Mind the Gap

Resources required to Receive, Process, & Interpret Research-Returned Whole Genome Data

Farren Briggs, PhD SCM
Assistant Professor, Case Western Reserve University

ndge Neuroimmunological Disorders Gene-Environment Epidemiology Lab

Department of Population and Quantitative Health Sciences

School of Medicine 1843 Case Western Reserve University

Case Western Reserve University Est. 1826 think beyond the possible

https://nathanjamail.com/the-knowledge-and-execution-gap/

Overview of Returning Whole Genome Data

- Where it all began
- Who are potential study participants?
- What genetic results/data might be Returned?
- How might genetic results/data be returned?
- How to interpret returned genetic data?
- Explore My Genetic Data

U.S. Federal Investment

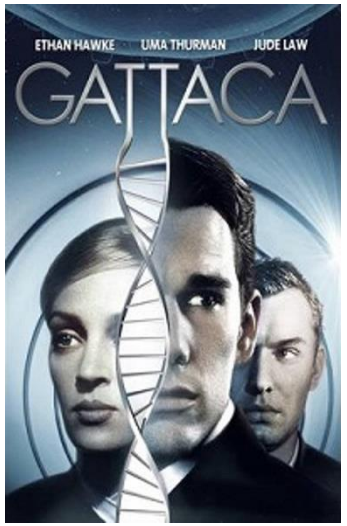
"Tonight I'm launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes.

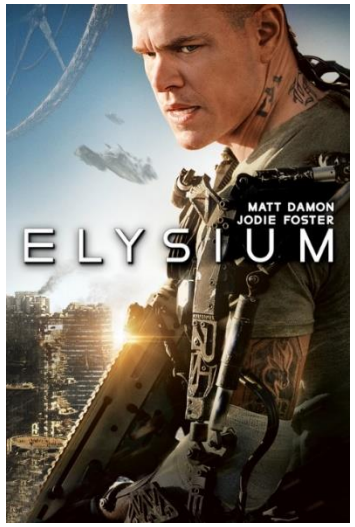
And to give us all access to the personalized information we need to keep ourselves and our families healthier."

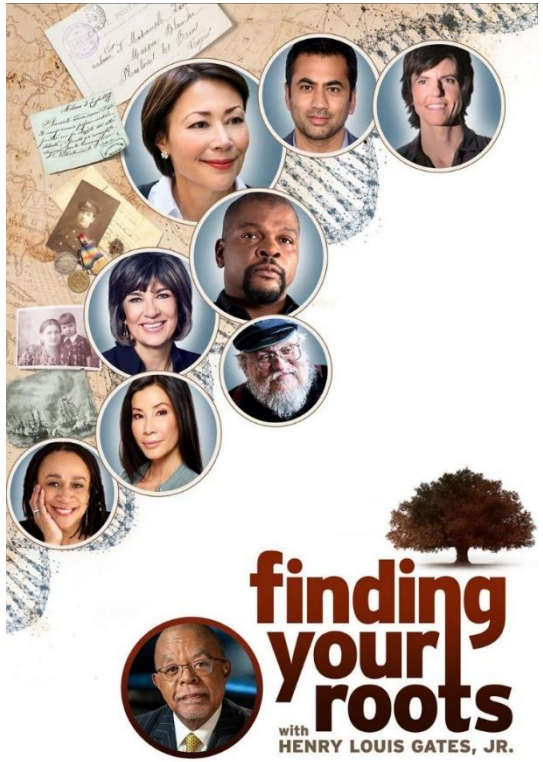
President Barack Obama
2015 State of the Union Address | January 20, 2015

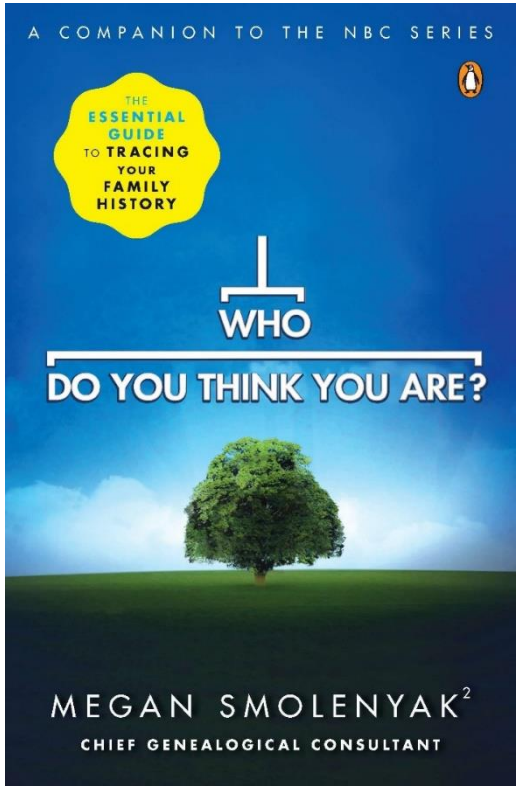
https://obamawhitehouse.archives.gov/precision-medicine

GENETICS GOES HOLLYWOOD TO DOCU-SERIES









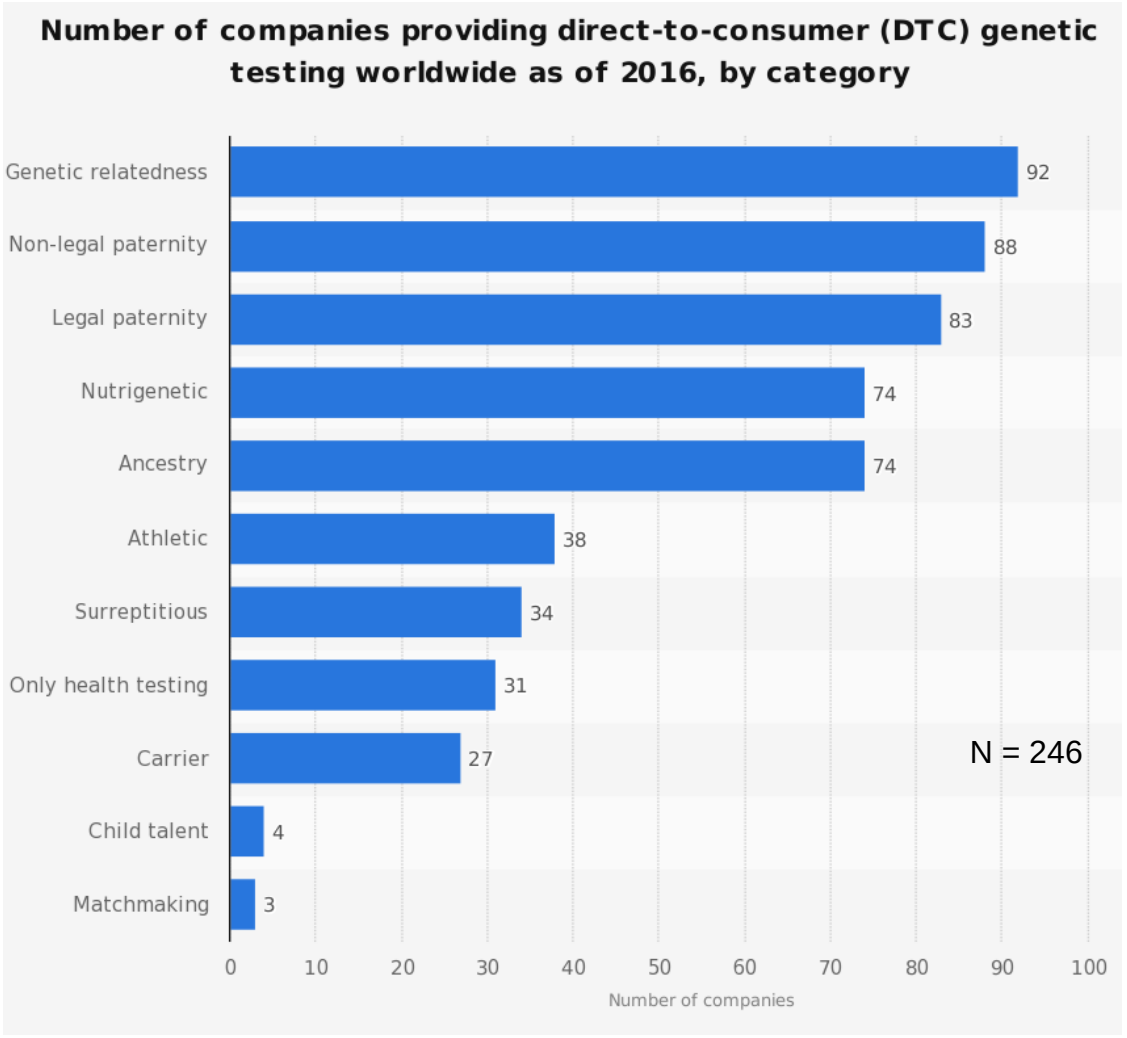
Direct To Consumer Genetic Testing (DTC-GT)

23andMe®

ancestryDNA™

MyHeritage

FamilyTreeDNA



Phillips AM, Appl Transl Genom, 2016 Feb 2; 8:16-22. http://dx.doi.org/10.1016/j.atg.2016.01.001

CELEBRITY TESTIMONIALS

https://www.youtube.com/watch?v=W5nyIAJlky4
https://www.aarp.org/health/healthy-living/info-2014/sheryl-crow-melissa-etheridge-beat-cancer.html
https://www.etonline.com/news/209150_exclusive_christina_applegate_youth_oregon_bad_moms_married_with_children

POTENTIAL RESEARCH PARTICIPANTS WANT THEIR RAW GENETIC DATA

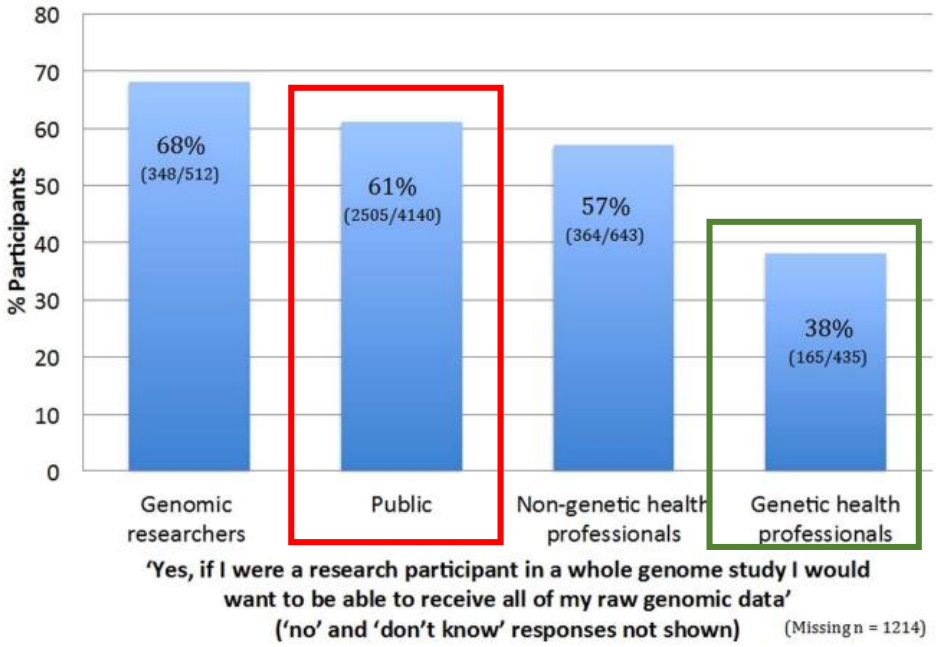


Figure 1 Interest in receiving raw genomic data.

Q: If you were given all of your raw genomic data from a research study, what would you do with this? (n=6944)
A: "I would seek out an interpretation of it" 62% (n=4320)

- 60% said "I'd analyse it myself" (n=2581)
  (Within the different professional groups, these are the percentages who would analyse the data themselves: 81% genomic researchers, 68% genetic health professionals, 56% other health professionals, 56% public)
- 57% said "I would ask for a referral to my local clinical genetics service" (n=2459)
- 43% said "I would ask my GP or Primary Care Physician" (n=1844)
- 41% said "would find a genomics researcher and ask them" (n=1775)
- 15% said "I would pay a commercial genetics company to analyse the data" (n=658)
- 5% had other suggestions: eg, "use google", "I would ask my bioinformatician colleagues", "I would share it on GitHub", "ask a genetic counsellor", "I would open source it to anyone online", "I would refer the raw data in a zip file to a company like 23andMe", "I would want information about interpreting the data before deciding how to proceed" (n=237)

Research Programs are now Returning Genetic data

Project	Dates	# genomes sequenced to-date	Platform	Results Returned	Report to Health Record	Uninterpreted Data to Participants	Accredited Lab	Last updated
Harvard PGP	2005-	352	WGS	Filtered Variants w/ Lit Annot	No	Yes (Variants)	No	Nov 2017
BWH/Harvard MedSeq	2011-	110	WGS	Monogenic, Common, PGx	**Yes**	FASTQ	Yes	Nov 28, 2017
Mount Sinai HealthSeq	2012–2015	40	WGS	Monogenic, Common, PGx	No	BAM, VCF	No	paper
Mayo "10 scientists"	2012–2014	10	WES	Monogenic	No	Yes	No	paper
Institute for Systems Biology (ISB) Pioneer 100	2014	108	WGS	Monogenic, Common, PGx	No	BAM, VCF	No	paper
BWH/BCH/Harvard BabySeq Project	2015–	160	WGS	Monogenic, PGx	**Yes**	FASTQ	Yes	Nov 2017
Nevada Institute of Personalized Medicine	2015–	0	WES	Monogenic, PGx	No	BAM, VCF	No	paper
NYGC Seeq.io	2016-	~500	WGS	ancestry, microbiome	No	BAM	No	Feb 2017
NIH All of Us	**2017-**	**?**	**WGS**	**ACMG 59, PGx**	**?**	**?**	**Yes**	**Paper 8/15/2019**
100,000 Genomes Project (UK)	2015-	44,633	WGS	Monogenic, PGx	**Yes**	Yes	Yes	January 2018

12/10/2018 NIH *All of Us* Webinar:

Genomic Data returned includes: PGx, AMCG pathogenic findings, Ancestry data, and **Raw data files**

Modified table from https://github.com/jasonbobe/sharing-genome-studies/blob/master/table.md; Hum Genomics. 2018 Feb 17;12(1):7. doi: 10.1186/s40246-018-0139-5.
https://allofus.nih.gov/sites/default/files/genetic-counseling-resource-funding-opportunity-webinar-december-10-2018.pptx

Who are Potential Study Participants?

Example

WHO WILL BE A PART OF ALL OF US?

- Longitudinal cohort of **≥ 1,000,000 or more people** living in the United States
- **Goal: "to accelerate research and improve health**.. Uncover(ing) paths toward delivering **precision medicine** – or individualized prevention, treatment, and care – for all of us"
- **How:** By taking into account individual differences in **lifestyle, socioeconomics, environment, and biology**.

