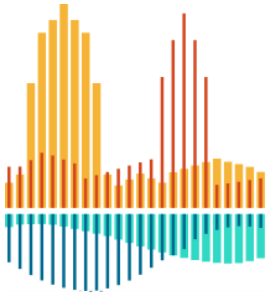
# Precisely Precision Medicine
# A Primer on Translational Research



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BIOLOGY

SCHOOL OF MEDICINE
CASE WESTERN RESERVE
UNIVERSITY

DEPARTMENT OF POPULATION AND
QUANTITATIVE HEALTH SCIENCES

# PRESENTERS AND TOPICS

Dana Crawford, PhD

Will Bush, PhD, MS

Farren Briggs, PhD, ScM

Jessica Cooke Bailey, PhD, MA

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# Presenters and Topics

Electronic Health Records: Not Your Parents' Paper Charts

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

Annotating Genomics Sequence for Human Health

The intersection of bioethics and genomics in precision medicine

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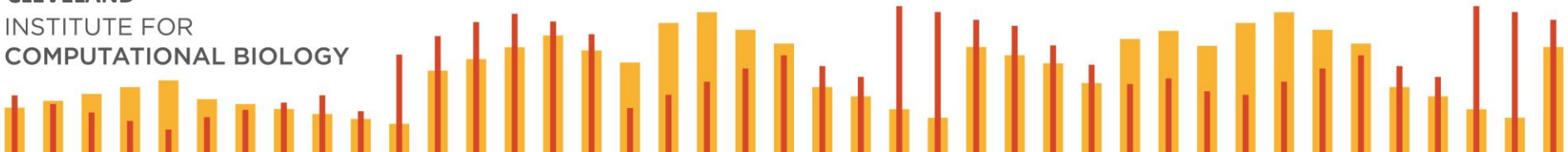
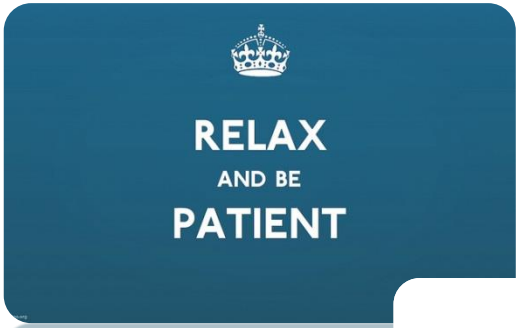


# Precision Medicine

## The Concept




Right Patient

Right Drug


Right Dose

First Time

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# Precision Medicine Research

## Age of Genomic Discovery

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https://www.ebi.ac.uk/gwas/

GWAS as of Sept 2020:

4,694 publications

197,708 associated SNPs

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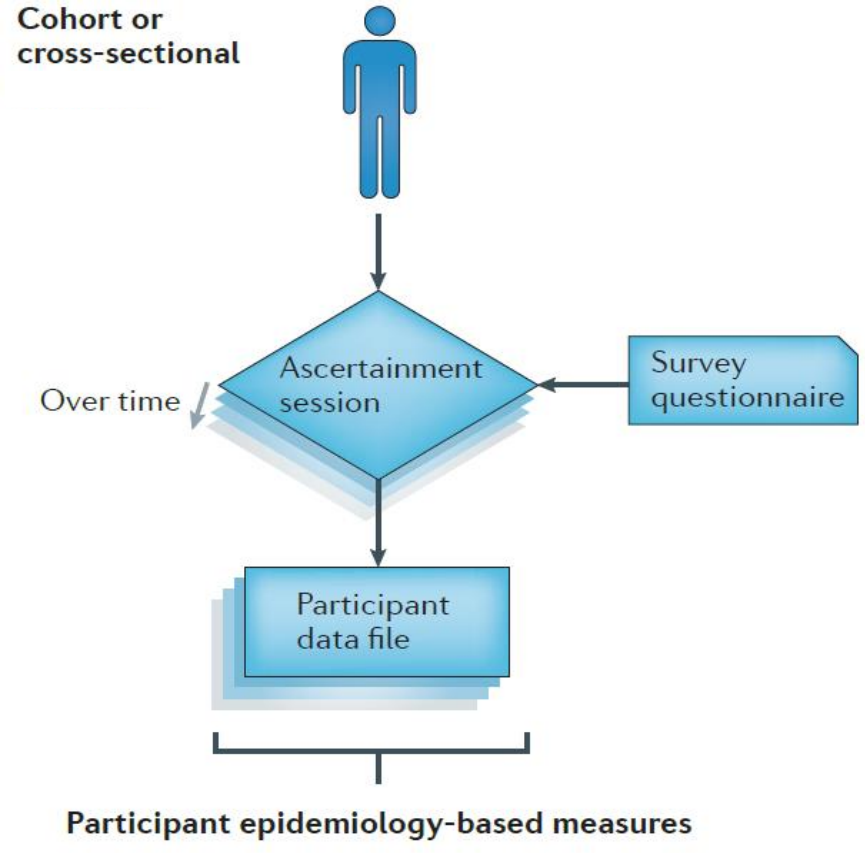
# PRECISION MEDICINE RESEARCH

## AGE OF GENOMIC DISCOVERY




Bush, Oetjens, Crawford (2016) *Nat Rev Genet* 17(3):129-45

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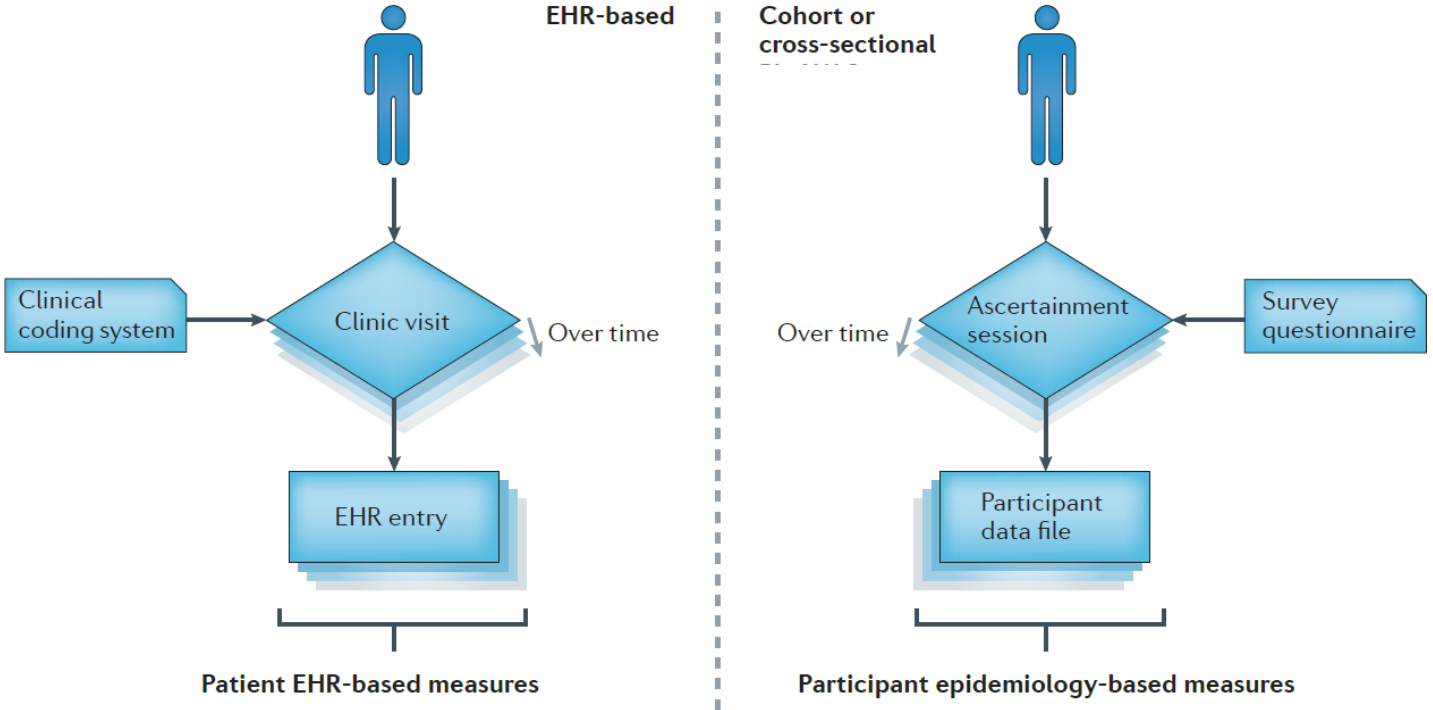
# ELECTRONIC HEALTH RECORDS

