Alabama Genomic HEALTH INITIATIVE

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UAB MEDICINE
The University of Alabama at Birmingham

HudsonAlpha
INSTITUTE FOR BIOTECHNOLOGY

2017-2020 Two Cohorts

2021 - Present

Population Cohort (transitioning to clinical enrollment in 2021)

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

- Pharmacogenetic Report
- 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

DNA/Tissue Bank

Genomic Database

Medical Records (i2b2)

Protocol: Clinical Cohort

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HUDSONALPHA INSTITUTE FOR BIOTECHNOLOGY

GDA → ACMG59 → Sanger confirm → Positive ROR / Negative ROR

PGx → Translational software

AGMG SF Gene List

Expected positive ROR return 1.5%

Cerner UAB MEDICINE

PDF Report/ CDS Build

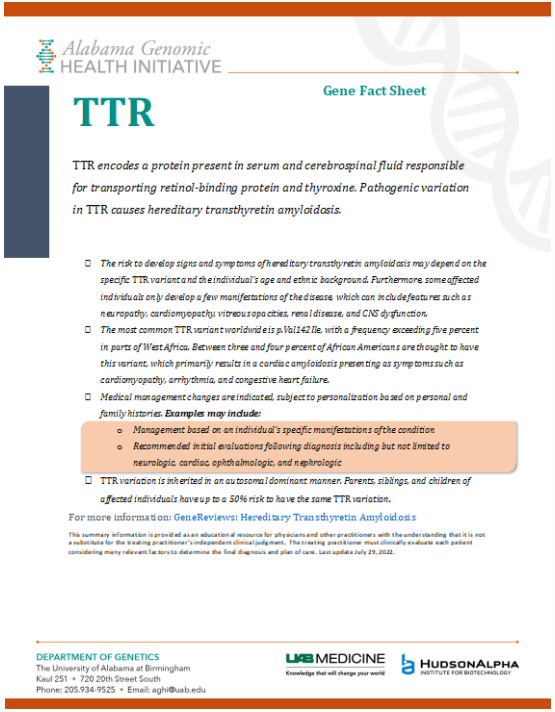
PGx Pharmacist to provide education, contacts MD if change recommended

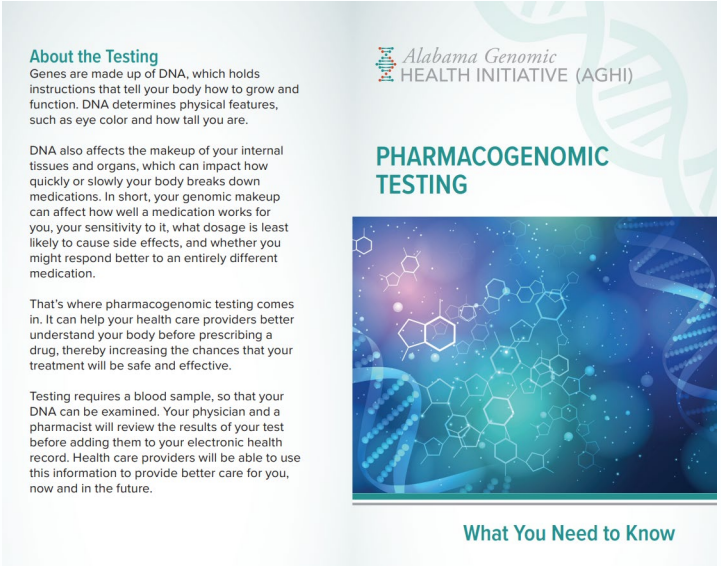
MD Orders Consult

PGx Pharmacist to review patient record and provide a PGx consult note

Expected positive PGx return~100 %

Clinician Resource Hub



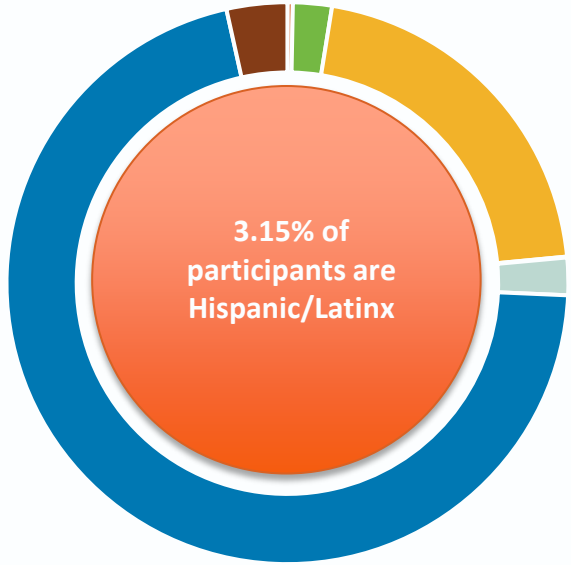


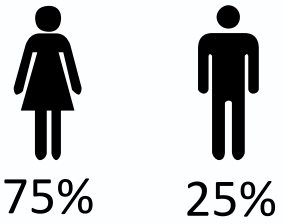
https://www.hudsonalpha.org/clinician-resource-hub/aghi/