Persons in underrepresented populations will be **prioritized.**

The target percentage of persons in racial and **ethnic minorities** is **>45%** and that of persons in **under-represented** populations is **>75%.**

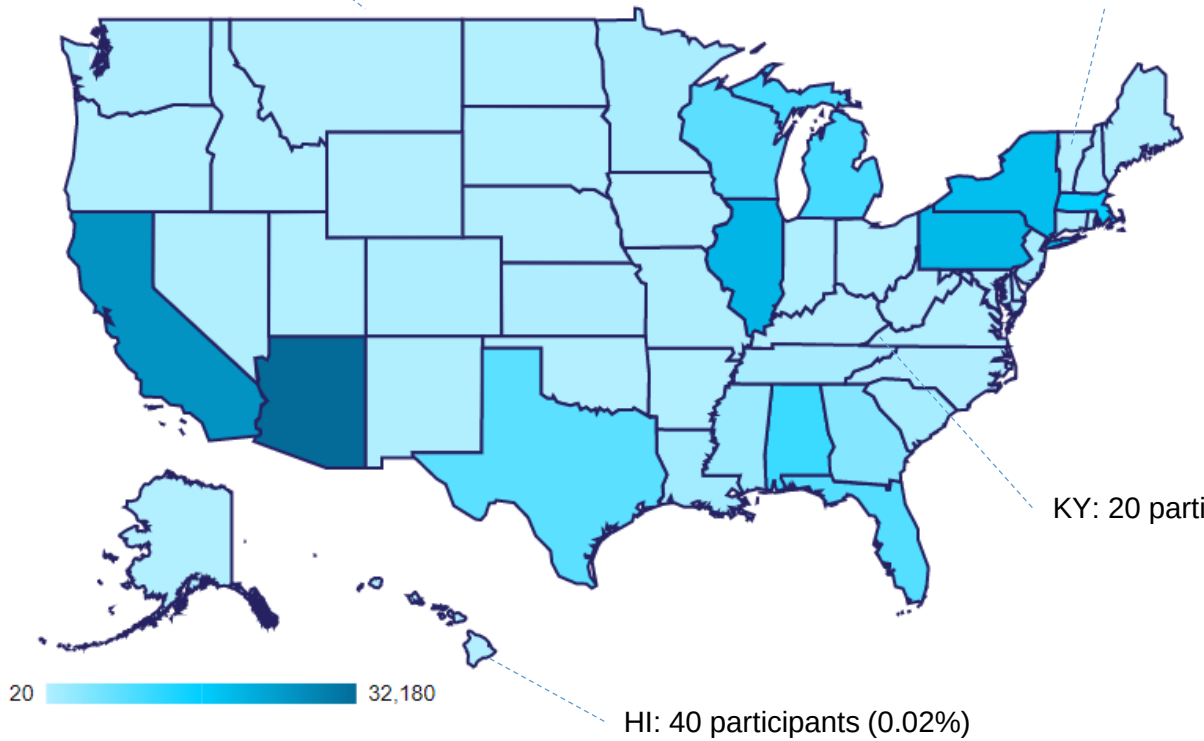
N Engl J Med 2019; 381:668-676 DOI: 10.1056/NEJMsr1809937

GEOGRAPHY

All of Us RESEARCH PROGRAM | The Future of Health Begins With You

256,000+
Participants

Geography



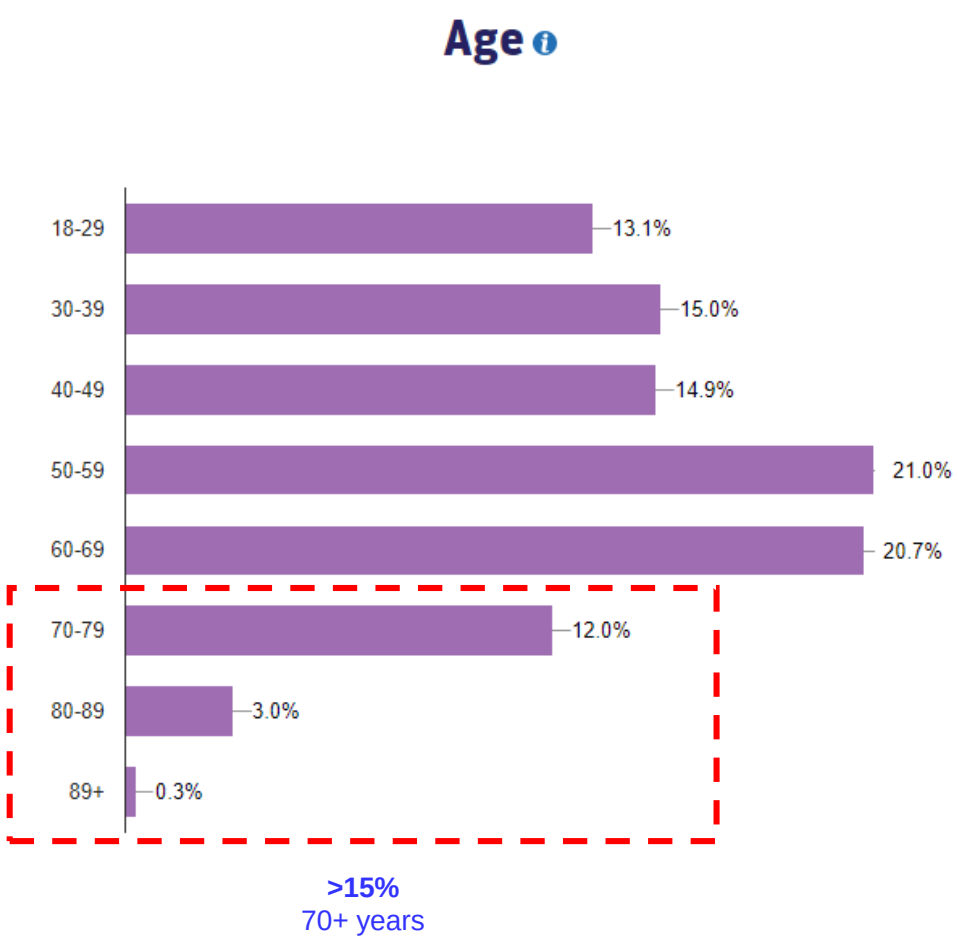
Outreach

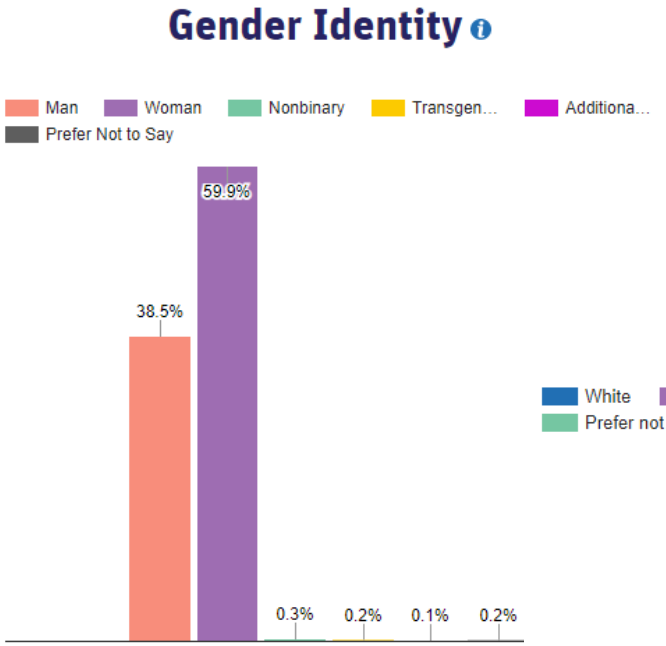
100+
Funded Partner Organizations

370+
Sites Collecting Samples and Measurements

AGE, SEX, & RACE/ETHNICITY

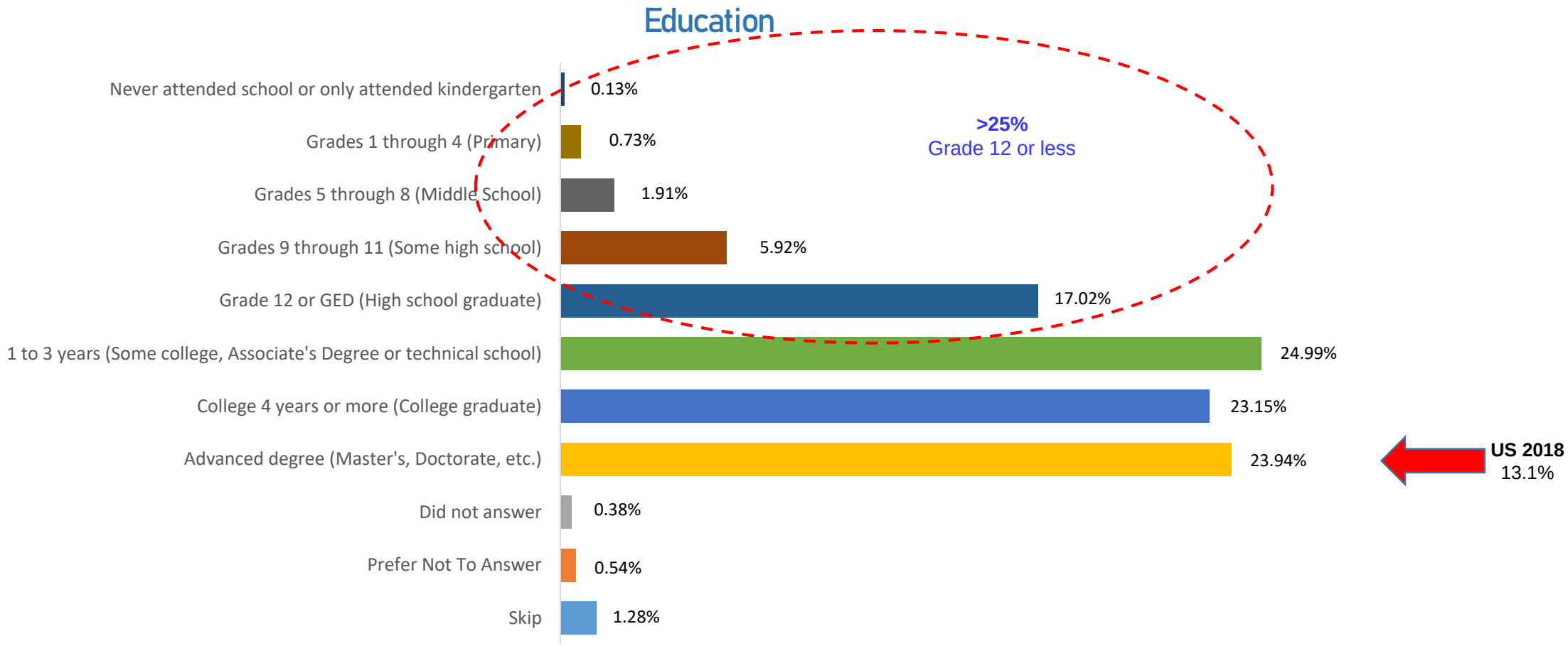
All of Us RESEARCH PROGRAM
The Future of Health Begins With You





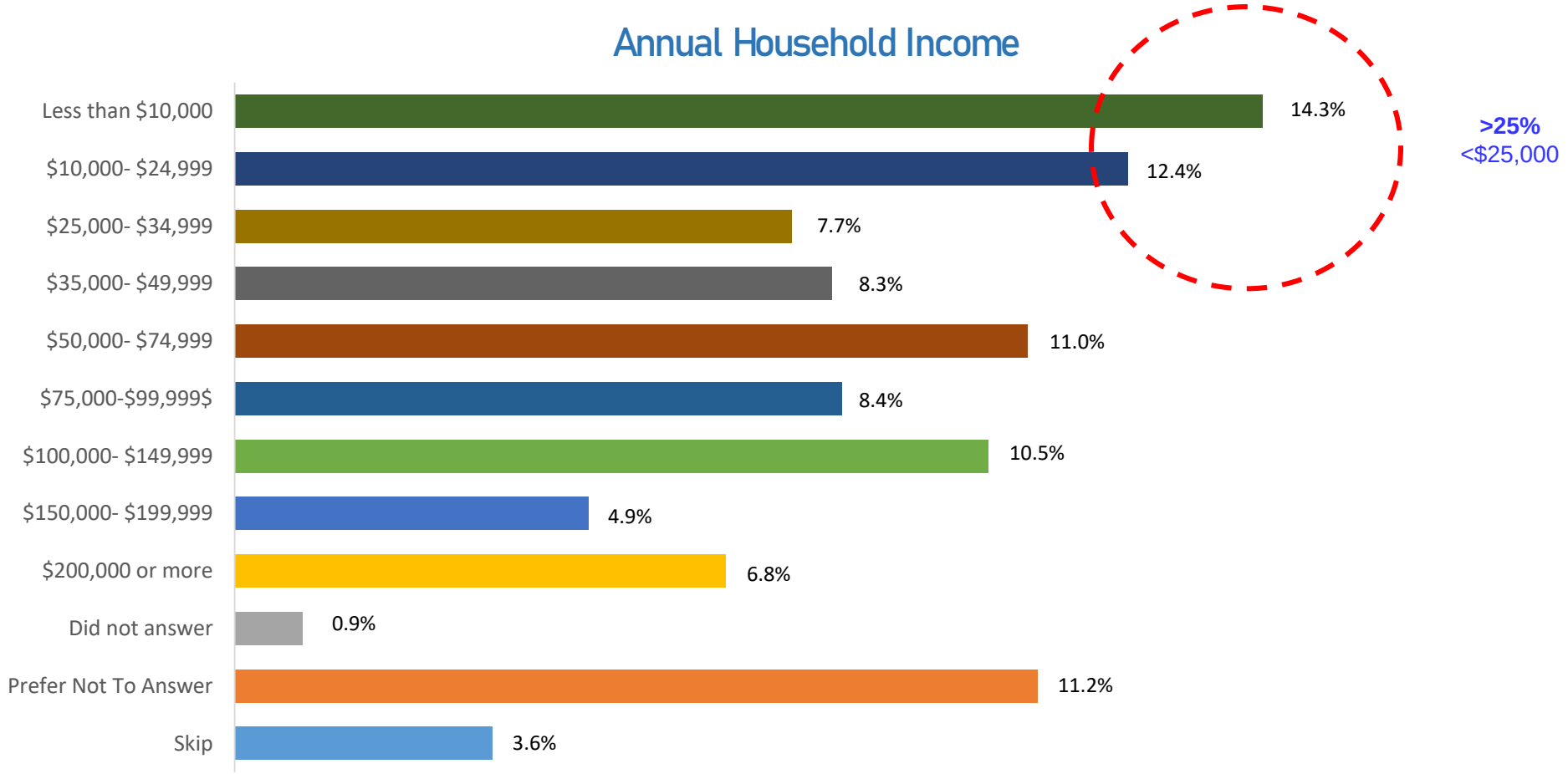
https://www.researchallofus.org/data/data-snapshots/ accessed 09/06/2019