## ACCELERATING PRECISION MEDICINE RESEARCH

Bush, Oetjens, Crawford (2016) *Nat Rev Genet* 17(3):129-45

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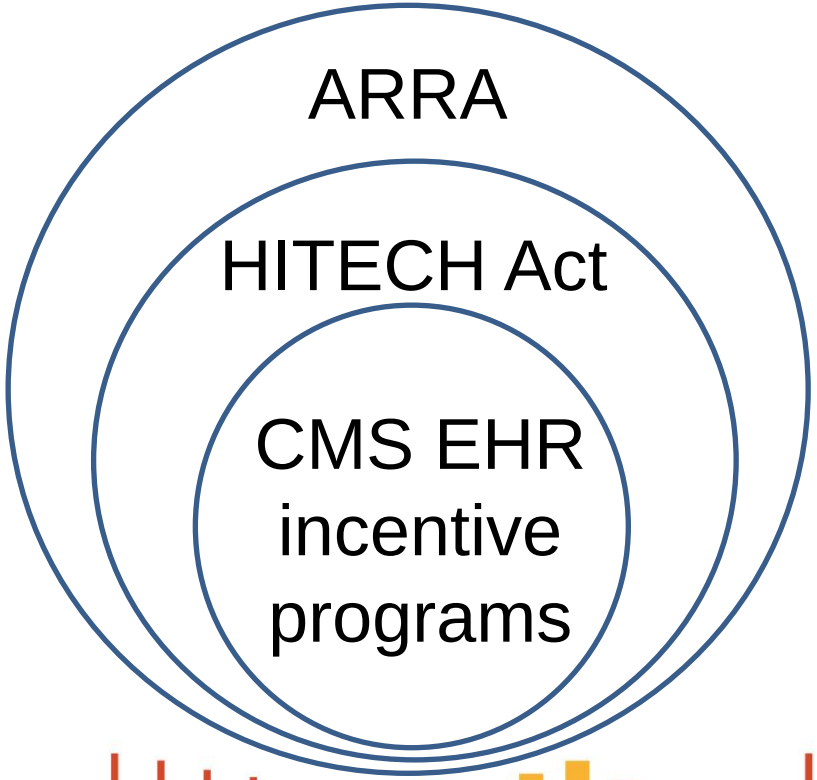
# The Rapid Rise of EHRs


**ARRA**

American Recovery and Reinvestment Act of 2009

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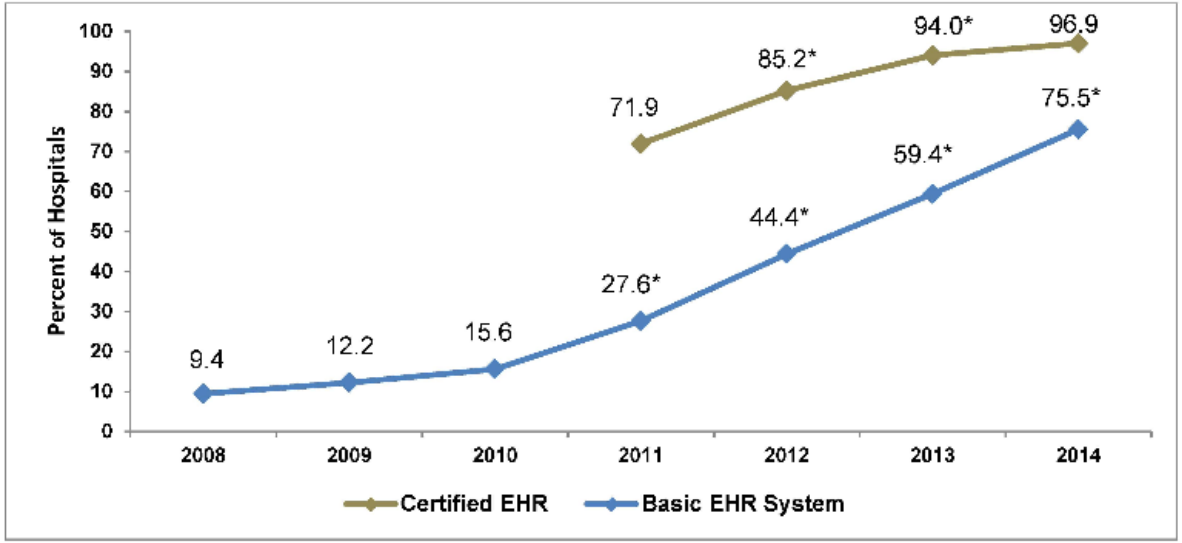
# The Rapid Rise of EHRs

96% of reporting US hospitals have at least a basic EHR




https://www.healthit.gov/sites/default/files/data-brief/2014HospitalAdoptionDataBrief.pdf

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# Electronic Health Records

## Accelerating Precision Medicine Research

**Patient EHR-based measures**

| | |
|---|---|
| 250.0 T2DM | Yes |
| 411.1 coronary syndrome | Yes |
| 414.01 coronary artery disease | No |
| 278.01 obesity | Yes |
| Alanine aminotransferase | 15.6 units per l |
| Blood albumin | 3.7 g per dl |
| Aspartate aminotrasferase | 22 units per l |
| Bicarbonate ($HCO_3$) | 24 mEq per l |
| Carbon dioxide ($CO_2$) | 27 mEq per l |
| Blood cholesterol | 240 mg per dl |
| Blood creatinine | 1.2 mg per dl |