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

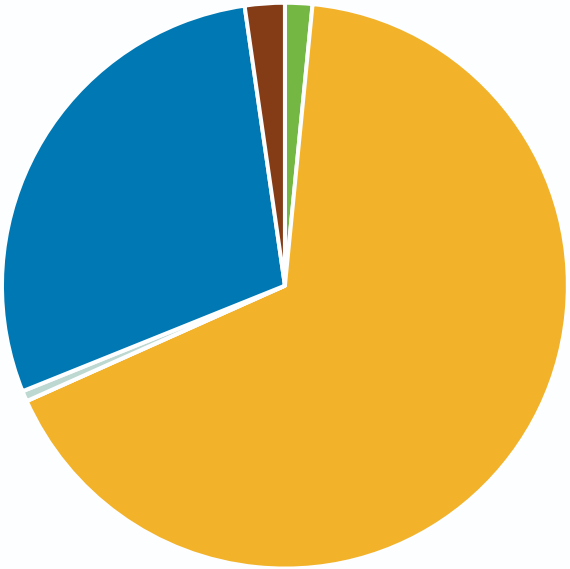
Kelly East, MS, CGC, Certified Genetic Counselor
Clinical Applications Lead
HudsonAlpha Institute for Biotechnology

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%)



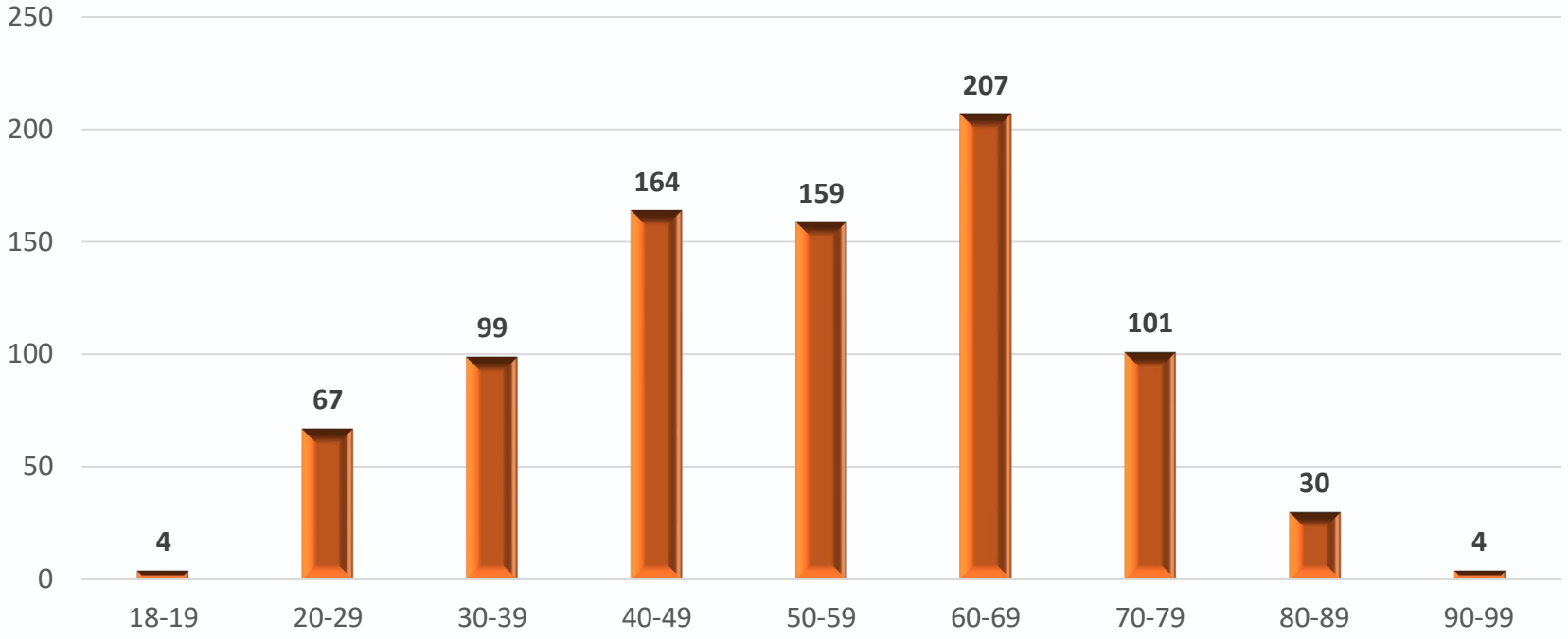
73% FEMALE ♀ **27% MALE** ♂