EDUCATION



https://www.researchallofus.org/data/data-snapshots/ accessed 09/06/2019

ANNUAL HOUSEHOLD INCOME

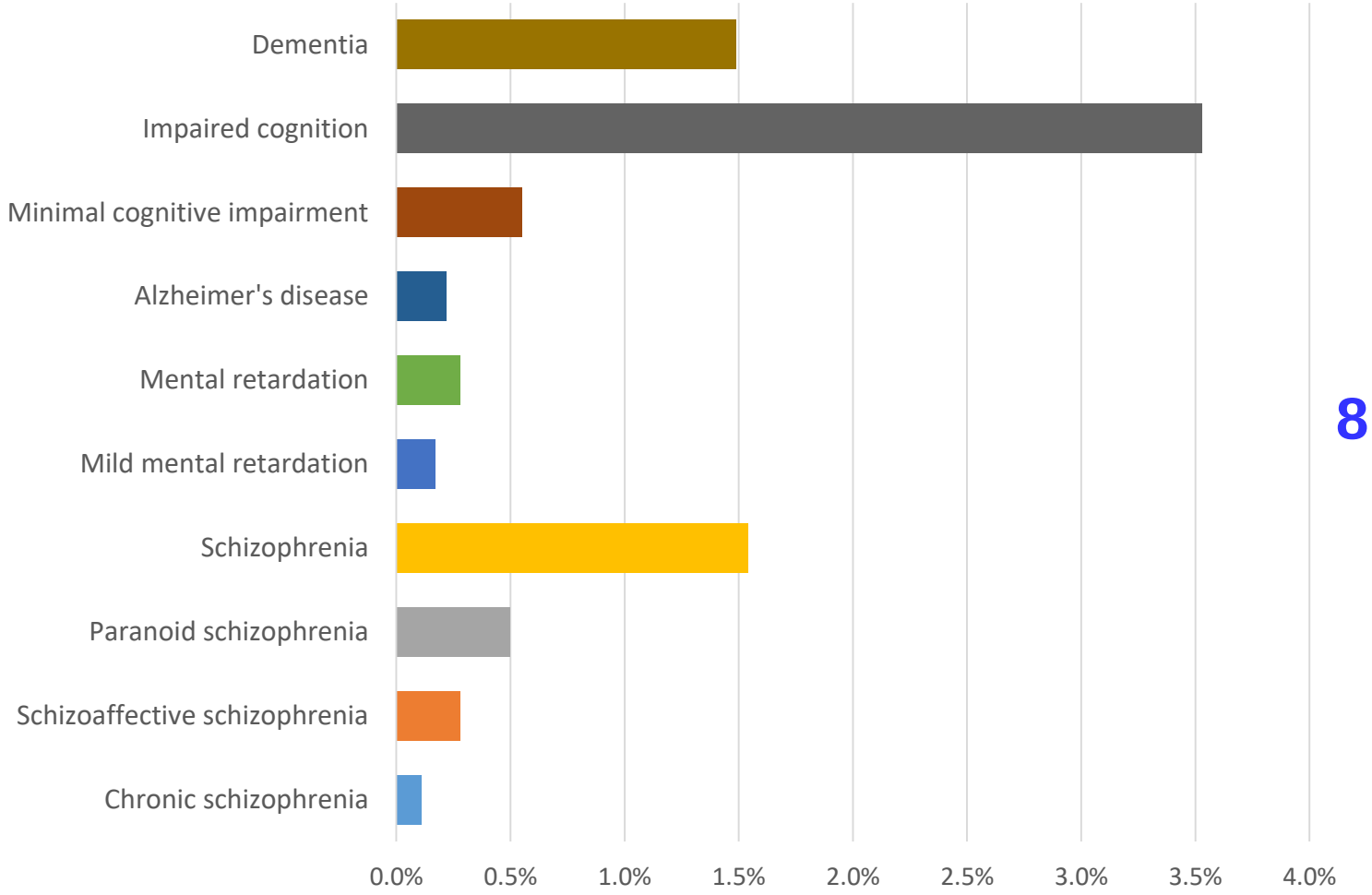


https://www.researchallofus.org/data/data-snapshots/ accessed 09/06/2019

HEALTH STATES

All of Us RESEARCH PROGRAM | The Future of Health Begins With You

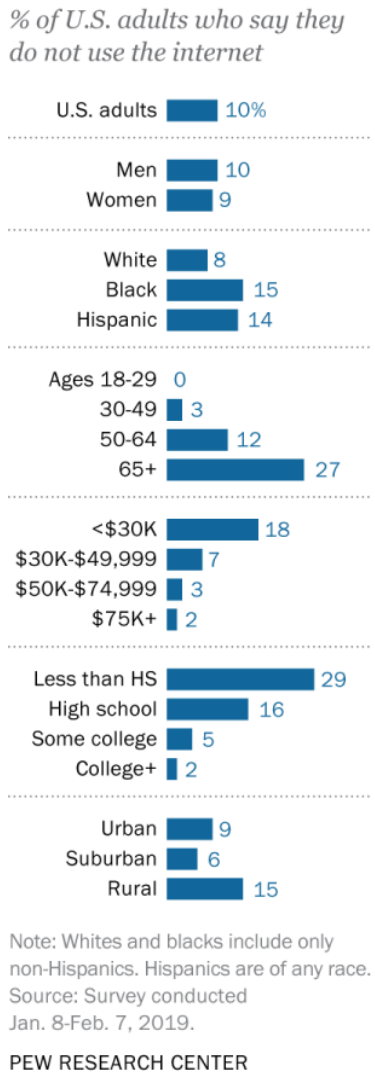
36,260 Participants

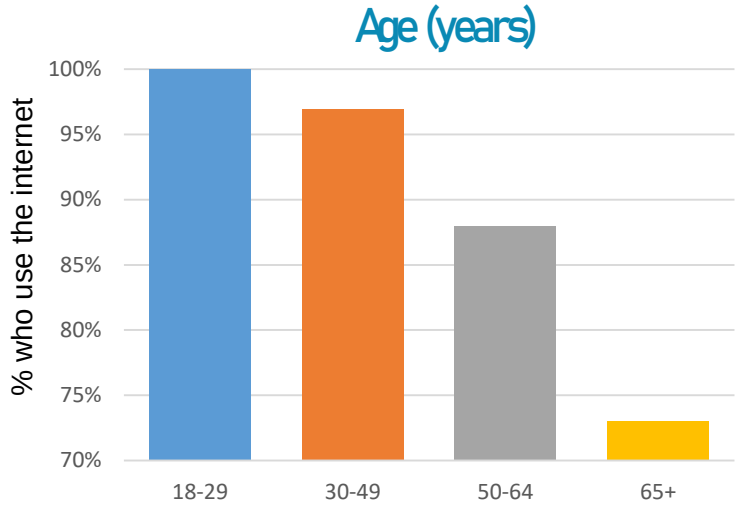


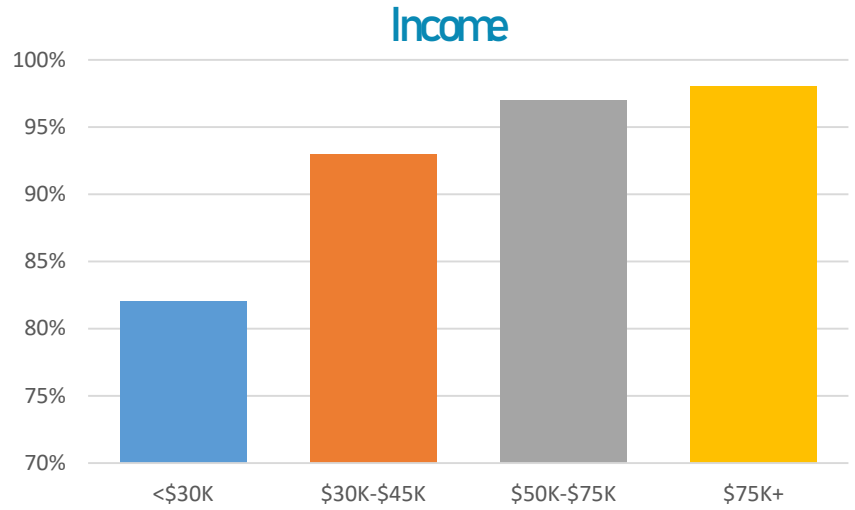
8.7%

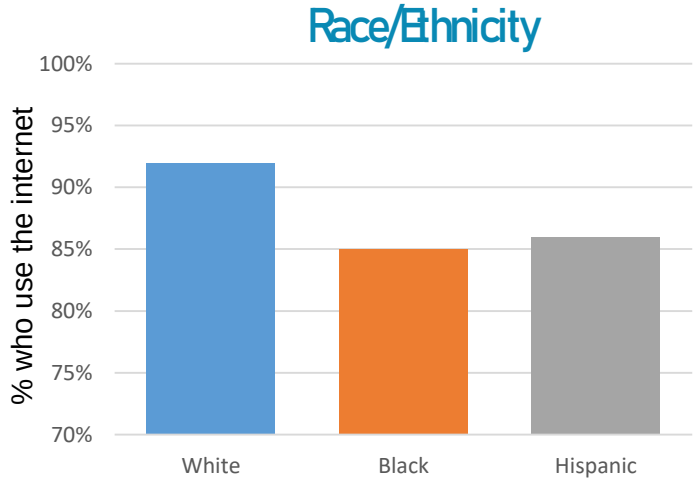
https://databrowser.researchallofus.org/ accessed 09/06/2019

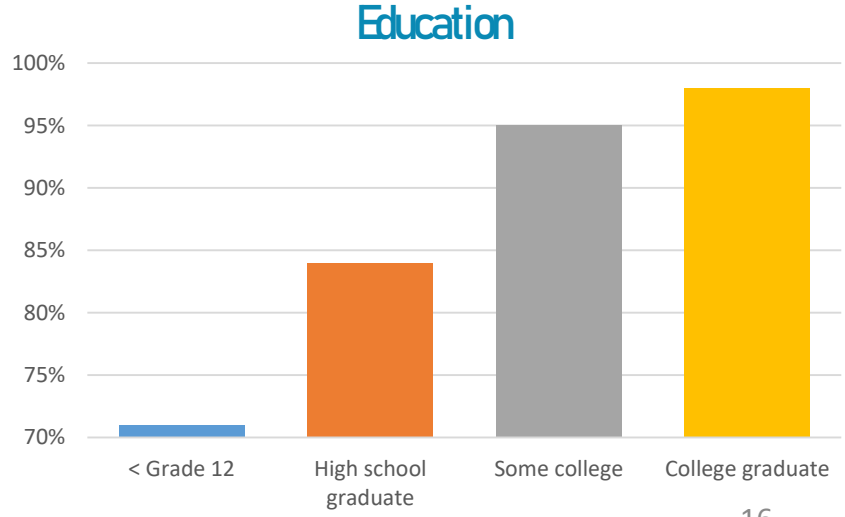
Other Major USA Population Traits
2019 Internet Access









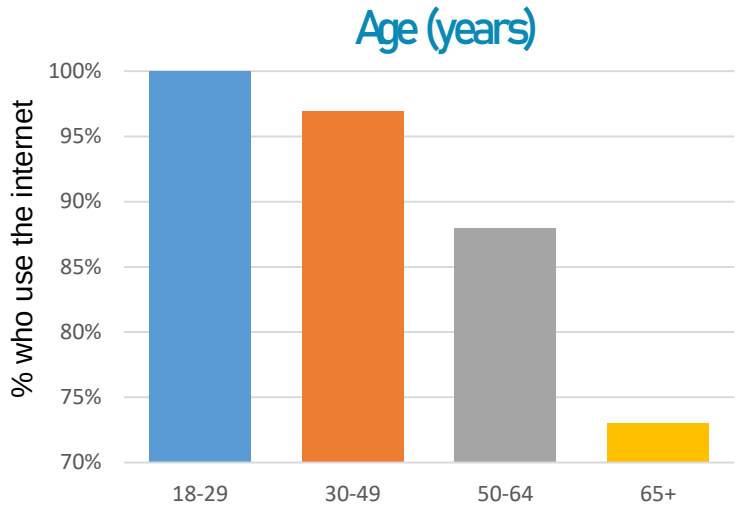


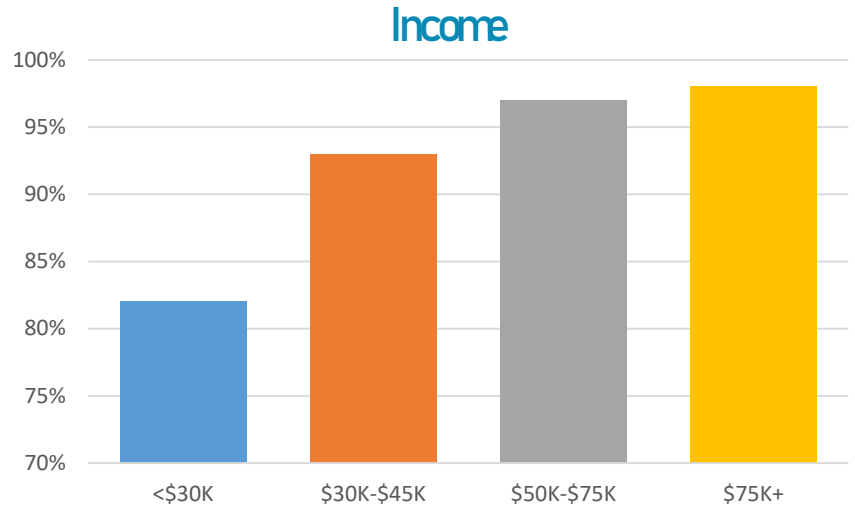
https://www.pewresearch.org/fact-tank/2019/04/22/some-americans-dont-use-the-internet-who-are-they/

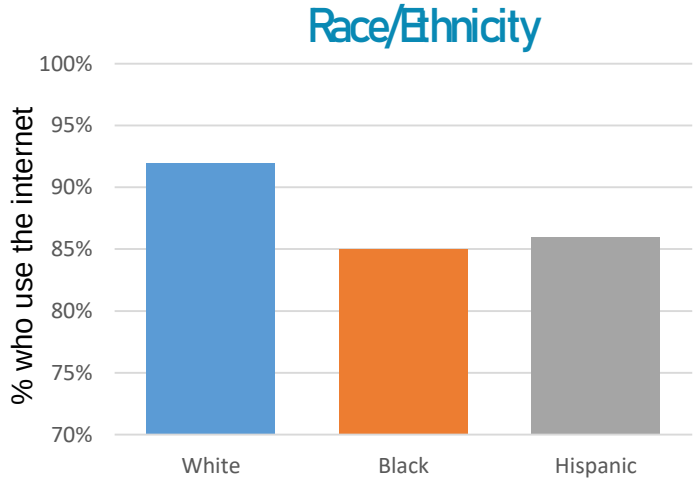
https://www.pewinternet.org/fact-sheet/internet-broadband/

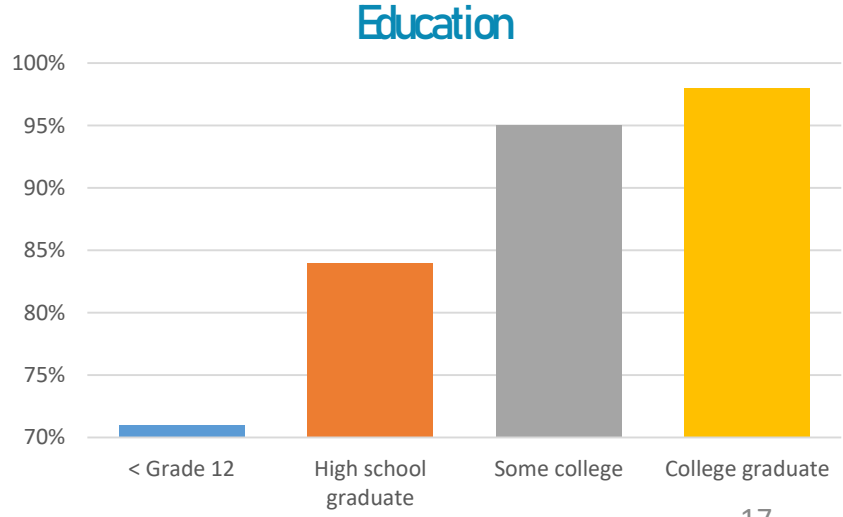
Other Major USA Population Traits
2019 Internet Access

Access to broadband and non-handheld computers **much lower**









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https://www.pewinternet.org/fact-sheet/internet-broadband/

