

A watercolor illustration at the top of the slide. On the left, a family of four (two adults and two children) is depicted in warm yellow and orange tones, holding hands. To their right, a large, stylized DNA double helix is rendered in shades of blue and purple. Further right, another family of four is shown in cool purple and blue tones, also holding hands. The background is a soft, abstract watercolor wash of blues, greens, and purples, with a tree on the far right.

Telling Alabama's
GENOMIC STORY

ALABAMA GENOMIC HEALTH INITIATIVE



Alabama Genomic
HEALTH INITIATIVE

Bruce R. Korf, MD, PhD
UAB Heersink School of Medicine

2017-2020 Two Cohorts

Population Cohort
(transitioning to
clinical enrollment
in 2021)

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

Affected Cohort
Continues

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

2021 - Present

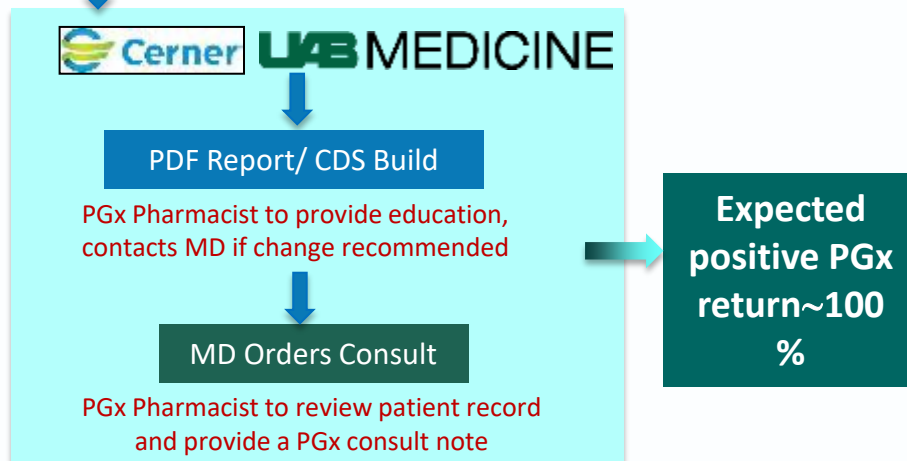
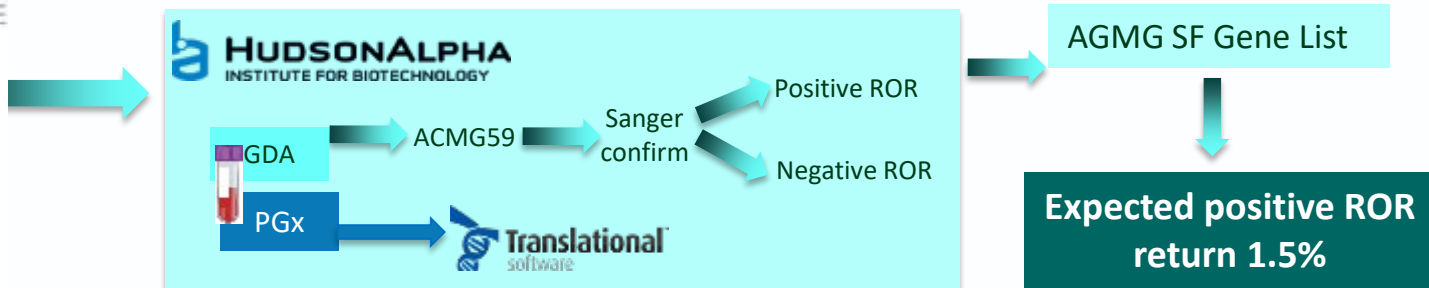
Pharmacogenetic Report
Genotyping array
Variant analysis
Return of results of actionable variants
Genetic counseling
Supportive care

DNA/Tissue Bank
Genomic Database
Medical Records (i2b2)



Protocol: Clinical Cohort

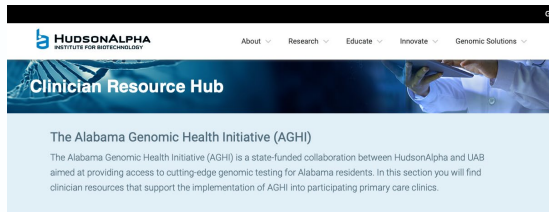
Alabama Genomic
HEALTH INITIATIVE



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Clinician Resource Hub



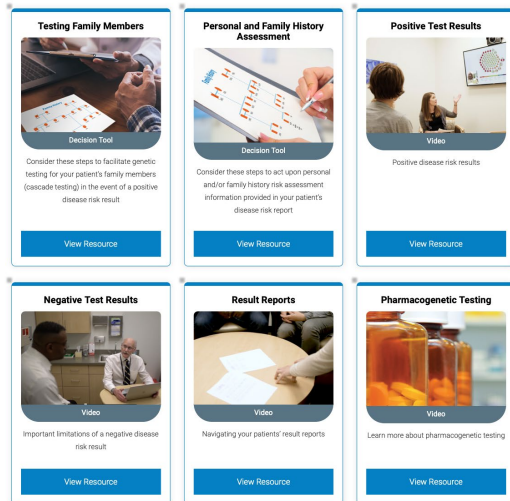
HUDSONALPHA
INSTITUTE FOR BIOTECHNOLOGY

About ▾ Research ▾ Educate ▾ Innovate ▾ Genomic Solutions ▾

Clinician Resource Hub

The Alabama Genomic Health Initiative (AGHI)

The Alabama Genomic Health Initiative (AGHI) is a state-funded collaboration between HudsonAlpha and UAB aimed at providing access to cutting-edge genomic testing for Alabama residents. In this section you will find clinician resources that support the implementation of AGHI into participating primary care clinics.