0.07% of Participants Are Hispanic/Latinx

Updated 11/4/22

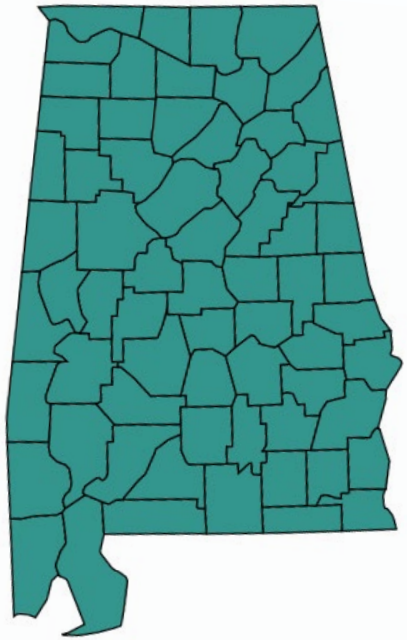
Alabama Genomic HEALTH INITIATIVE

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

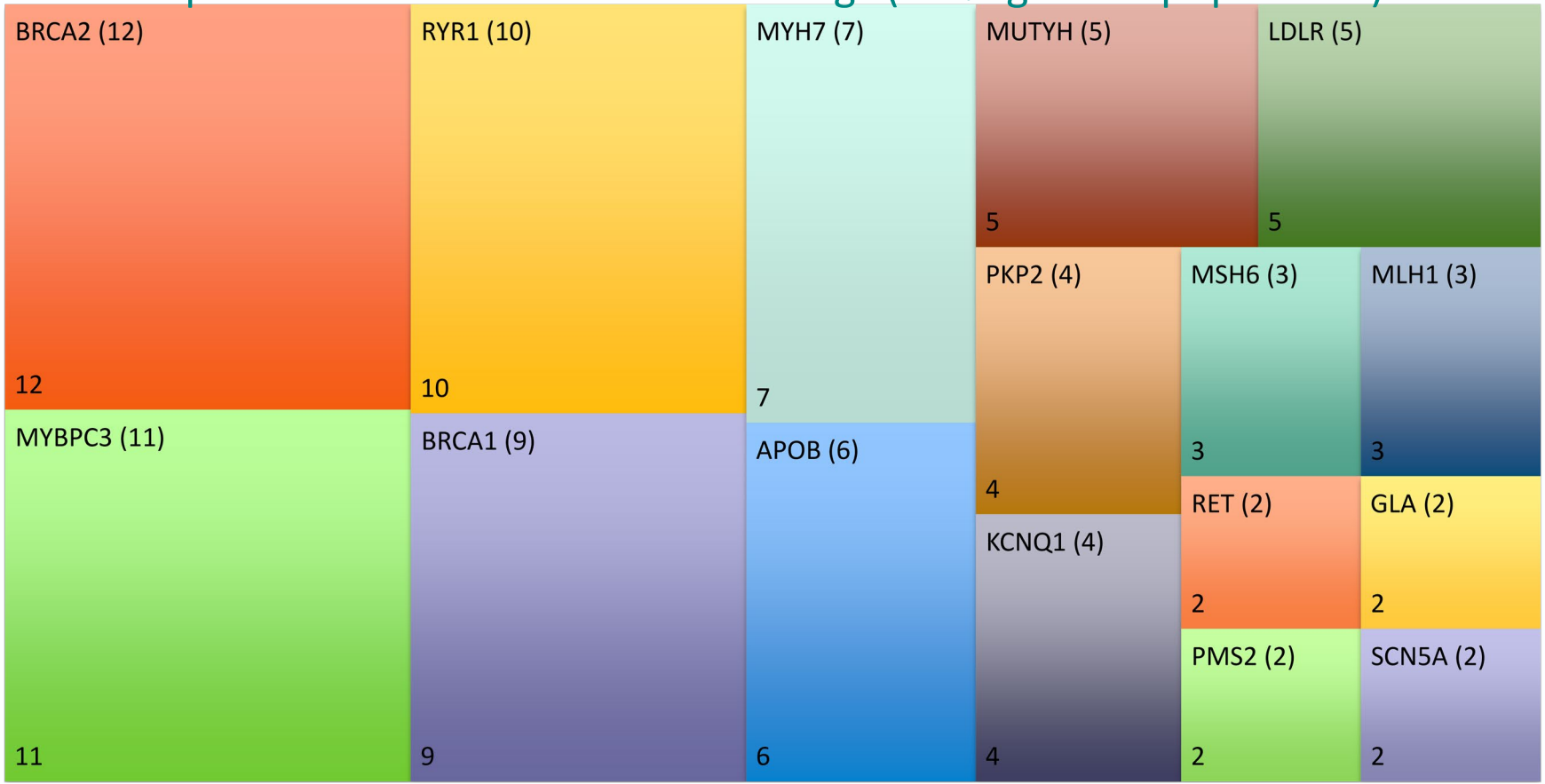
Updated 11/4/22

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	*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 11/4/22

