Informed Consent When Considering Returning Genetic Results to Survey Participants: The Informed Consent *Process*

Michelle N. Meyer, PhD, JD

Associate Professor and Chair, Department of Bioethics & Decision Sciences
Faculty Co-Director, Behavioral Insights Team
Geisinger

Geisinger

Disclosures

- Member, All of Us Consent Working Group (and several other AoU working groups/task forces), 2016–2017; no current relationship with AoU, views expressed are not those of AoU

- Relevant funding : NIH

Granularity & timing of participant choices regarding RoR

Minimal choice

RoR bundled w/biobank study; decision made up front about enrollment + R0R

Considerations:

- Participant preference
- Selection bias due to bundling RoR and study?

Can choose to receive/decline results *by category* (e.g., all hereditary disease reports, all PGx)

Maximal choice

Can choose to receive/decline *each and every* result (e.g., BRCA1/2, APOE)

Considerations:

- Resource/logistical challenges of tracking granular choices
- Preferences may change over time, while participants may forget they are in the study, creating solicitation/tracking challenges
- Ethical issues/moral distress when you have actionable information you can't disclose

eConsent: A scalable approach to improve comprehension?

- Research consent forms are long, complex, and suboptimally relevant (Kass et al., J Gen Intern Med 2011)
- Post-consent comprehension generally poor (Joffe et al., Lancet 2001; Appelbaum, AJOB 2012)
- Studies of interventions to improve consent comprehension (multimedia, concise forms, extended conversations) are mixed (Grady et al., PLoS ONE 2017; Flory & Emanuel, JAMA 2004; Kass et al., Clin Trials 2015)
- Lots of enthusiasm for eConsent for a variety of reasons (Bieseker et al., RTI Press 2019; Kraft, Garrison, Wilfond, AJOB 2019; De Sutter et al., JMIR 2020), but dearth of high-quality RCT evidence supporting it (De Sutter et al., JMIR 2020)
- One prominent version of eConsent is the open source, smartphone-based eConsent developed by Sage Bionetworks, led by Megan Doerr, John Wilbanks (Doerr, Suver & Wilbanks, SSRN 2016; Wilbanks, JLME 2018)
  - 2017: Adopted by Apple's ResearchKit
  - 2018: Adopted by *All of Us* (with brief animated videos added)
- Sage Bionetworks eConsent has been shown to be feasible, with positive indications of informedness about most of the key concepts tested (Doerr et al., JMIR mHealth and uHealth 2017; Doerr et al., AJOB Empirical 2021), but never compared to standard (human conversation-based) consent in an RCT
- NAS: Promising, but "dearth of evidence regarding the advantages and disadvantages of electronic methods in terms of understanding of information" (Returning Individual Research Results to Participants, 2018, pp. 207–8)

Trial to Compare eConsent With Standard Consent Among Prospective Biobank Participants

(NCI R01CA211723-03S1; ClinicalTrials.gov Identifier: NCT04131062)

Collaborators

John Wilbanks
Megan Doerr, MS, LGC
Jennifer Wagner, JD, PhD
Randi Vogt, PhD
Rebecca Mestechkin, BS
Tami Gjorgieva, BS
Daniel Rosica, MS
Anh Huynh, BS

Acknowledgements

MyCode consenters
Alanna Rahm, PhD (parent award PI)
MyCode PIs and leadership
Geisinger patient-participants

Geisinger IRB NUMBER: 2006-0258
IRB Approved: 12/14/2018

RESEARCH CONSENT/AUTHORIZATION FORM

TITLE OF STUDY: Geisinger MyCode® Community Health Initiative
PRINCIPAL INVESTIGATORS: DJ Carey, PhD, DH Ledbetter, PhD, AC Sturm, MS, LGC
QUESTIONS OR PROBLEMS: 1-855-636-0019 (toll free)
24-HOUR HOSPITAL SWITCHBOARD: 570-271-6211

Geisinger Clinic invites you to take part in a project called the MyCode® Community Health Initiative (MyCode for short). By signing up for MyCode you agree to allow Geisinger to save your blood and saliva samples and use them for research. You also agree to allow scientists doing research with your samples to use information in your health record.

The goal of this research is to learn more about human health and disease to find better ways to keep people healthy and to help them when they are sick.

Please read this whole document carefully before you decide whether or not to take part in this research. Please keep this document for your records.

THIS FORM WILL TELL YOU:

- Why we are doing this research
- The benefits and risks of being a part of this research
- How we will collect samples of your blood or saliva
- How we will use your samples for research
- How we will protect your privacy

WHY DOES GEISINGER WANT TO KEEP MY BLOOD AND SALIVA SAMPLES?
Information that is in your blood or saliva can provide clues about your health and diseases you have or might get. Geisinger doctors and scientists want to do research to find these clues and learn how to use them to improve health.