Other Major USA Population Traits
Digital Illiteracy

16%

16-65 yrs

35%

Hispanics

41%

< Grade 12

28%

55-65 yrs

22%

Blacks

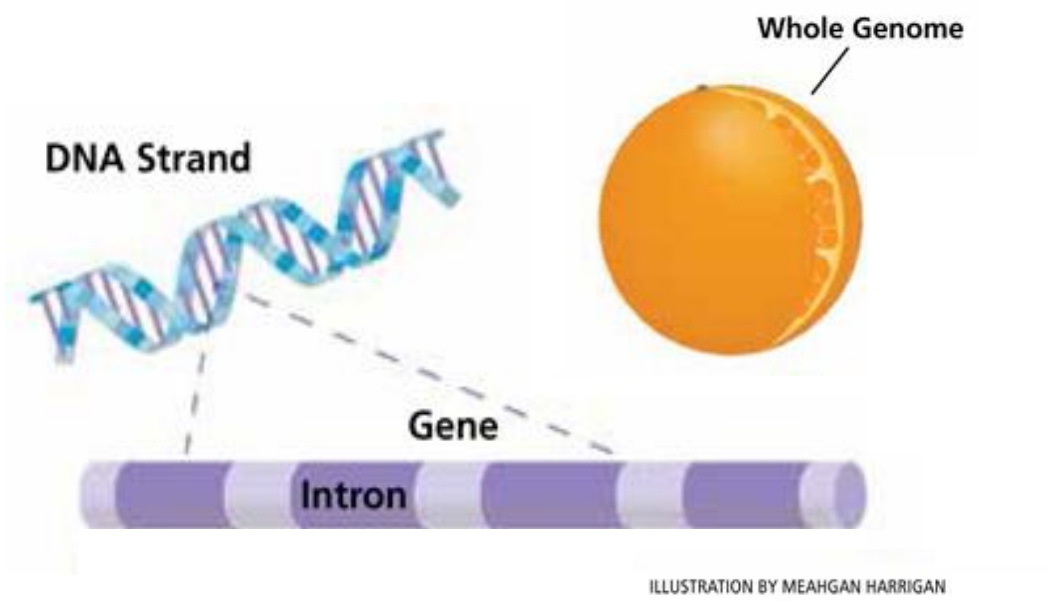
17%

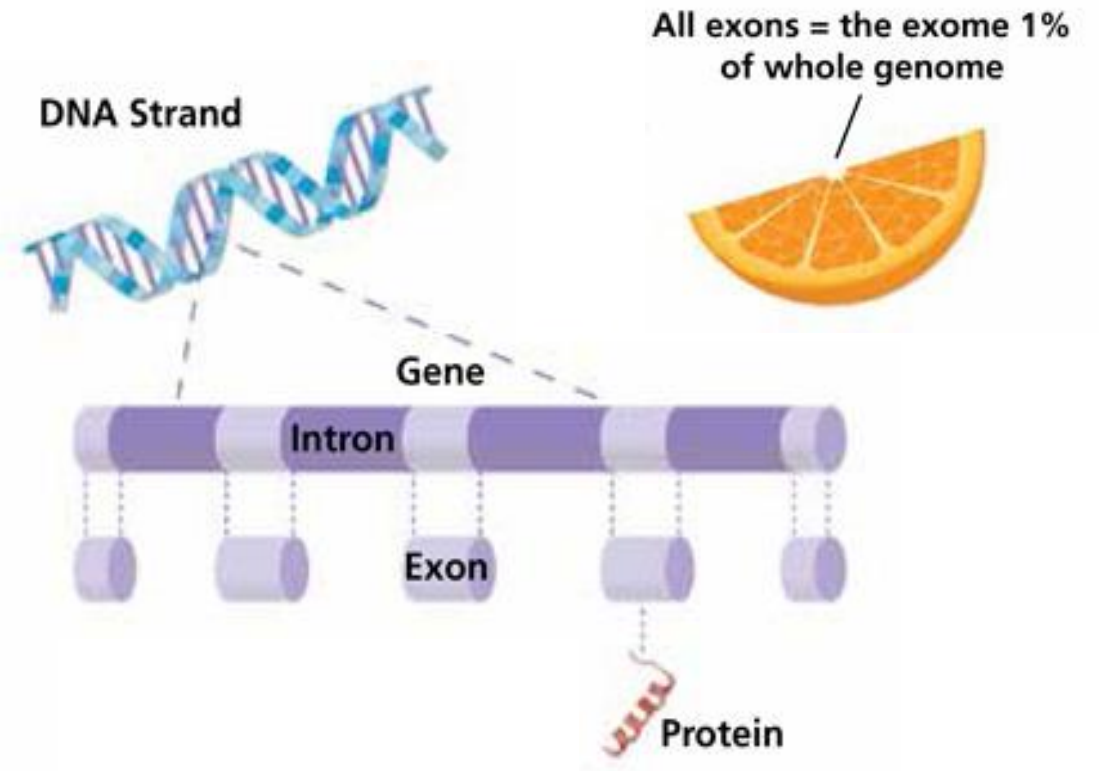
High school Grad

Mamedova S, Pawlowski E (2018) A description of US adults who are not digitally literate. In: Hudson L (ed) Stats in Brief. US Department of Education, Washington DC

What Curated Genetic Results/Data Might be Returned?

Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES)

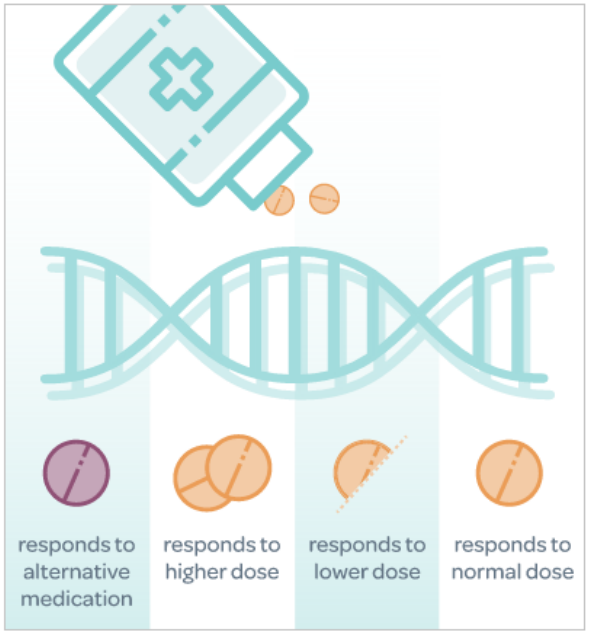




Returning Curated Genetic Findings

All of Us RESEARCH PROGRAM
The Future of Health Begins With You

ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®



ACMG 59

Pharmacogenes

www.acmg.net

https://www.genelex.com/what-is-pharmacogenetics/

CURRENT RECOMMENDATIONS FOR 2º FINDINGS IN CLINICAL WES/WGS

ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

Secondary finding – a result not related to test indication

Example: WES was ordered for a female patient with family history of breast and ovarian cancer

- Order was likely for ***BRCA1/BRCA2*** variants
- Data also reveal an ***LDLR*** mutation associated with familial hypercholesterolemia
- ACMG recommends reporting both *BRCA1/BRCA2* **AND** *LDLR* findings to patient

CURRENT RECOMMENDATIONS FOR 2º FINDINGS IN CLINICAL WES/WGS

ACMG
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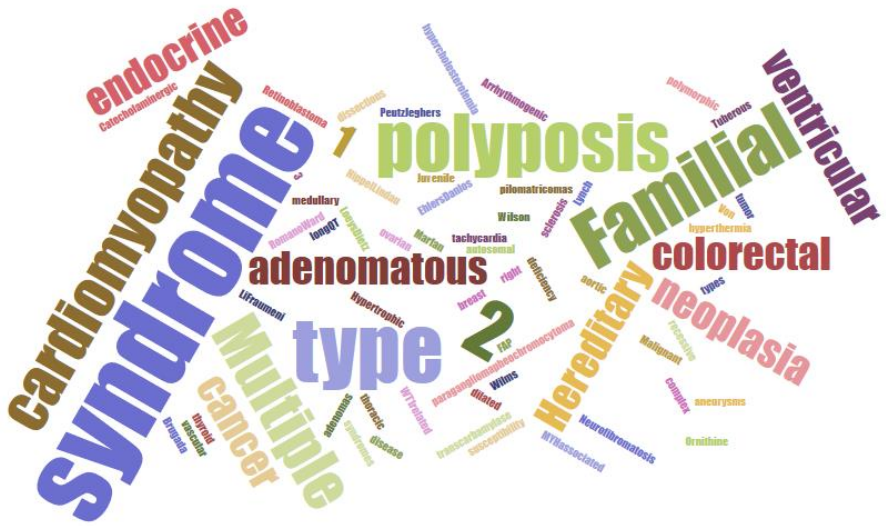
Translating Genes Into Health®

ACMG maintains and updates lists of gene-condition pairs to be reported

Current list is ACMG SF v2.0



(27 conditions)

(59 genes)

Kalia et al (2017) *Genet Med* 19:249-255

Current Recommendations for 2º Findings in Clinical WES/WGS

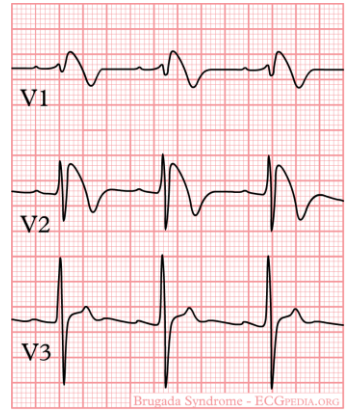
ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

Characteristics of "**ACMG 59**":

Condition has established prevention, intervention, or treatment strategies

Gene has **known** highly penetrant mutations

Example: Brugada syndrome and ***SCN5A*** Ile176Val (LOF)



Cardiac arrhythmia associated with sudden death

Implantable cardioverter-defibrillator is established prevention strategy

Ecgpedia.org

CHALLENGES FOR SECONDARY FINDINGS IN CLINICAL WES OR WGS

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Translating Genes Into Health®

ACMG recommends reporting **known** and **expected** pathogenic variants

ClinVar Variant Classification

ACMG STANDARDS AND GUIDELINES | Genetics inMedicine

Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology

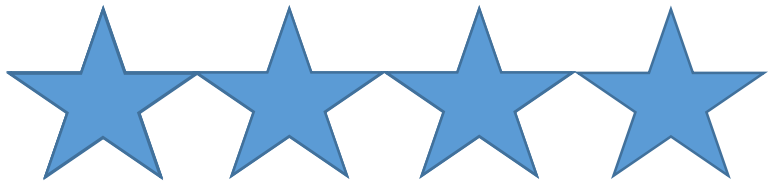
Sue Richards, PhD[1], Nazneen Aziz, PhD[2,16], Sherri Bale, PhD[3], David Bick, MD[4], Soma Das, PhD[5], Julie Gastier-Foster, PhD[6,7,8], Wayne W. Grody, MD, PhD[9,10,11], Madhuri Hegde, PhD[12], Elaine Lyon, PhD[13], Elaine Spector, PhD[14], Karl Voelkerding, MD[13] and Heidi L. Rehm, PhD[15]; on behalf of the ACMG Laboratory Quality Assurance Committee

Genet Med. 2015 May;17(5):405-24. doi: 10.1038/gim.2015.30. Epub 2015 Mar 5.

KNOWN/EXPECTED PATHOGENIC VARIANTS: CLINVAR RESOURCE

Variants are classified by consequence

The **star rating** represents variant's review status, an indication of classification confidence



Practice Guideline

KNOWN/EXPECTED PATHOGENIC VARIANTS: CLINVAR RESOURCE

Variants are classified by consequence

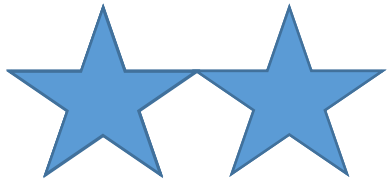
The **star rating** represents variant's review status, an indication of classification confidence

Reviewed by Expert Panel
(e.g., CPIC)

KNOWN/EXPECTED PATHOGENIC VARIANTS: CLINVAR RESOURCE

Variants are classified by consequence

The **star rating** represents variant's review status, an indication of classification confidence



Criteria provided; multiple submitters; no conflicts

KNOWN/EXPECTED PATHOGENIC VARIANTS: CLINVAR RESOURCE

Variants are classified by consequence

The **star rating** represents variant's review status, an indication of classification confidence

★ Criteria provided; multiple submitters; conflicts

★ Criteria provided; single submitter

KNOWN/EXPECTED PATHOGENIC VARIANTS: CLINVAR RESOURCE

Variants are classified by consequence

The **star rating** represents variant's review status, an indication of classification confidence

No assertion criteria provided

An Application of Reporting 2º Findings in Clinical WES/WGS

American College of Medical Genetics and Genomics
Translating Genes Into Health®

Example: Geisinger required "pathogenic" variants to have

1) ★★ or ★★★ ClinVar rating

OR

2) Predicted loss of function

OR

3) Both

JAMA Network | Open

Original Investigation | Genetics and Genomics

Exome Sequencing–Based Screening for *BRCA1/2* Expected Pathogenic Variants Among Adult Biobank Participants

CHALLENGES WITH RETURN OF ACMG RESULTS

ACMG recommendations evolve over time

2013

56 gene-condition pairs

including

~~*MYLK* and Familial thoracic aortic aneurysm and dissection~~

2016

59 gene-condition pairs

now including

ATP7B and Wilson disease
BMPR1A and Juvenile polyposis
SMAD4 and Juvenile polyposis
OTC and ornithine transcarbamylase deficiency

Kalia et al (2017) *Genet Med* 19:249-255

CHALLENGES WITH RETURN OF ACMG RESULTS

The use of ACMG secondary findings recommendations for general population screening: a policy statement of the American College of Medical Genetics and Genomics (ACMG)

ACMG Board of Directors[1]

All of Us

Population screening (?)

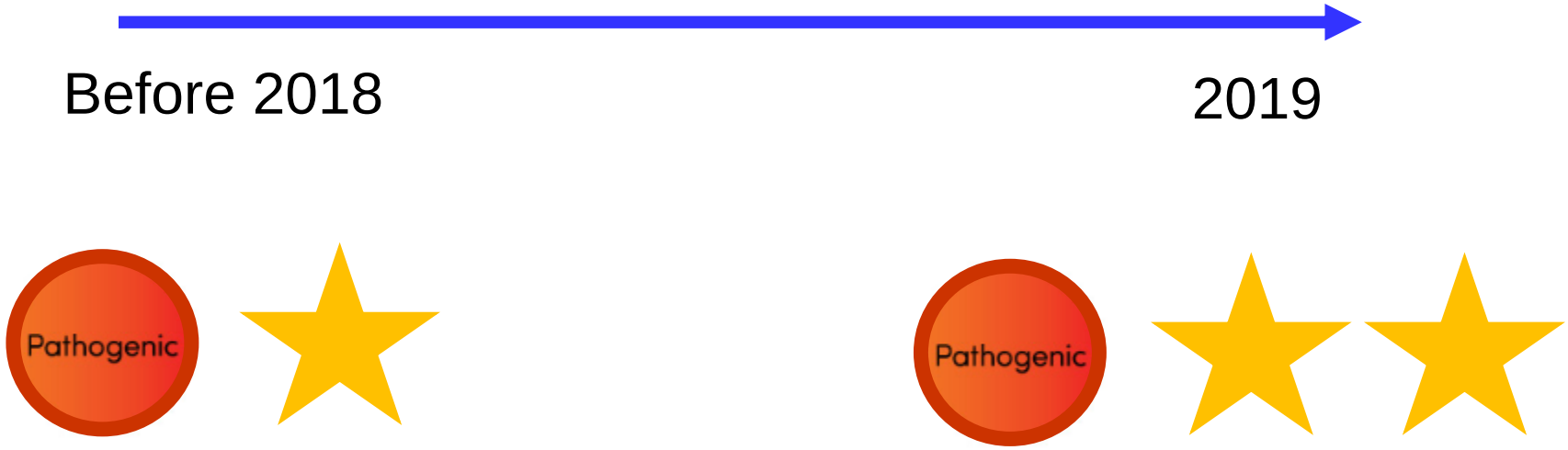
The American College of Medical Genetics and Genomics (ACMG) has previously published policy statements on the reporting of secondary findings in clinical exome and genome sequencing (ACMG SF v1.0 and ACMG SF v2.0), also known as the "ACMG 56" and "ACMG 59," respectively.[1,2] These recommendations specifically stated that "reporting some incidental [a.k.a. secondary] findings would likely have medical benefit for the patients and families of patients undergoing ***clinical sequencing***" (ACMG board's emphasis). The ACMG SF v2.0 list of genes was not validated for general population screening. The use of ACMG SF v2.0 for purposes other than reporting incidental findings after clinical sequencing is not endorsed by ACMG.