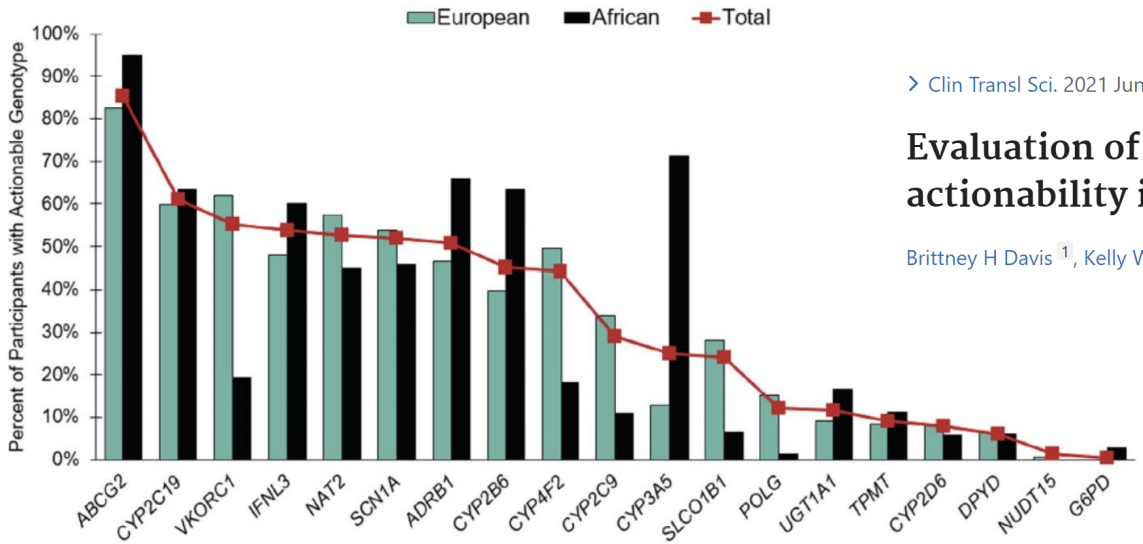
Population Cohort Actionable Findings (1-2% general population)



Family History Review

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

AGHI and Pharmacogenetics



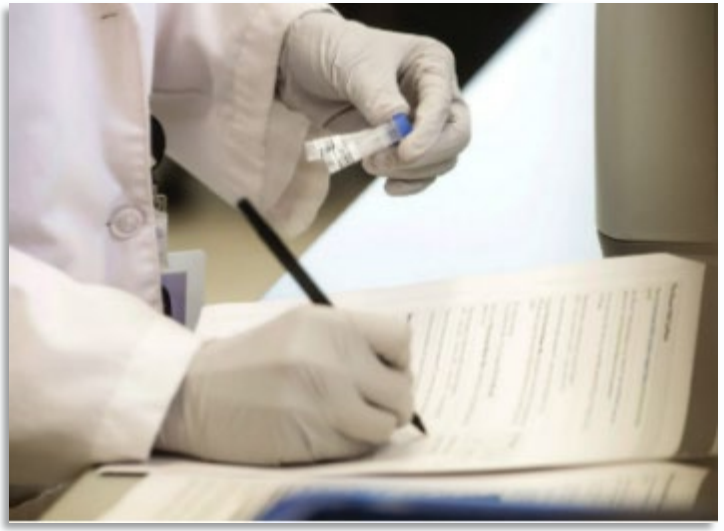
Clin Transl Sci. 2021 Jun 13. doi: 10.1111/cts.13097. Online ahead of print.

