualified Health Centers, to bring in diverse and underrepresented communities.

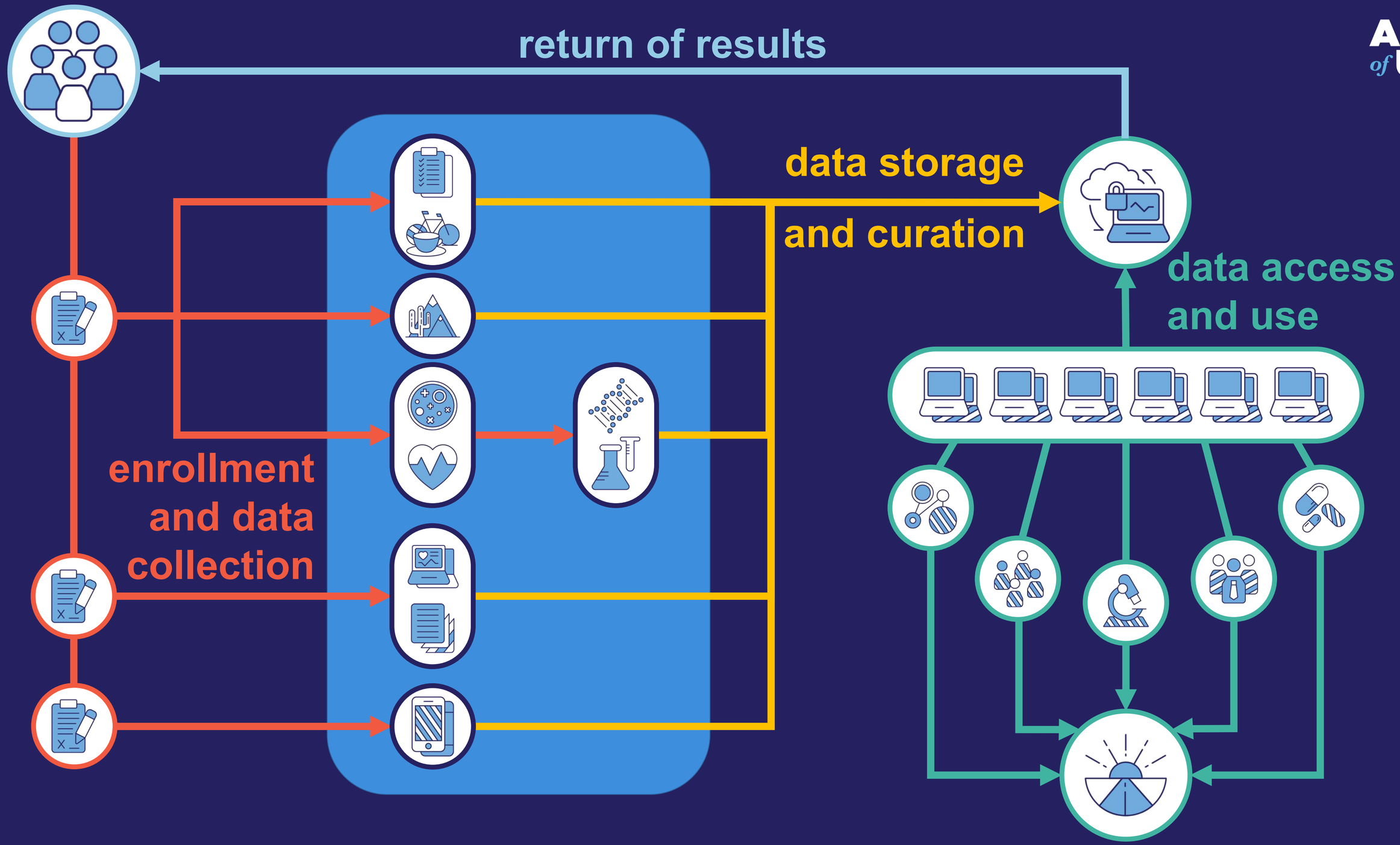
For researchers

- Testing digital engagement strategies to recruit and retain diverse participants.
- Opening new pathways to bring in data:
  - Investments in pilots to gather rich, longitudinal electronic health records.
  - Developing APIs and apps to leverage wearable health technologies.
- Empowering and democratizing research to bring “more brainpower per problem.”
  - *All of Us* will be open to all researchers, including citizen scientists.
- Built a network of partners to make it possible for anyone, anywhere in the country to participate in biomedical research.

All of Us RESEARCH PROGRAM

Program Structure

NIH National Institutes of Health


return of results
data storage
and curation
data access
and use
enrollment
and data
collection

Major building blocks of the *All of Us* Research Program consortium

DATA AND RESEARCH CENTER

Big data capture, cleaning, curation, & sharing in secure environment

Vanderbilt, Verily, Broad Institute

BIOBANK

Repository for processing, storing, and sharing biosamples (35+M vials)

Mayo Clinic

PARTICIPANT TECHNOLOGY SYSTEMS CENTER

Web and phone-based platforms for participants

Vibrent Health

GENOMICS PARTNERS

Genotyping and whole genome sequencing of biosamples; counseling and educational resources for participants

Baylor College of Medicine, Broad Institute, University of Washington, Color, HudsonAlpha, and partners

PARTICIPANT CENTER / DV NETWORK

Direct volunteer participant enrollment, digital engagement innovation, and consumer health technologies

Scripps Research Institute (with multiple partners)

HEALTH CARE PROVIDER ORGS NETWORK

HPOs with clinical & scientific expertise, enrollment & retention of participants

30+ regional medical centers, FQHCs, and VA

COMMUNICATIONS & ENGAGEMENT NETWORK

Communications, marketing, and design expertise; engagement coordination and community partners network

Wondros, Pyxis Partners, University of Utah, and many community engagement partner organizations

All of Us Consortium Members *(beyond community partners, as of March 2021)*

The Participant Center

Scripps Research Translational Institute
BlueCross BlueShield
SENSIS
DXC.technology
waves
Walgreens
Bloodworks Northwest
New York Blood Center
Gulf Coast Regional Blood Center — Commit for Life.
careevolution HEALTHCARE TECHNOLOGY
MONTAGE MARKETING
WebMD
THE BEHAVIOURAL INSIGHTS TEAM
Medscape
patientslikeme
PicnicHealth
San Diego Blood Bank
URBAN ONE
ACHA American College Health Association — advocacy • education • research
SYNC FOR SCIENCE
Quest Diagnostics
Sage BIONETWORKS
NATIONAL BLOOD COLLABORATIVE — BLOOD SOLUTIONS | TRUSTED SOURCE
fitbit
QTC — A Leidos Company

Communications & Engagement

WONDROS
THE UNIVERSITY OF UTAH
RTI INTERNATIONAL
PYXISPARTNERS — PATHWAYS TO PROGRESS

HPO Network

(Health Care Provider Organizations)

RMCs

All of Us California

UC San Diego Health
UCI Health
UCDAVIS HEALTH
UCSF — University of California San Francisco
Cedars Sinai
USC University of Southern California

IllinoisPrecision Medicine Consortium

Northwestern Medicine
THE UNIVERSITY OF CHICAGO
NorthShore University HealthSystem
RUSH
COOK COUNTY HEALTH
THE UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE — PEORIA CHICAGO ROCKFORD URBANA
UI Health | UIC

All of Us New England

BRIGHAM HEALTH — BRIGHAM AND WOMEN'S HOSPITAL
MASSACHUSETTS GENERAL HOSPITAL
Mass General Brigham
BOSTON MEDICAL — EXCEPTIONAL CARE. WITHOUT EXCEPTION.

Trans America Consortium

Henry Ford HEALTH SYSTEM
Spectrum Health
Essentia Health
BaylorScott&White HEALTH
RELIANT MEDICAL GROUP — Part of OptumCare®
HealthPartners Institute

New York City Consortium

COLUMBIA
Weill Cornell Medicine
NYC HEALTH+ HOSPITALS | Harlem
NewYork-Presbyterian

All of Us Southern Network

UAB MEDICINE
USA HEALTH
UAB SCHOOL OF MEDICINE — The University of Alabama at Birmingham — Montgomery Regional Medical Campus — Huntsville Regional Medical Campus — Selma Family Medicine Program
University Medical Center — College of Community Health Sciences — THE UNIVERSITY OF ALABAMA
Cooper Green Mercy HEALTH SERVICES AUTHORITY — AFFILIATE OF UAB HEALTH SYSTEM
TUSKEGEE UNIVERSITY
The University of Mississippi MEDICAL CENTER
LSU Health NEW ORLEANS
Tulane University
HUNTSVILLE HOSPITAL

All of Us SouthEast Enrollment Center

UHealth — UNIVERSITY OF MIAMI HEALTH SYSTEM | UNIVERSITY OF MIAMI MILLER SCHOOL of MEDICINE
EMORY UNIVERSITY
MOREHOUSE SCHOOL OF MEDICINE
UF UNIVERSITY of FLORIDA

All of Us Wisconsin

Marshfield Clinic Health System
WISCONSIN — UNIVERSITY OF WISCONSIN-MADISON
Froedtert & MEDICAL COLLEGE of WISCONSIN
GUNDERSEN HEALTH SYSTEM