(2019) *Genet Med* 21:1467-1468

CHALLENGES WITH RETURN OF ACMG RESULTS

ClinVar annotations change over time

LRRK2 rs34637584
Autosomal dominant Parkinson disease 8



CHALLENGES WITH RETURN OF ACMG RESULTS

ClinVar annotations change over time

HFE rs1800562
Hereditary hemochromatosis

RETURNING CURATED GENETIC FINDINGS

All of Us RESEARCH PROGRAM
The Future of Health Begins With You

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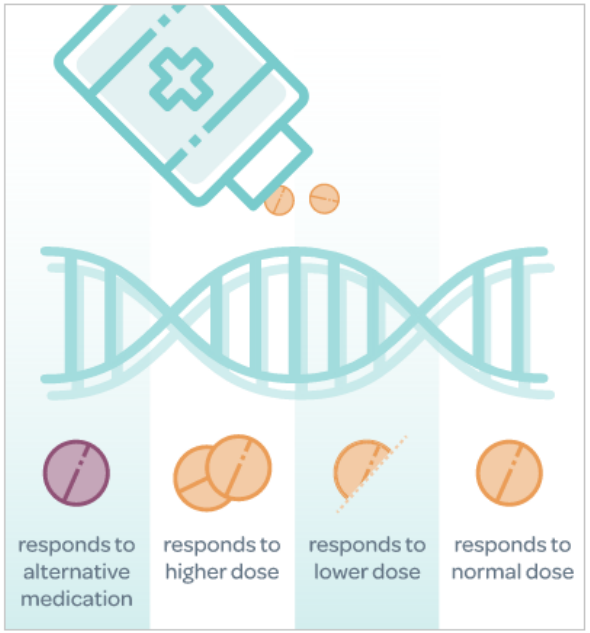


ACMG 59

Pharmacogenes

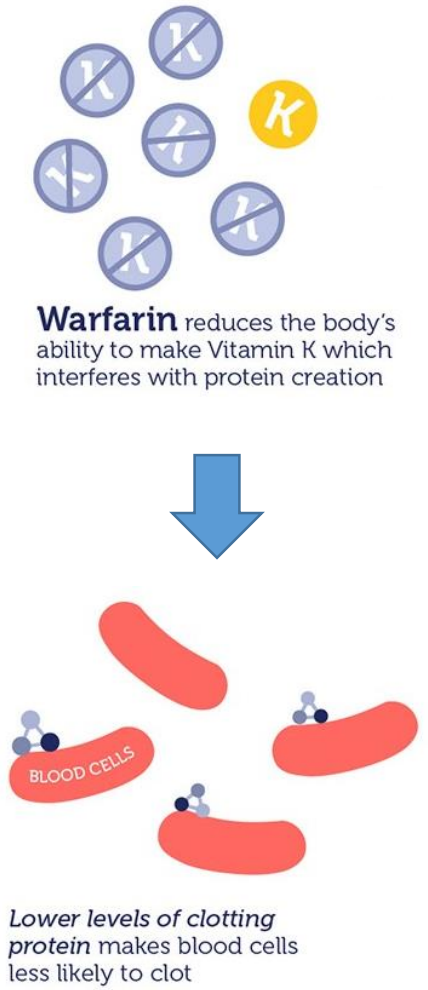
www.acmg.net

https://www.genelex.com/what-is-pharmacogenetics/

The Genetics of Drug Response Pharmacogenomics

FDA (2017) Drug Label for Warfarin dosing
(Prevention and treatment of various thrombotic disorder)

VKORC1	CYP2C9				
	*1/*1	*1/*2	*1/*3	*2/*2	*2/*3
GG	5-7 mg	5-7 mg	3-4 mg	3-4 mg	3-4 mg
AG	5-7 mg	3-4 mg	3-4 mg	3-4 mg	0.5-2 mg
AA	3-4 mg	3-4 mg	0.5-2 mg	0.5-2 mg	0.5-2 mg



The Genetics of Drug Response Pharmacogenomics

CPIC is an expert panel that
- Creates
- Curates
- Posts

Gene/drug Clinical Practice Guidelines that are
- Freely available
- Peer-reviewed
- Evidence-based
- Updatable

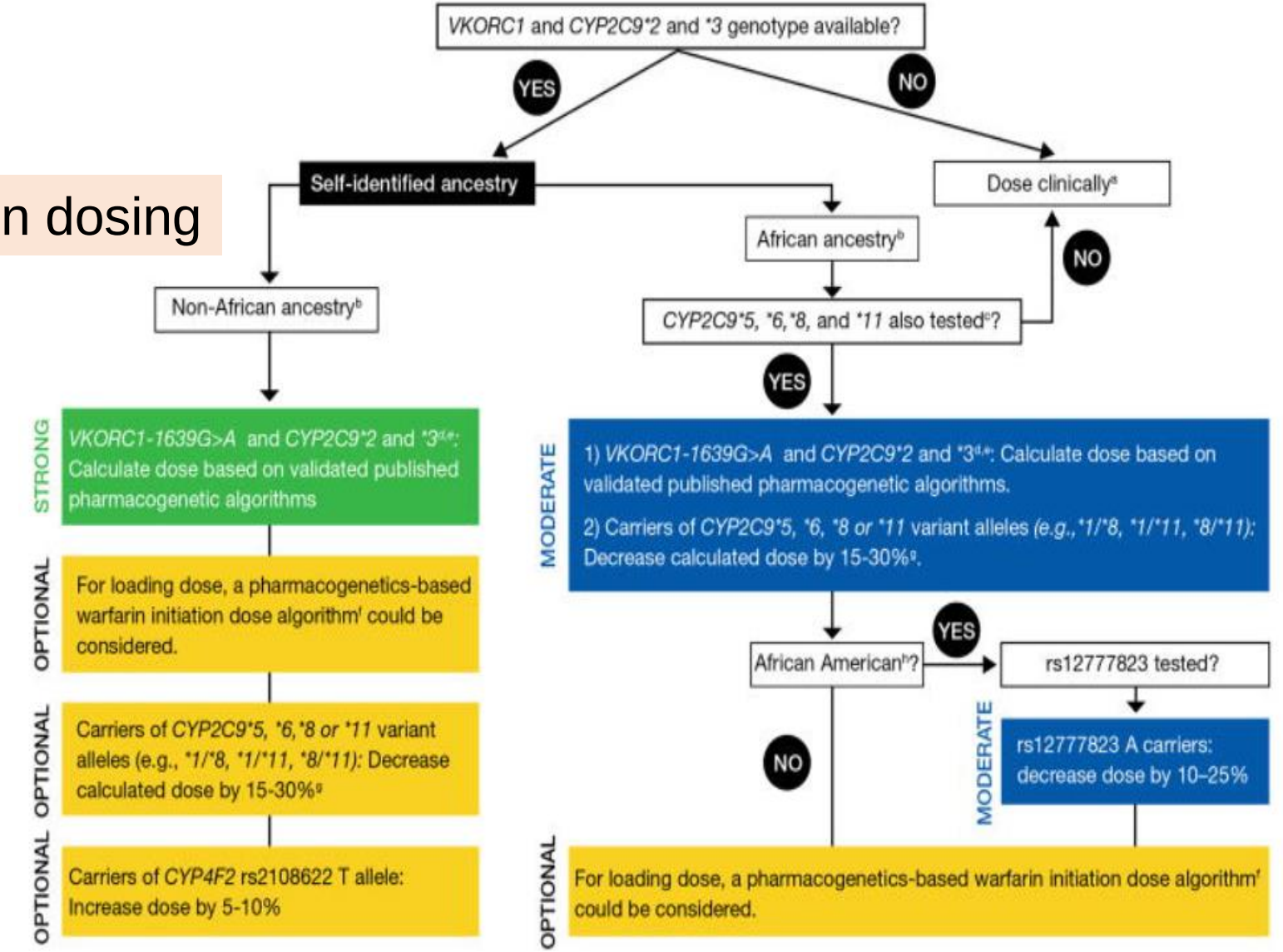
ClinVar 

61 dosing guidelines
19 genes
46 drugs

As of 9/8/2019

CHALLENGES WITH RETURN OF PGx RESULTS

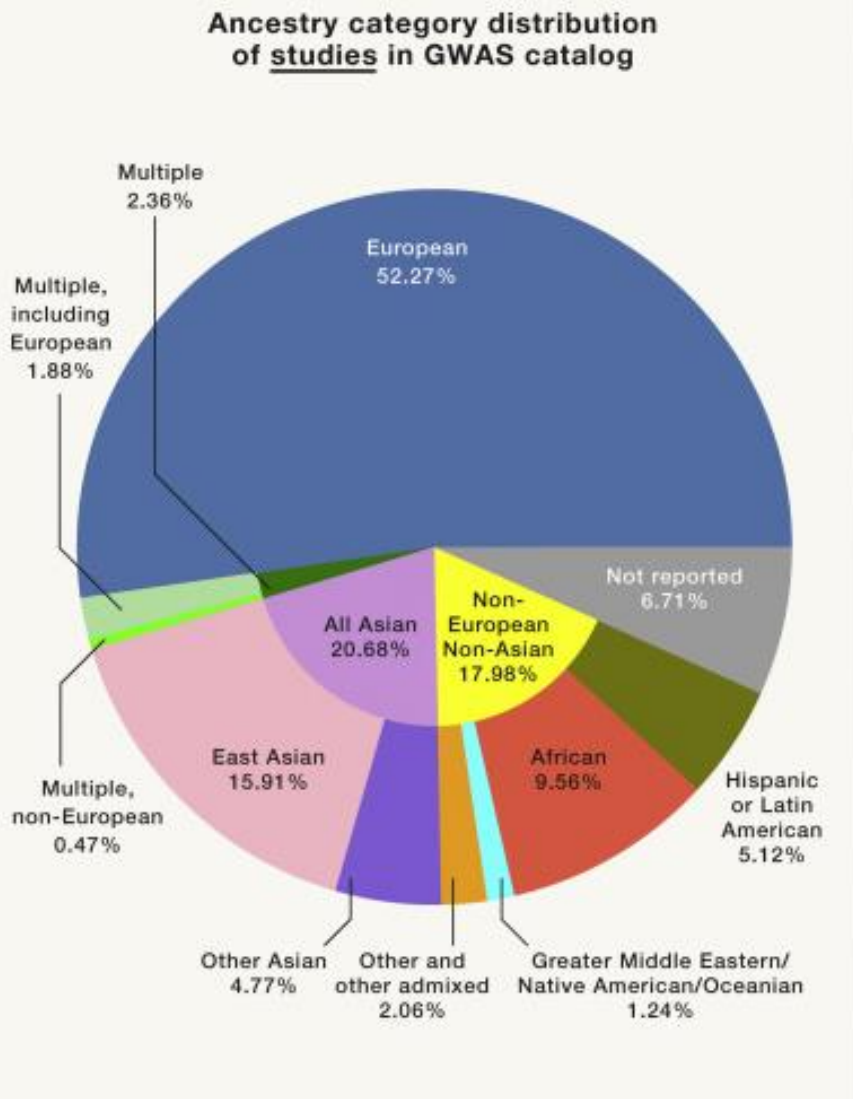
Warfarin dosing

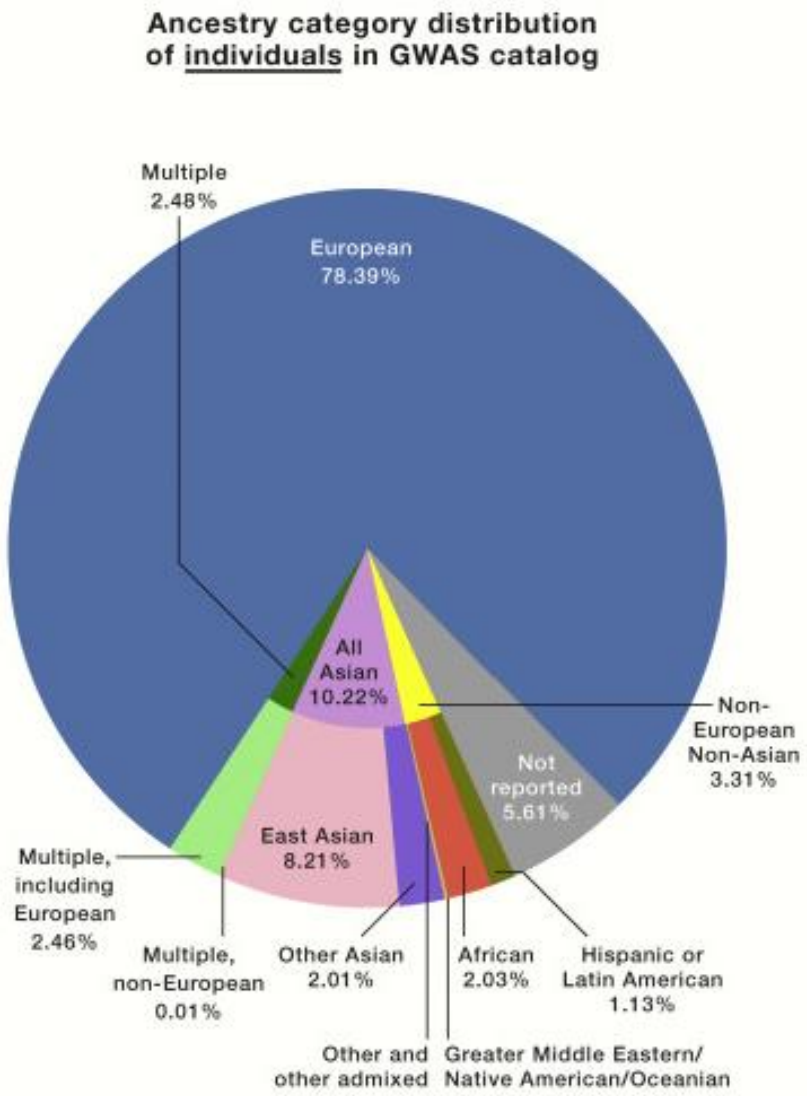


Pharmacogenomic recommendations **VARY** by race/ethnicity or genetic ancestry

Johnson et al (2017) *Clin Pharmacol Ther* 102(3):397-404

CHALLENGES WITH RETURN OF PGx RESULTS





Not enough data available in non-Europeans; therefore, the **discovery** of pharmacogenes for diverse populations are lagging

Sirugo, Williams, Tishkoff (2019) *Cell* 177(1):26-31

How might Curated Genetic Results/Data be Returned?