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

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

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
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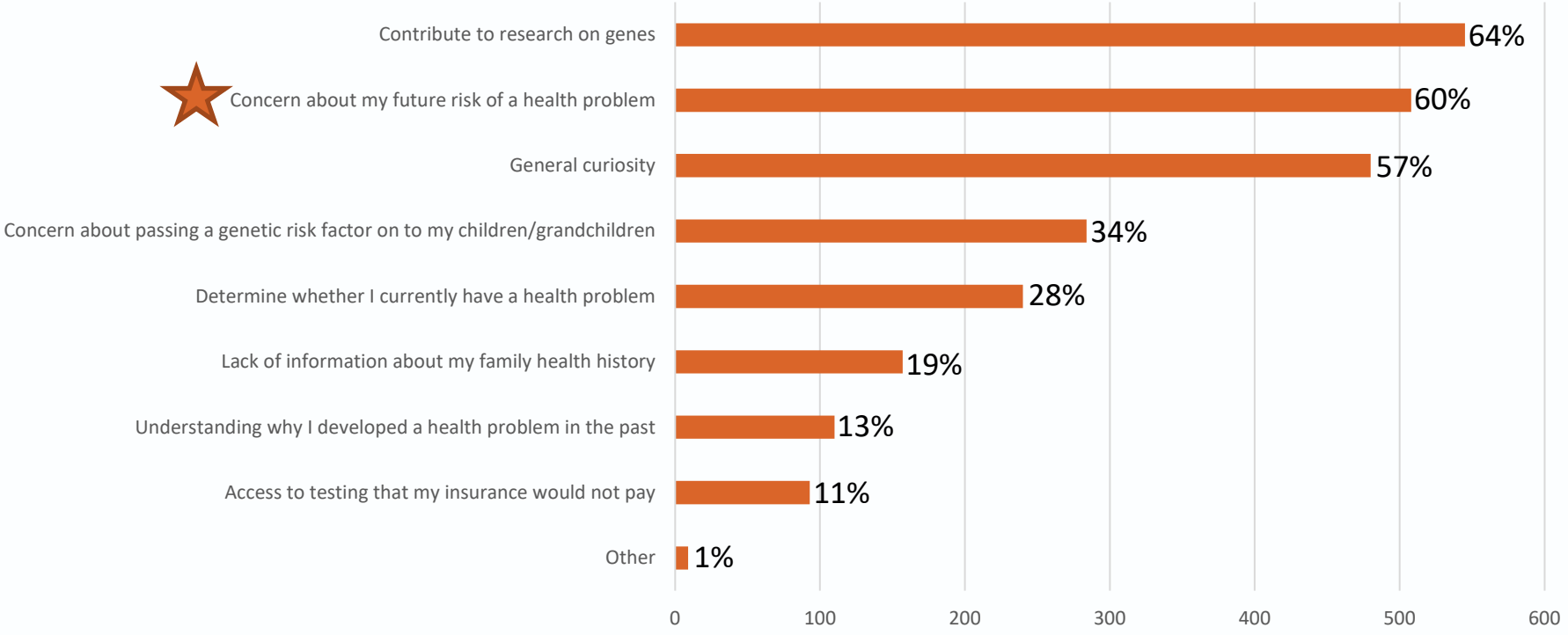
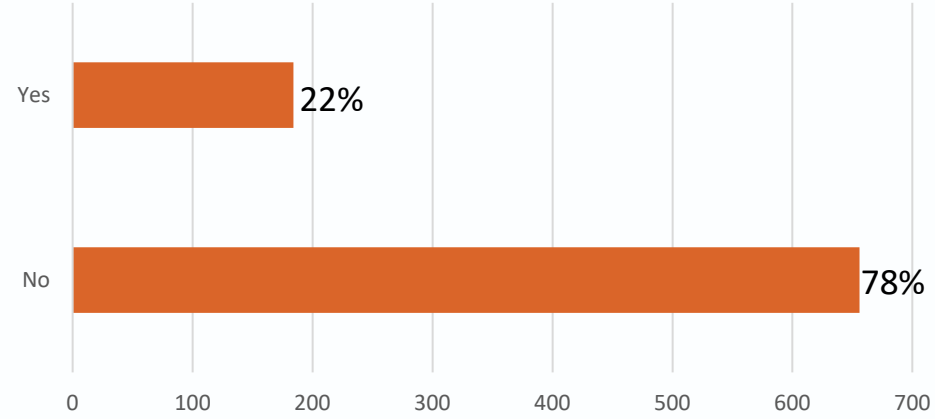
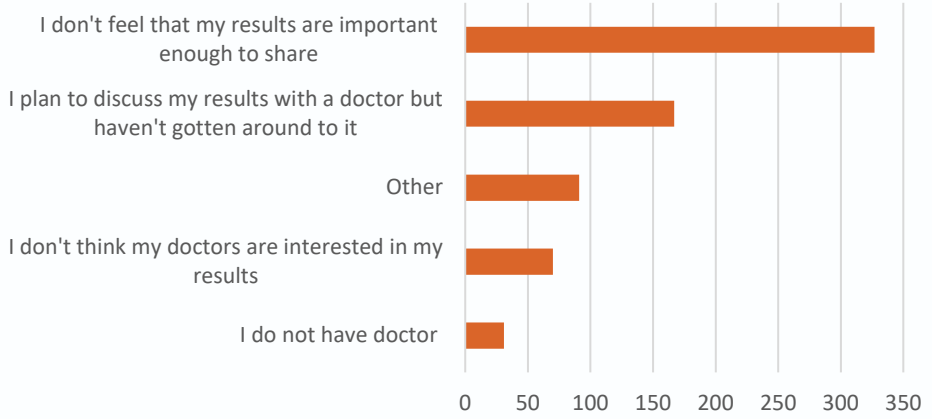
Motivations for Participating in AGHI