All of Us Pennsylvania

University of Pittsburgh

University of Arizona and Banner Health

THE UNIVERSITY OF ARIZONA
Banner Health
MARIPOSA — Your COMMUNITY HEALTH CENTER

FQHCs (Federally Qualified Health Centers)

Cherokee HEALTH SYSTEMS
JACKSON-HINDS COMPREHENSIVE HEALTH CENTER
SAN YSIDRO HEALTH
Community Health Center, Inc.
Cooperative Health
Sun River Health

VA Medical Centers

VA
U.S. Department of Veterans Affairs — Veterans Health Administration

Participant Technology Systems Center (PTSC)

vibrent

Biobank

MAYO CLINIC

Data & Research Center (DRC)

VANDERBILT UNIVERSITY MEDICAL CENTER
BROAD INSTITUTE
verily
COLUMBIA
SCHOOL OF PUBLIC HEALTH — UNIVERSITY OF MICHIGAN
Northwestern Medicine
UTHealth — The University of Texas Health Science Center at Houston

Genomics Partners

Baylor College of Medicine
JOHNS HOPKINS MEDICINE
UTHealth — The University of Texas Health Science Center at Houston
HUDSONALPHA INSTITUTE FOR BIOTECHNOLOGY
BROAD INSTITUTE
color
Mass General Brigham
UNIVERSITY of WASHINGTON

All of Us RESEARCH PROGRAM

The *All of Us* Policy Team

Katherine Blizinsky, Ph.D.
Director

Subhashini Chandrasekharan, Ph.D.
ELSI Lead

Tawina Clarke, M.P.H.
Policy Coordination Lead

Sally Enoh, J.D.
Legal Intern

Sonya Jooma, M.A.
Deputy Director

Aleek Kahramanian, M.P.A.
Policy Project Manager

Rosayma Lopez-Ramirez, M.A., CIPPG, CIPM
Privacy Officer

Teresa McEachern, B.B.A.
Special Assistant to the Director

Jessica Reusch, Ph.D.
Agreements Lead

Ericka Thomas, M.H.A.
Participant Priorities Lead

functional areas

Consideration

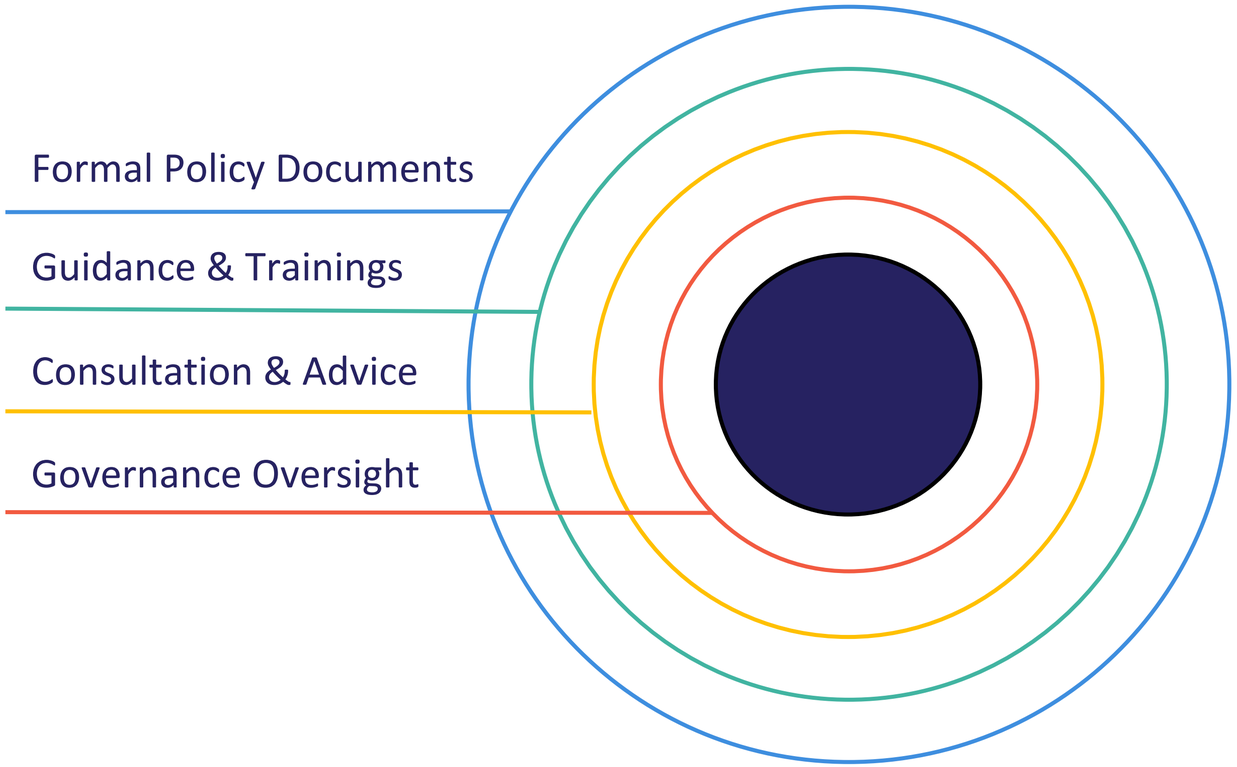
Evaluating ethical and social obligations for the program

Interpretation

Setting the terms for legal, regulatory, and policy compliance

Promulgation

Establishing and overseeing program-wide policies and principles



Consents and authorizations

Including vulnerable populations and protected classes

Privacy protections, controls, and measures

Access and use of *All of Us* data and research resources

Generation and sharing of genomic information

All of Us Policy Office

topical areas

- Agreements
- Participant Protections*
- Privacy
- Access and Use
- Genomics

All of Us RESEARCH PROGRAM

Sharing Data with Researchers

NIH National Institutes of Health

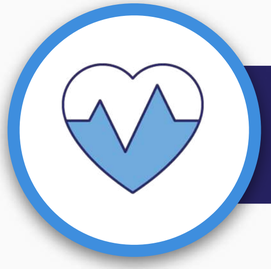
All of Us Data Collection

Participant Surveys

- The Basics
- Lifestyle
- Overall Health
- Personal Medical History
- Health Care Access & Utilization
- Family Medical History
- COVID-19 Participant Experience
- *Mental Health*

Electronic Health Records

- Medical Records
- *Claims Data*
- *Pharmacy Data*
- *Vision and Dental Records*



Physical Measurements

- Blood Pressure
- BMI
- Heart Rate
- Height
- Hip Circumference
- Waist Circumference
- Weight

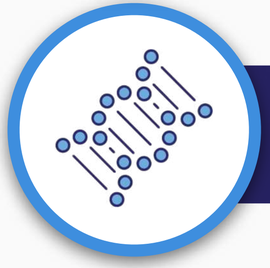
Biospecimens

- Blood
- Urine
- DNA (from blood or *saliva*)
- *Saliva*
- *RNA*

Mobile/Wearable Tech

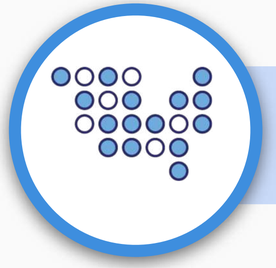
Assays

- COVID Serology*
- *HbA1c*
- *Heavy Metals*



Omics

- WGS*
- Arrays (Ancestry & Traits)
- *Other Omics*



Geospatial/Environmental Data

Selected Scientific Opportunities

- Develop quantitative **estimates of risk** for a range of diseases by integrating environmental exposures and genetic factors
- Identify the causes of individual variation in response to commonly used therapeutics = **pharmacogenomics**
- Discover **biological markers** that signal increased or decreased risk of developing common diseases
- Develop **solutions to health disparities**
- Use **mobile health technologies** to correlate activity, physiological measures, and environmental exposures with health outcomes
- **Empower study participants** with data and information to improve their own health
- Create a platform to enable **trials of targeted therapies**

All of Us Data Access and Use Principles

- **Participants are research partners**
  - Must protect their privacy to the greatest extent possible (while balancing the below principles)

- **Data is a non-scarce resource and should therefore be as accessible as possible for authorized users**
  - This includes researchers outside of academic medical centers to those affiliated with industry and citizen/community scientists