Some of these clues are found in your DNA (which is also known as deoxyribonucleic acid). DNA makes up your genes. Genes provide instructions for things like eye or hair color, height, and sometimes things that affect health. Everyone's DNA is slightly different. By studying the DNA of many different people and comparing it to information in their health records we hope to find differences in DNA that help people stay healthy or in some cases get sick. Your blood also contains proteins and other chemicals that can provide clues about your health and we may also study those.

Many people are needed to provide samples to do this research. We have samples from tens of thousands of Geisinger patients, and plan to collect more. Our goal is to enroll up to 500,000 Geisinger patients in this project.

MyCode is a project of Geisinger Clinic. MyCode activities (such as collecting, storing, or testing samples) may be paid for by the following sources:

- Geisinger's own funds;
- Government grants;
- Grants from non-profit agencies that support research; and/or
- Commercial partners (such as drug companies)

Study: 2006-0258
Version Number: 33
Date: 1/2/2019 Page 1 of 7

vs.

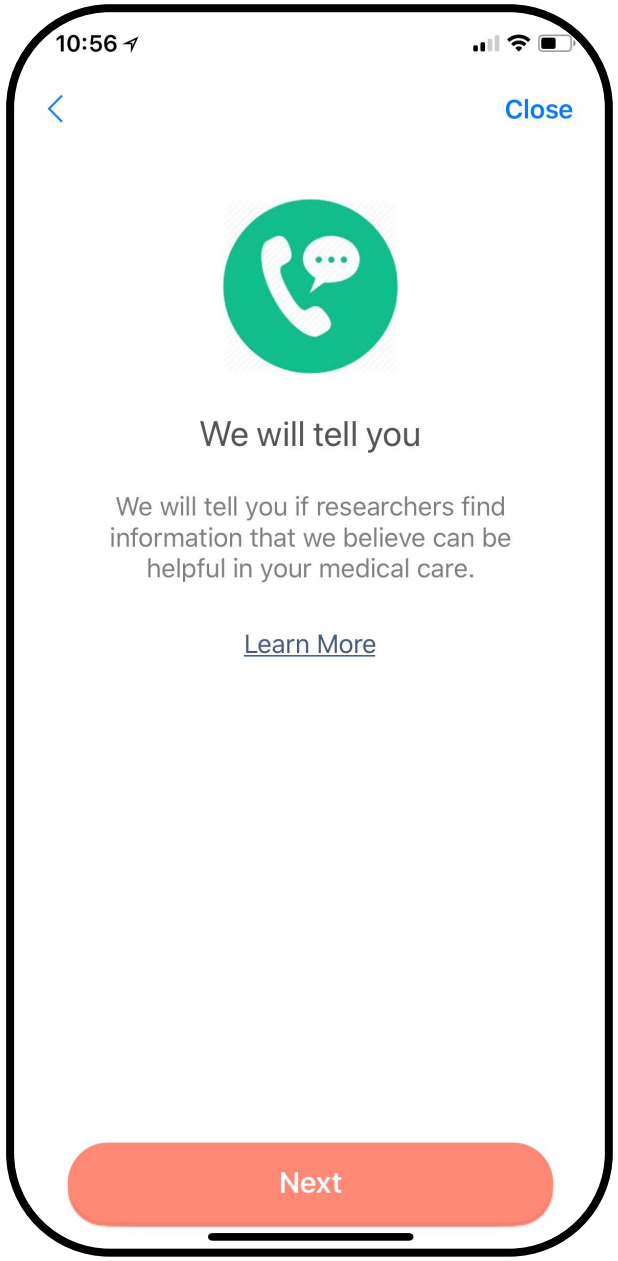
Trial to Compare eConsent With Standard Consent Among Prospective Biobank Participants

(NCI R01CA211723-03S1; ClinicalTrials.gov Identifier: NCT04131062)

<u>MyCode basics</u>:

- Based at Geisinger, non-profit, integrated health system serving ~2M patients in largely rural central and northeast PA
- Unselected research biobank; any Geisinger patient is eligible
- Primary recruitment: primary & specialty clinic waiting rooms
- Clinically actionable (ACMG+) only: ~3% of participants
- 320,125 consented participants
- No age minimum for MyCode, but eConsent study limited to adults
- 2018 survey (unpublished): “Was RoR relevant to your enrollment decision?”:
  - — Among those who *enrolled*: 61% Yes
  - — Among those who *declined*: 15% Yes
  - — Among those who were *undecided*: 28% Yes

Iconographic representation of key concepts



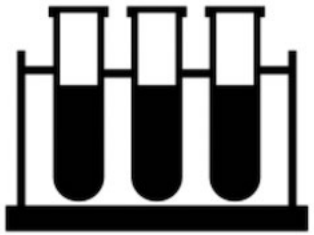
What do I need to do?

Your family

Risk To Privacy

You Get To Choose

Will you share my data?



How will we do this research?

What will we be looking for?

