Evidence of Uptake and Action in Response to Screening Programs

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Two Cohorts

Population Cohort

Genotyping array
Variant analysis
Return of results of actionable variants
Genetic counseling
Supportive care

Rare Disease Cohort

Whole genome sequencing
Variant analysis
Return of results of pathogenic variants
Genetic counseling
Supportive care

DNA/Tissue Bank

Genomic Database
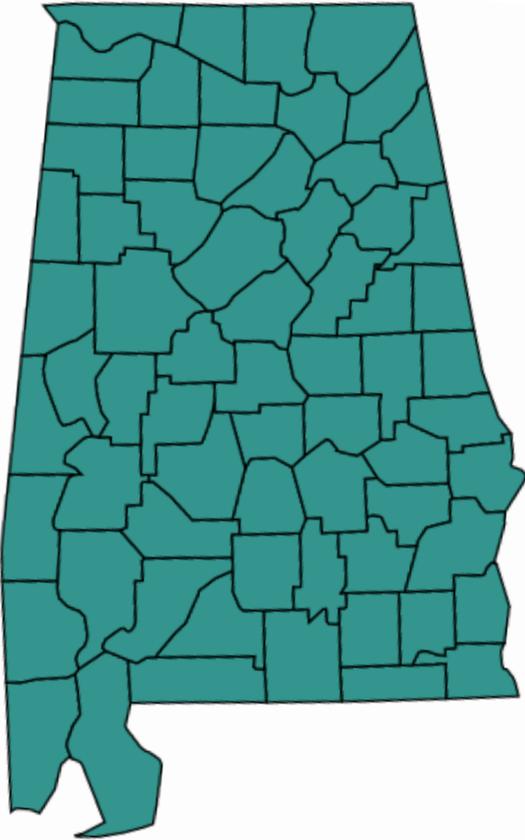
Medical Records (i2b2)

Population Cohort Enrollment Demographics

ENROLLMENT BY RACE

- ■ American Indian or Alaskan (0.33%)
- ■ Asian (2.24%)
- ■ Black or African American (20.99%)
- ■ Native Hawaiian or Other Pacific Islander (0.05%)
- ■ Unknown (2.15%)
- ■ White (70.84%)
- ■ More Than One Race (3.41%)

3.16% of participants are Hispanic/Latinx

75%   25%
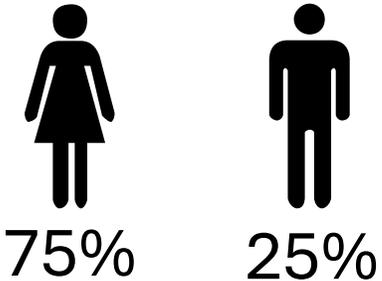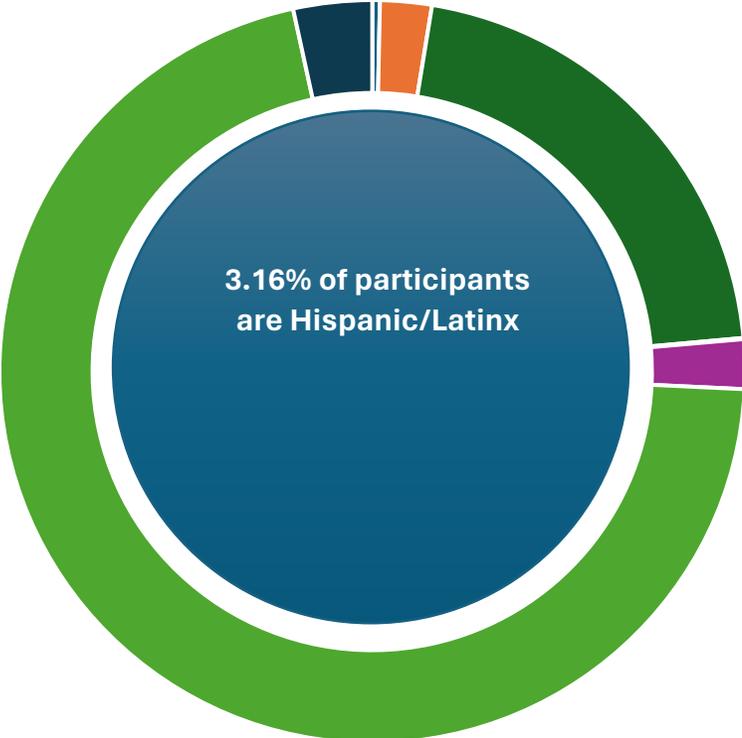
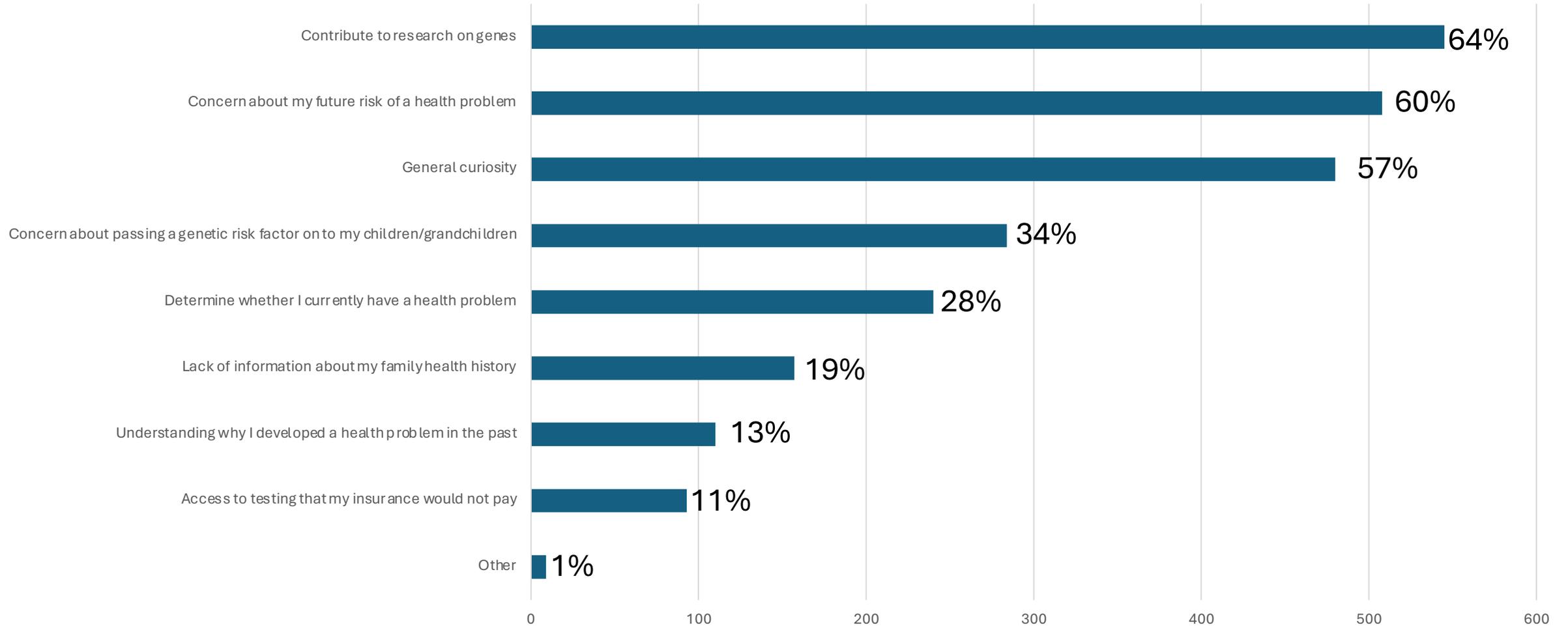# Cumulative Population and Clinical Cohort Enrollment