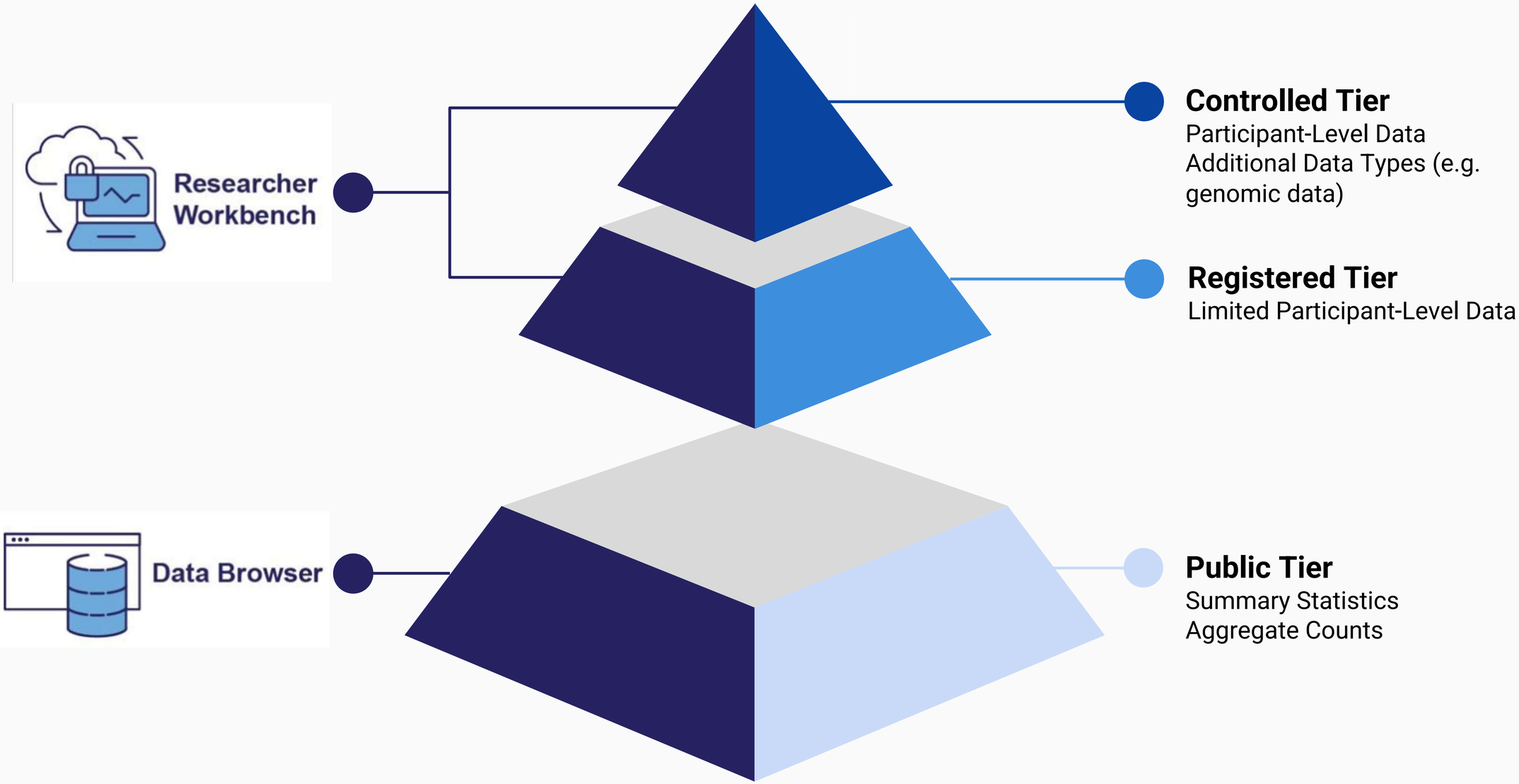
- **We should continuously seek to remove unnecessary barriers to accessing *All of Us* data**
  - No group of data users should have privileged access to *All of Us* resources based on anything other than data protection criteria

Considerations

- How do you balance broad access with programmatic oversight?
- How much do you trust your data users?
- What measures may be taken to render data hard to re-identify or (otherwise misuse) without sacrificing utility?
- How will you determine if/when a user has violated the terms of use and the gravity and intent of the violation?
- How will you enforce appropriate user behavior?

"They're harmless when they're alone, but get a bunch of them together with a research grant and watch out."

The *All of Us* Research Hub



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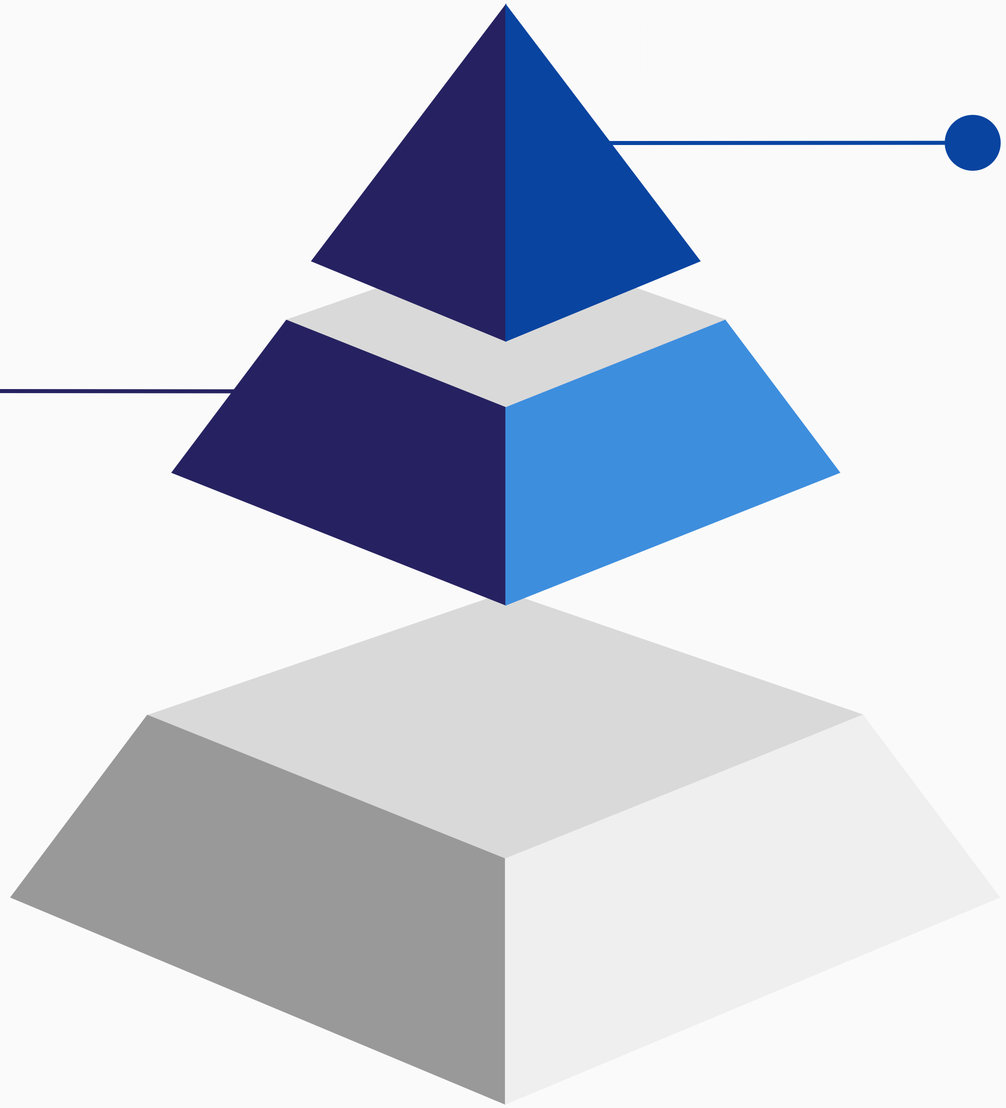


Controlled Tier

Granular Participant-Level Data

Registered Tier Data PLUS
Additional EHR Fields
Genomic Data

Fewer Data Transformations

Unshifted Dates (except Year of Birth)
More Precise Geographic Information (3-Digit Zip Codes)
Fewer Generalizations and Ontological "Roll-Ups"