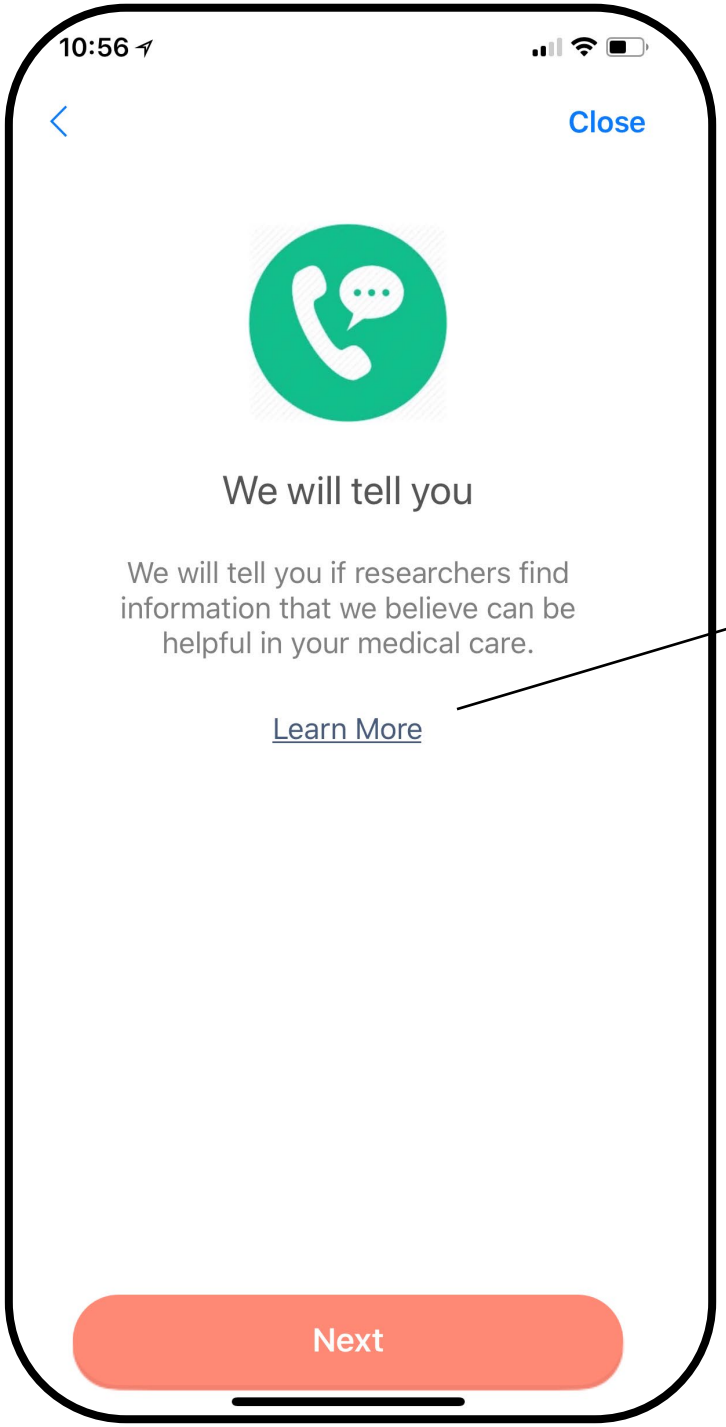
Information about your health

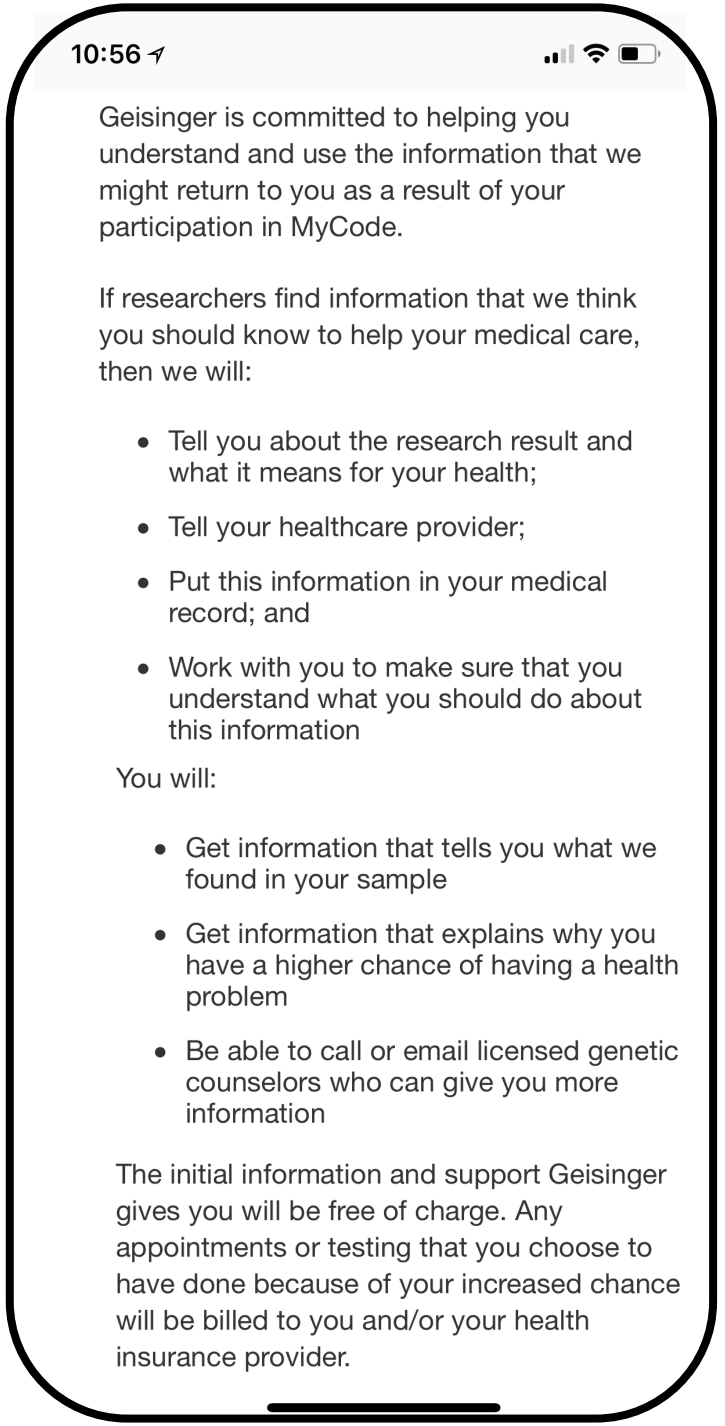
Other Risks