**Participant epidemiology-based measures**

| | |
|---|---|
| Ever had diabetes? | Yes |
| Cancer ever diagnosed? | Yes |
| Ever smoked? | No |
| Allergic to gluten? | No |
| Allergic to peanuts? | Yes |
| Current weight | 240 lb |
| Current height | 5'8" |
| Green vegetables per week | 2–4 servings |
| Red meat per week | 6–8 servings |
| Blood cholesterol | 275 mg per dl |
| Exercise time per week | 30 min |

Bush, Oetjens, Crawford (2016) *Nat Rev Genet* 17(3):129-45

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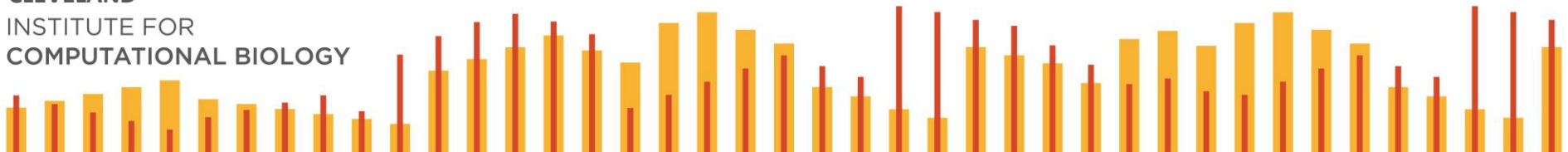

# Electronic Health Records

## Accelerating Precision Medicine Research

| | |
|---|---|
| • Demographics | Structured and unstructured text |
| • Vitals | Structured |
| • Medical History | Structured and unstructured text |
| • Medical encounter | Structured and unstructured text |
| • Orders and prescriptions | Structured |
| • Laboratory tests | Structured |

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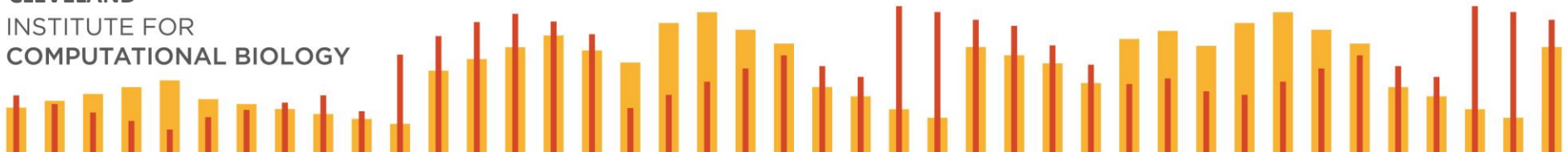
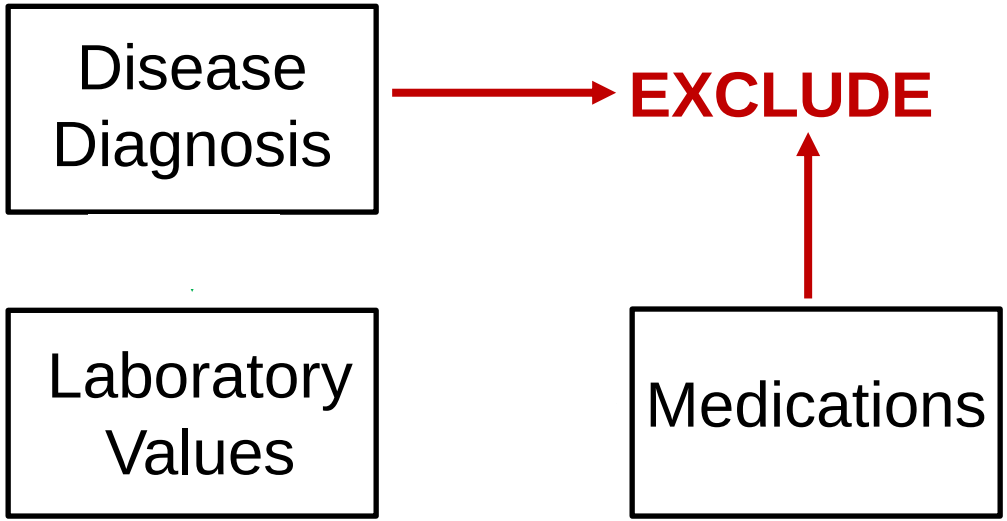


# Electronic Health Records

## Accelerating Precision Medicine Research

Billing codes
Procedure codes
Problems lists




Pendergrass and Crawford (2019)
*Curr Proc Hum Genet* 100:e80

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# Electronic Health Records

## Not Your Parents' Paper Charts

https://en.wikipedia.org/wiki/Medical_record

- ✓ Accessible
- ✓ Computable
- ✓ Scalable

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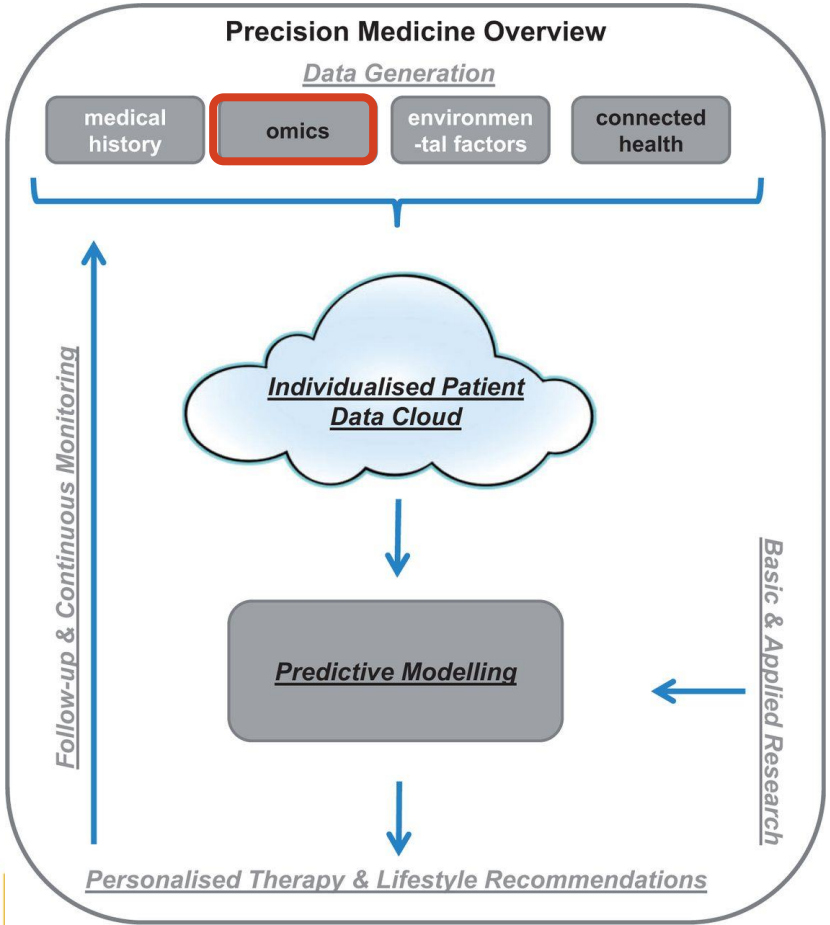
# Electronic Health Records