Registered Tier

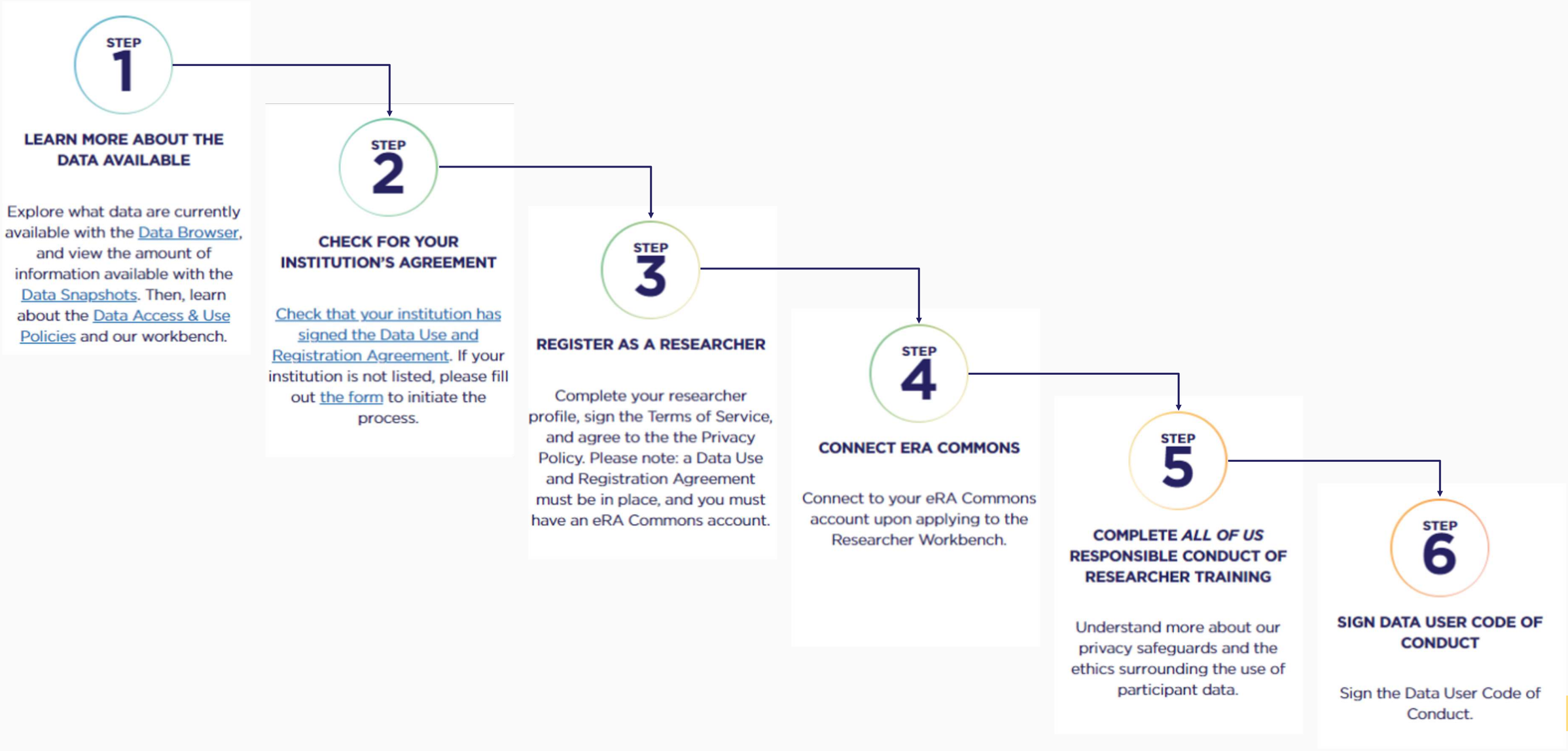
Limited Participant-Level Data

Physical Measurements
Some Electronic Health Record Data
Survey Data
Fitbit Data

Many Data Transformations

Date Shifting
Generalization (e.g. State-Level Geographic Information)
Ontological "Roll-Ups"

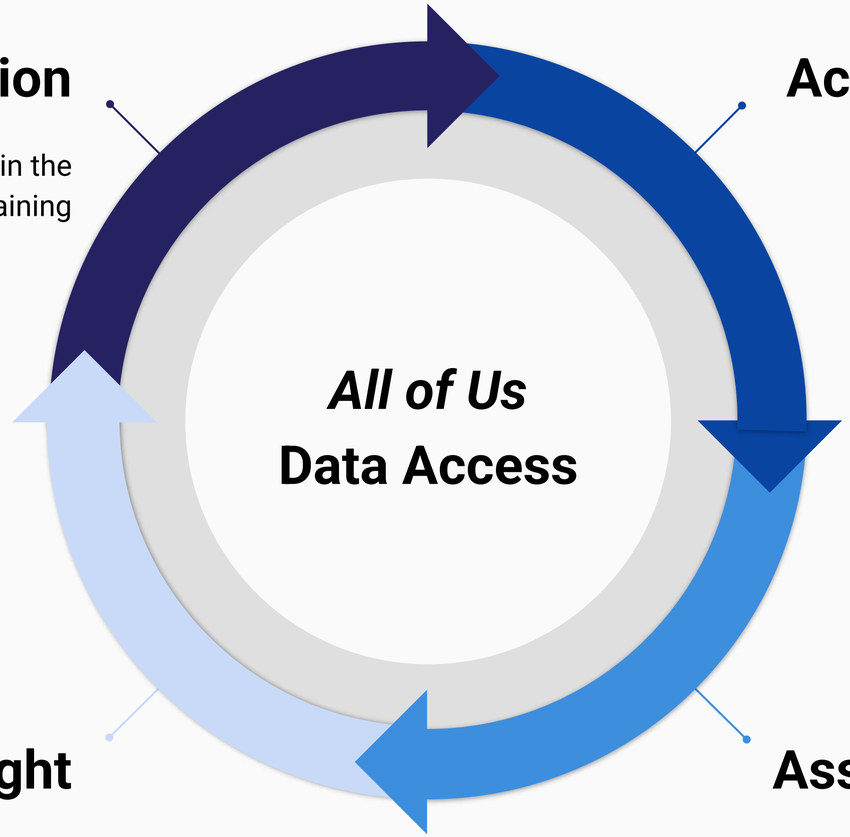
The User Application Process



Preventing Misuse, Building Trust

Education

Raising Awareness and Setting Expectations in the Responsible Conduct of Research Training