Costs and Payments

Tiers of Information Architecture

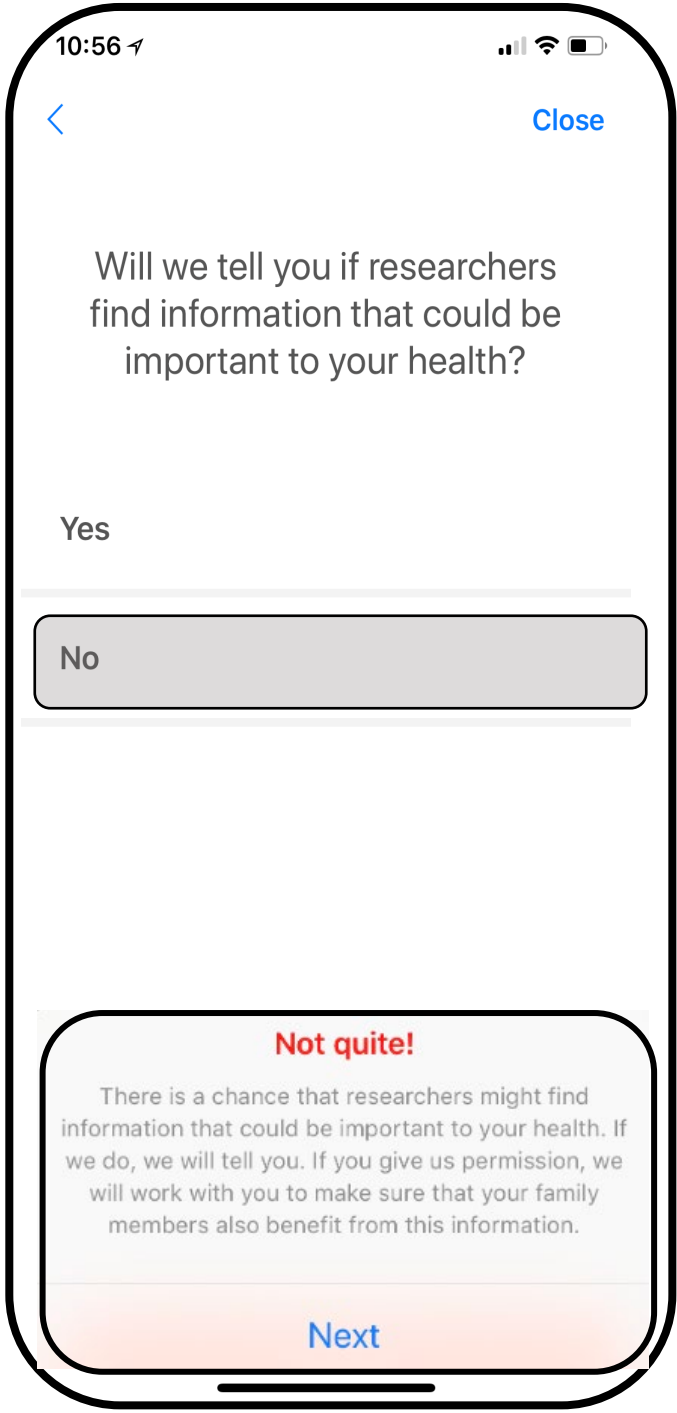
Facilitates different informational needs