## Accelerating Precision Medicine in the Clinic




Duffy DJ (2016) *Brief Bioinform* 17(3):494-504

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

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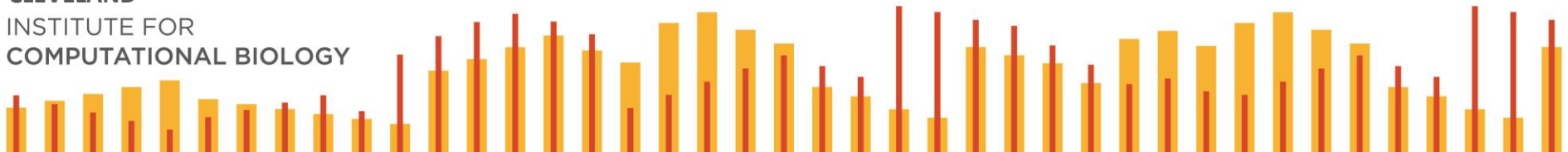
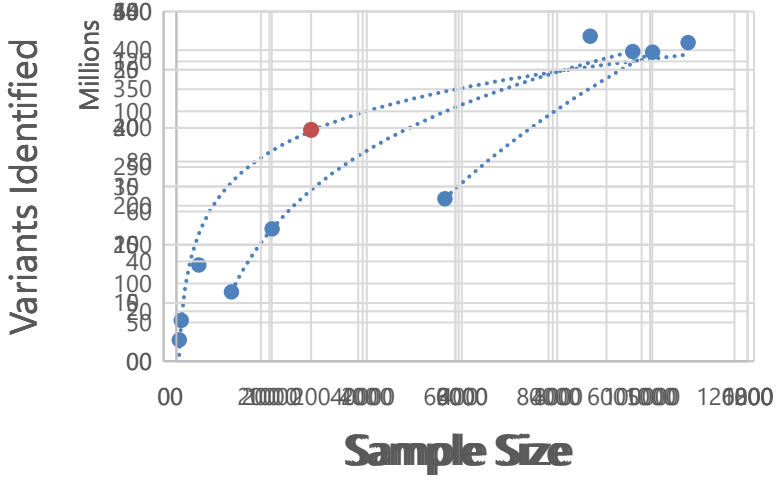


# The Scale of Whole Genome Sequencing Data

- ADSP Discovery (578)
  27,896,774
- ADSP Disc-Ext (1005)
  53,041,134
- ADSP Expansion (4795)
  124 Million
- TOPMED (110,000)
  410 Million
- ADSP FUS (30,000)
  ~300 Million




46% Singleton

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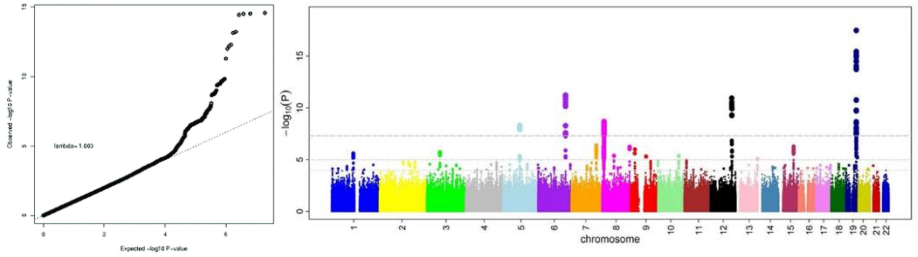
# What do we do with these Variants?

## GWAS – Unit is a Variant

"Hypothesis-Free" – Statistically Driven



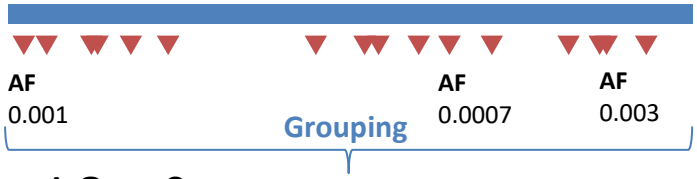

| Variant | Chr | Pos | Alleles | AF | OR |
|---|---|---|---|---|---|
| rs190982 | 5 | 88223420 | G/A | 0.41 | 0.93 (0.90–0.95) |

"We identified a seventh signal adjacent to *MEF2C* (encoding myocyte enhancer factor 2). The MEF2C protein limits excessive synapse formation during activity-dependent refinement of synaptic connectivity and thus may facilitate hippocampal-dependent learning and memory"

Lambert et al (2013) *Nat Genet* 45(12):1452–1458

## Sequencing – Unit is…

Hypothesis-Based – Biologically Driven




- A Gene?
  - UCSC, Ensembl, or Entrez gene definition?
- Only interested in coding variants?
  - What are the exons of those genes?
    - RefSeq or Ensembl Transcript definition?
  - Care where those variants are expressed?

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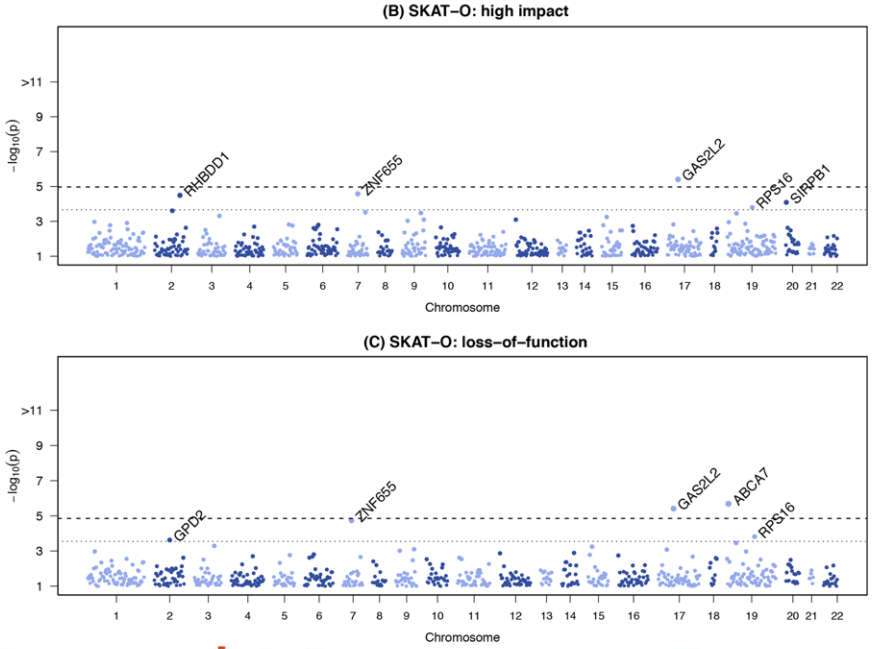
# WES Analysis of Alzheimer's

Bis et al (2020) *Mol Psychiatry* 25(8):1859-1875

- Custom Annotation Pipeline
- High, Moderate, Low, Modifier impact categories
- Loss of Function

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Bis et al (2020) *Mol Psychiatry* 25(8):1859-1875

Molecular Psychiatry
https://doi.org/10.1038/s41380-018-0112-7

ARTICLE

## Whole exome sequencing study identifies novel rare and common Alzheimer's-Associated variants involved in immune response and transcriptional regulation