Accountability

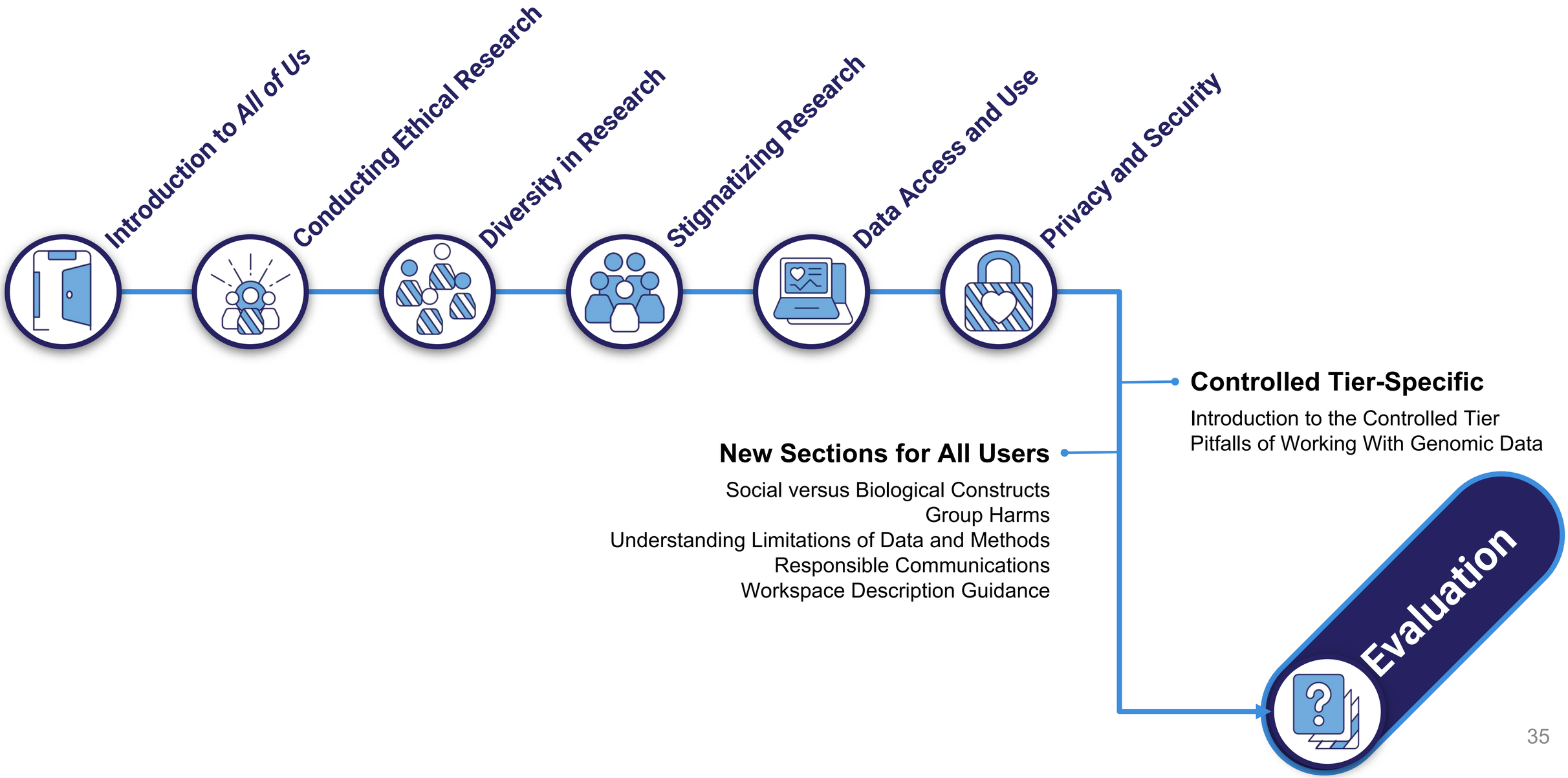
Oversight

Assistance

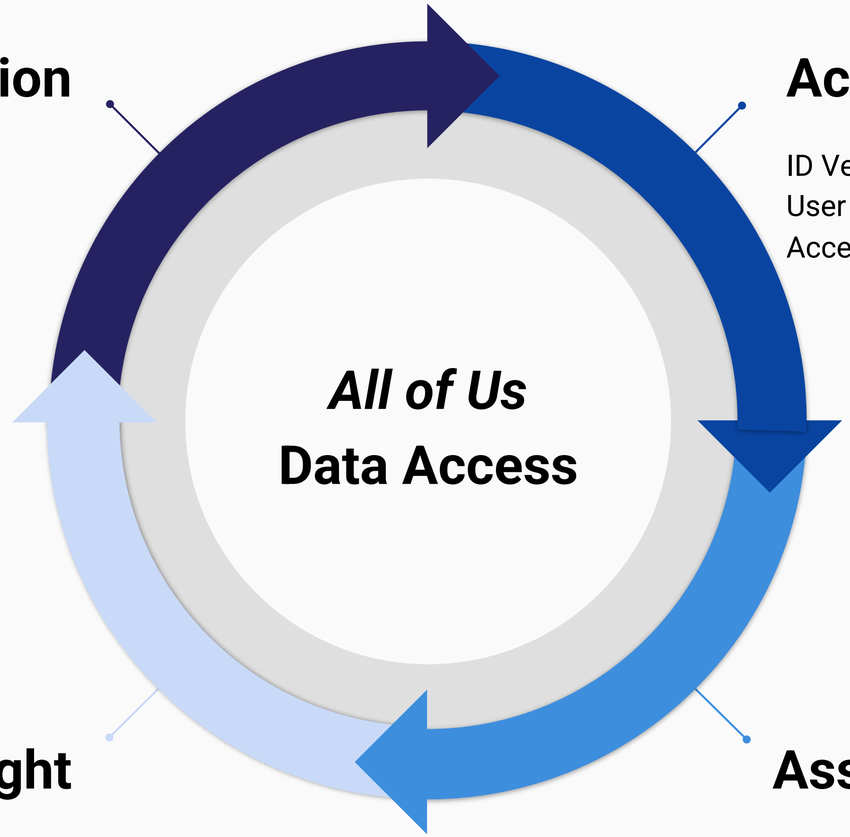
Education

Responsible Conduct of Research Training

Additional Modules

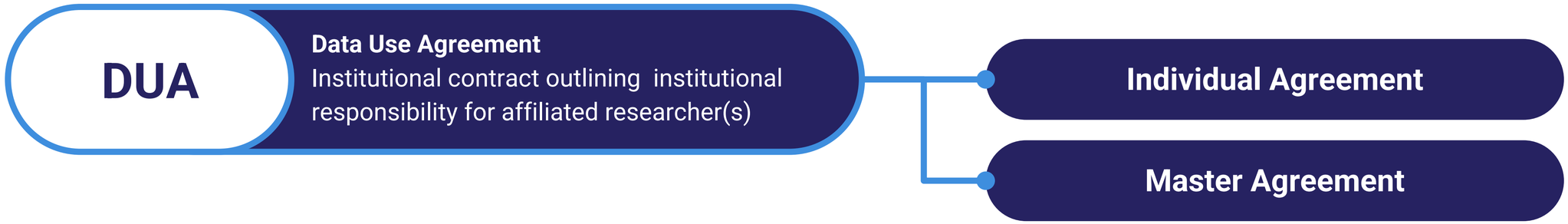


Preventing Misuse, Building Trust



Accountability

Data Use Contracts and Policies



Accountability

Data Use Contracts and Policies

DUA

Data Use Agreement
Institutional contract outlining institutional responsibility for affiliated researcher(s)

DUCC

Data User Code of Conduct
Individual agreement outlining individual use responsibilities

The *All of Us* Data User Code of Conduct (select clauses)

I **WILL**:

- read and adhere to the ***All of Us*** **Research Program Core Values**.
- know and follow **all applicable federal, state, and local laws** regarding human data access and privacy.
- provide a **meaningful and accurate** description of my research purpose every time I create an *All of Us* Research Program Workspace.
- use the *All of Us* Research Program data ONLY for the purpose of **biomedical or health research**.

I will **NOT**:

- use *All of Us* Research Program data, or any external data, files or software that I upload... for **research that is discriminatory or stigmatizing** of individuals, families, or communities.
- **attempt to re-identify** research participants or their relatives.
- **make copies of or download individual-level data** resources outside of the *All of Us* research environment without approval from RAB.
- **share my login information with anyone**, including another Authorized Data User...

Certificates of Confidentiality

42 u.s.c. § 241(d)

applies to identifiable, sensitive information collected during the course of federally-funded research

ensures limited disclosures to protect participant identities

radically overhauled by the 21st century cures act

before

optional

issuance

mandatory and automatic for federally funded research*

participant identities

coverage

identifiable and *potentially* identifiable information and all copies

at researcher discretion

withholding

mandatory, with some exceptions*

n/a

immunity

immune from legal process and inadmissible in proceedings

after

Accountability

Data Use Contracts and Policies

DUA

Data Use Agreement
Institutional contract outlining institutional responsibility for affiliated researcher(s)

DUCC

Data User Code of Conduct
Individual agreement outlining individual use responsibilities

I WILL:

conduct research that follows **all policy requirements** and conforms to the ethical principles of the *All of Us* Research Program.

Accountability

Data Use Contracts and Policies

DUA

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DUCC

Data User Code of Conduct
Individual agreement outlining individual use responsibilities

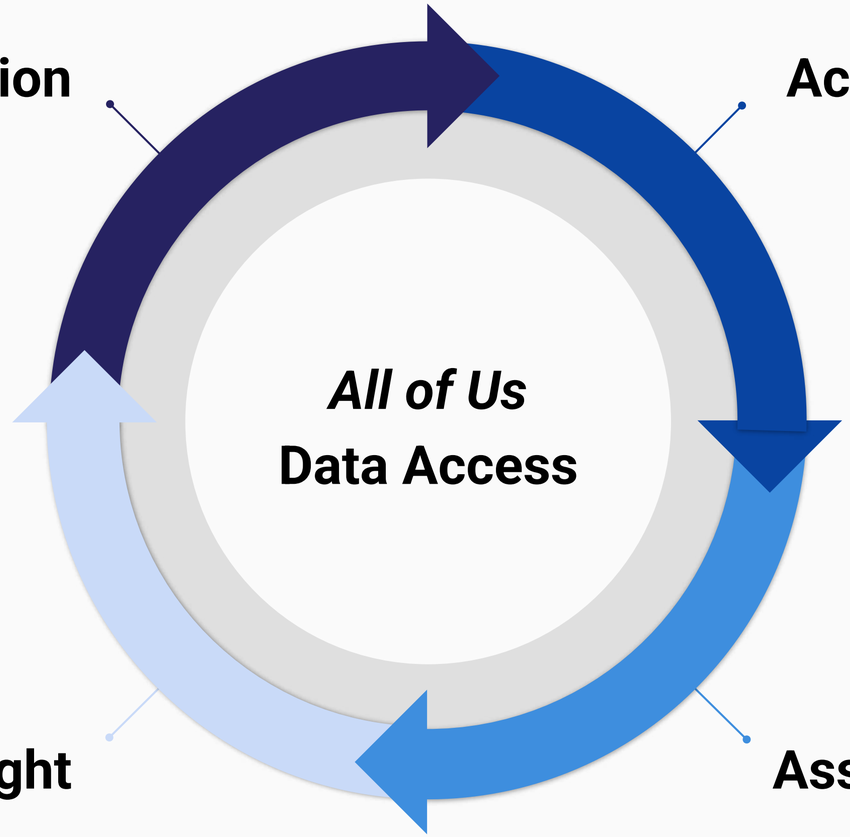
Policies

Collection of detailed directives for appropriate use, compliance with which is required by the DUCC

- Ethical Conduct of Research
- Stigmatizing Research
- Data and Statistics Dissemination
- Publications and Presentations
- User Appeals
- … and more to come

https://www.researchallofus.org/data-tools/data-access/

Preventing Misuse, Building Trust

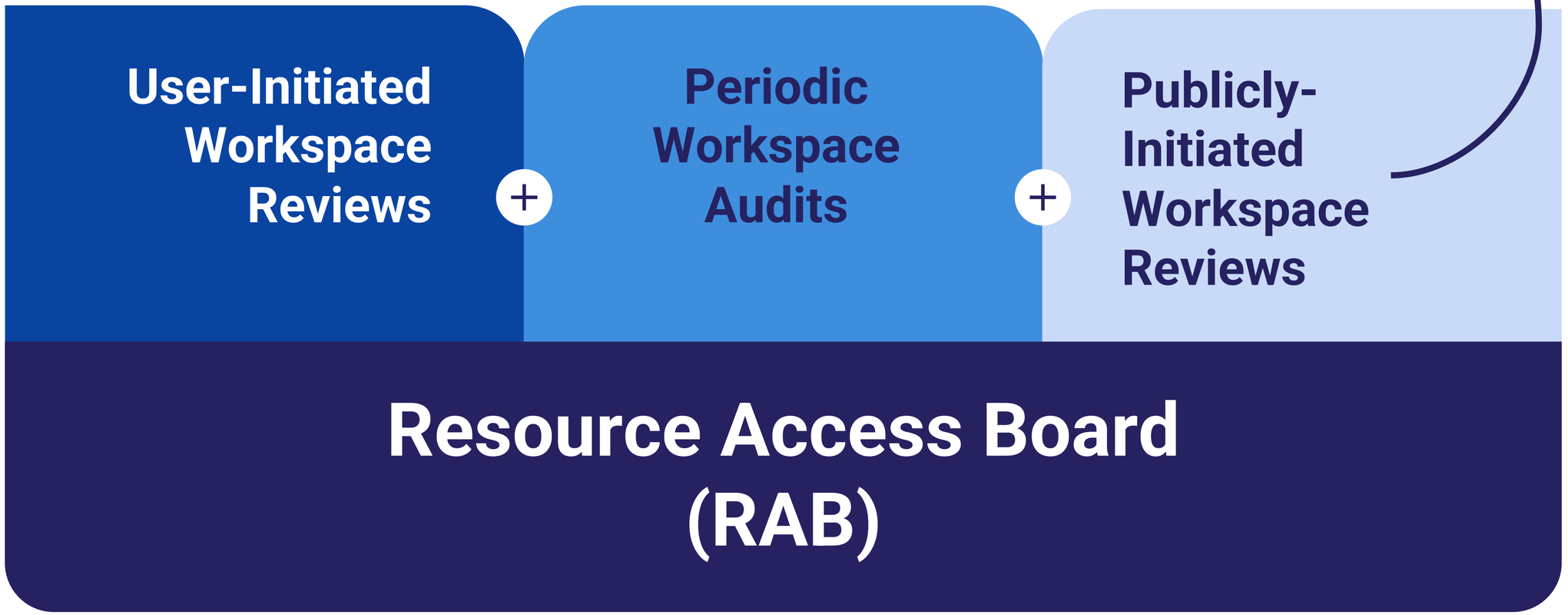


Continual monitoring by Data and Research Center and periodic audits and publicly-initiated reviews conducted by the Resource Access Board

User-initiated reviews and assistance from the Resource Access Board available at any stage

Assistance

https://www.researchallofus.org/research-projects-directory/



Oversight

Has a violation actually occurred?