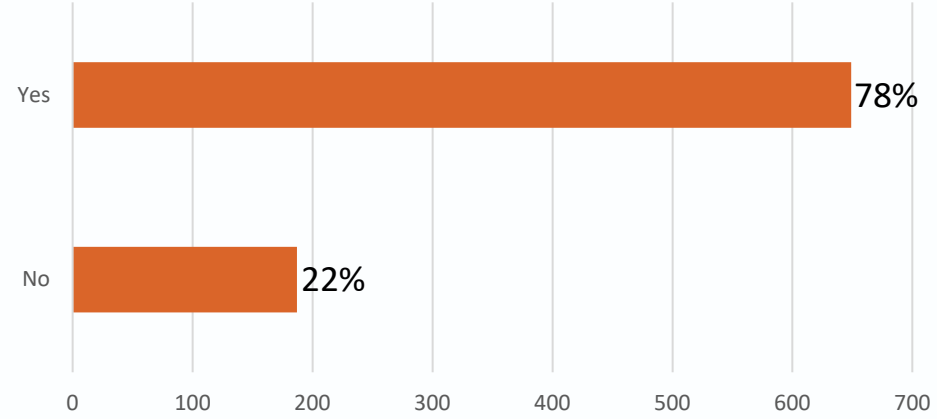
Have you discussed your AGHI results with your physician or another healthcare provider?



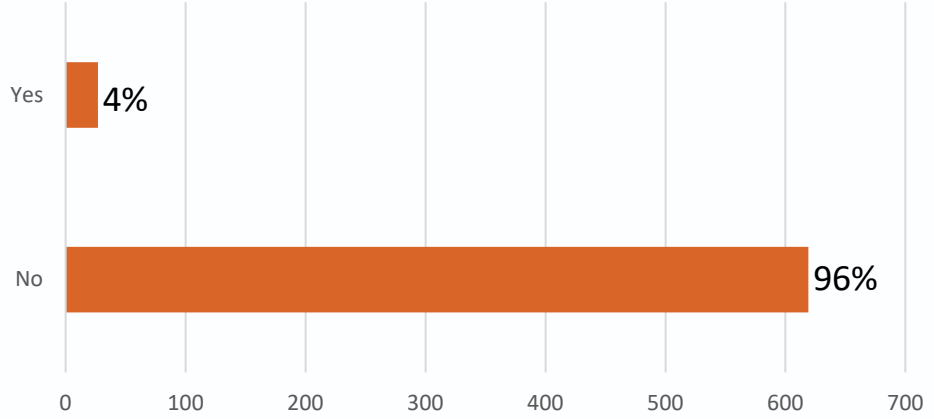
Please share the reason(s) for not discussing your AGHI results with your doctor(s)



Have you shared your AGHI results with your family members?



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



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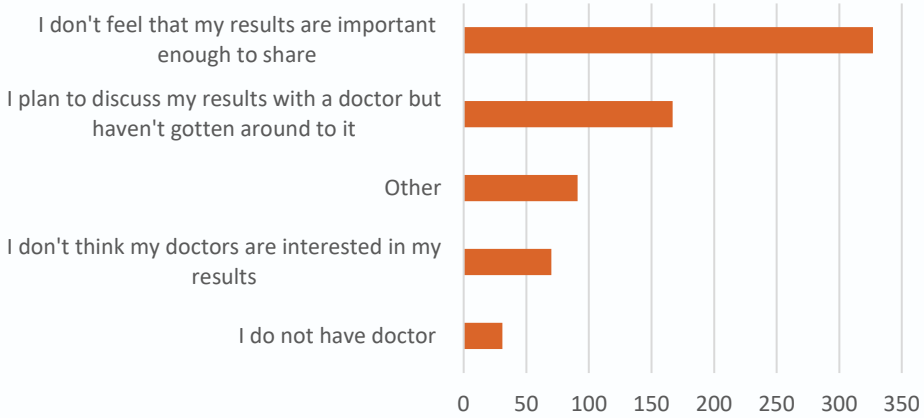