RETURN OF CURATED RESEARCH GENETIC RESULTS

Personal report
via snail mail

but

Not easily scalable
Expensive (?)
Mobile population

http://womenobgyn.net/education/gynecology-genetics/

RETURN OF CURATED RESEARCH GENETIC RESULTS

Through your healthcare provider

but

RETURN OF CURATED RESEARCH GENETIC RESULTS

Through a Web-based tool

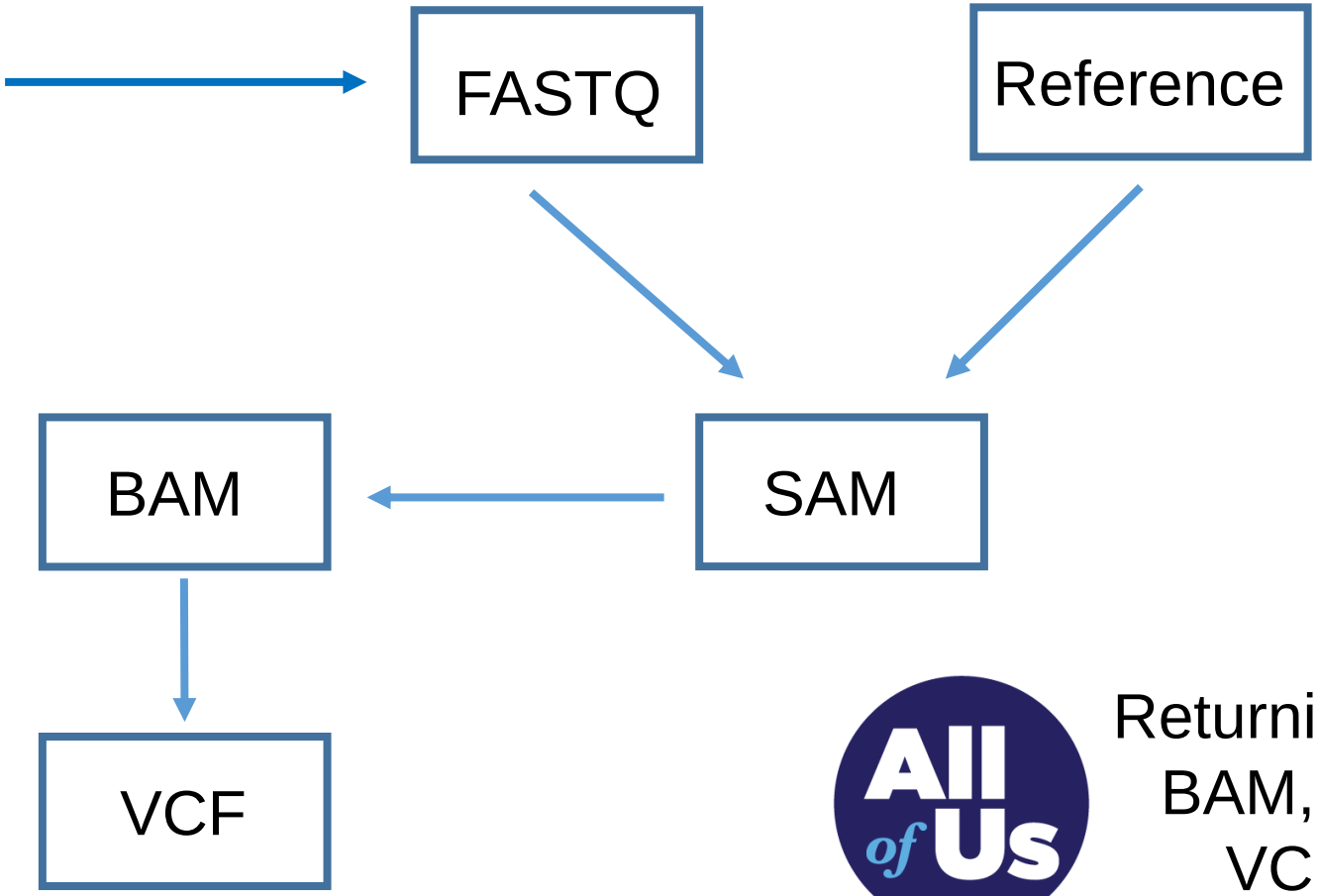
but

My46 enables individuals to manage their results from genetic testing, whether it is a single result being offered for return or the hundreds of results that can be offered for return from tests based on WES and WGS

What RAW WGS/WES Data Might be Returned?

RETURNING RAW WGS/WES DATA

Sequencer



All of Us

Returning SAM, BAM, and/or VCF (?)

RETURNING RAW WGS/WES DATA

Name	Description	WES file size (GB)	WGS files size (GB)
BAM	*Binary Alignment/Map format*: nucleotide sequence with corresponding quality scores mapped to the reference genome, derived from raw data files using an alignment algorithm	~5–15	~150–250
VCF	*Variant Call Format*: files for storing variant bases relative to the reference genome, which are derived from sequence files using a variant calling algorithm; usually annotated with allele frequency and predicted consequence	~0.02	~0.2

+ 1GB reference

RETURNING RAW WGS/WES DATA
VCF FORMAT

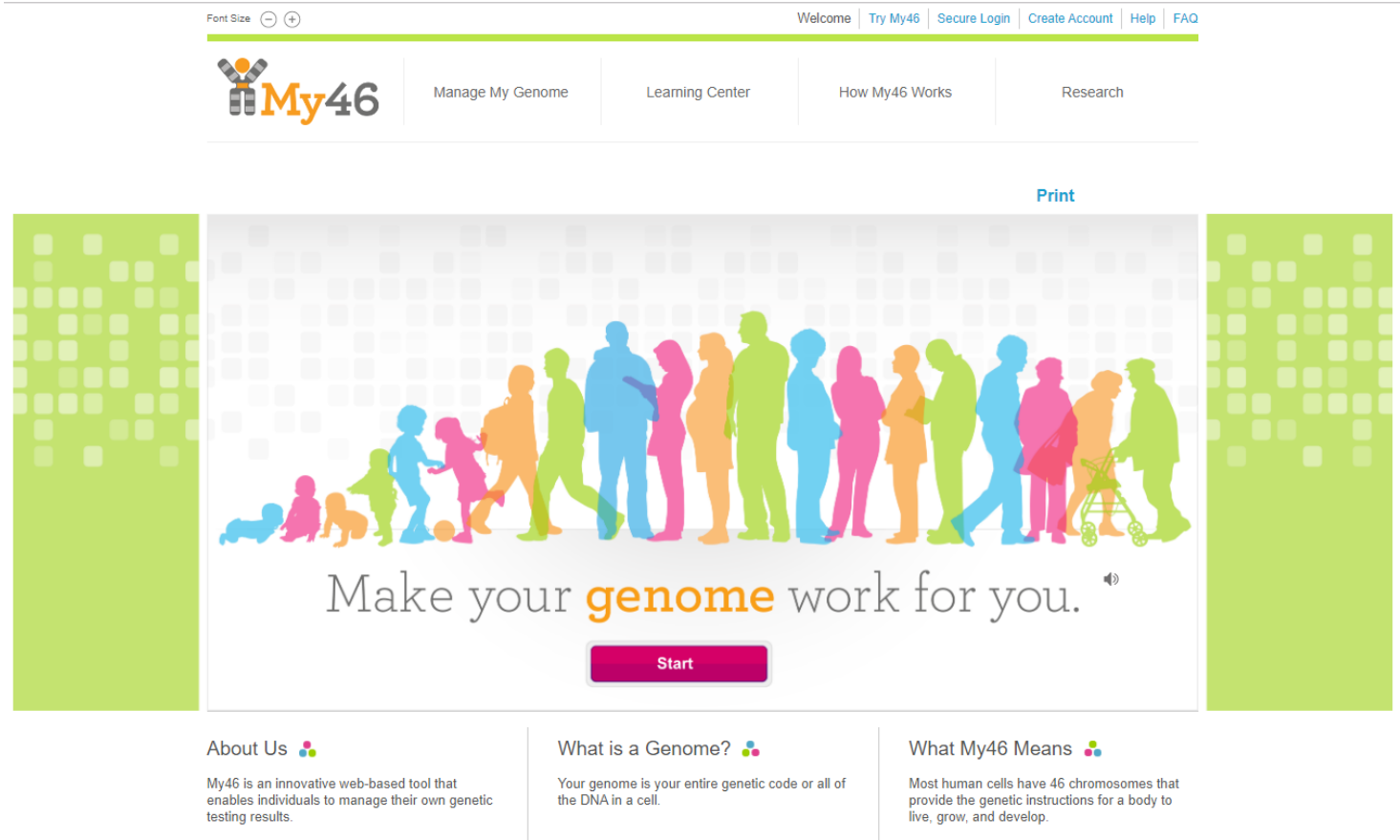
```
##fileformat=VCFv4.2
##FORMAT=<ID=GT,Number=1,Type=Integer,Description="Genotype">
##FORMAT=<ID=GP,Number=G,Type=Float,Description="Genotype Probabilities">
##FORMAT=<ID=PL,Number=G,Type=Float,Description="Phred-scaled Genotype Likelihoods">
#CHROM  POS     ID      REF     ALT     QUAL    FILTER  INFO    FORMAT  SAMP001 SAMP002
20      1291018 rs11449 G       A       .       PASS    .       GT      0/0     0/1
20      2300608 rs84825 C       T       .       PASS    .       GT:GP   0/1:.   0/1:0.03,0.97,0
20      2301308 rs84823 T       G       .       PASS    .       GT:PL   ./.:.   1/1:10,5,0
```

VCF considered “interpreted” data files and **may** require an investigational device exemption from the FDA

https://faculty.washington.edu/browning/beagle/intro-to-vcf.html#example

How might RAW WGS/WES be Returned?

RETURN OF RAW WGS/WES DATA



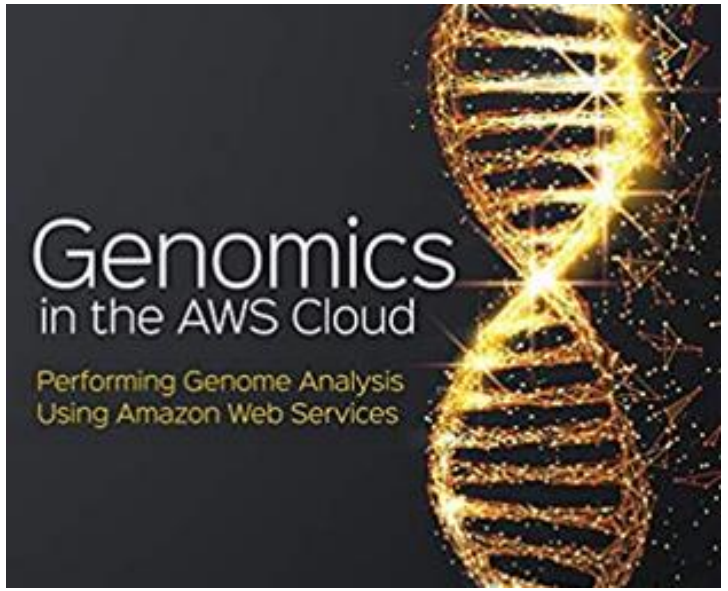
Through a Web-based tool

but

My46 enables individuals to manage their results from genetic testing, whether it is a single result being offered for return or the hundreds of results that can be offered for return from tests based on WES and WGS

RETURN OF RAW WGS/WES DATA

Other private storage tools

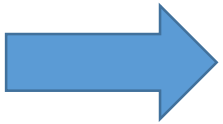


but

What to Do with RAW WGS/WES Data?

What to Do with Raw WGS/WES Data

Q: If you were given all of your raw genomic data from a research study, what would you do with this? (n=6944)
A: "I would seek out an interpretation of it" 62% (n=4320)



- 60% said "I'd analyse it myself" (n=2581)
  (Within the different professional groups, these are the percentages who would analyse the data themselves: 81% genomic researchers, 68% genetic health professionals, 56% other health professionals, 56% public)
- 57% said "I would ask for a referral to my local clinical genetics service" (n=2459)
- 43% said "I would ask my GP or Primary Care Physician" (n=1844)
- 41% said "would find a genomics researcher and ask them" (n=1775)
- 15% said "I would pay a commercial genetics company to analyse the data" (n=658)
- 5% had other suggestions: eg, "use google", "I would ask my bioinformatician colleagues", "I would share it on GitHub", "ask a genetic counsellor", "I would open source it to anyone online", "I would refer the raw data in a zip file to a company like 23andMe", "I would want information about interpreting the data before deciding how to proceed" (n=237)

Middleton A, et al. J Med Genet 2015;52:571–574. doi:10.1136/jmedgenet-2015-103119

What to Do with Raw WGS/WES Data

gyanwali

Converting .vcf to .csv??

Personally I use vcftools
http://vcftools.sourceforge.net/index.html

The quickest way to convert a vcf to 23andMe assuming you have Linux, and your vcf already has dbSNP IDs assigned is with Plink, using the following plink command:

./plink --vcf example.vcf --recode 23 --chr 1-23 --out example.txt

gyanwali

How do you use that? I tried opening it but it doesnt exactly run.

What to Do with Raw WGS/WES Data

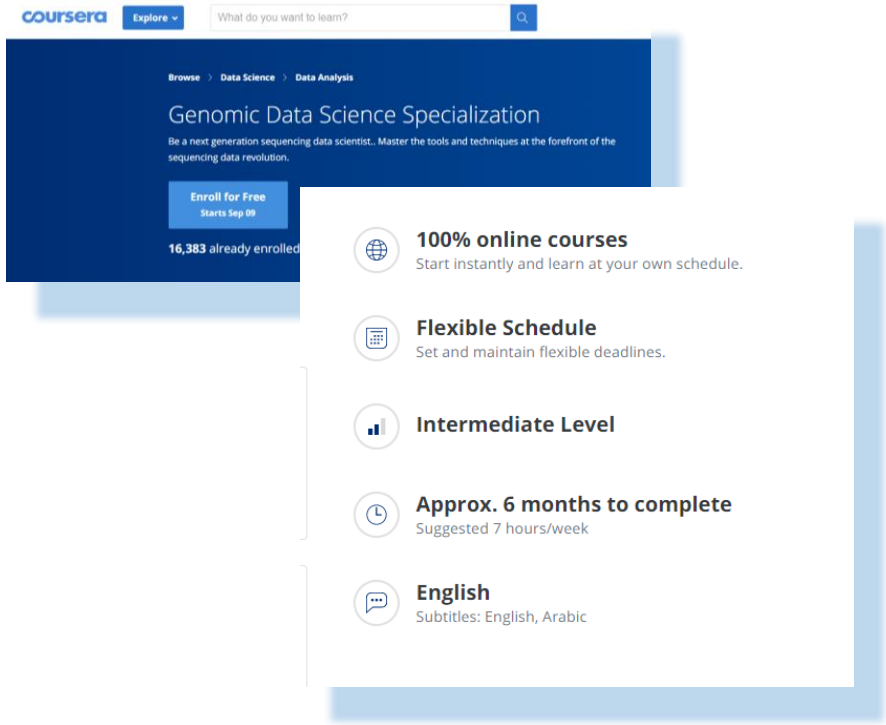
gyanwali

How do you use that? I tried opening it but it doesnt exactly run.

1. Download Plink 1.9 from here: https://www.cog-genomics.org/plink/1.9/.
2. Extract the zip file to the same folder where your VCF file is located.
3. Download these two text files to the same folder: v3snps.txt & Xv3.txt
4. Start the command prompt (type cmd in your windows search bar) and change the directory to where your file is located.
Command example (just copy-paste your file directory after cd): cd your_file_directory
5. Then type: plink --vcf your_filename.vcf.gz --extract v3snps.txt --snps-only --out 23andme.txt
6. Open the 23andme.txt, go to the end of the document and copy-paste the content of Xv3.txt, and save.
Done. Shouldn't take more than 5 minutes.