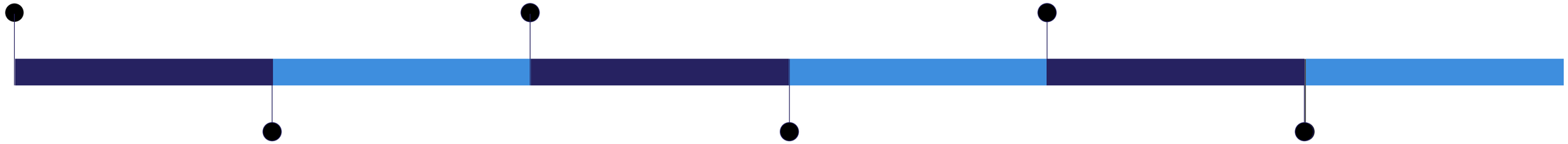
Occurrence

Is it reasonable to believe that the perceived violation was intentional?

Intentionality

Has the user always otherwise been in good standing with *All of Us*?

User History



Type

What is the type of the perceived violation?

- Legal or Regulatory Violation
- Participant/Group Reidentification
- Stigmatizing Research
- Group Harm
- Insufficient Workspace Description
- Marketing
- Other

Type specific-considerations

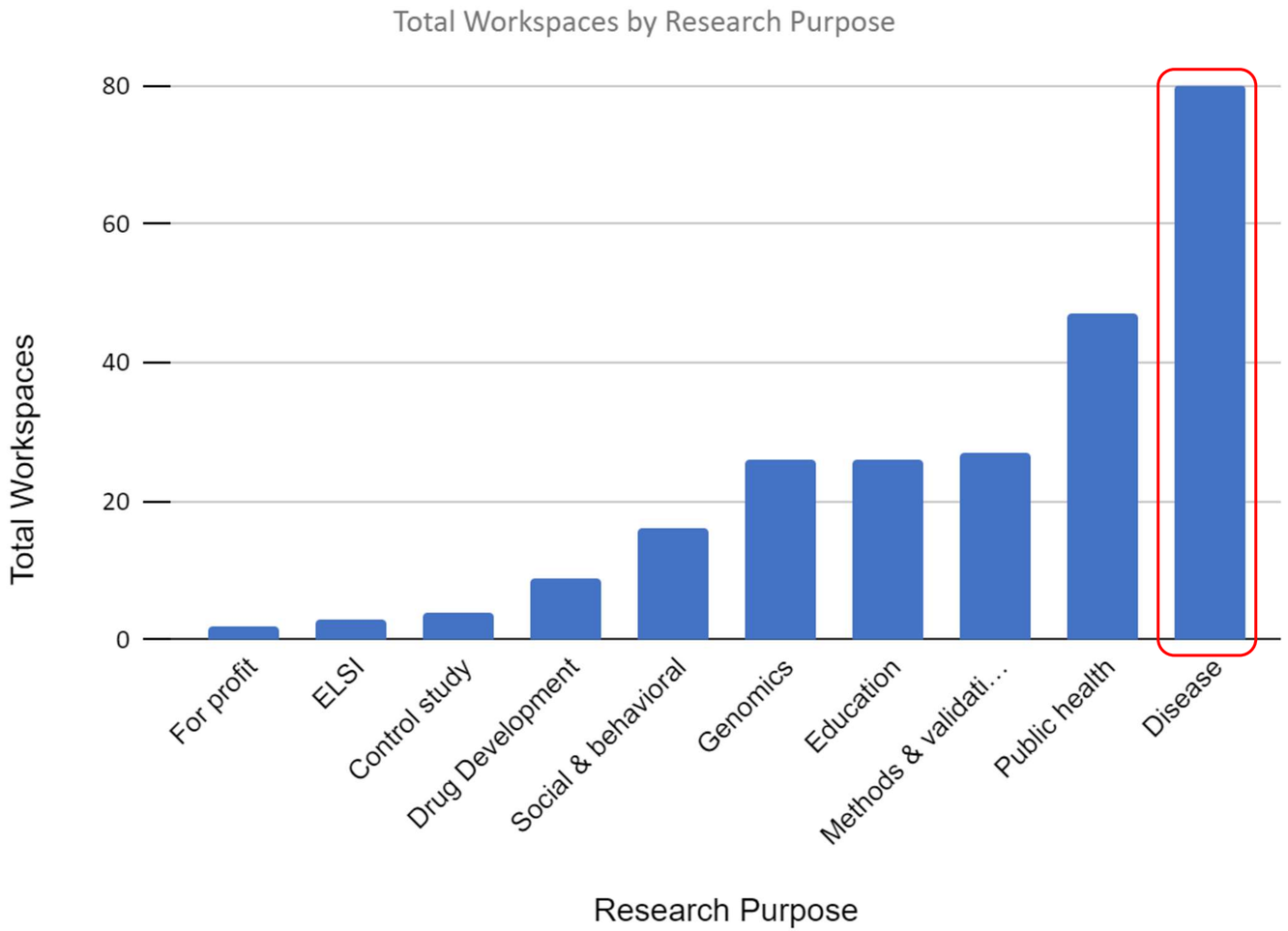
Scale and Scope

- How many individuals or how much information was affected?
- How significant was the effect?

Pattern Recognition

Are there patterns in violations in the user's history or across users (either total or affiliated with a particular insitution)?

Researchers are accessing *All of Us* for many reasons

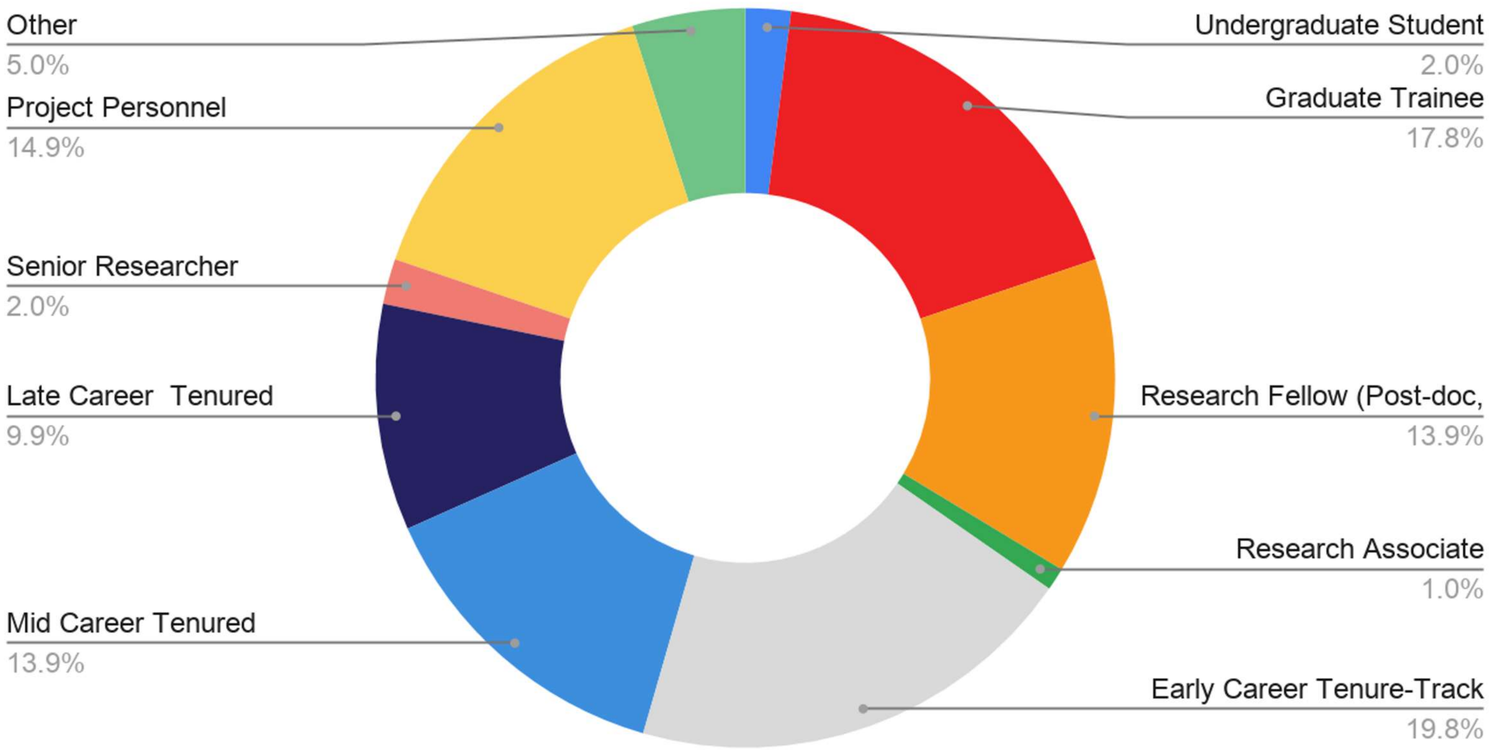


*Please note: researchers may select multiple categories per workspace

Disease Foci (Workspace Count)
Cancer (12)
Diabetes (8)
Depression (7)
Cardiovascular Disease (6)
Autoimmune Disease (6)
and many more….