- 7628 participants

- 67 of 67 counties

- 93 actionable results returned in population cohort (ended in March 2020)

- 30 actionable results return in clinical cohort

    = 1.5% of general population

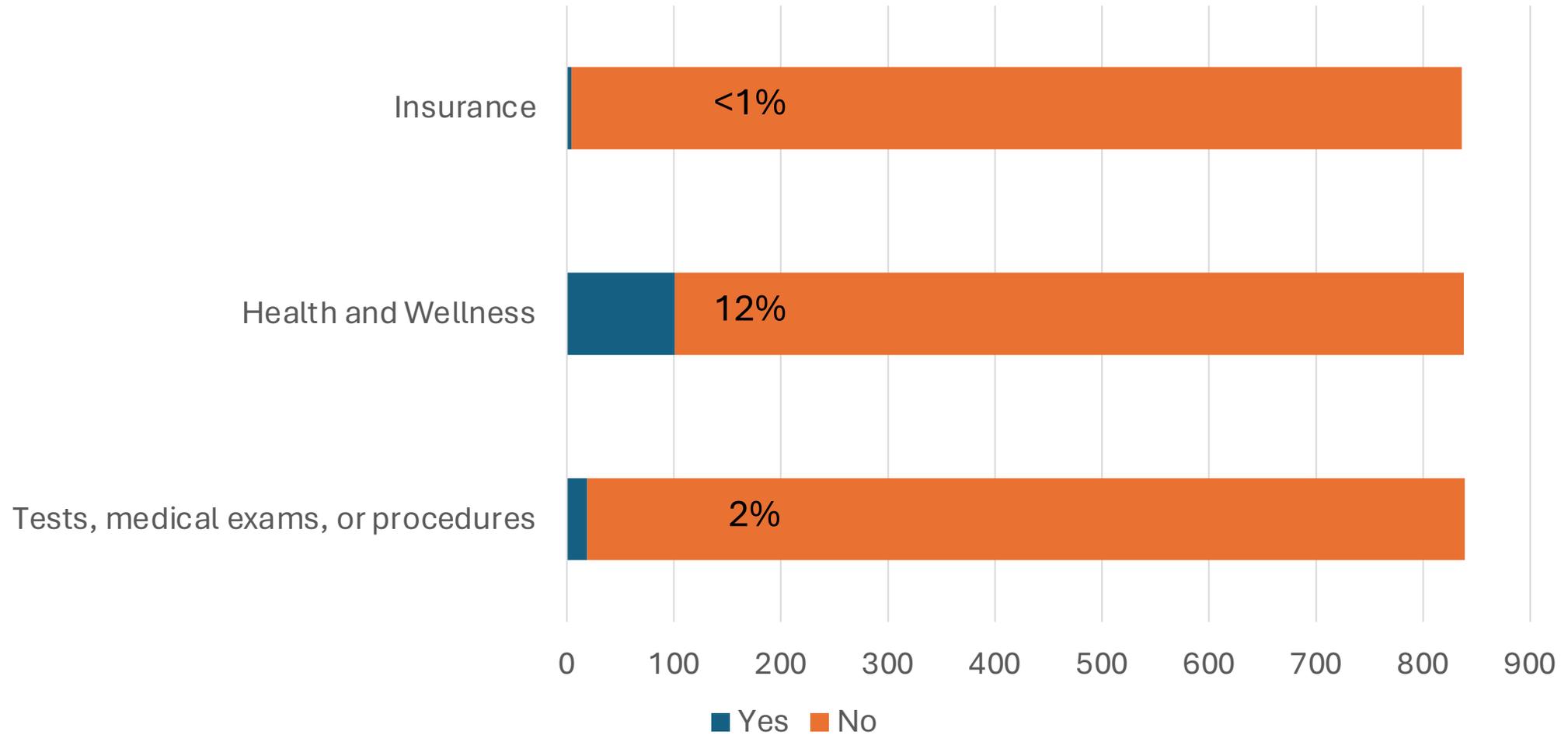# Actionable Findings in the Clinical and Population Cohort