Joshua C. Bis[1] et al · Alzheimer's Disease Sequencing Project

Received: 21 December 2017 / Revised: 1 May 2018 / Accepted: 14 May 2018


**Abstract**

The Alzheimer's Disease Sequencing Project (ADSP) undertook whole exome sequencing in 5,740 late-onset Alzheimer disease (AD) cases and 5,096 cognitively normal controls primarily of European ancestry (EA), among whom 218 cases and 177 controls were Caribbean Hispanic (CH). An age-, sex- and *APOE* based risk score and family history were used to select cases most likely to harbor novel AD risk variants and controls least likely to develop AD by age 85 years. We tested ~1.5 million single nucleotide variants (SNVs) and 50,000 insertion-deletion polymorphisms (indels) for association to AD, using multiple models considering individual variants as well as gene-based tests aggregating rare, predicted functional, and loss of function variants. Sixteen single variants and 19 genes that met criteria for significant or suggestive associations after multiple-testing correction were evaluated for replication in four independent samples; three with whole exome sequencing (2,778 cases, 7,262 controls) and one with genome-wide genotyping imputed to the Haplotype Reference Consortium panel (9,343 cases, 11,527 controls). The top findings in the discovery sample were also followed-up in the ADSP whole-genome sequenced family-based dataset (197 members of 42 EA families and 501 members of 157 CH families). We identified novel and predicted functional genetic variants in genes previously associated with AD. We also detected associations in three novel genes: *IGHG3* ($p = 9.8 \times 10^{-7}$), an immunoglobulin gene whose antibodies interact with β-amyloid, a long non-coding RNA *AC099552.4* ($p = 1.2 \times 10^{-7}$), and a zinc-finger protein *ZNF655* (gene-based $p = 5.0 \times 10^{-6}$). The latter two suggest an important role for transcriptional regulation in AD pathogenesis.

### Introduction

Genomic studies have revealed that late-onset Alzheimer disease (LOAD) is highly polygenic, with as many as 30 susceptibility loci identified through large-scale meta-analysis of genome-wide association studies (GWAS), targeted exome genotyping array, and several early whole exome sequencing (WES) studies [1–12]. Although AD susceptibility is highly heritable ($h^2 = 0.58–0.79$) [13], much of its genetic architecture is still unknown and few rare variants have been detected thus far [3, 6, 7, 14–19]. Discovery of rare variants in genomic studies, even those with large sample sizes and examining highly heritable diseases, remains challenging due to statistical power limitations in detecting all but the most strongly associated variants (odds ratio (OR) > 1.5) [20–23]. The protein coding regions of the genome, or exome, are the best characterized and most conserved portions of the genome and the source of most variants identified to date that are responsible for Mendelian diseases [24]; thus, the exome is a more

Alzheimer's Disease Sequencing Project members are listed below the Acknowledgement

These authors contributed equally: Joshua C. Bis, Xueqiu Jian, Brian W. Kunkle, Yuning Chen

These authors equally supervised the study: Adam C. Naj, Myriam Fornage, Lindsay A. Farrer

**Electronic supplementary material** The online version of this article (https://doi.org/10.1038/s41380-018-0112-7) contains supplementary material, which is available to authorized users. Variant summary data can be found at the NIA Genetics of Alzheimer's Disease Data Storage site (https://www.niagads.org) under accession number NG00065.

✉ Lindsay A. Farrer
farrer@bu.Edu

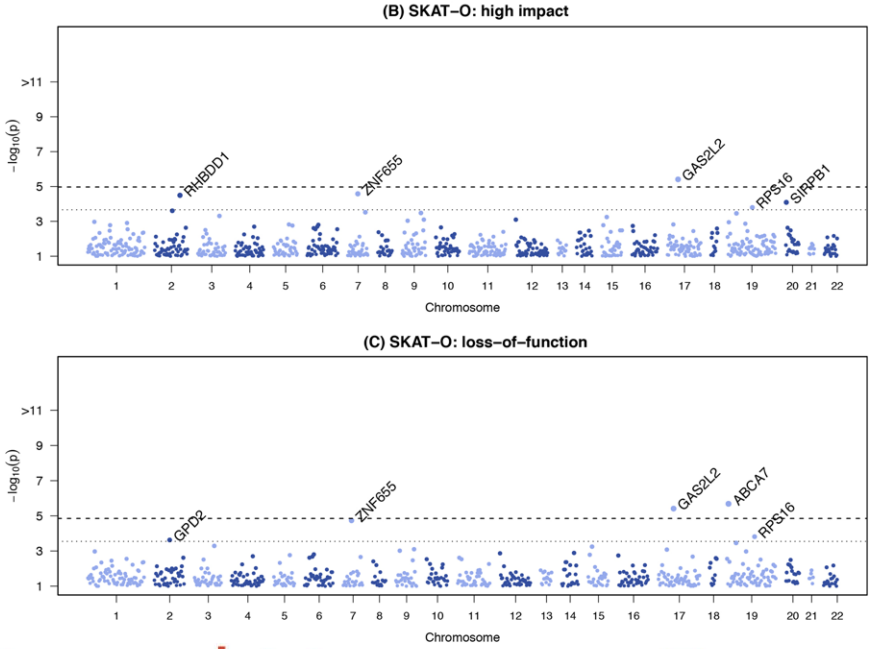
Extended author information available on the last page of the article