Testing Family Members Decision Tool Consider these steps to facilitate genetic testing for your patient's family members (cascade testing) in the event of a positive disease risk result. View Resource	Personal and Family History Assessment Decision Tool Consider these steps to act upon personal and/or family history risk assessment information provided by your patient's disease risk report. View Resource	Positive Test Results Video Positive disease risk results View Resource
Negative Test Results Video Important limitations of a negative disease risk result View Resource	Result Reports Video Navigating your patients' result reports View Resource	Pharmacogenetic Testing Video Learn more about pharmacogenetic testing View Resource

Alabama Genomic HEALTH INITIATIVE

TTR

Gene Fact Sheet

TTR encodes a protein present in serum and cerebrospinal fluid responsible for transporting retinol-binding protein and thyroxine. Pathogenic variation in TTR causes hereditary transthyretin amyloidosis.

- The risk to develop signs and symptoms of hereditary transthyretin amyloidosis may depend on the specific TTR variant and the individual's age and ethnic background. Furthermore, some affected individuals only develop a few manifestations of the disease, which can include features such as neuropathy, cardiomyopathy, vitreous opacities, renal disease, and CNS dysfunction.
- The most common TTR variant worldwide is p.Val142Ile, with a frequency exceeding five percent in parts of West Africa. Between three and four percent of African Americans are thought to have this variant, which primarily results in a cardiac amyloidosis presenting as symptoms such as cardiomyopathy, arrhythmia, and congestive heart failure.
- Medical management changes are indicated, subject to personalization based on personal and family history. **Example may include:**
 - Management based on an individual's specific manifestations of the condition
 - Recommended initial evaluations following diagnosis including but not limited to neurologic, cardiac, ophthalmologic, and nephrologic
- TTR variation is inherited in an autosomal dominant manner. Parents, siblings, and children of affected individuals have up to a 50% risk to have the same TTR variation.

For more information: [GeneReviews: Hereditary Transthyretin Amyloidosis](#)

This summary information is provided as an educational resource for physicians and other practitioners with the understanding that it is not a substitute for the treating practitioner's independent clinical judgment. The treating practitioner should clinically evaluate each patient considering many relevant factors to determine the final diagnosis and plan of care. Last update July 25, 2022.

DEPARTMENT OF GENETICS
The University of Alabama at Birmingham
Kaul 251 • 720 20th Street South
Phone: 205.934.9525 • Email: aghi@uab.edu

UAB MEDICINE
Knowledge that will change your world

HUDSONALPHA
INSTITUTE FOR BIOTECHNOLOGY

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

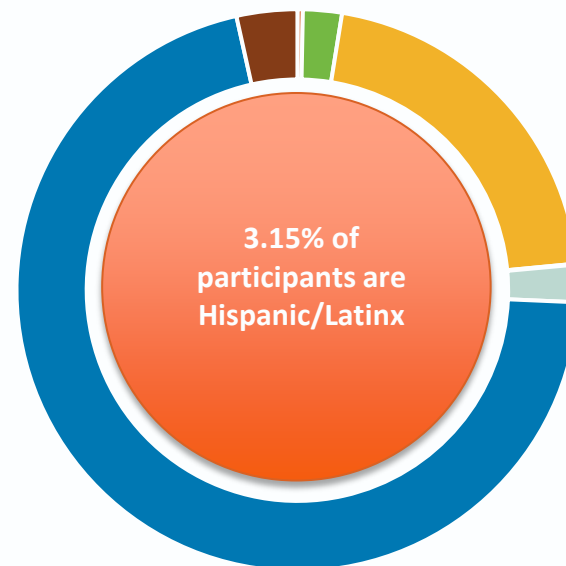
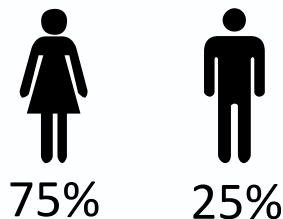
What You Need to Know



Population Cohort Enrollment Demographics

ENROLLMENT BY RACE

- American Indian or Alaskan (0.31%)
- Asian (2.24%)
- Black or African American (20.94%)
- Native Hawaiian or Other Pacific Islander (0.05%)
- Unknown (2.15%)
- White (70.82%)
- More Than One Race (3.49%)



Updated 3/4/22

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



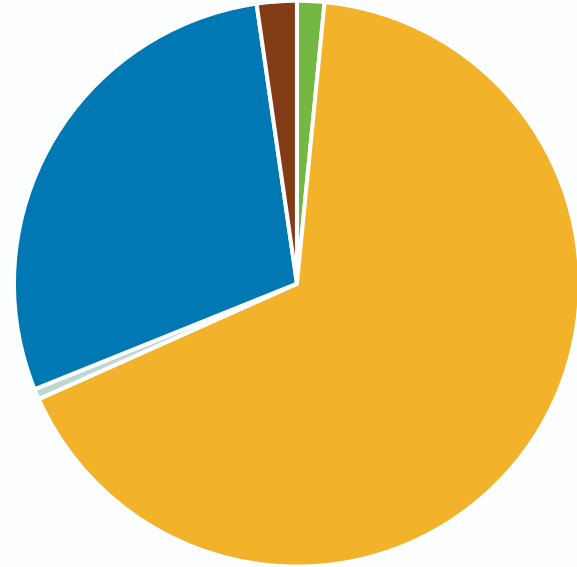
Tiffany Osborne, Program Director II
Minority Health & Health Disparities Research Center
UAB School of Medicine/Division of Preventive
Medicine