Type	Genes
Tumor Predisposition Breast/ovarian, Li-Fraumeni, Peutz-Jeghers, Lynch, Polyposis, Von Hippel-Lindau, MEN1/2, Medullary thyroid cancer, PTEN hamartoma syndrome, Retinoblastoma, Paraganglioma/pheochromocytoma, Tuberous sclerosis complex, WT1-related Wilms' tumor, NF2	*BRCA1/2, TP53, STK11, MLH1, MSH2, MSH6, PMS2, APC, MUTYH, BMPR1A, SMAD4, VHL, MEN1, RET, PTEN, RB1, SDHD, SDHAF2, SDHC, SDHB, TSC1, TSC2, WT1, NF2* *New: PALB2, MAX, TMEM127*
Connective Tissue Dysplasia Ehlers-Danlos vascular type, Marfan, Loeys-Dietz, Familial aortic aneurysms and dissections	*COL3A1, FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYH11*
Cardiac Hypertrophic cardiomyopathy, dilated cardiomyopathy, Arrhythmia	*MYBPC3, MYH7, TNNT2, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, GLA, MYL2, LMNA, RYR2, PKP2, DSP, DSC2, TMEM43, DSG2, KCNQ1, KCNH2, SCN5A* *New: CASQ2, TRDN, FLNC, TTN*
Metabolic Hypercholesterolemia, Wilson disease, Ornithine transcarbamylase deficiency	*LDLR, APOB, PCSK9, ATP7B, OTC* *New: BTD, GAA, HFE, TTR*
Pharmacogenetic Malignant Hyperthermia	*RYR1, CACNA1S*
Other	*New: HFE, ACVRL1, ENG, HNF1A, RPE65*

Updated 7/18/23

Motivations for Participating in AGHI

Motivation	Percentage
Contribute to research on genes	64%
Concern about my future risk of a health problem	60%
General curiosity	57%
Concern about passing a genetic risk factor on to my children/grandchildren	34%
Determine whether I currently have a health problem	28%
Lack of information about my family health history	19%
Understanding why I developed a health problem in the past	13%
Access to testing that my insurance would not pay	11%
Other	1%

Ashley Cannon, PhD, MS

Changes made following AGHI results:

Ashley Cannon, PhD, MS

AGHI Integration into Family Medicine

About the Testing

Genes are made up of DNA, which holds instructions that tell your body how to grow and function. DNA determines physical features, such as eye color and how tall you are.

DNA also affects the makeup of your internal tissues and organs, which can impact how quickly or slowly your body breaks down medications. In short, your genomic makeup can affect how well a medication works for you, your sensitivity to it, what dosage is least likely to cause side effects, and whether you might respond better to an entirely different medication.

That's where pharmacogenomic testing comes in. It can help your health care providers better understand your body before prescribing a drug, thereby increasing the chances that your treatment will be safe and effective.

Testing requires a blood sample, so that your DNA can be examined. Your physician and a pharmacist will review the results of your test before adding them to your electronic health record. Health care providers will be able to use this information to provide better care for you, now and in the future.

Alabama Genomic HEALTH INITIATIVE (AGHI)

PHARMACOGENOMIC TESTING

What You Need to Know

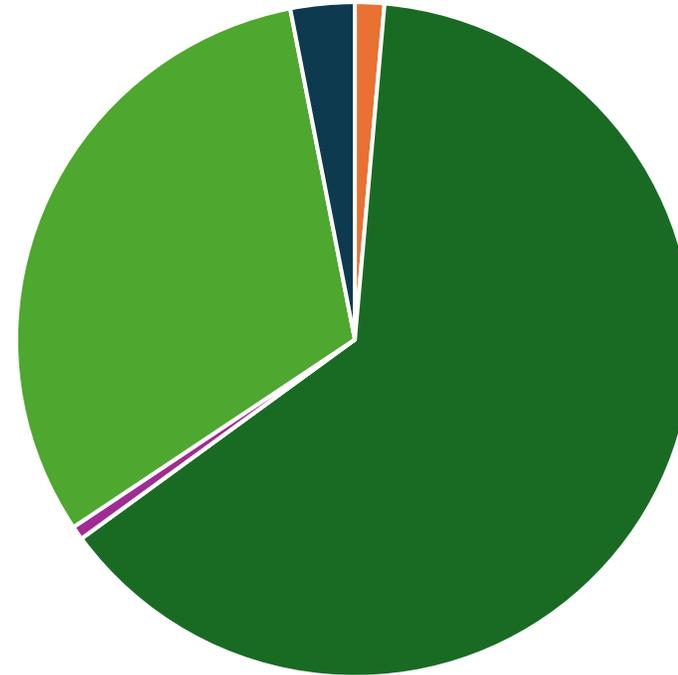| Enroll	Return Genomic Findings	Clinician Education
• Three Family Medicine Clinics	• Actionable Results • Pharmacogenetics	• Genomic Medicine • PGx

Clinical Cohort Recruitment By the Numbers

- American Indian or Alaskan (0%)

- Asian (1.4%)

- Black or African American (63.55%)

- Native Hawaiian or Other Pacific Islander (0%)

- Unknown (0.66%)

- White (31.32%)

- More Than One Race (3.06%)

73% FEMALE ♀   **27% MALE ♂**

1.24% of Participants Are Hispanic/Latinx

Updated 7/18/23

AGHI Community Advisory Board

Opportunity for AGHI leaders to share information about the project's goals, strategies, and findings with the advisory board through quarterly, virtual meetings. During these meetings, members of the board will participate in active discussion about these topics and provide feedback on behalf of the communities they represent.