Published online: 14 August 2018

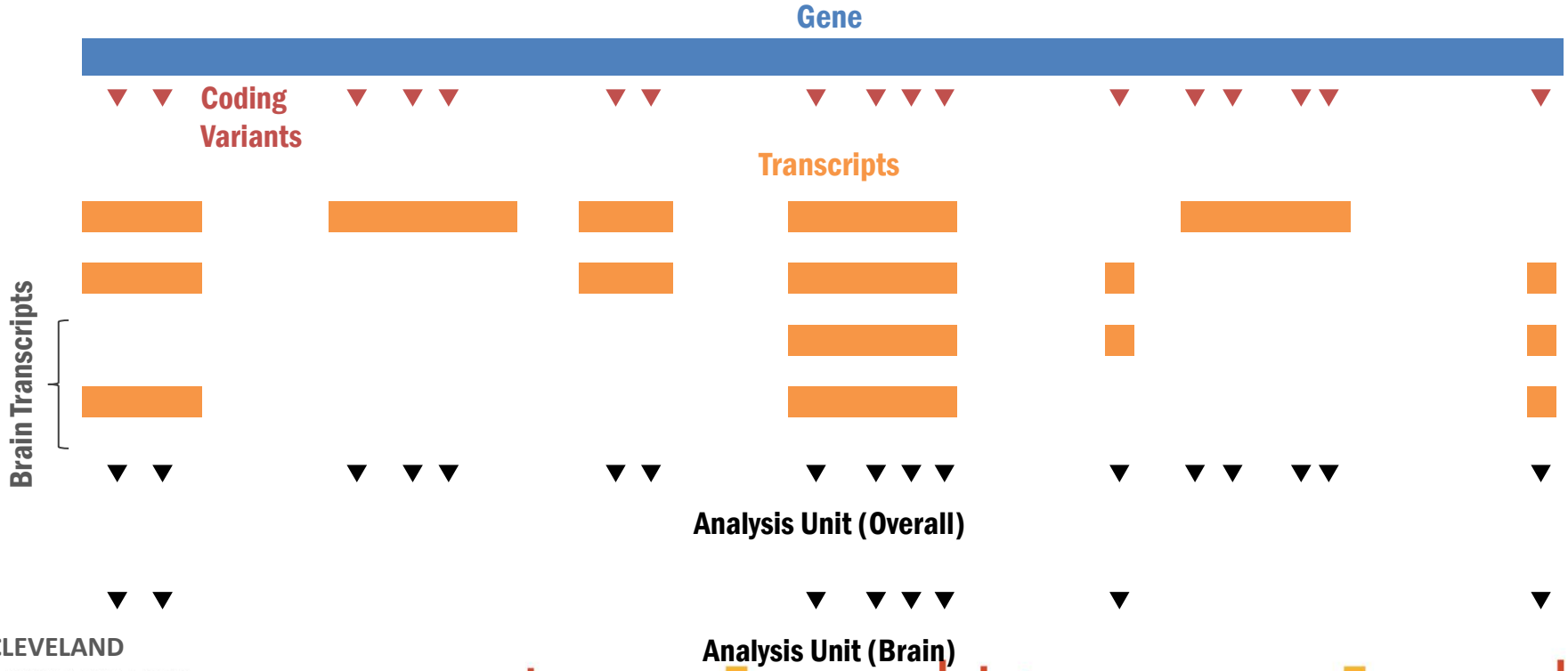


on

Low,



# Tissue Context is Important

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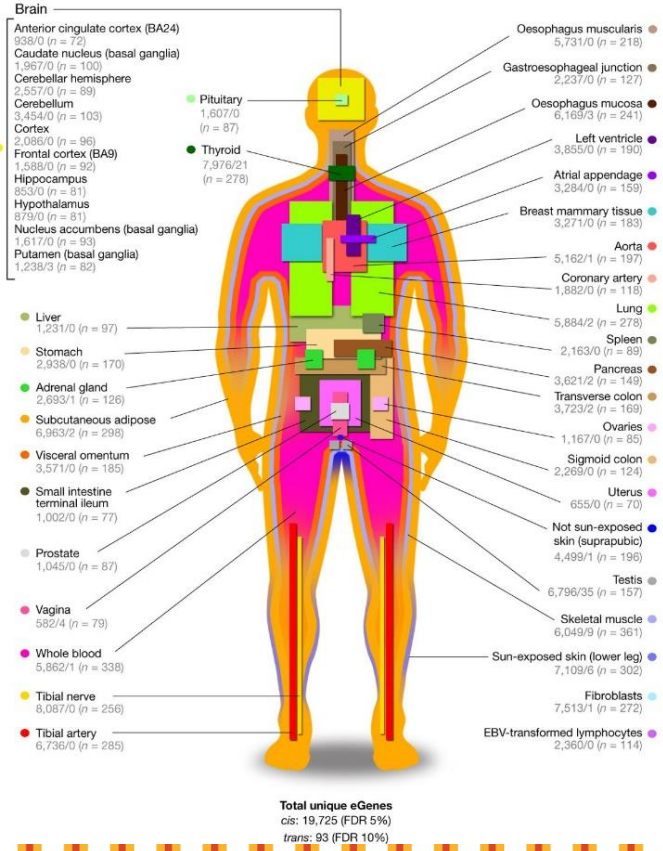
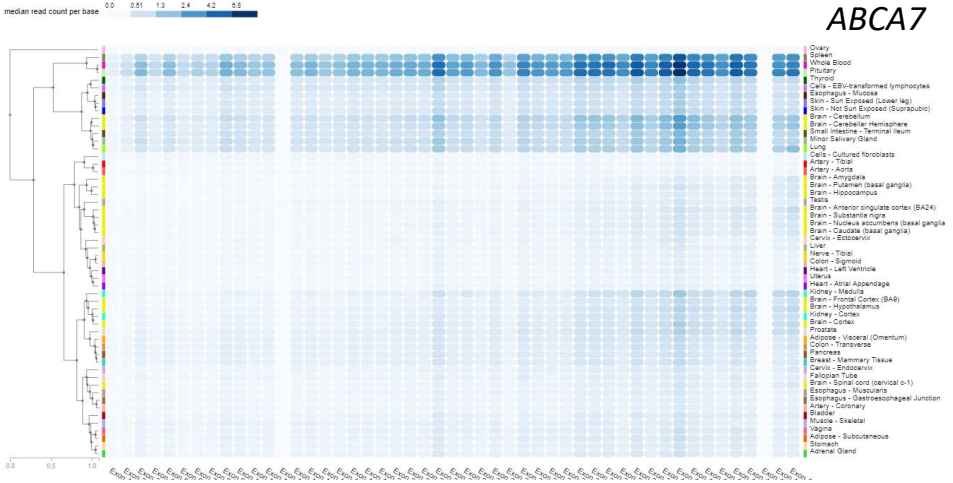
# TISSUE CONTEXT IS IMPORTANT



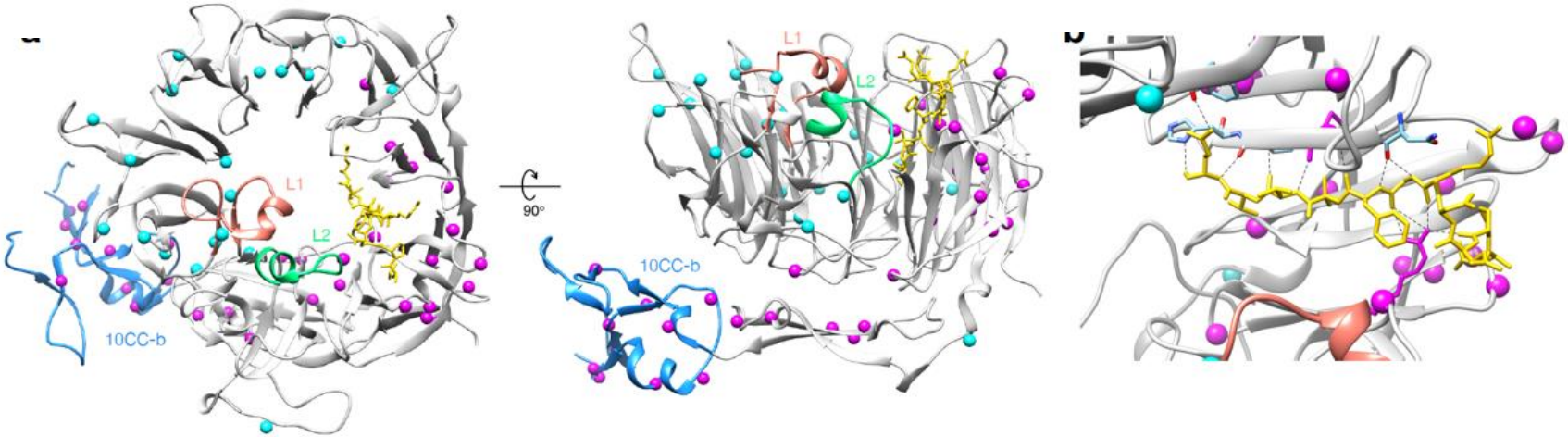




*ABCA7*

**4% of variant effects change**

**25% of gene units have at least one effect change**

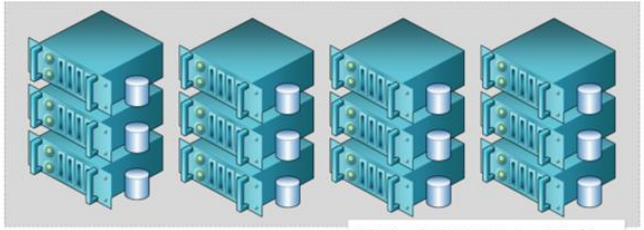
# PROTEIN-BASED INFORMATION




- AD signal region of 34 variants (out of a total of 214 considered) in SORL1
- Variants localize to the peptide binding tunnel and the dynamic 10CC region