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

Clinical Cohort Recruitment By the Numbers

- American Indian or Alaskan (0%)
- Asian (1.56%)
- Black or African American (66.75%)
- Native Hawaiian or Other Pacific Islander (0%)
- Unknown (0.6%)
- White (28.81%)
- More Than One Race (2.28%)



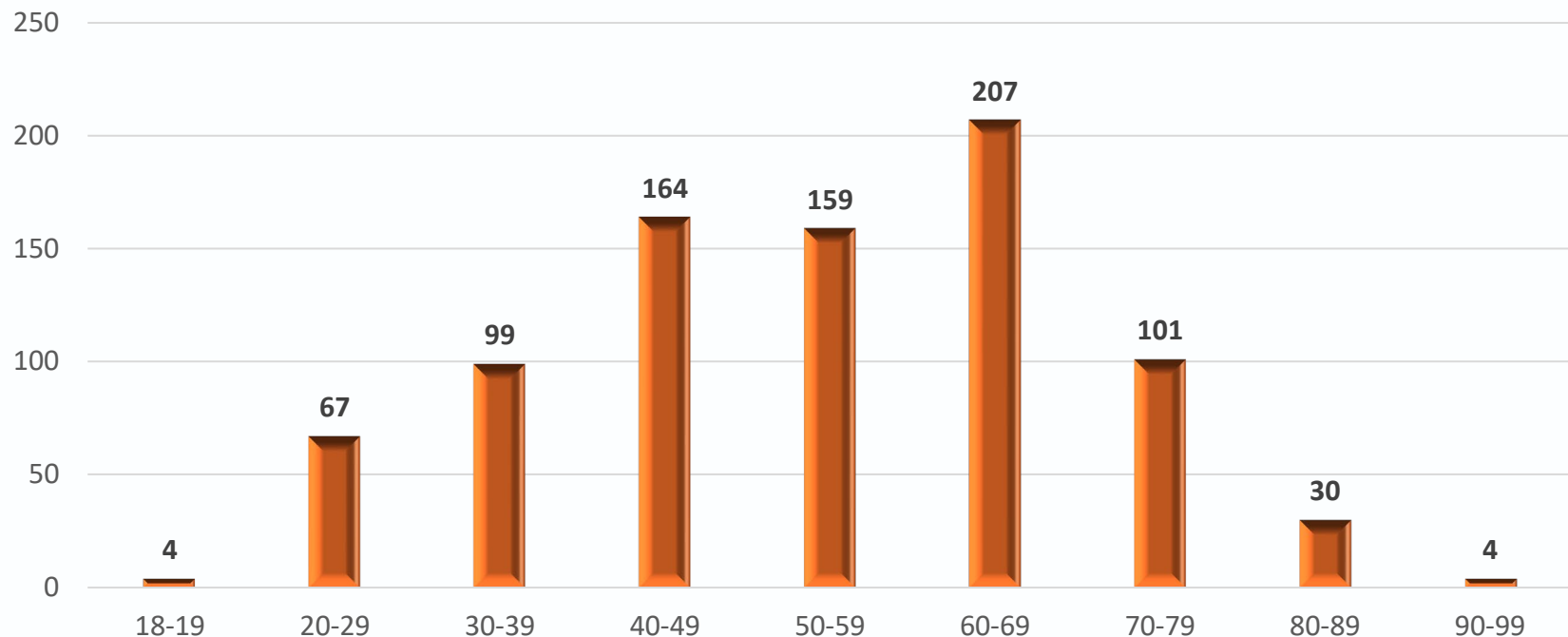
73%  **FEMALE**

27%  **MALE**

0.07% of Participants Are Hispanic/Latinx

Updated 11/4/22

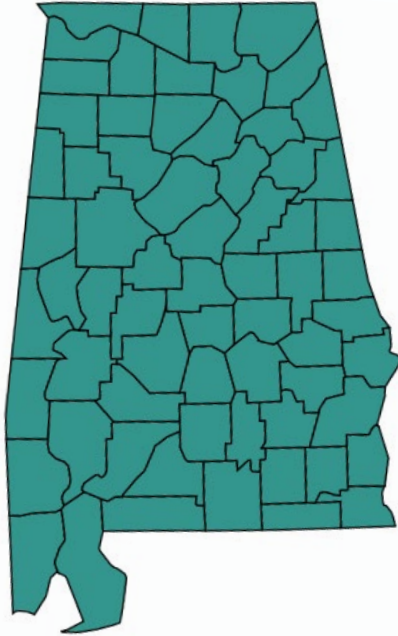
FY20-22 AGHI Clinical Cohort Participants by Age



Updated 11/4/22



Cumulative Population and Clinical Cohort Enrollment



- 7254 participants
- 67 of 67 counties
- 105 actionable results returned to participants
= 1% of general population