What to Do with Raw WGS/WES Data

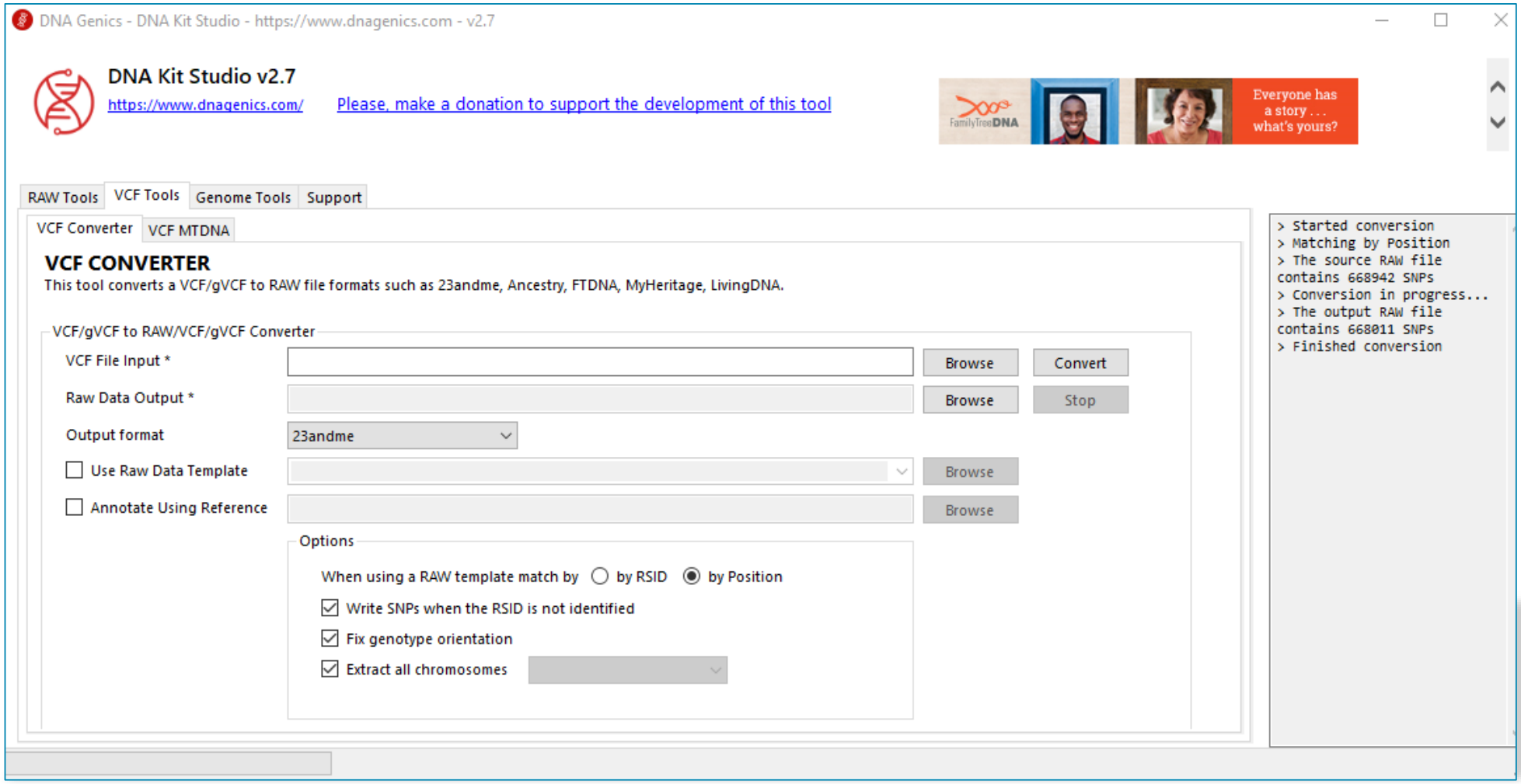
Using the UNIX/LINUX Environment…



Q: Who of the public will be able to do this?

https://www.coursera.org/specializations/genomic-data-science

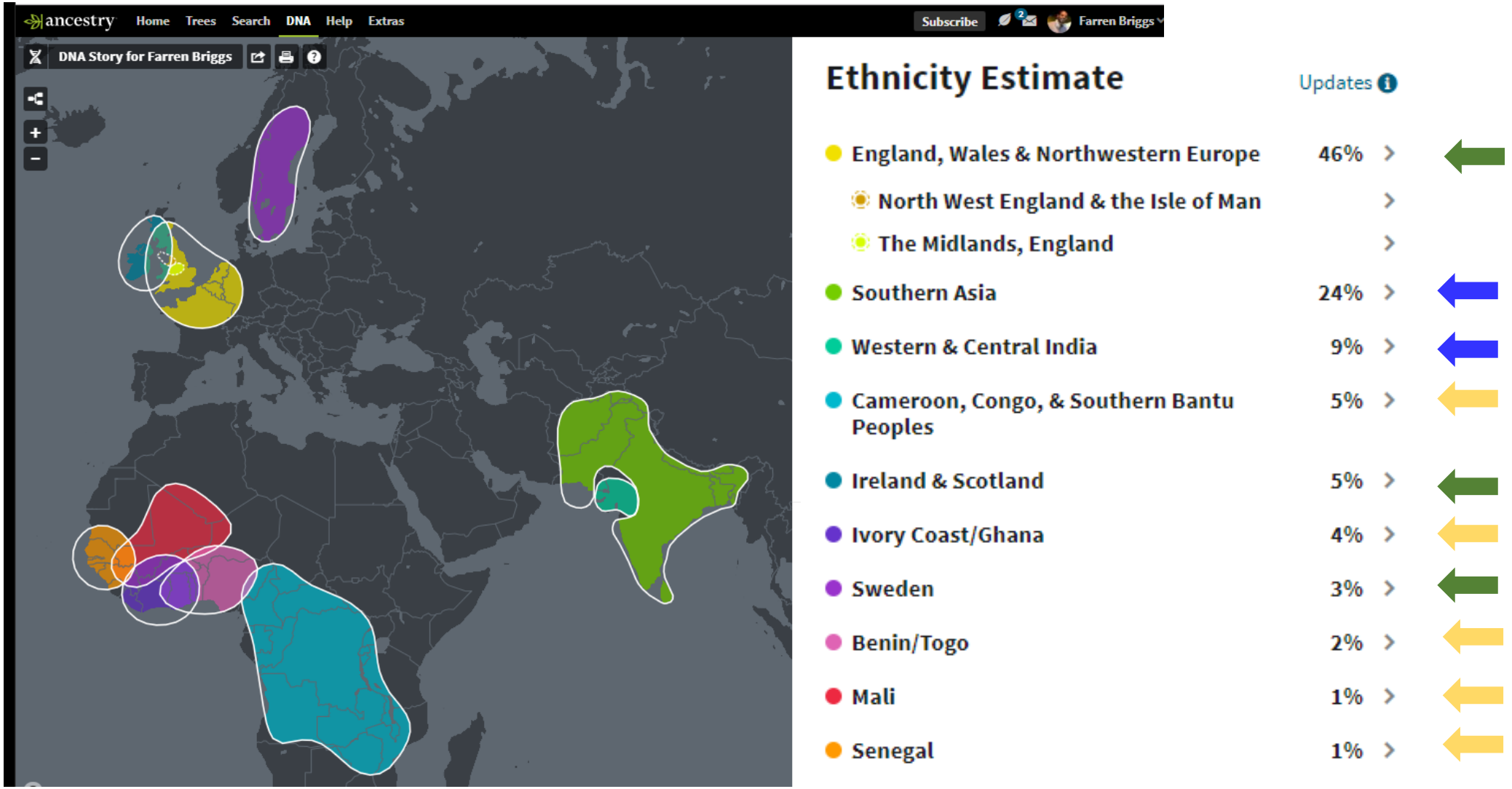
What to Do with Raw WGS/WES Data



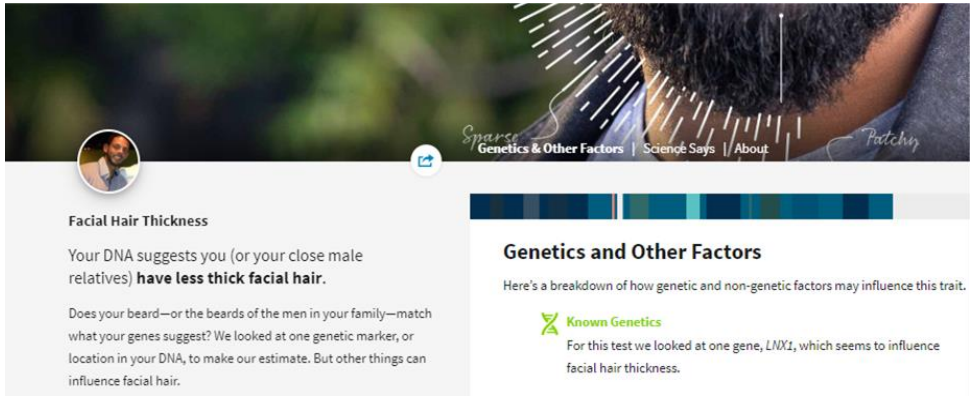
How to Interpret Genetic Data?

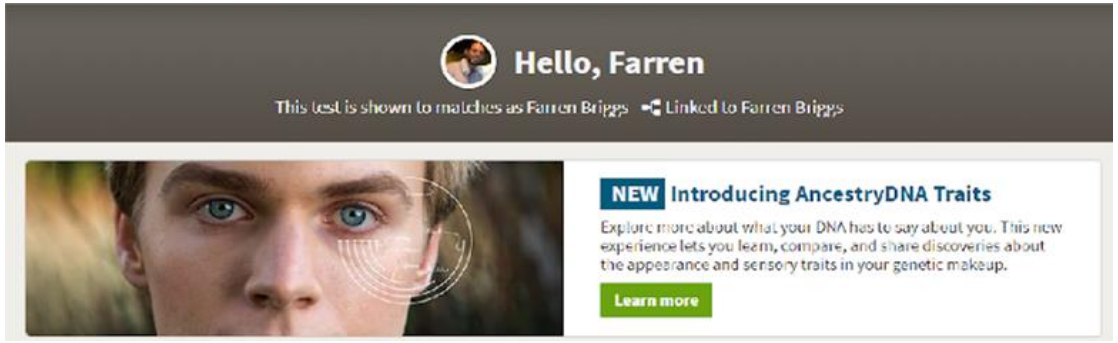
My Genetic Profile

* Immediate family approved *public* sharing



My Genetic Traits

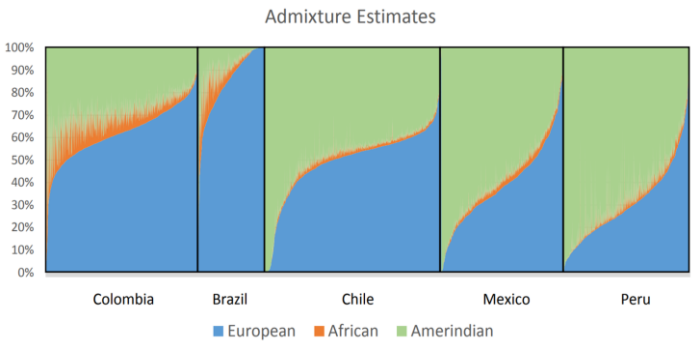


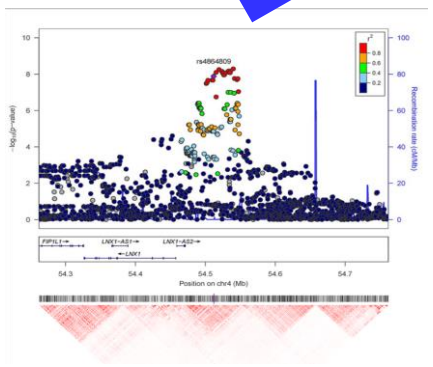


ARTICLE

Received 13 Jul 2015 | Accepted 25 Jan 2016 | Published 1 Mar 2016 DOI: 10.1038/ncomms10815 OPEN

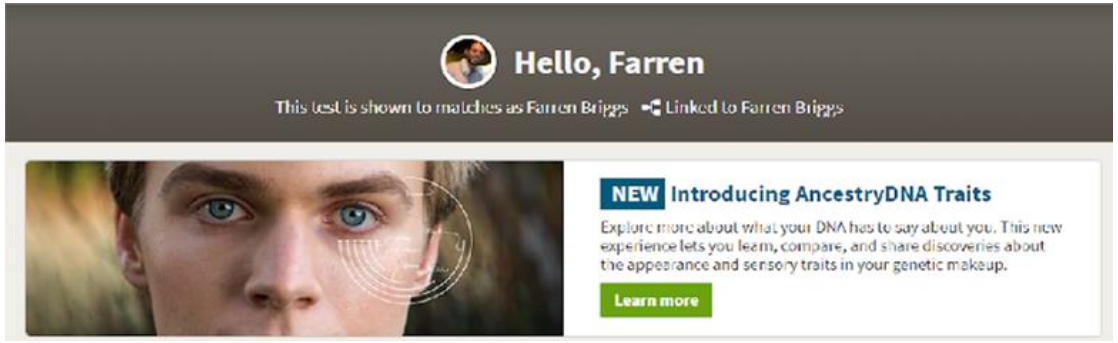
A genome-wide association scan in admixed Latin Americans identifies loci influencing facial and scalp hair features





Study	Population	Sample Size	G (ref allele)
The PAGE Study	Native Hawaiian	4,478	**0.37**
The PAGE Study	Asian	8,232	**0.38**
1000Genomes	South Asian	978	**0.41**
1000Genomes	East Asian	1,008	**0.41**
1000Genomes	African	1,322	**0.41**
gnomAD - Genomes	East Asian	1,546	**0.42**
The PAGE Study	South Asian	846	**0.42**
gnomAD - Genomes	African	8,676	**0.45**
The PAGE Study	African American	32,212	**0.46**
The PAGE Study	Dominican	3,782	**0.52**
The PAGE Study	Cuban	4,198	**0.57**
The PAGE Study	Central American	2,412	**0.58**
gnomAD - Genomes	Ashkenazi Jewish	288	**0.58**
The PAGE Study	Puerto Rican	7,844	**0.58**
The PAGE Study	Native American	1,246	**0.61**
gnomAD - Genomes	American	846	**0.61**
The PAGE Study	Mexican	10,684	**0.61**
1000Genomes	Europe	1,006	**0.64**
The PAGE Study	South American	1,958	**0.64**
gnomAD - Genomes	Other	1,086	**0.65**
1000Genomes	American	694	**0.65**
gnomAD - Genomes	European	18,842	**0.67**

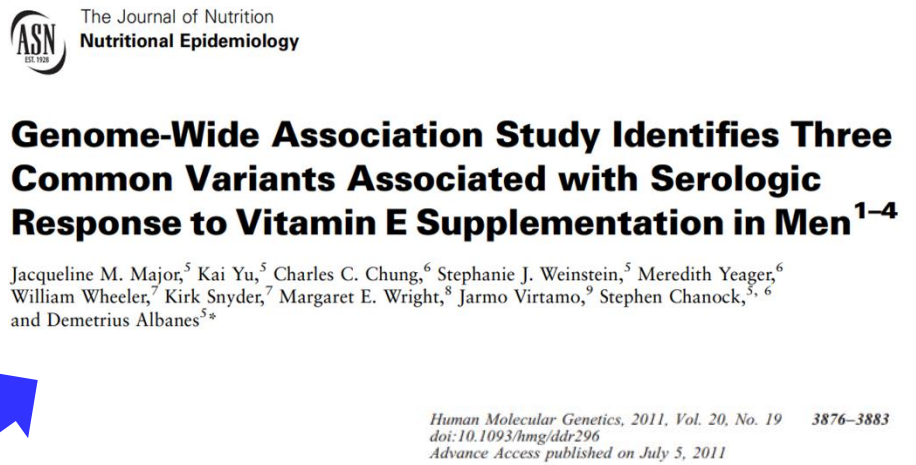
My Genetic Traits



Cleft Chin
The DNA we tested tells us you probably **have a cleft chin**.