Dr. Lori Bateman, PhD, RD, Assistant Professor
UAB Division of Preventive Medicine|School of Medicine

Kelly East, MS, CGC, Certified Genetic Counselor
Clinical Applications Lead
HudsonAlpha Institute for Biotechnology

Tiffany Osborne, Program Director II
Minority Health & Health Disparities Research Center
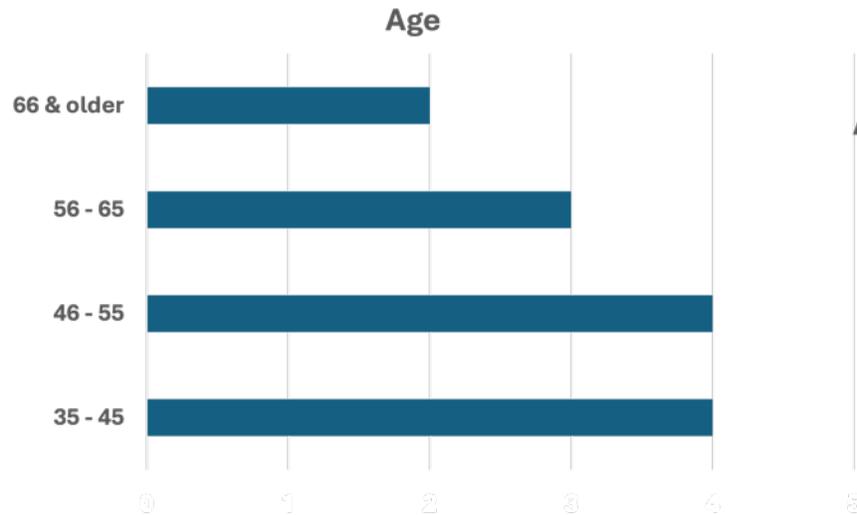UAB School of Medicine/Division of Preventive Medicine

Whitley Kelley, MS, CGC, Certified Genetic Counselor
HudsonAlpha Institute for Biotechnology

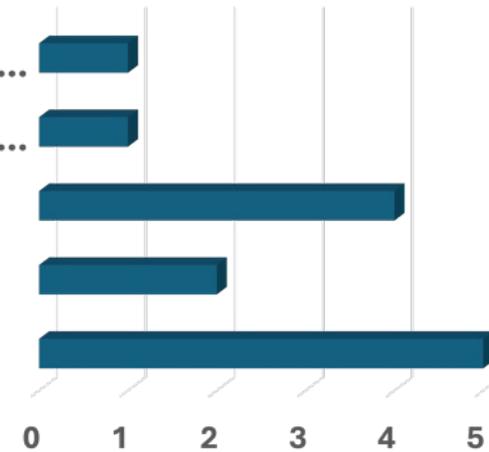# CAB Demographics

Gender

7 Males

7 Females

Age

66 & older	2
56 - 65	3
46 - 55	4
35 - 45	4

Race

Amer Indian/Native...	1
Ashkenazi Jewish...	1
White	4
Latinx	2
AA/Black	5

Ethnicity

2 - Hispanic

12 – Non - Hispanic

- Education
  - Graduate – 7
  - Bachelors – 3
  - Some college - 3

Method: CAB Meeting Topics

- December, 2021 – Participation, Increasing Access
- February, 2022—Recruitment
- May, 2022—Return of Results, Receiving Results
- October, 2022 – Genetic test results, family health risks
- June, 2023 – Experience being in the CAB

Survey Results- Participants

- Survey completion:
  - Pretest: N_{pre} = 14
  - Post-test: N_{post}=10
  - Matched: N = 10 (took pre and post-tests)
- Testing
  - Too small of Ns for significance testing; instead, focus on trends
- Note: Interpreting results:
  - Results from highly optimistic (+2) to highly pessimistic (-2), with "0" as neutral.

Optimism Toward Genomic Medicine

- Mean (M) SCALE: Very Likely = +2; Very unlikely = -2
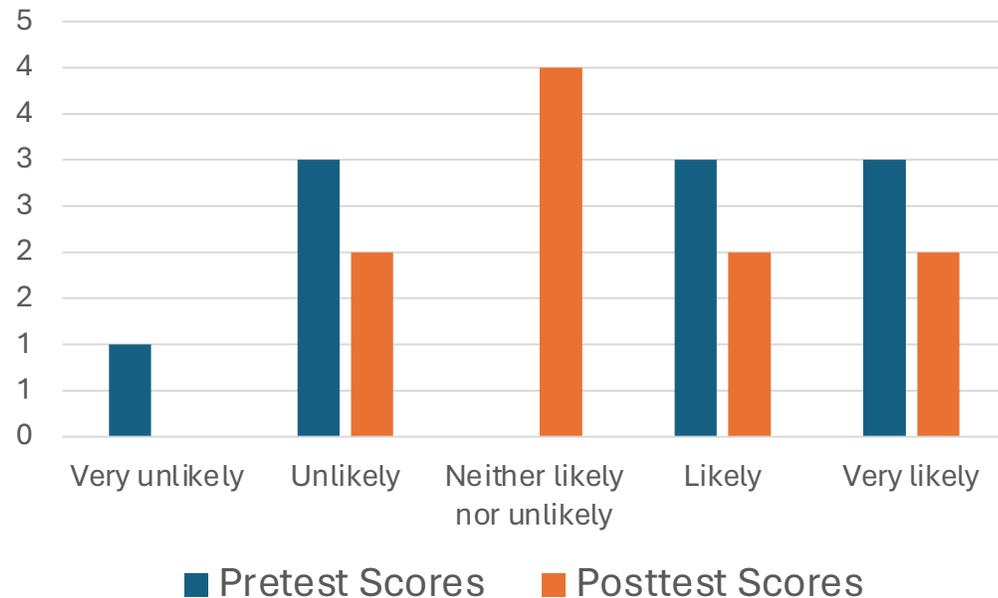
> *Optimism slightly **decreases***

  - (M_{pre}=1.12, M_{post}=0.79)
  - Overall, there is a small change, with a slight decrease (0.33) in optimism