Updated 11/4/22

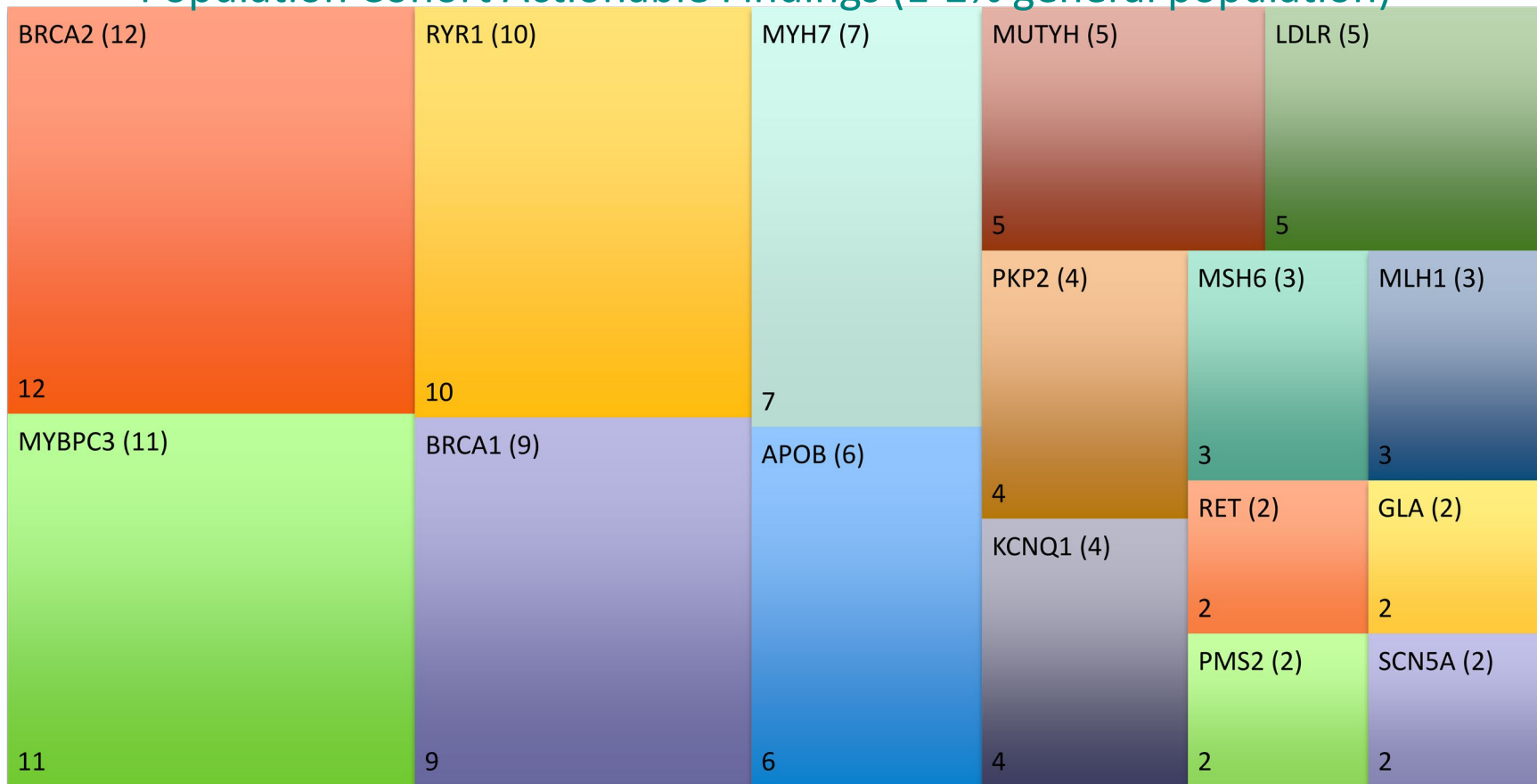


Actionable Findings in the Clinical and Population Cohort

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	<i>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</i> New: <i>PALB2, MAX, TMEM127</i>
Connective Tissue Dysplasia Ehlers-Danlos vascular type, Marfan, Loeys-Dietz, Familial aortic aneurysms and dissections	<i>COL3A1, FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYH11</i>
Cardiac Hypertrophic cardiomyopathy, dilated cardiomyopathy, Arrhythmia	<i>MYBPC3, MYH7, TNNT2, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, GLA, MYL2, LMNA, RYR2, PKP2, DSP, DSC2, TMEM43, DSG2, KCNQ1, KCNH2, SCN5A</i> New: <i>CASQ2, TRDN, FLNC, TTN</i>
Metabolic Hypercholesterolemia, Wilson disease, Ornithine transcarbamylase deficiency	<i>LDLR, APOB, PCSK9, ATP7B, OTC</i> New: <i>BTD, GAA, HFE, TTR</i>
Pharmacogenetic Malignant Hyperthermia	<i>RYR1, CACNA1S</i>
Other	New: <i>HFE, ACVRL1, ENG, HNF1A, RPE65</i>

Updated 11/4/22

Population Cohort Actionable Findings (1-2% general population)



Family History Review

- Forms focus on ACMG SFv2.0 conditions
- Reviewed by Genetic Counselors
- Triageed into 3 categories using published testing criteria guidelines

"If you want to
discuss further..."