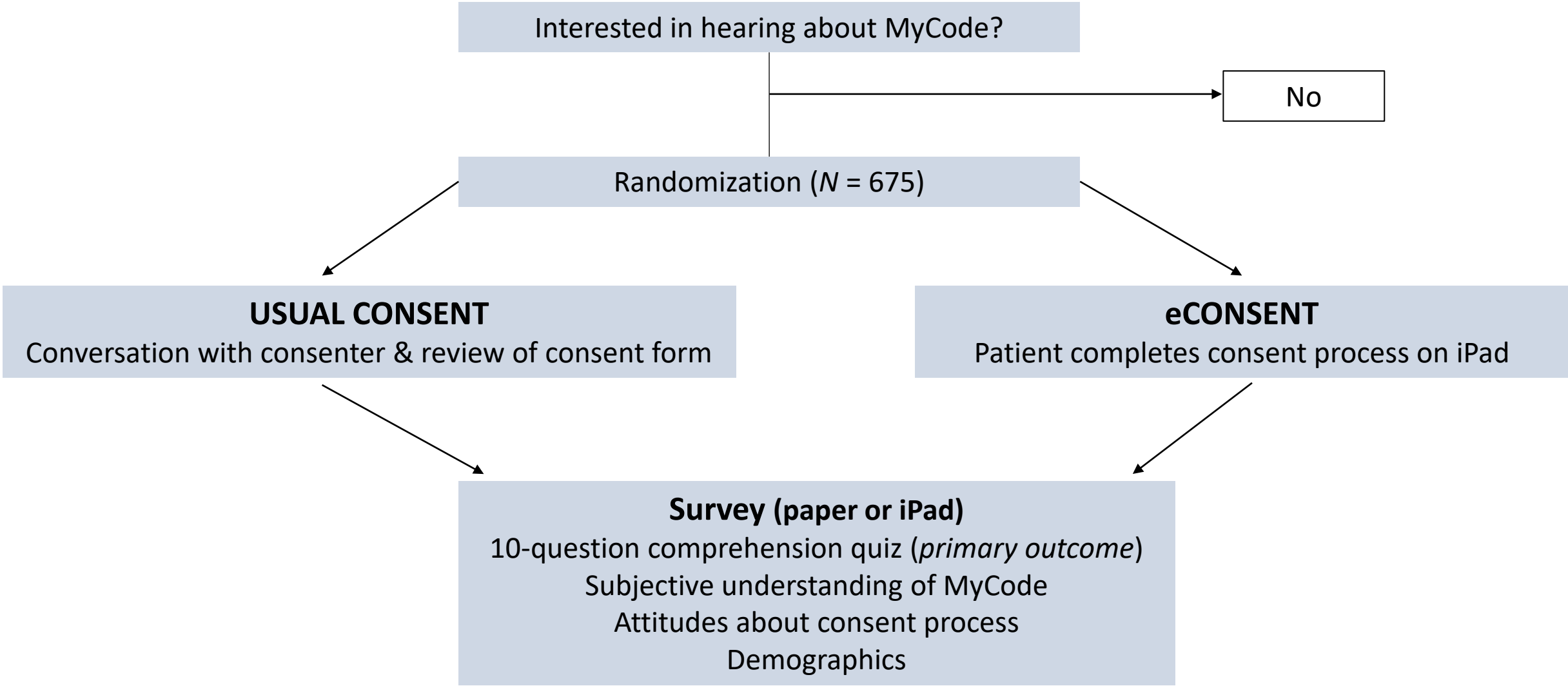
Teachback Questions

Reinforces learning of key concepts



Trial to Compare eConsent With Standard Consent Among Prospective Biobank Participants

(NCI R01CA211723-03S1; ClinicalTrials.gov Identifier: NCT04131062)