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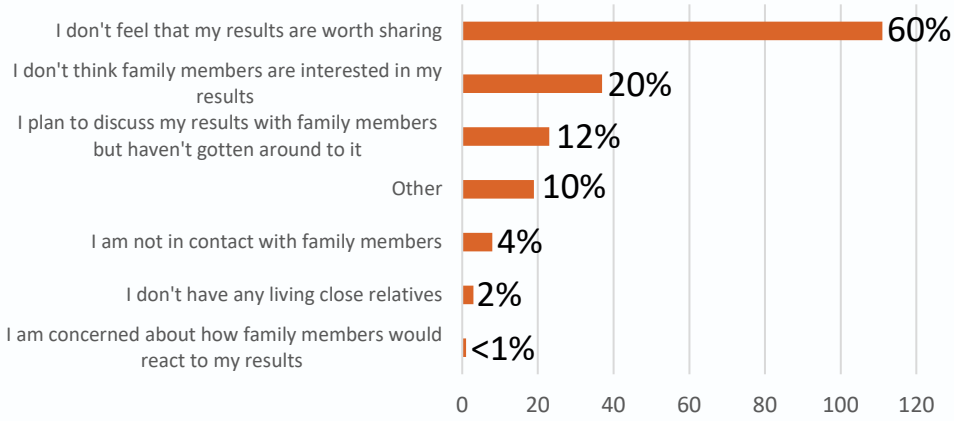
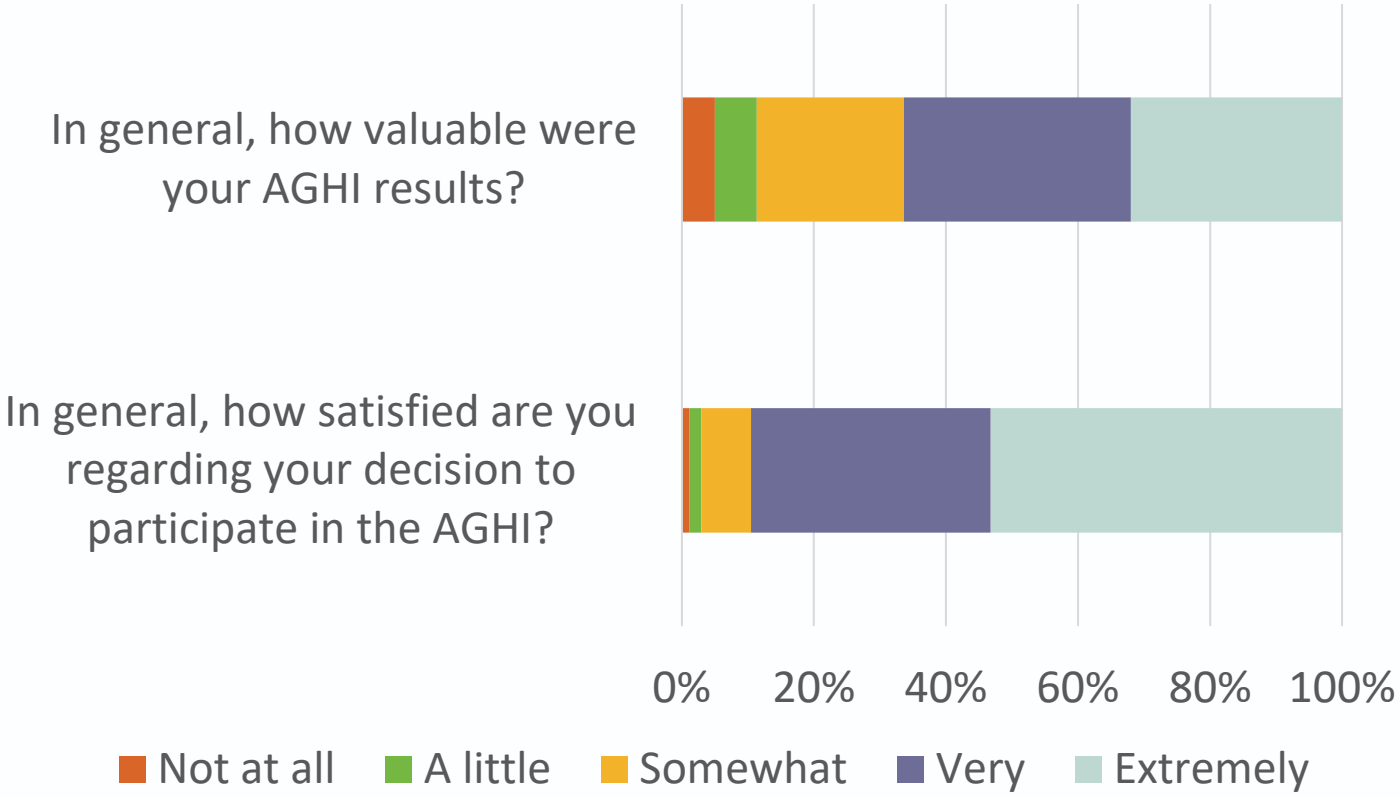
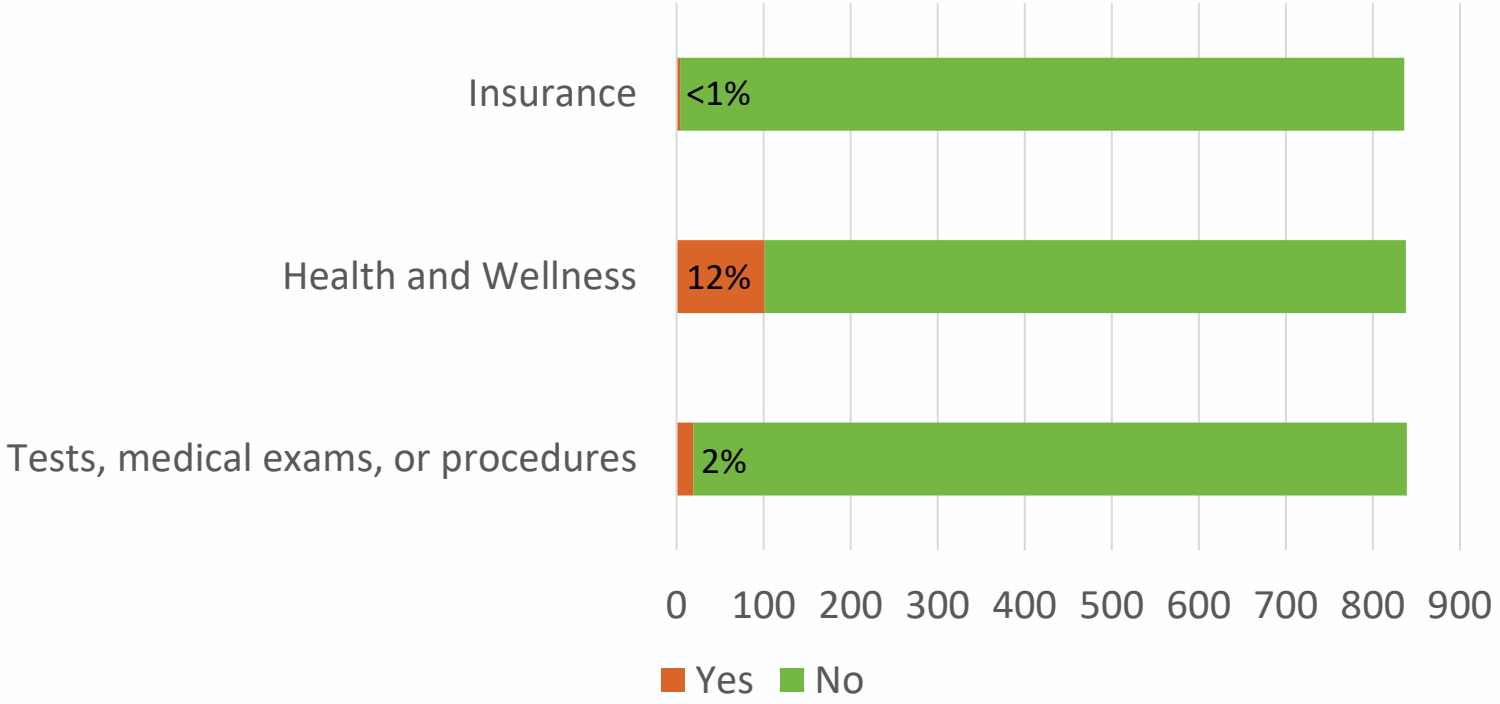



In general, how valuable were your AGHI results?
In general, how satisfied are you regarding your decision to participate in the AGHI?
0%
20%
40%
60%
80%
100%
Not at all
A little
Somewhat
Very
Extremely

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

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

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

Jim Cimino, MD
Director of UAB Informatics Institute

Informatics

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Biobank

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Engagement

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

Bioethics

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

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

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