49%

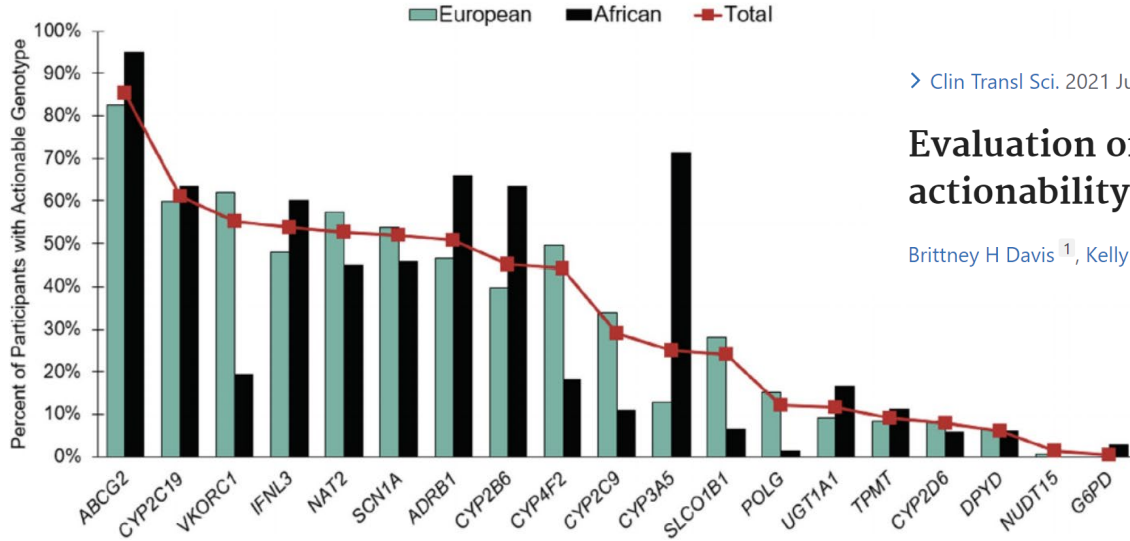
"Follow-up
may be
beneficial..."

5%

"We encourage
further
discussion..."

46%

AGHI and Pharmacogenetics



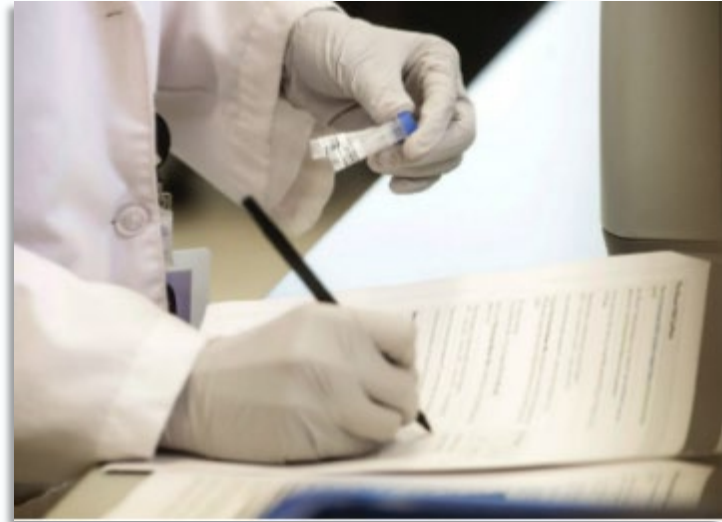
> Clin Transl Sci. 2021 Jun 13. doi: 10.1111/cts.13097. Online ahead of print.

Evaluation of population-level pharmacogenetic actionability in Alabama

Brittney H Davis ¹, Kelly Williams ², Devin Absher ², Bruce Korf ³, Nita A Limdi ¹

Biobank

- 19685 plasma aliquots
- 6573 DNAs
- 6350 buffy coats
- 5042 whole blood



Bioinformatics

- 5950 annotated chips from population cohort
- 444 annotations from the WGS cohort
- 92% consent to biobank and share data in population cohort
- 82% consent to biobank and share data in the clinical cohort

Updated 4/18/22



Telling Alabama's
GENOMIC STORY

ALABAMA GENOMIC HEALTH INITIATIVE

AGHI Participant Experience and Outcomes

Ashley Cannon, PhD, MS, CGC

Purpose

- To assess motivation for participation, satisfaction, and actions taken based on AGHI results from the first 2 years of the population study