Tang ZZ, Sliwoski GR, Chen G, Jin B, Bush WS, Li B, Capra JA (in press) *Genome Res*

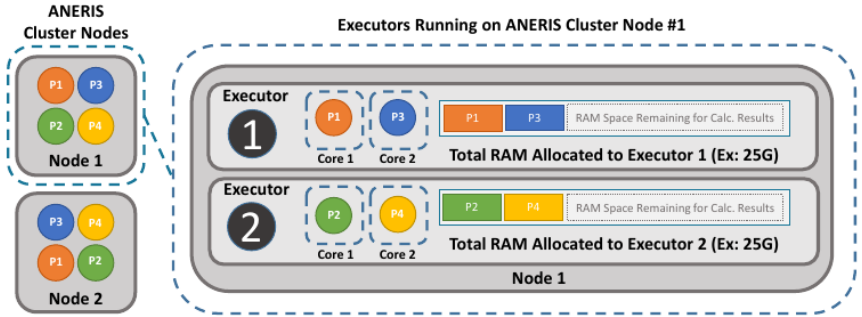
# BIG DATA TECHNOLOGIES



**R330** - 64GB RAM, 4 x 6TB drive, 200GB SSD, E3-1280 4 cores, 10Gb

**R430** - 2 x E5-2650v4 (12-core), 128GB RAM, 2 x 1Gb, 2 x Intel X520 10Gb SFP+, 1 x Intel X520 DP 10Gb DA/SFP+, 8 x 600GB 10k SAS 12 Gbps, PERC H730, 1GB Cache

| Name | # | HD | RAM | Cores |
|---|---|---|---|---|
| Data | 12 | 4*6TB | 64GB | 4 |
| Service | 3 | 8*600GB | 512GB | 2*12 |
| Head | 1 | 8*600GB | 512GB | 2*12 |




**Executor Parameters: 2 Cores, 25G RAM (To fit 2 executors, a node must have 4 cores and 50G RAM)**

hadoop cloudera APACHE Spark jupyter R hail python™

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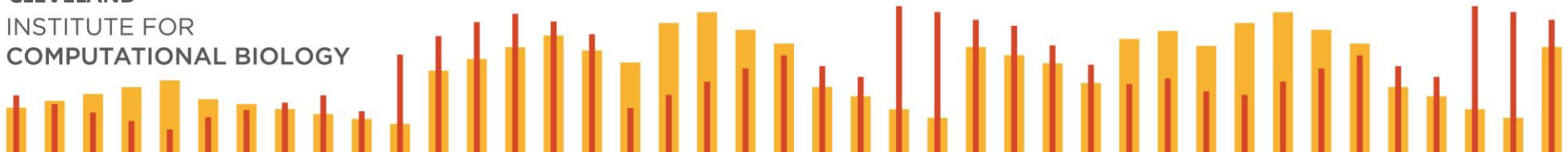

# OVERVIEW
## RETURNING GENETIC RESULTS/DATA

- How we got here
- How might genetic results/data be returned?
- How to interpret returned genetic data?

# U.S. Federal Investment

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

*"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

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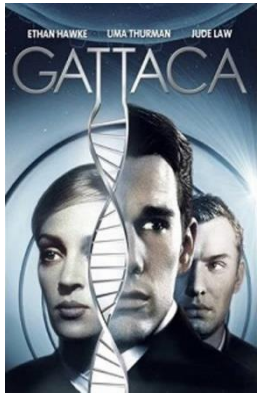
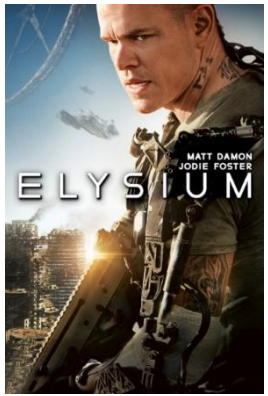
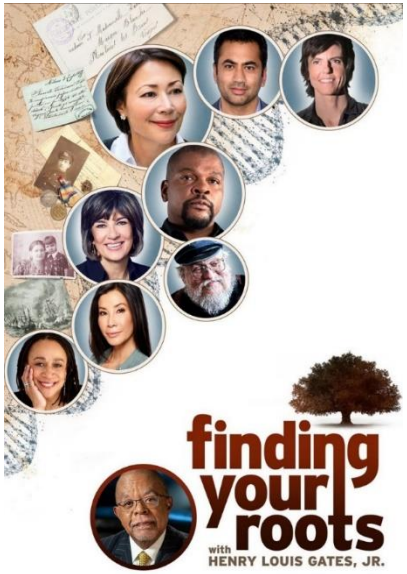
# GENETICS

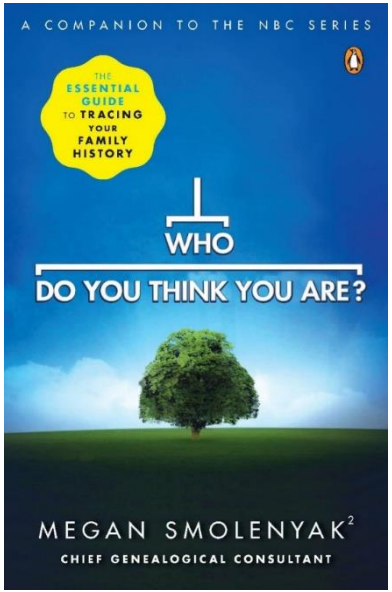
## HOLLYWOOD TO DOCU-SERIES





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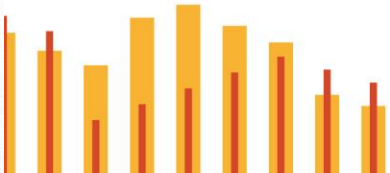
# Direct To Consumer Genetic Testing (DTC-GT)