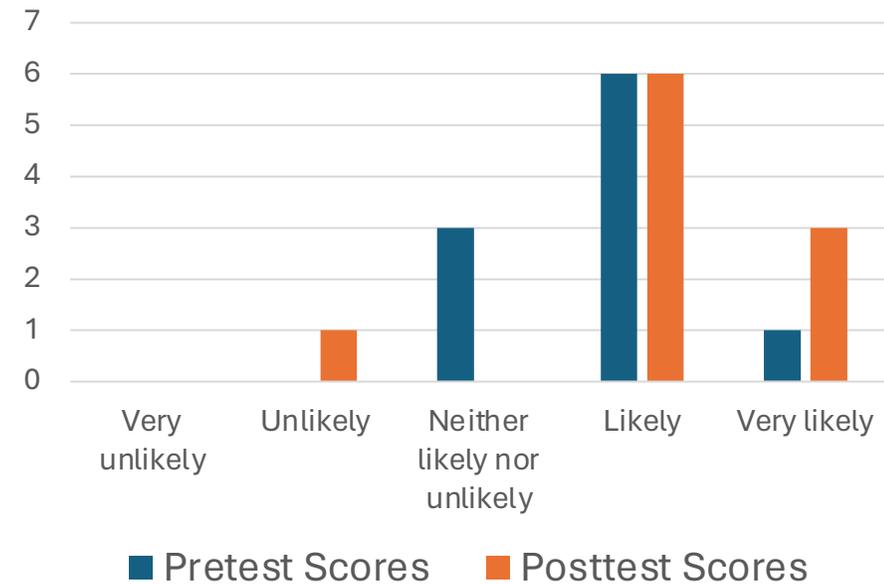Mean Scores for Optimism toward Genomic
Category of Questions
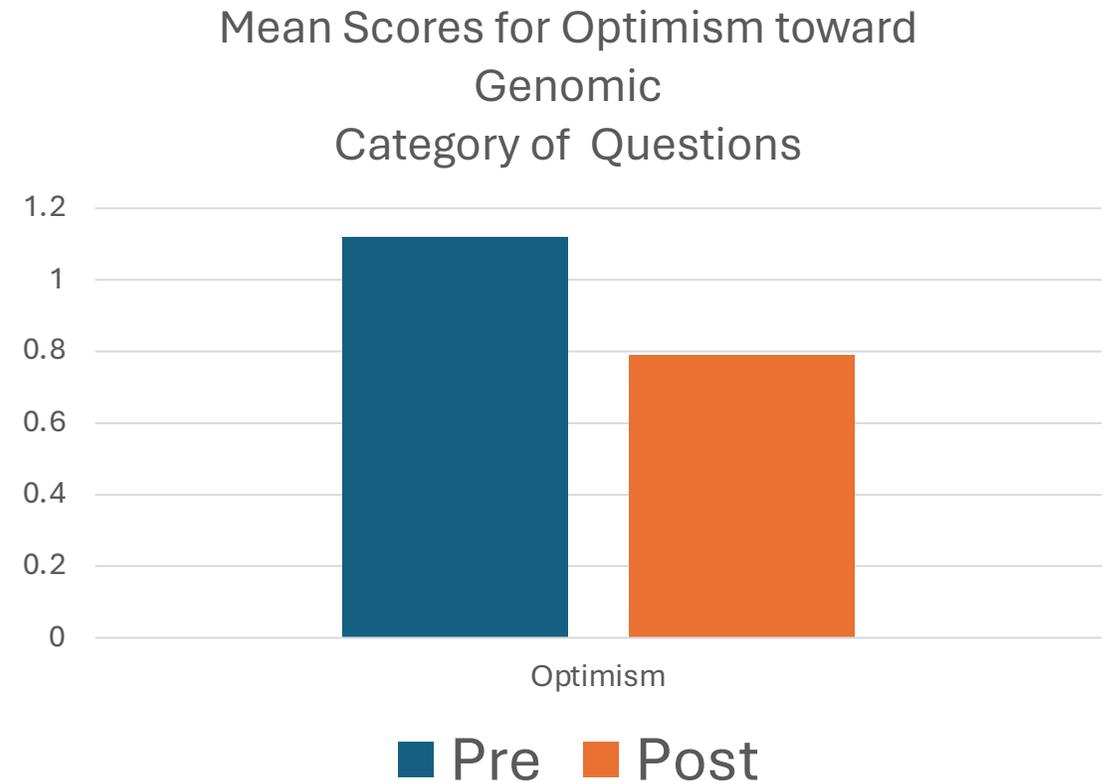
Response Distribution