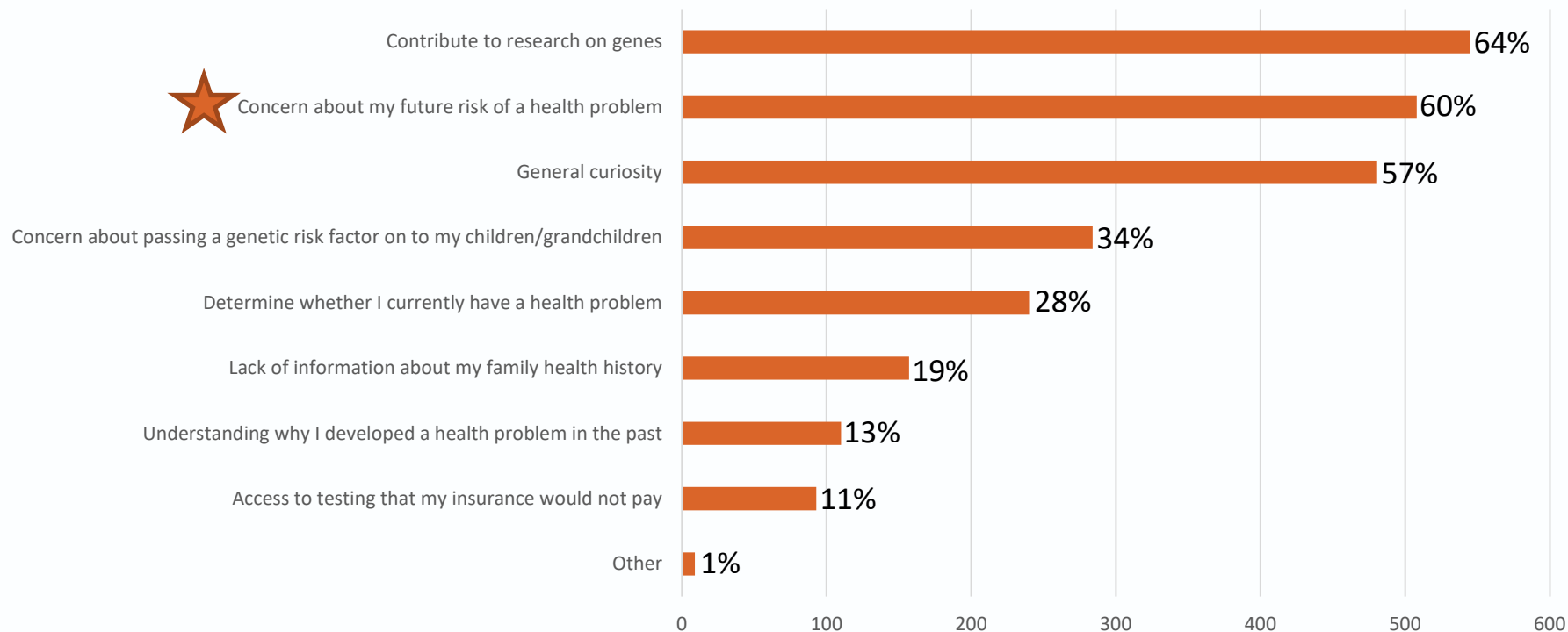
Methods

- An online survey was developed
- A unique survey link was sent via email and postcard to 3874 AGHI participants that received a result and agreed to be re-contacted
- 59 participants that received a medically-actionable result were also contacted by phone call and given the option to complete the survey during the call

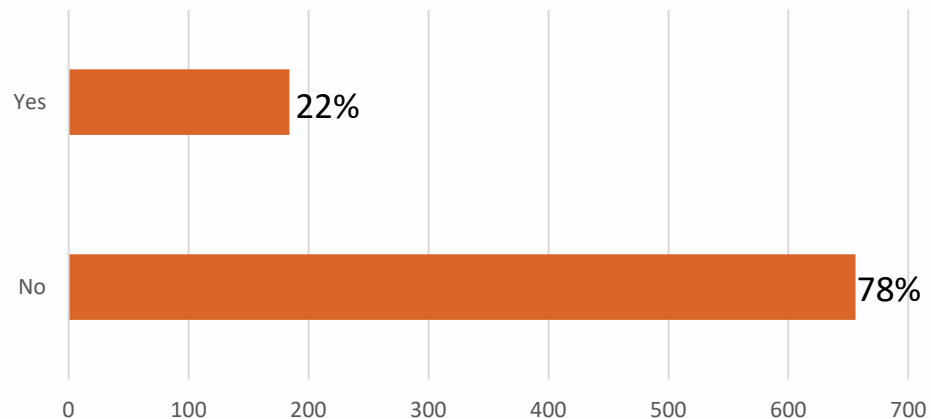
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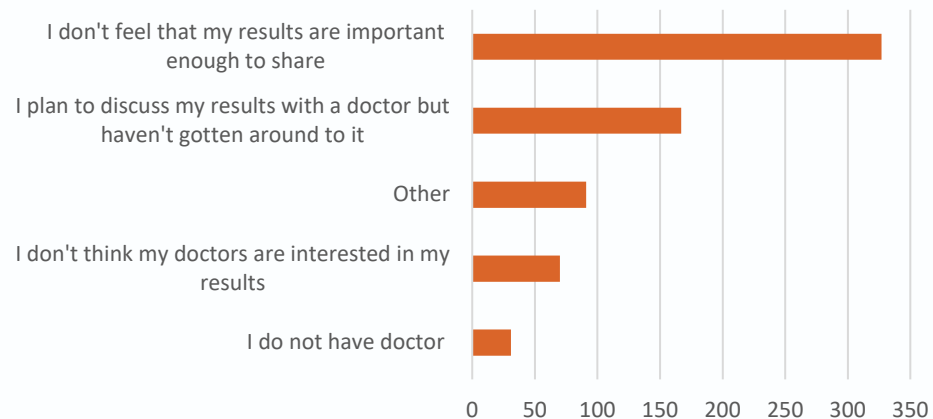
Motivations for Participating in AGHI



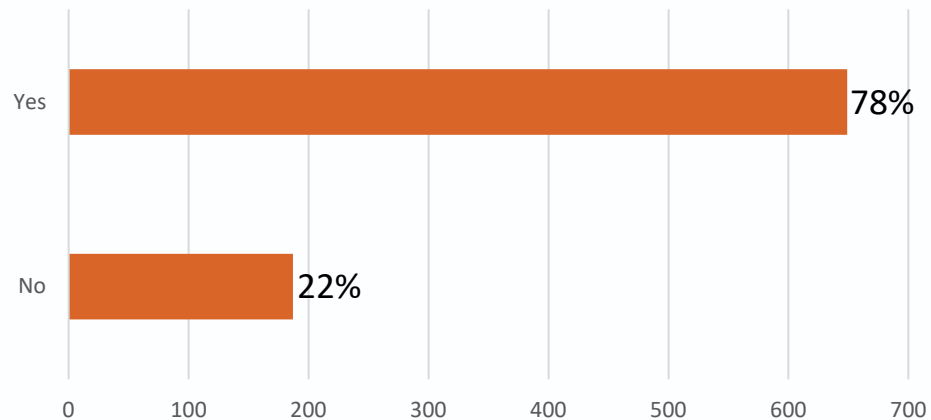
Have you discussed your AGHI results with your physician or another healthcare provider?