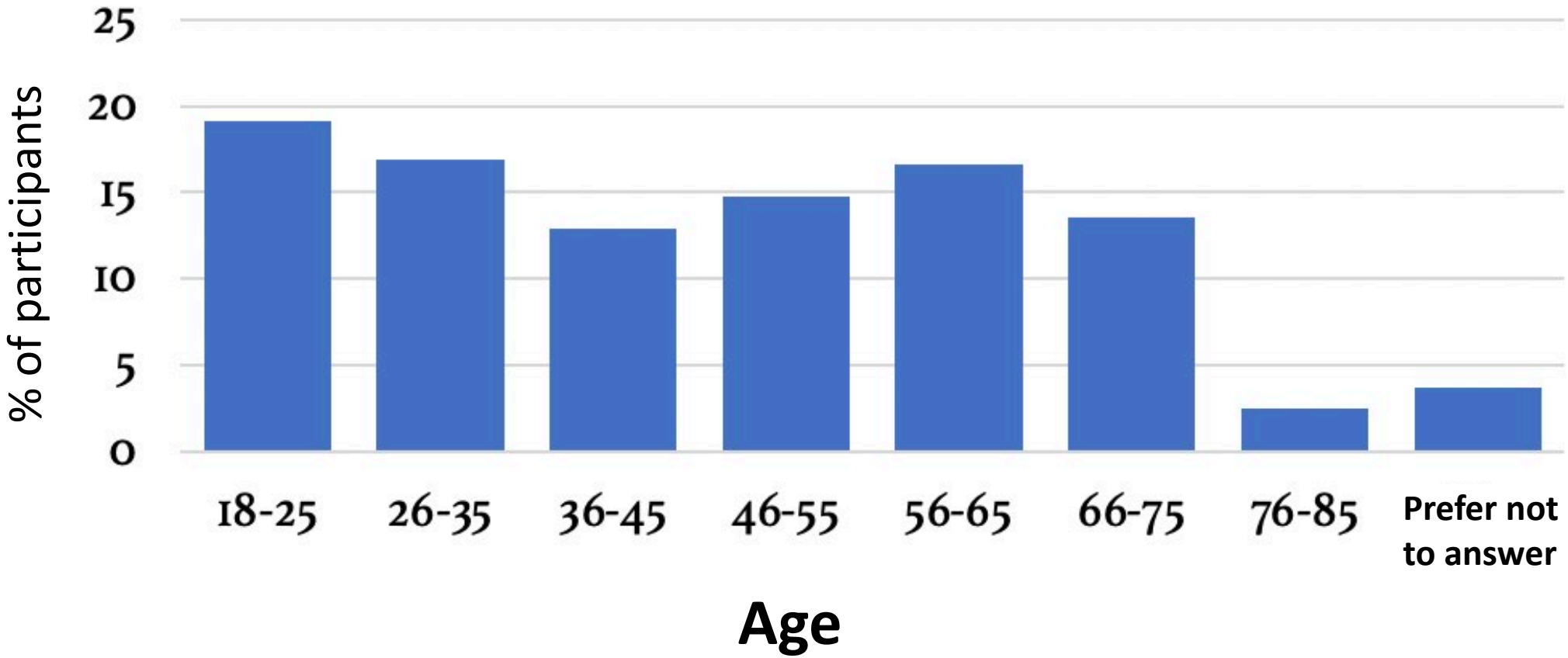


Sample Characteristics (self-reported)

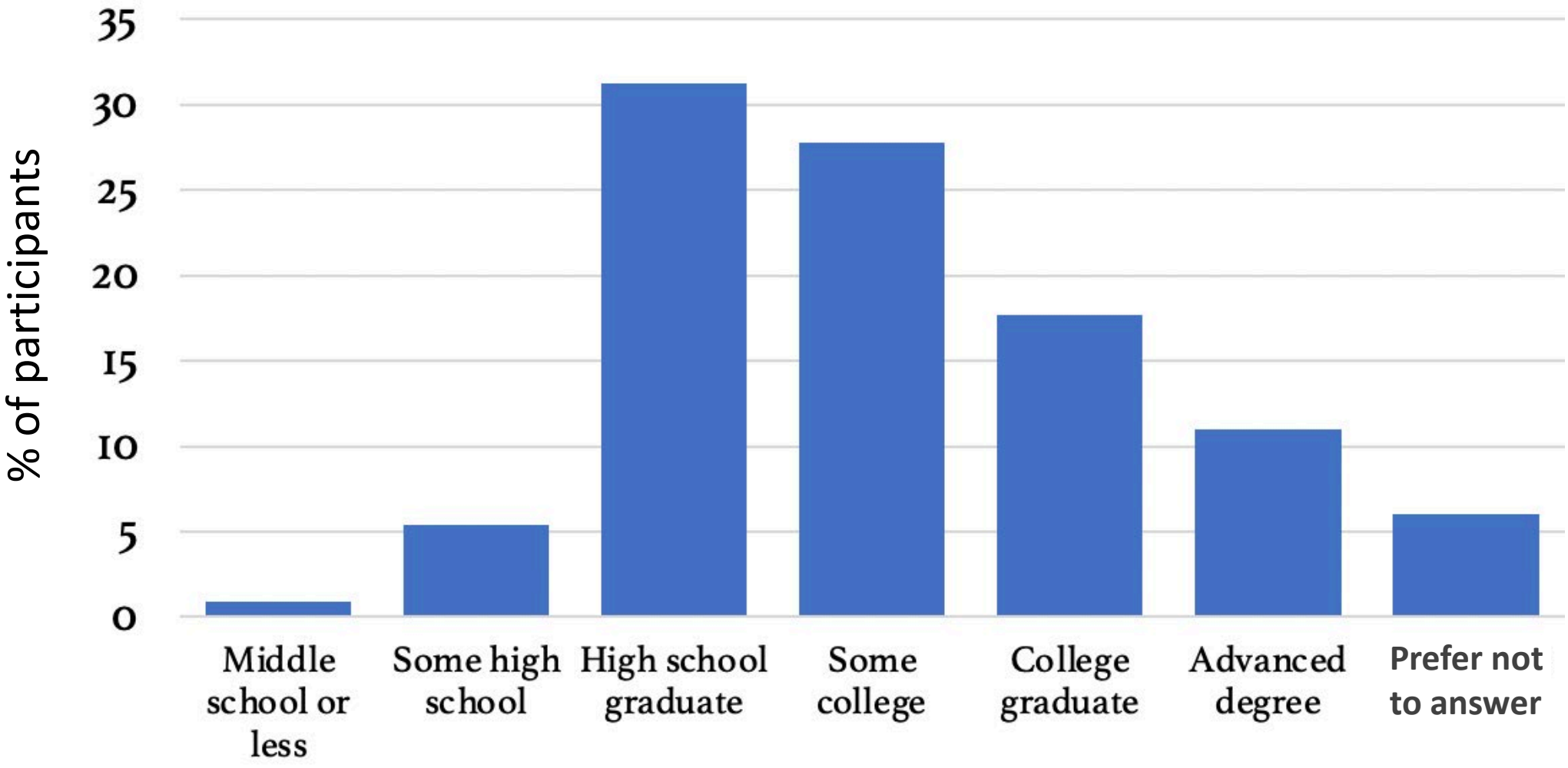
- Sex assigned at birth: 63% female
- Gender identity: 63% woman
- 17% declined/deferred needed healthcare because they couldn't afford it
- "How often have you gotten healthcare information that was easy to understand?": 15% said none or some of the time
- Use a personal computer (66%); use a smartphone (85%)