All of Us DATA & RESEARCH CENTER

Who are our researchers?



Researcher Demographics*

- **>50%** Trainees, Fellow, & Early Career Investigators
- **86%** have graduate degrees (**72%** doctorate)
- **48%** White, **40%** Asian, **10%** None/PNTA, **1%** AA, **1%** AI/AN
- **94%** Non-Hispanic
- **61%** Man, **33%** Woman, **5%** Non binary, transgender, or PNTA

*Percentages provided are out of the total number of researchers who responded to each optional demographic question as of 8/4/2020. Response rates for demographic questions range from ~63% for Ethnicity to ~71% for race.

All of Us DATA & RESEARCH CENTER

Sharing Data with Participants

National Institutes of Health

All of Us RESEARCH PROGRAM

Participants Want Results

PLOS ONE published a public opinion survey conducted by the Foundation for the NIH.

2,601 responses were analyzed.

79% supported the program after reading a short description.

54% said they would definitely or probably participate if asked—not predictive of enrollment numbers, but encouraging.

- Little variability among demographic groups
- Most important incentive for participation: **learning about one's health information**

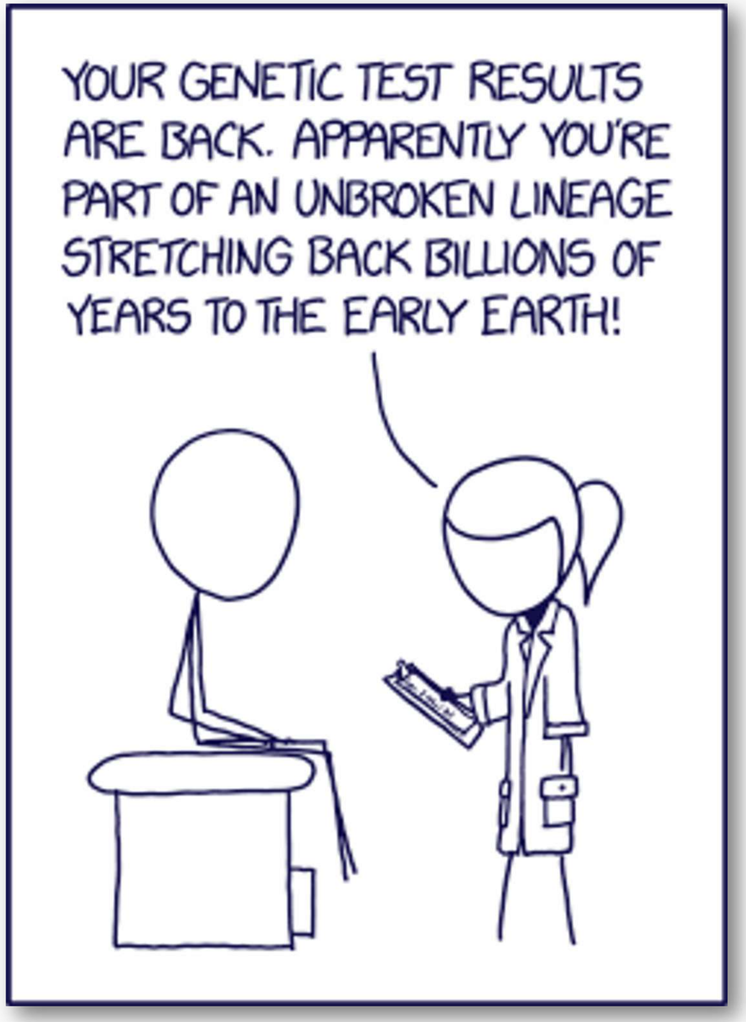
Kaufman DJ, Baker R, Milner LC, Devaney S, Hudson KL (2016):
A Survey of U.S. Adults' Opinions about Conduct of a Nationwide Precision Medicine Initiative Cohort Study of Genes and Environment.
PLOS ONE 11(8): e0160461. doi:10.1371/journal.pone.0160461

National Academies Report

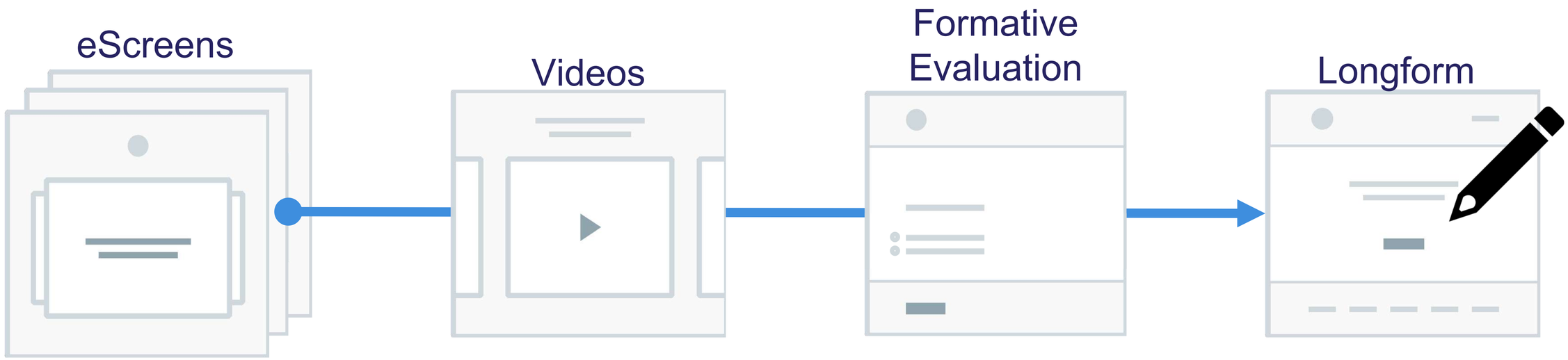
- Support decision making regarding the return of results on a study-by-study basis
- Promote high-quality individual research results
- Foster participant understanding of individual research results
- Revise and harmonize current regulations

Considerations

- What are the legal and regulatory obligations?
- Where is the appropriate balance between paternalism and participant autonomy?
- What information should and should not be returned to participants?
- How should you support participant decision-making and receipt of information?
- How can you overcome issues of equity and cultural sensitivity?



Broad Accessibility | Informed Consent



https://allofus.nih.gov/about/protocol/all-us-consent-process

yes means yes.

everything else means no.

Consent vs . Informing Loops | DNA Results Example

Consent to Get DNA Results

Overall potential risks and benefits of learning DNA results

General overview of DNA, variants, limitations of current knowledge

Legal information, disclaimers, and resources

Choice to be offered for each DNA result type in the future (as available)

Shared Emphasis on…

Participant Choice

Research Results

Informing Loops

Potential risks and benefits of that specific type of DNA result

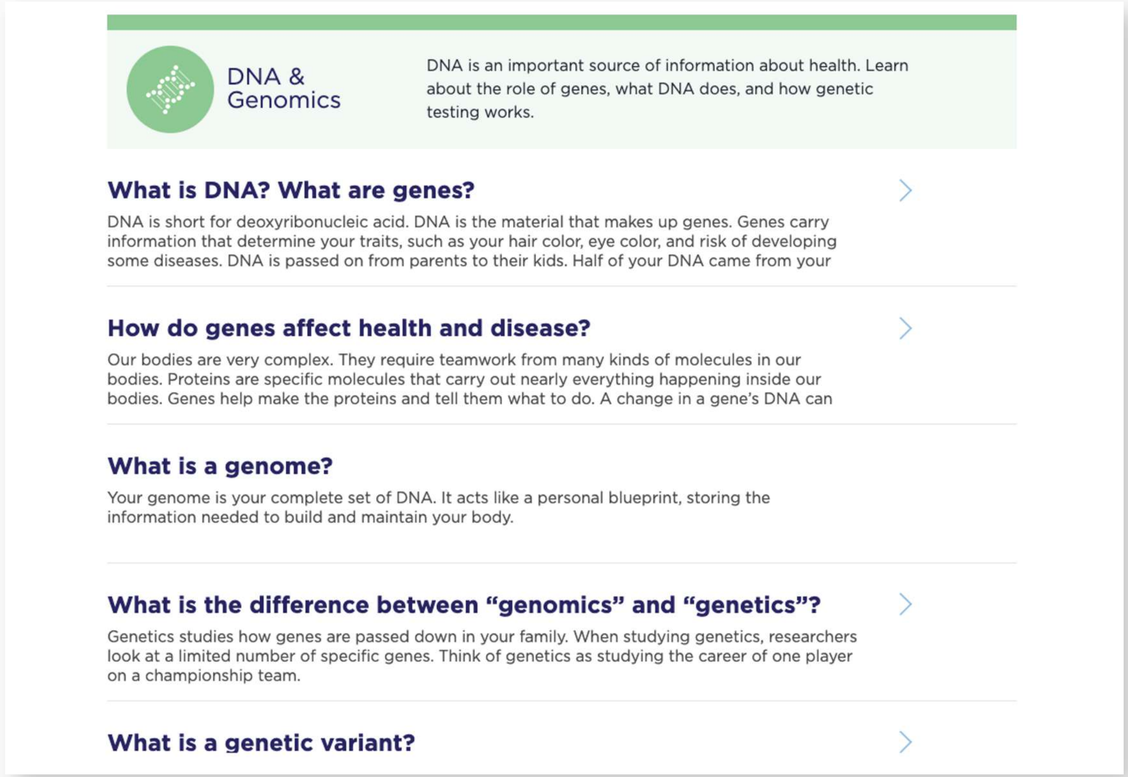
Examples of the type of information one could learn from that type of DNA result and limitations of those results