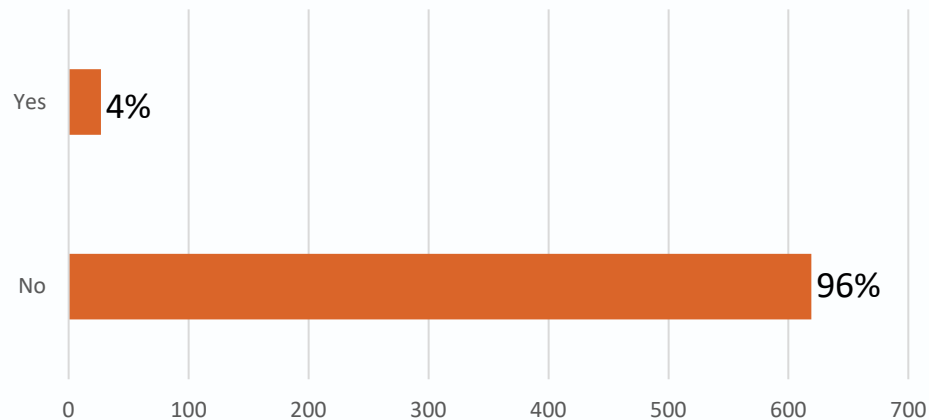
Please share the reason(s) for not discussing your AGHI results with your doctor(s)



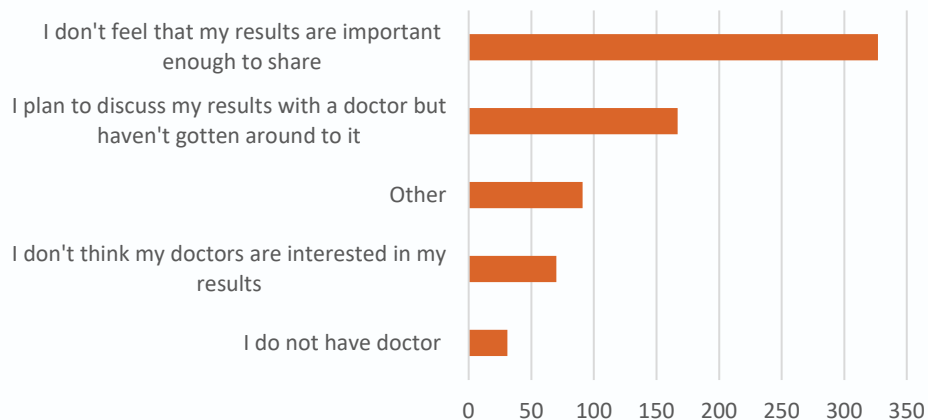
Have you shared your AGHI results with your family members?



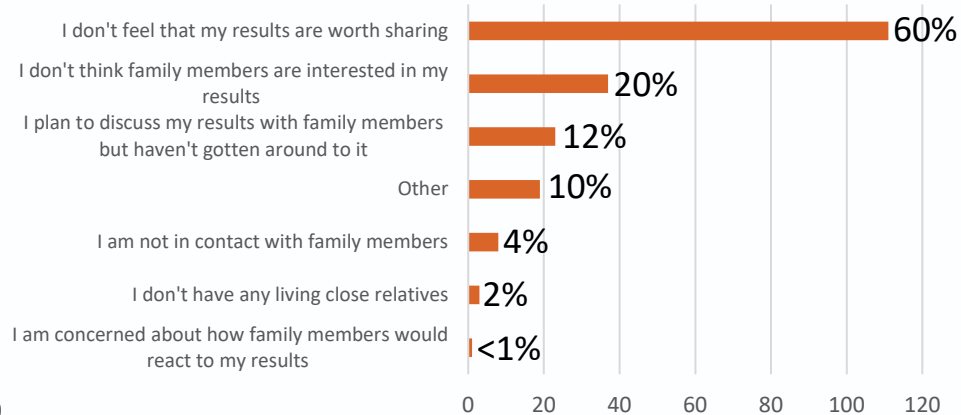
Have your family members taken any action based on your test results?



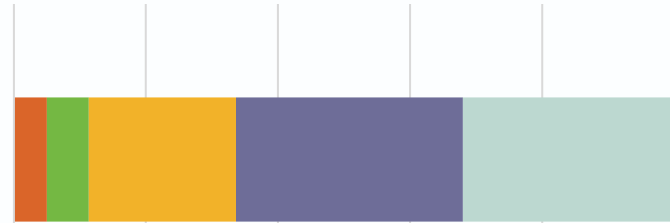
Please share the reason(s) for not discussing your AGHI results with your doctor(s)



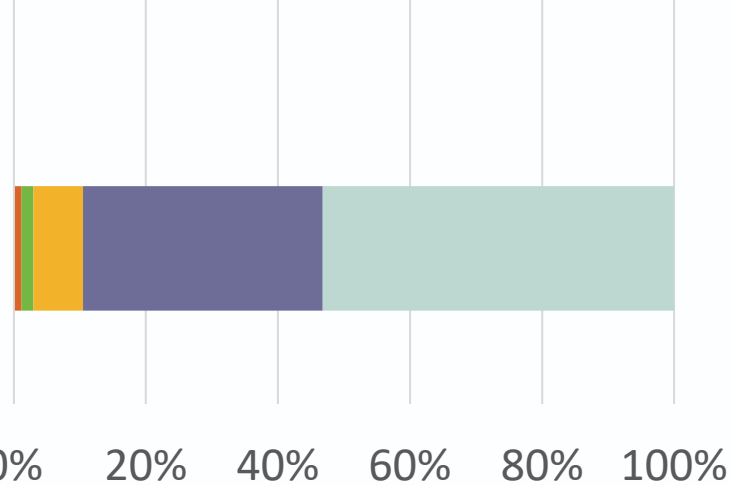
Please share the reason(s) for not discussing your AGHI results with your family members



In general, how valuable were your AGHI results?