- Sample Questions: Medical tests and control over health
  - Shift toward likely for both increasing medical tests and increasing control over health
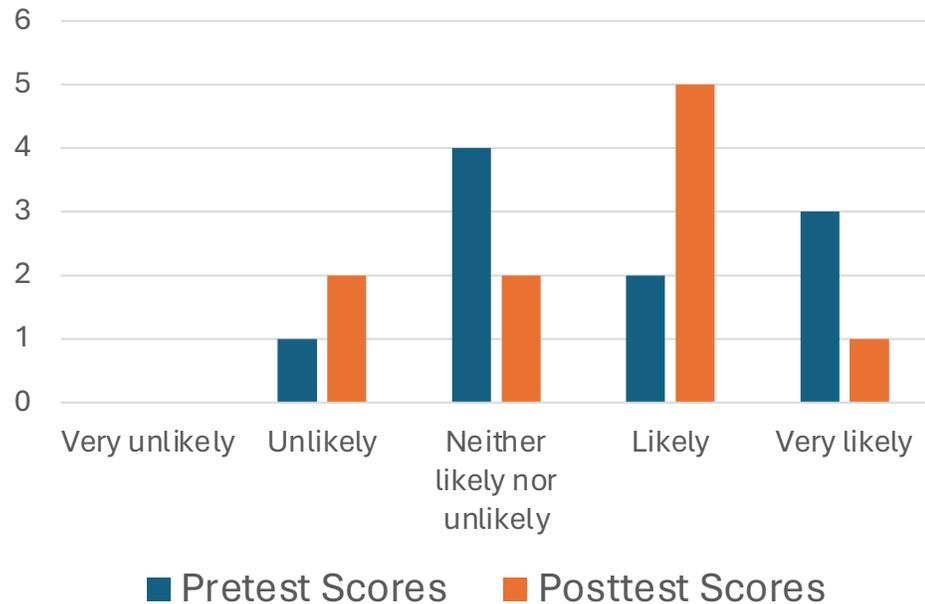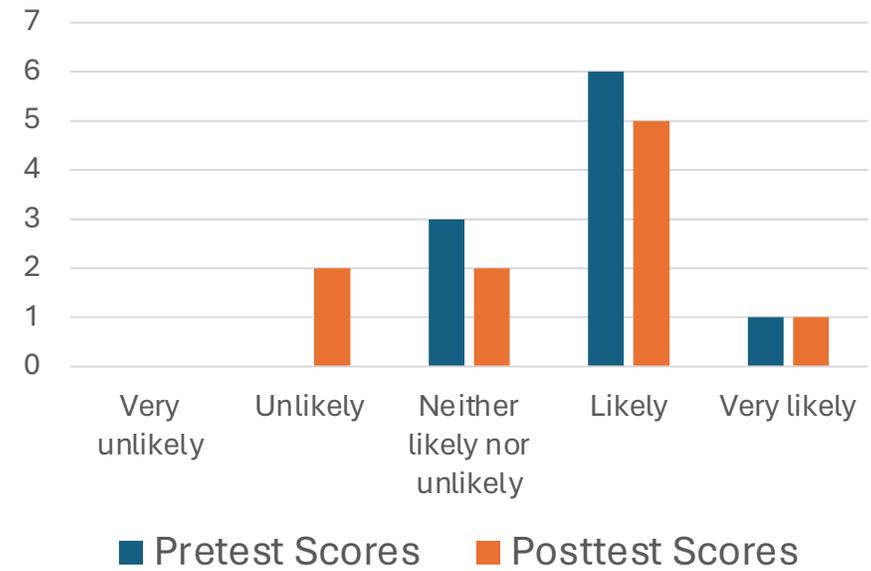
Response Distribution

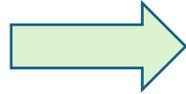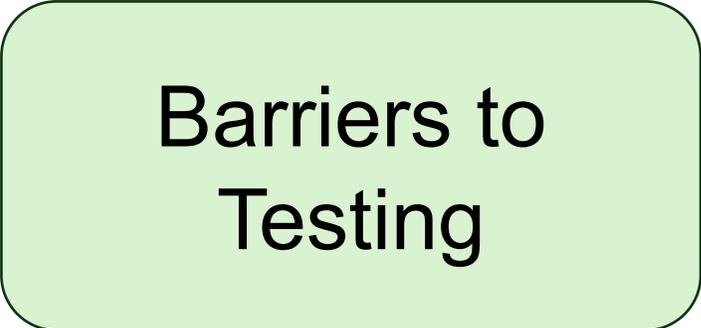- Sample Questions: Shift toward likely received well by doctors and toward unlikely received well by patients