Race/Ethnicity (select all that apply)	Share of participants (rounded)
American Indian or Alaska Native	0.6%
Asian	1.5%
Black, African American, or African	3.0%
Hispanic, Latino, or Spanish	4.0%
Middle Eastern or North African	0.0%
Native Hawaiian or other Pacific Islander	1.0%
White	86.0%
None of these fully describe me	0.3%
Prefer not to answer	4.0%

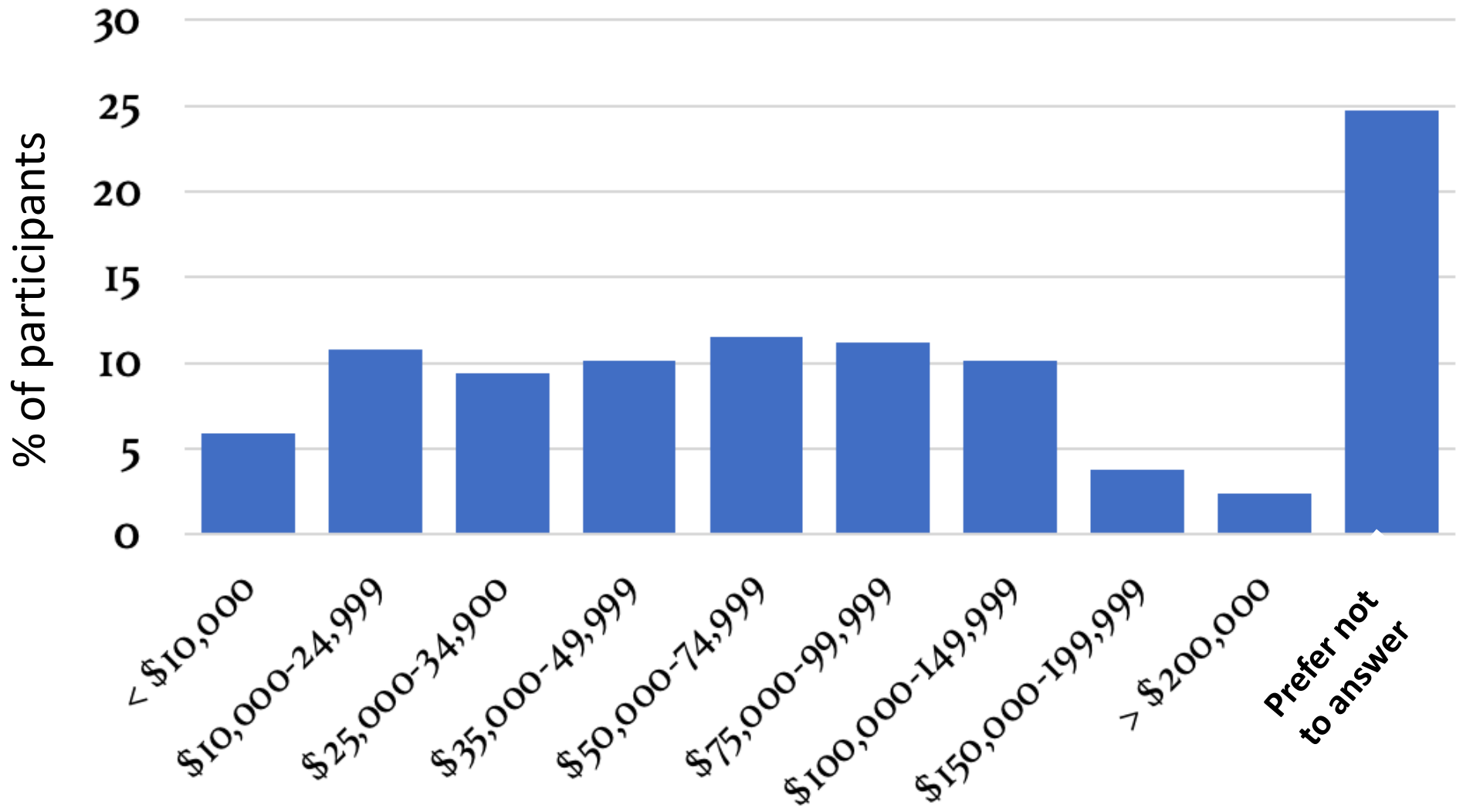
Sample Characteristics (self-reported)