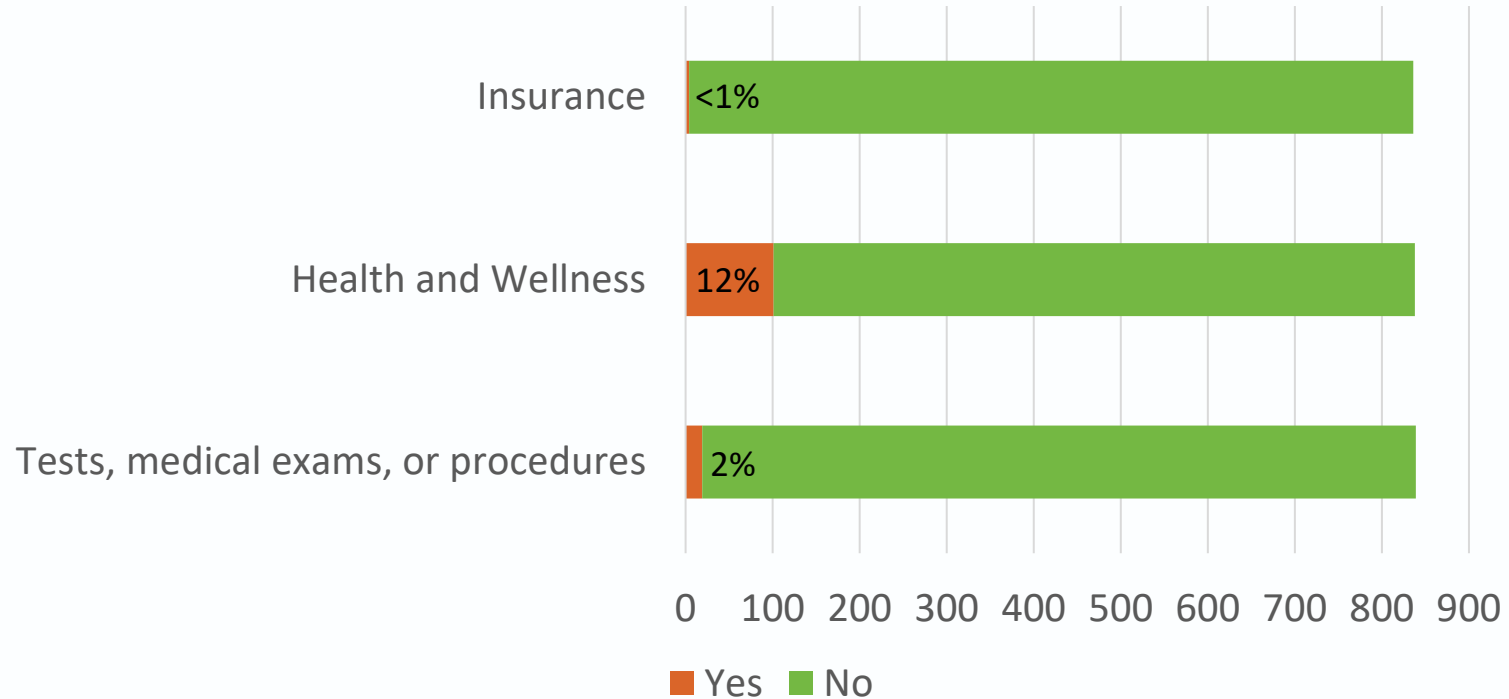


In general, how satisfied are you regarding your decision to participate in the AGHI?



■ Not at all ■ A little ■ Somewhat ■ Very ■ Extremely

Changes made following AGHI results:



Conclusions

- There is strong community interest in population genomic screening
- The rate of returnable results is 1-3% based on ACMG SF list
- Need to avoid false reassurance
- Non-penetrance is common at time of testing



AGHI Team



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



Ety 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

Oversight Committee



Bruce R. Korf, MD, PhD
Chief Genomics Officer
of UAB Medicine



Greg Barsh, MD, PhD
Faculty Investigator and
Faculty Chair at HudsonAlpha
Institute for Biotechnology



Matthew Might, PhD
Director of UAB Hugh Kaul
Precision Medicine Institute



**Nita Limdi, PharmD, PhD,
MSPH**
Director, Program for
Translational
Pharmacogenomics

Co-PIs



Jim Cimino, MD
Director of UAB
Informatics Institute

Informatics



Jeff Edberg, PhD
Professor in UAB Division
of Clinical Immunology
and Rheumatology

Biobank



Ashley Cannon, PhD
Assistant Professor
& Certified Genetic Counselor
at UAB

Engagement



Tom May, PhD
Research Faculty Investigator
at HudsonAlpha Institute
for Biotechnology



Mariko Nakano, PhD
Assistant Professor
of Bioethics at UAB School
of Medicine

Bioethics



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



Renie Moss
Program Director
rpmoss@uab.edu
(205) 934-9525

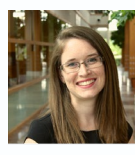


Mona Fouad, MD
UAB Senior Associate
Dean for Diversity &
Inclusion

Outreach and Enrollment



William Curry, MD
UAB Senior Associate
Dean for Rural Health &
Primary Care



Kelly East, CGC
Certified Genetic
Counselor at
HudsonAlpha Institute
for Biotechnology

Education



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



Greg Cooper, PhD
Faculty Investigator at
HudsonAlpha Institute
for Biotechnology

Genomics



Anna Hurst, MD
Assistant Professor
in UAB Department
of Genetics