Theme Based Quotes

Barriers to Testing

→ "I wouldn't take the test because of the simple fact I would worry myself to death trying to figure out what's gonna happen and, for me, just because of my relationship with the healthcare facility…"
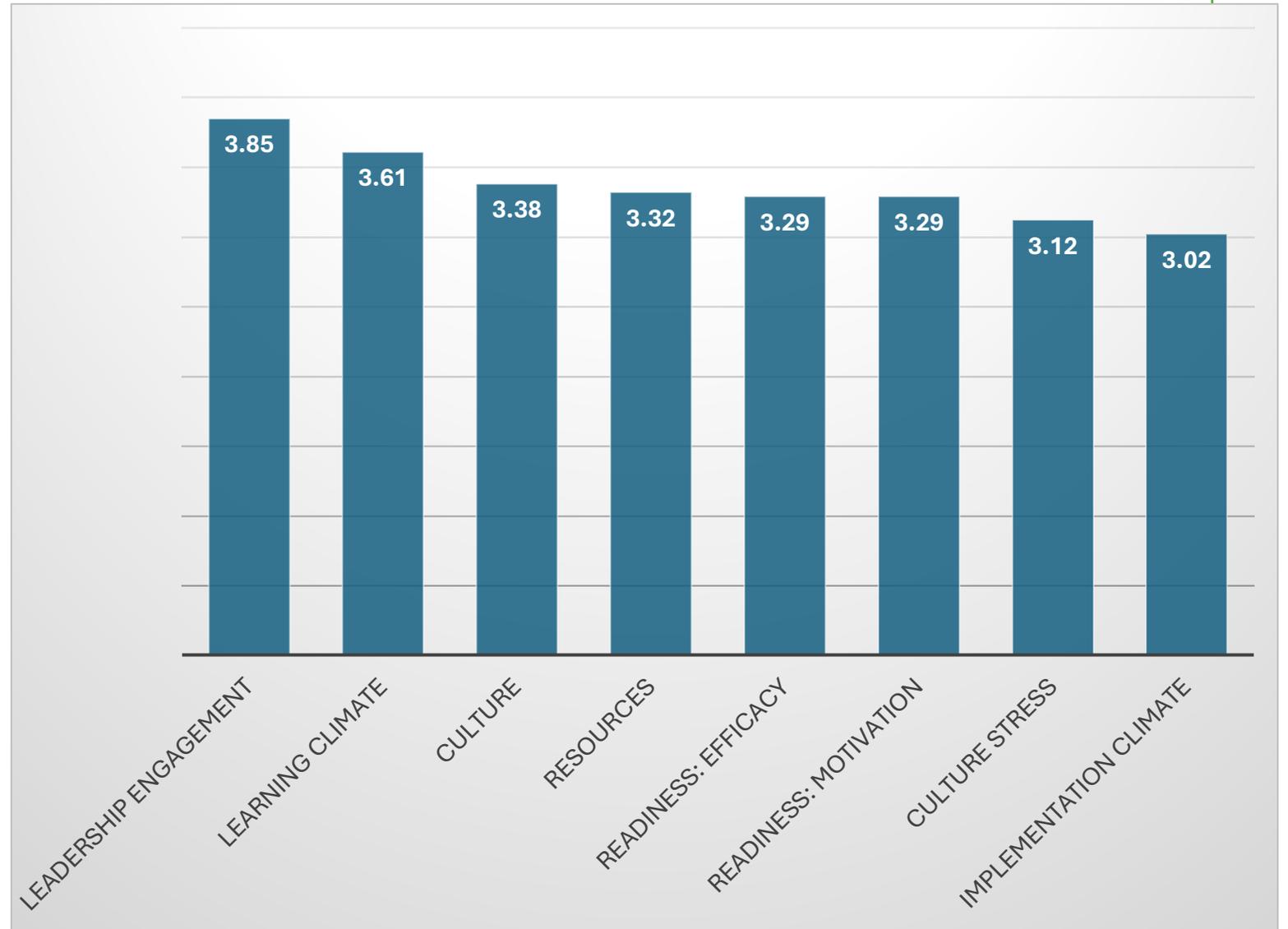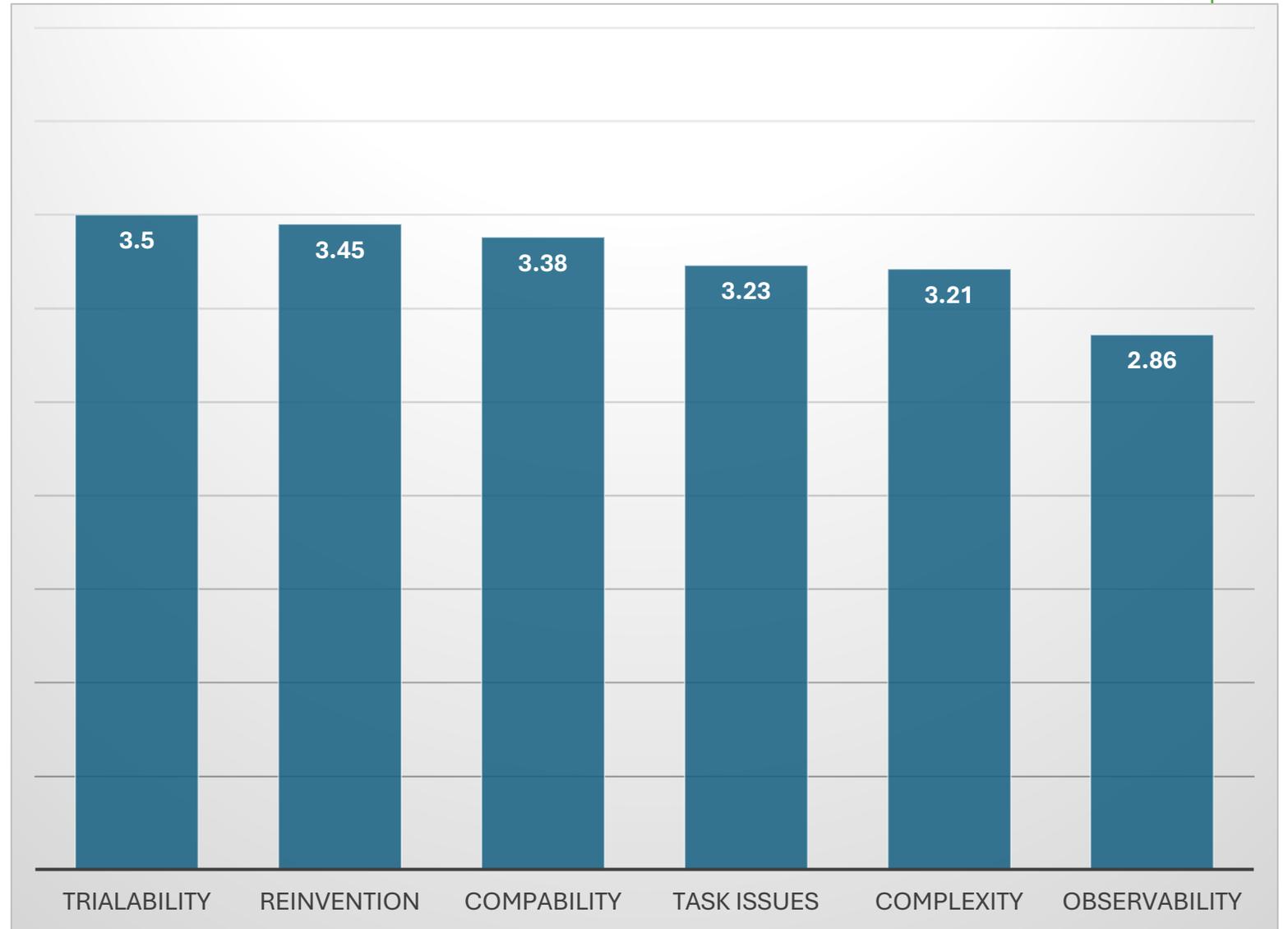
Life Insurance