Sample Characteristics (self-reported)



Sample Characteristics (self-reported)



Select Results: Objection & Subjective Comprehension

	Standard Consent	eConsent	*p* value
Mean quiz score (out of 10)	76%	87%	<0.0001
Mean score is directionally better in eConsent arm for every question			
Mean quiz score (out of # of questions attempted)	82%	88%	<0.0001
Mean score is directionally better in eConsent arm for every question			

Select Results: Objection & Subjective Comprehension

	Standard Consent	eConsent	*p* value
Mean quiz score (out of 10)	76%	87%	<0.0001
Mean score is directionally better in eConsent arm for every question			
Mean quiz score (out of # of questions attempted)	82%	88%	<0.0001
Mean score is directionally better in eConsent arm for every question			
% of participants who correctly answered each teachback question	—	73%* , 100%, 96%, 99%, 94%, 100%	—

* Five of six questions ranged from 94–100% correct. The *first* question ("What will we study?") is the outlier (73% answering correctly). This may have prompted participants to start paying attention.

Select Results: Objection & Subjective Comprehension

	Standard Consent	eConsent	*p* value
Mean quiz score (out of 10)	76%	87%	<0.0001
Mean score is directionally better in eConsent arm for every question			
Mean quiz score (out of # of questions attempted)	82%	88%	<0.0001
Mean score is directionally better in eConsent arm for every question			
% of participants who correctly answered each teachback question	—	73%* , 100%, 96%, 99%, 94%, 100%	—
"How well do you think you understand MyCode?" (4-pt Likert)	Not at all/a little: 28% Pretty/very well: 72%	Not at all/a little: 26% Pretty/very well: 74%	0.60
"How difficult did the informed consent process feel to you?" (4-pt Likert)	Pretty/very difficult: 3% Pretty/very easy: 97%	Pretty/very difficult: 3% Pretty/very easy: 97%	0.75

* Five of six questions ranged from 94–100% correct. The *first* question ("What will we study?") is the outlier (73% answering correctly). This may have prompted participants to start paying attention.

Select Results: Actual & Sense of Consent Process Length

	Standard Consent	eConsent	*p* value
Mean consent process time (minutes)	1.5	3.6	<0.0001
"How long did the informed consent process feel to you?" (4-pt Likert)	Very/pretty long: 4% Very/pretty quick: 96%	Very/pretty long: 12% Very/pretty quick: 88%	0.004

Select Results: Predictors of Comprehension

No significant correlation in *either arm* between quiz score and:

- age
- sex assigned at birth
- gender identity
- health literacy
- race/ethnicity (due to power, binarized as white/non-Hispanic (85%) vs. all others (15%))

Education and income predict comprehension in both arms . . . but no more in the eConsent arm (and with respect to education, the correlation is directionally smaller in the eConsent arm):

Variables	Standard Consent Correlation	eConsent Correlation	*p* value
Education & quiz score (out of 10)	0.30 (p = 0.0001)	0.18 (p = 0.06)	0.30
Income & quiz score (out of 10)	0.21 (p = 0.02)	0.29 (p = 0.005)	0.54

Select Results: Choosing to “Learn More”

Choosing to “learn more” about a concept was an infrequent behavior: only 14% of participants clicked on *any* of the 13 “learn more” links

About which topics did participants most frequently choose to “learn more”?

- privacy risks (7%)
- data sharing (6%)
- what do I need to do (4%)
- relevance to your family (4%)
- we will tell you (3%)
- 8 others: ≤ 3%

eConsent vs. Standard Consent: Concluding Considerations

1. Length of consent process
   - On one hand, eConsent takes (and feels) longer ☹
   - On the other hand, eConsent takes (and feels) longer ☺

2. Not everyone is comfortable with technology
   - Of those randomly assigned to iPad, **6.7%** declined the iPad
   - Can switch these individuals to standard consent (in-person or phone)
   - That % likely to drop over time due to demographics and continued technology diffusion

3. Scalability/outreach, preference tracking, and standardization
   - eConsent may allow consenters with minimal genomics expertise to facilitate the consent process (or for consent to be entirely self-serve for many); can be critical for reaching rural populations)
   - eConsent can facilitate tracking of participant choice (e.g., re: RoR)
   - Human-mediated consent can reflect bias (e.g., presumptions about who might want results or need/not need to hear certain things) or simply unwarranted variation in consenter approach that eConsent helpfully standardizes

4. Teachback questions → comprehension thresholds?
   - Any threshold for enrollment should reflect risks of enrollment/RoR with poor comprehension of the *particular* concept(s)—*and* risks of *excluding* participants from study/RoR (Personal Genome Project vs. AoU)

Thank You