Omega-3
People with DNA like yours can sometimes have **average omega-3 levels**

Vitamin E
People with DNA like yours can sometimes have **slightly lower vitamin E levels**


The Journal of Nutrition
Nutritional Epidemiology

Genome-Wide Association Study Identifies Three Common Variants Associated with Serologic Response to Vitamin E Supplementation in Men[1–4]

Jacqueline M. Major,[5] Kai Yu,[5] Charles C. Chung,[6] Stephanie J. Weinstein,[5] Meredith Yeager,[6] William Wheeler,[7] Kirk Snyder,[7] Margaret E. Wright,[8] Jarmo Virtamo,[9] Stephen Chanock,[5, 6] and Demetrius Albanes[5]*

Human Molecular Genetics, 2011, Vol. 20, No. 19 **3876–3883**
doi:10.1093/hmg/ddr296
Advance Access published on July 5, 2011

Genome-wide association study identifies common variants associated with circulating vitamin E levels

I also probably have a **unibrow**, **skin pigmentation**, **lighter hair…**

Third Party Interpretation (TPI) Tools

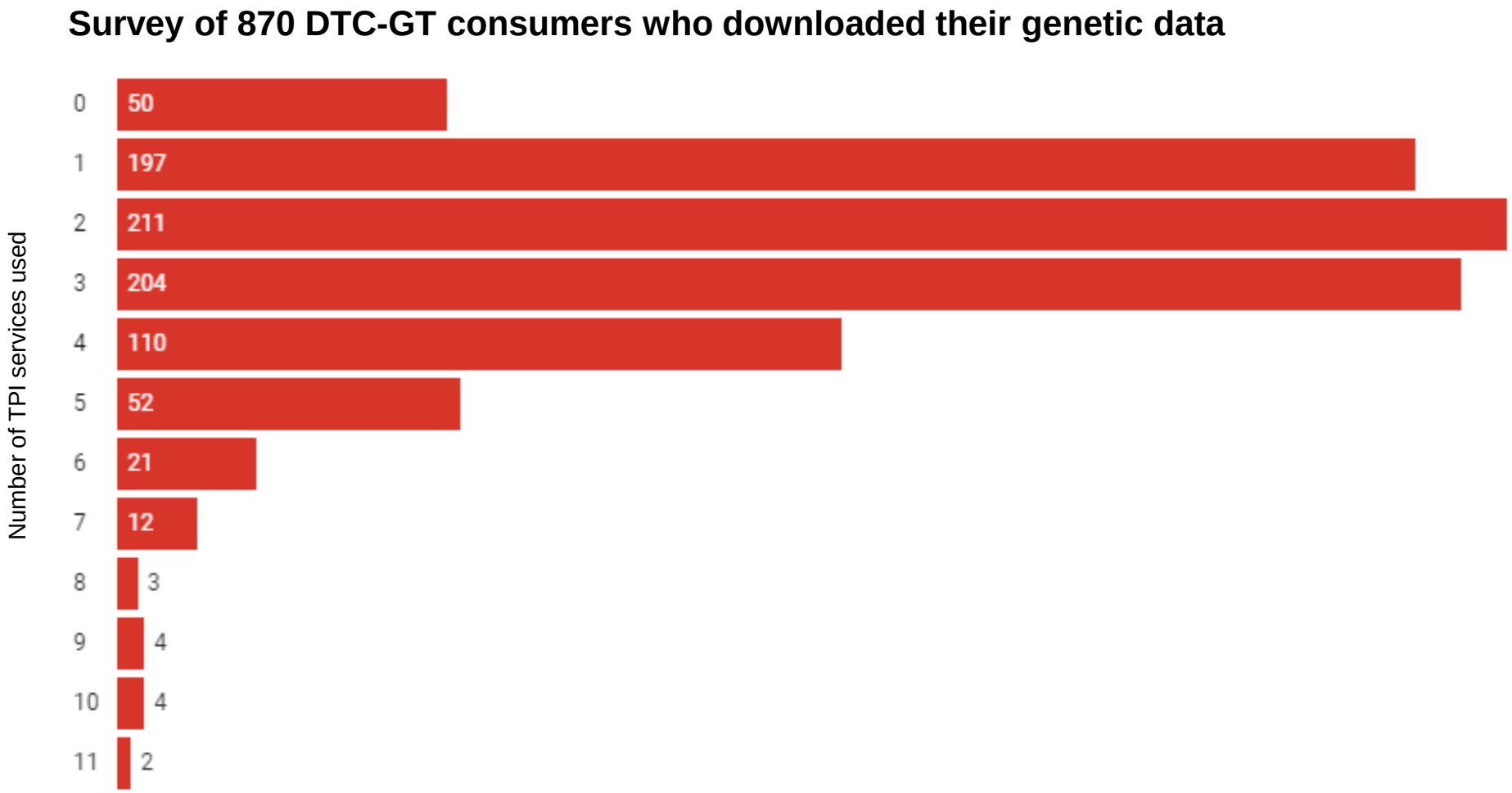
"Personalize your list of supplements unique to your genetics"

NUTRAHACKER

"Learn how to fix your brain according to your DNA make-up."

ANABOLICGenes
TRAINING AT A CELLULAR LEVEL

How many TPI tools would people use?



WHICH TPI TOOLS DID USERS TURN TO?

Survey of 870 DTC-GT consumers who downloaded their genetic data

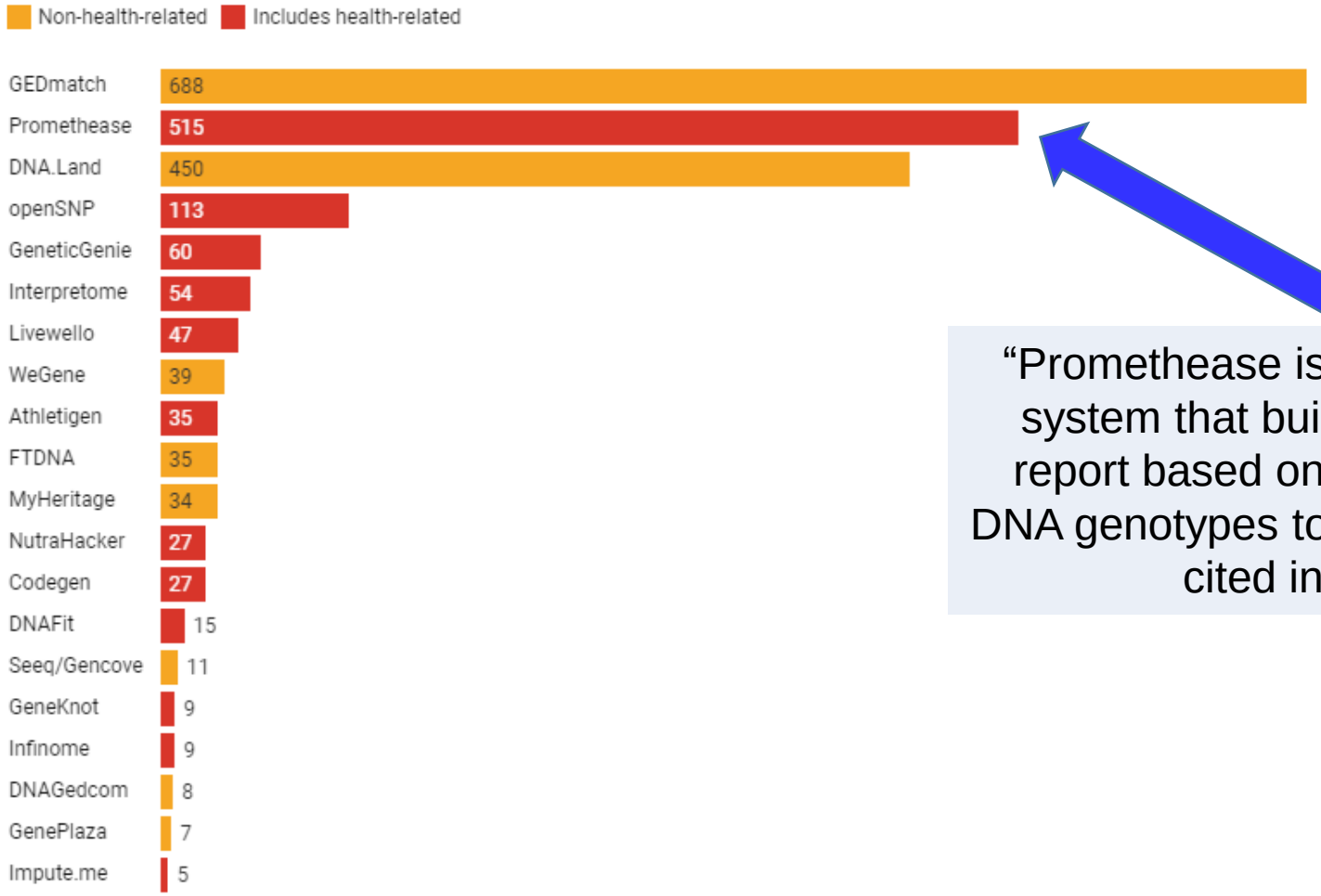
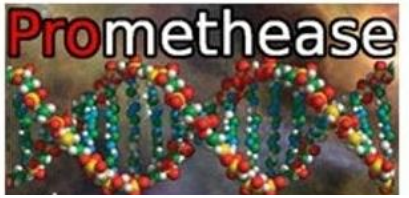


Chart includes tools mentioned by five or more users.

Chart: The Conversation, CC-BY-ND • Source: American Journal of Human Genetics, Nelson SC, et al. AJHG 105, 122-133, July 3, 2019

"Promethease is a literature retrieval system that builds a personal DNA report based on connecting a file of DNA genotypes to the scientific findings cited in SNPedia."

My Health-Related Genetic Traits



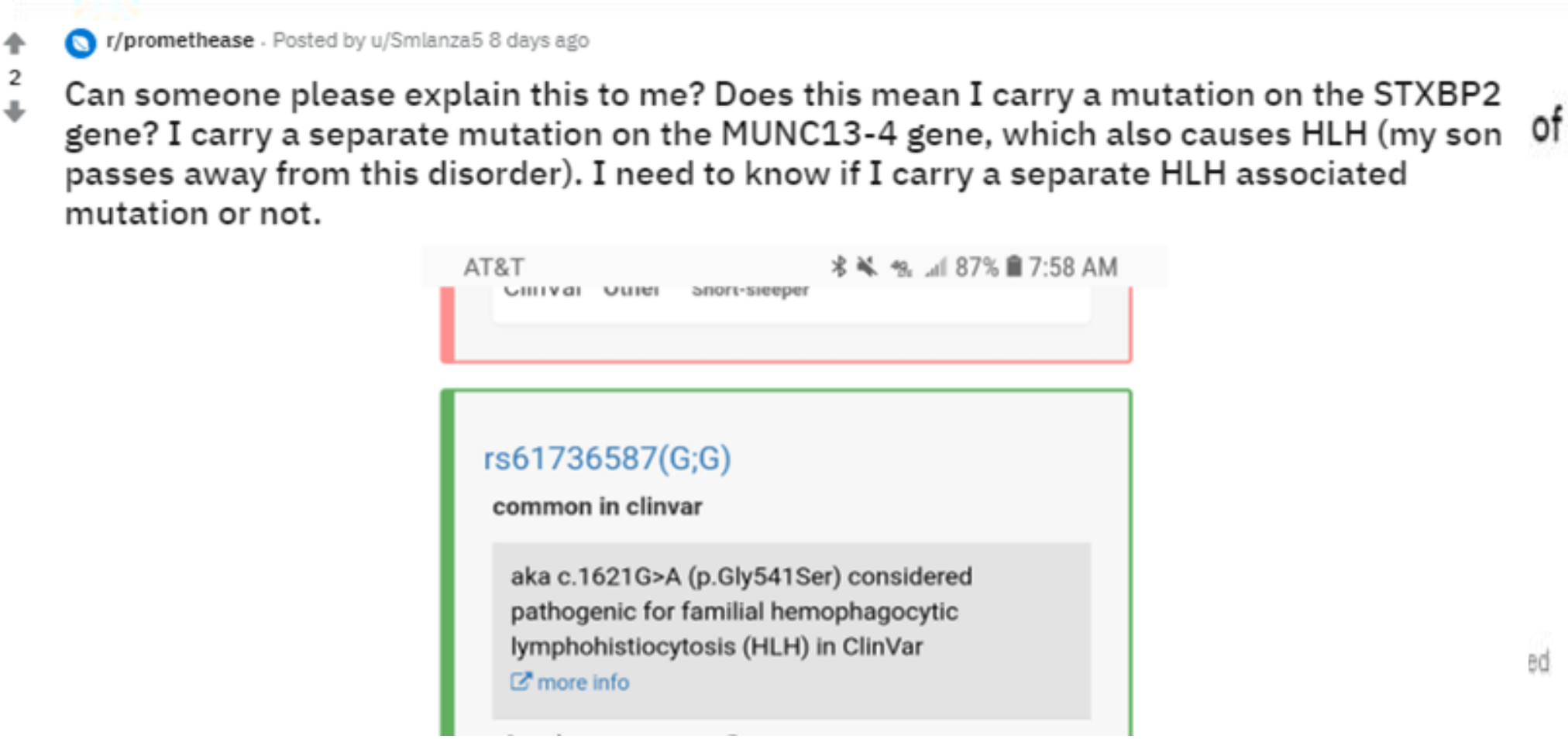
SNPedia

$12 USD + 47K SNPs from AncestryDNA

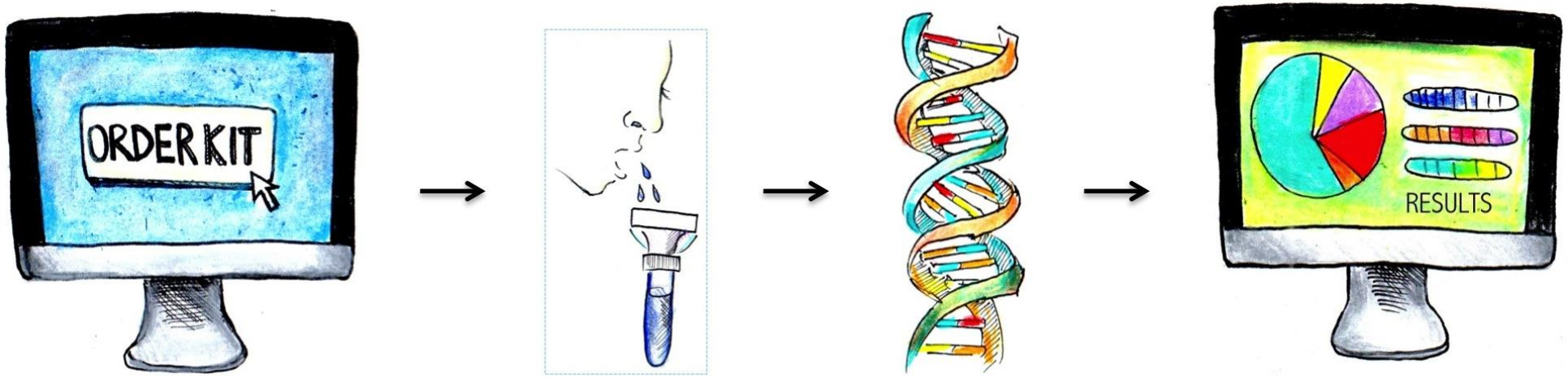
SNP	Summary	Repute	Publications	Magnitude
rs1426654	probably light-skinned, European ancestry		18	2.7
rs189798	normal high myopia risk		1	2
rs10825992	decreased high myopia risk	Good	1	2
rs2802292	Less likely to live to 100.	Bad	10	2.5
rs1935949	1.27X likelihood of 'exceptional longevity'	Good	1	2

Where to Seek Help?

reddit



WHERE TO SEEK HELP?



Next steps:

PCP, Genetic Health Professional, Test family members, Share data…. Re-test ???

https://pged.org/direct-to-consumer-genetic-testing/

MACRO SUMMARY – *MIND THE GAPS*

WHO ARE OUR STUDY PARTICIPANTS?

EDUCATION, HEALTH STATUS, RESOURCES, LITERACY

HOW DO WE ENSURE EQUITY IN ACCESS, INTERPRETATION, & OPPORTUNITIES FOR ACTION?

DOES IT NEED TO BE EQUAL? WHAT ABOUT PRIVACY? RELATIVES?

HOW DO WE SUPPORT PARTICIPANTS OVER TIME?

ACMG/PGX/CLINVAR FINDINGS CHANGE…

WHO BEARS THE ONUS?

PARTICIPANT, RESEARCHER, FUNDING AGENCY, GOVERNMENT?

ACKNOWLEDGEMENTS

DANA CRAWFORD, PHD
Associate Professor
Department of Population and Quantitative Health Sciences
Cleveland Institute for Computational Biology
Case Western Reserve University

JESSICA COOKE BAILEY, PHD
Assistant Professor
Department of Population and Quantitative Health Sciences
Cleveland Institute for Computational Biology
Case Western Reserve University

Human Genetics (2019) 138:691–701
https://doi.org/10.1007/s00439-019-02033-5

REVIEW

Mind the gap: resources required to receive, process and interpret research-returned whole genome data

Dana C. Crawford[1,2,3] · Jessica N. Cooke Bailey[1,3] · Farren B. S. Briggs[1,3]

Received: 4 April 2019 / Accepted: 27 May 2019 / Published online: 3 June 2019

Thank you

(and mind the gap)