→ "Now will the life insurance consider that as being somewhat of a screening and not really affect the eligibility on life insurance, or do we not really know?"
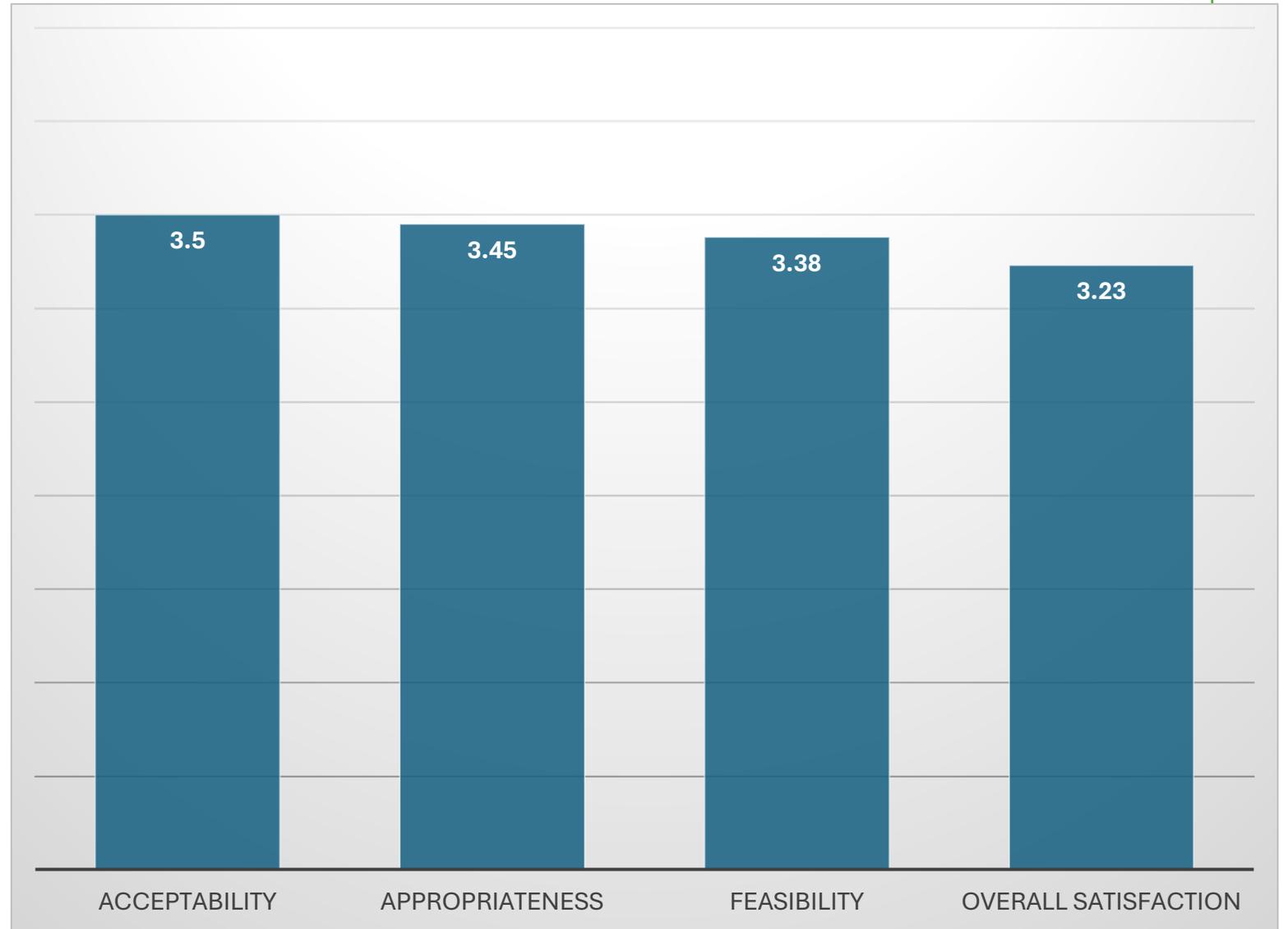
Health Provider Survey

Clinic Climate

Attitudes Toward Genomic Testing

Implementation Outcomes

Benefits of the Genomic Testing

- Help patients take a more proactive approach to their health and focus on prevention

    I think … that it's a tool that's very underutilized … it's very valuable to give insight to help patients … take ownership with their health and be more preventive with it." (Clinical Research Coordinator)

    To me, the huge benefit is explaining to them how unique they are, the benefit of knowing.

- Customized prescribing

    It's really interesting to me to figure out the implications of changes in dosing or avoiding certain medications that we would be able to do on the front end and get that information into a patient's

Perceived Patient Reactions to Genomic Medicine in Primary Care

- Mostly positive…

    "Yeah, it's been positive I haven't had any negative reactions…When they do get the results, it's like, "Oh, okay. This is super cool to know." (Physician 1)

- ..but may still benefit from focused application and/or patient education.

    Those are the people who are just interested in saying, 'Hey, what other things can we add to my health record that's gonna help us make good decisions?' Then I have a group of patients that are just saying, 'Hey, I don't really know what this is, and I'm concerned that this is going to give me information that I don't really want to know.

    I feel like for patients that struggle particularly with anxiety, and I even have had patients that self-profess that too, that if they are more anxious in general, that sometimes that knowledge is not helpful for them because it tends to lead to a lot more worry. Ultimately we don't know entirely how that's gonna play out for them. We can't predict what the future looks like for them 100 percent. I think that kind of in the middle kind of gray zone is really hard for some people. Those patients of mine have chosen not to pursue enrollment.

Conclusions

Public

• Wide public interest in participation in AGHI screening…

• but, not clear that this applies to all populations…

• and, expectations are not always realistic.

Providers

• Leadership engagement is critical

• Requires a lot of support (? sustainability)

• Needs to be integrated into normal clinical workflow

AGHI Team

Oversight Committee

Mitchell B. Cohen, MD
Chair of UAB Department of Pediatrics and AGHI Oversight Committee Chair

Richard M. Myers, PhD
President and Science Director at HudsonAlpha Institute for Biotechnology

Etty Benveniste, PhD
Senior Vice Dean for Basic Sciences at UAB

Robert Kimberly, MD
Senior Associate Dean for Clinical and Translational Research at UAB

Toni Leeth, MPH
Associate Dean for Strategic Planning and Administration at UAB

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Mariko Nakano, PhD
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Stephen Sodeke, PhD
Bioethicist & Professor of Allied Health Sciences, National Center for Bioethics in Research & Healthcare, Tuskegee University

Engagement and Implementation

Informatics

Biobank

Bioethics

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Outreach and Enrollment

Education

Genomics