Link to Learning Center to help participants find more information

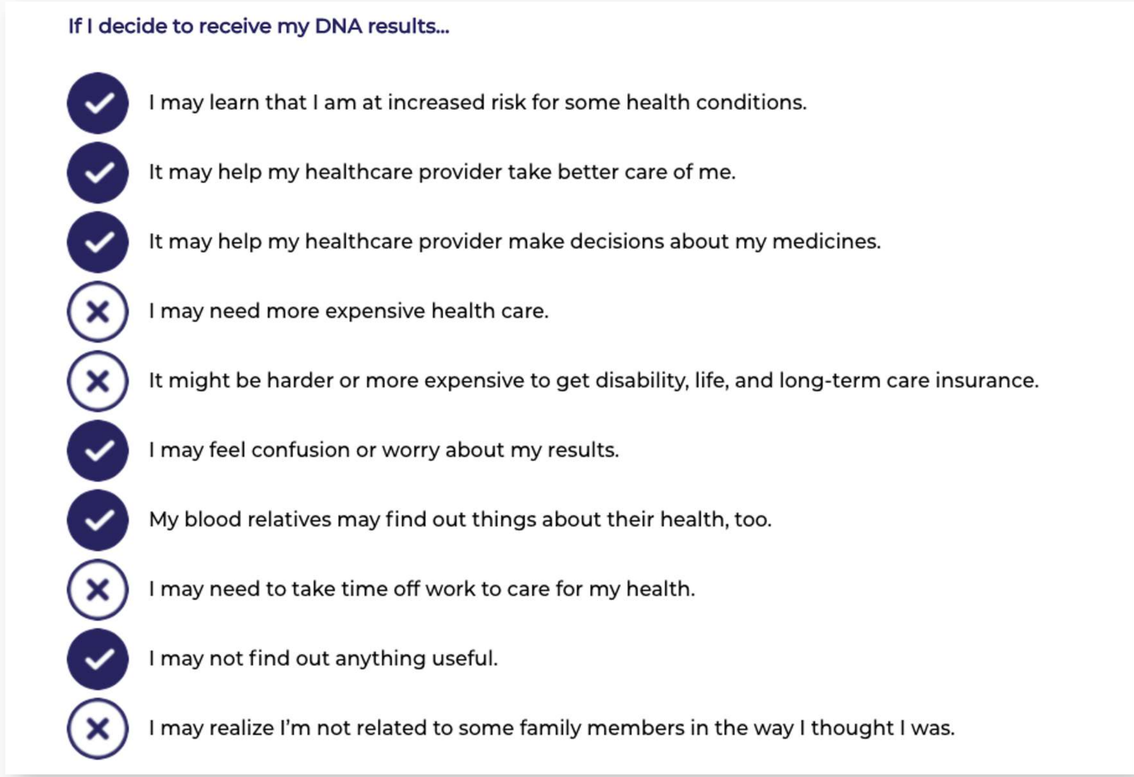
Choice to receive that specific type of result

All of Us Participant Educational and Decision Support

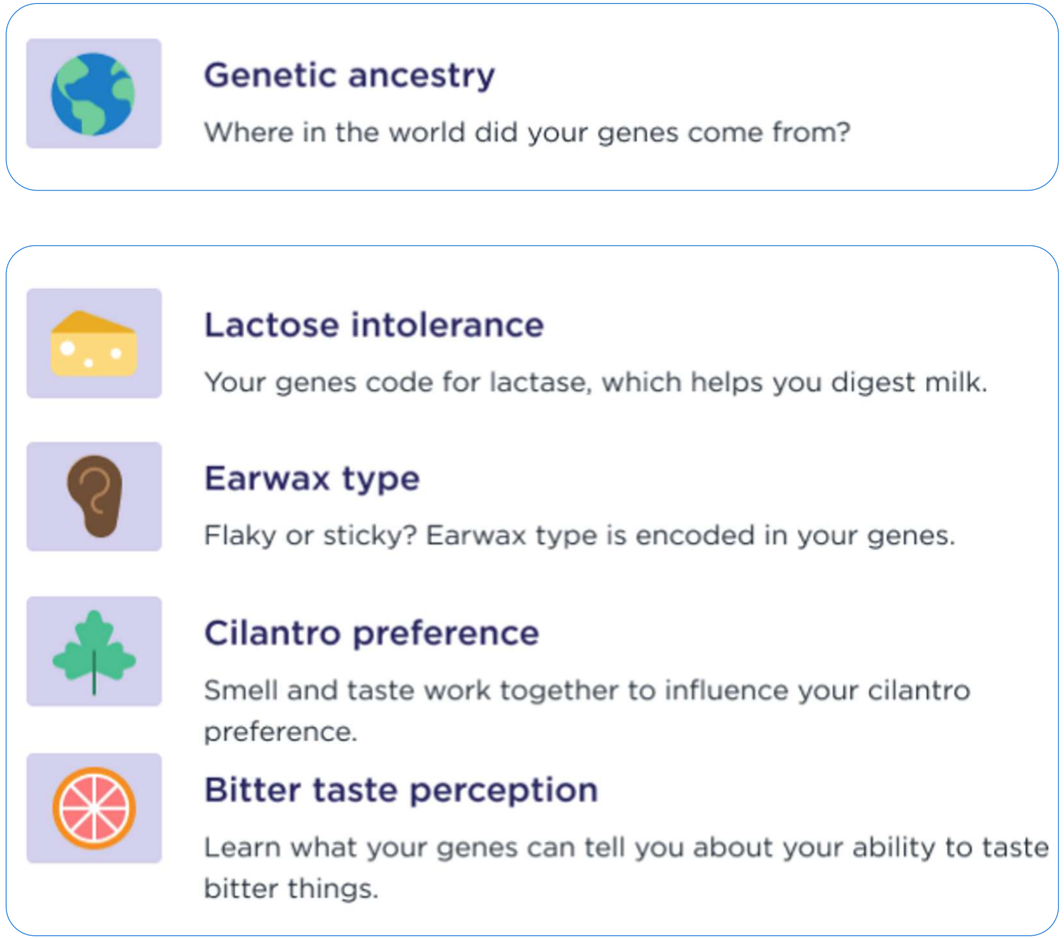
Participant Learning Center



Decision Tool



DNA Results | Ancestry and Traits



- Began returning results in late 2020
- >34 K notified they can get results if they want to
- >25 K said “Yes” to getting Genetic Ancestry and Traits results
- >20 K viewed genetic ancestry results
- >18 K have viewed at least one trait result
- **Biggest complaint: “I want to know more.”**

Available Now

DNA Results | Health-Related Information

IDE approved July 2020

- DNA from blood; supplement for saliva in process
- Returning ACMG 59 and PGx CPIC A

Genetic counselors will return P/LP results

Downloadable/Printable Reports

- Ability to send report directly to health care provider
- Technical section for health care providers

not quite here yet!

Lessons Learned | Genetic Ancestry and Traits

- **Commercial Product vs. Government Research Product**
  - We are not a DTC testing service, but we are returning many of the same results
  - Need to set appropriate expectations
- **Fine Line Between Traits and Health-Related Information**
- **Diverse Population Needs**
  - Cultural Competency/Sensitivity - returning results with appropriate contextual information
  - Return of Value - who determines what is of value?
- **Clarity** - Clear information on key concepts to prevent biologizing of social and other non-biological constructs
  - Race/Ethnicity
  - Ancestry
  - Genetic Ancestry

Lessons Learned | Health-Related Results

- **Participant Choice**
  - Learn about and decide on each result type *before* results are generated
  - Can choose for each result type independently

- **Bridging the Digital Divide**
  - PDF reports vs. interactive web results

- **State-level laws for genetic analysis**
  - Florida law - must offer to send results of genetic testing to physician. Why not offer to all participants, regardless of state?

- **Obtaining an Investigational Device Exemption (IDE) from the FDA**
  - Ties the program’s consent to FDA purview
  - Providing comprehensive overview and all related materials helped establish a clearer picture