23andMe®

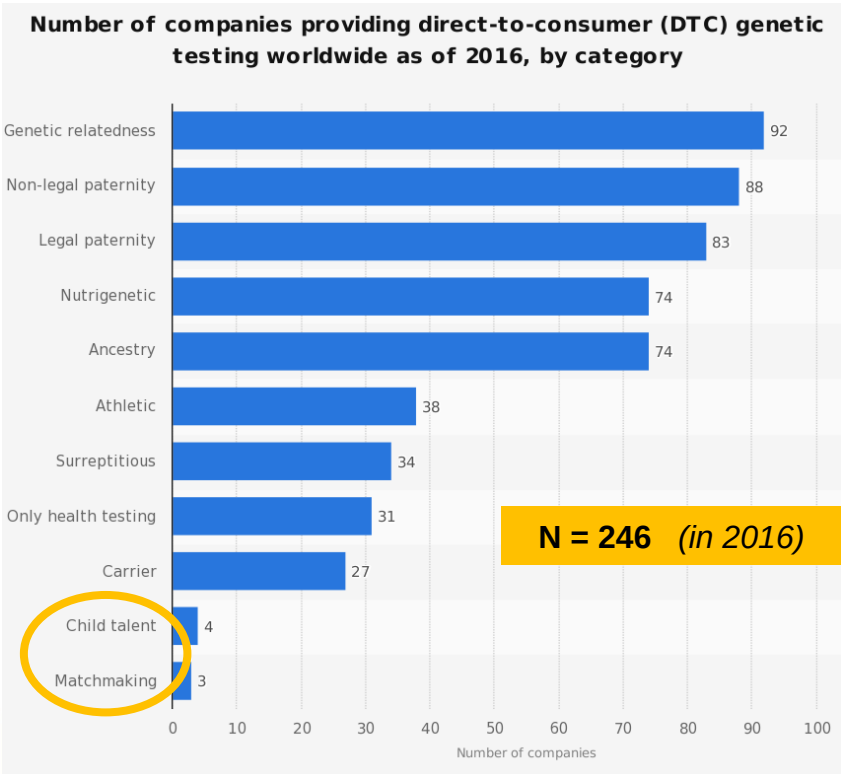
ancestryDNA™

MyHeritage

FamilyTreeDNA

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



# Potential Research Participants Want their Raw Genetic Data

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

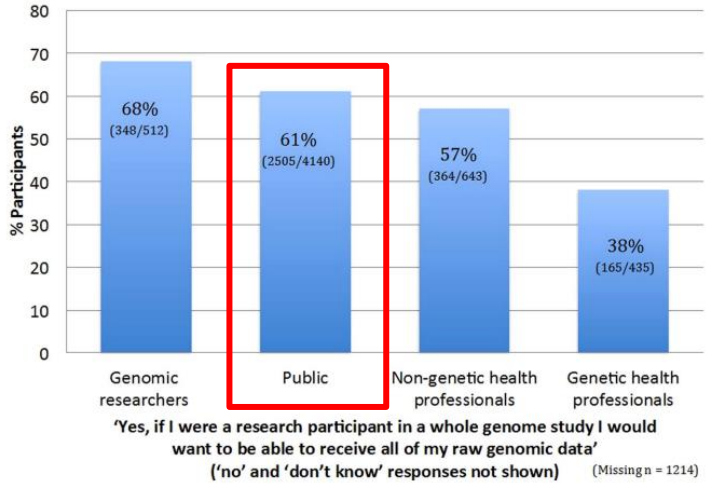



**Figure 1** Interest in receiving raw genomic data.

**Q:** If you were given your **raw genomic data** from a research study, what would you do? (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)

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# How might Genetic Results/Data be Returned?

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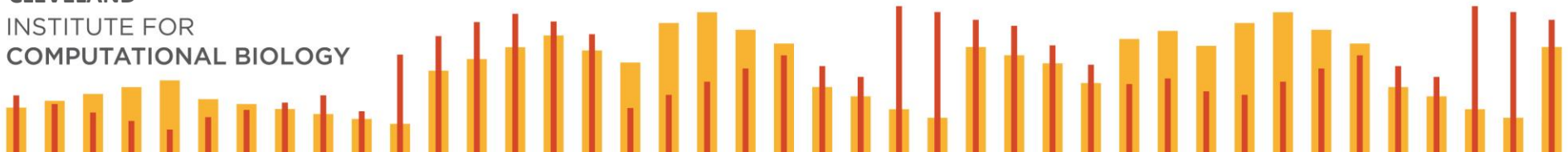
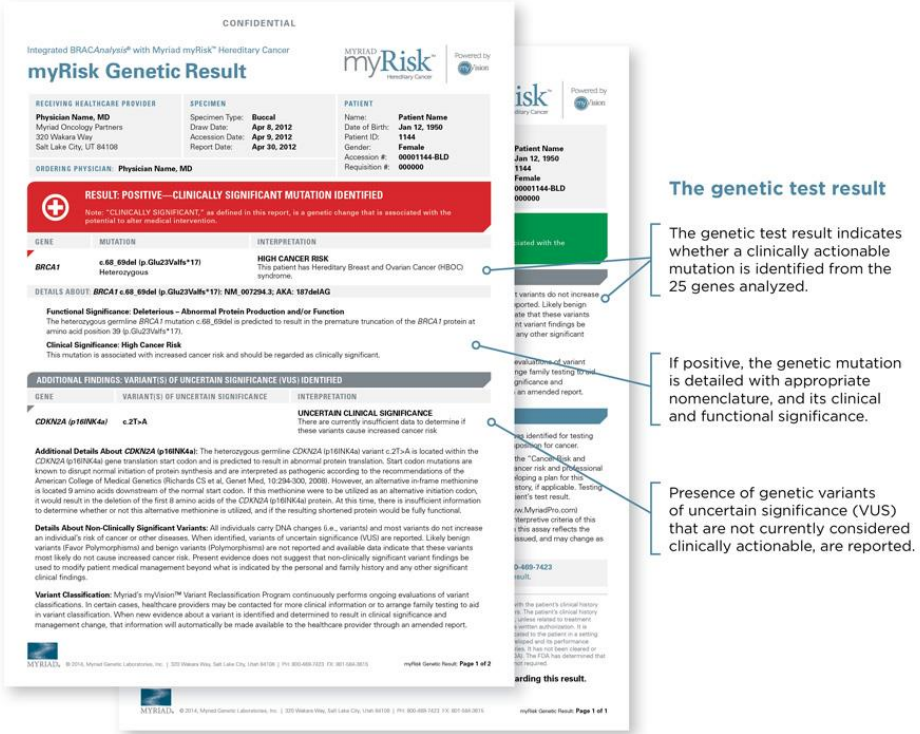


# Return of Curated Research Genetic Results

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



CONFIDENTIAL

Integrated BRACAnalysis® with Myriad myRisk® Hereditary Cancer

**myRisk Genetic Result**

myRisk Hereditary Cancer — Powered by myVision

| RECEIVING HEALTHCARE PROVIDER | SPECIMEN | PATIENT |
|---|---|---|
| Physician Name, MD<br>Myriad Oncology Partners<br>320 Wakara Way<br>Salt Lake City, UT 84108 | Specimen Type: Buccal<br>Draw Date: Apr 8, 2012<br>Accession Date: Apr 9, 2012<br>Report Date: Apr 30, 2012 | Name: Patient Name<br>Date of Birth: Jan 12, 1950<br>Patient ID: 1144<br>Gender: Female<br>Accession #: 00001144-BLD<br>Requisition #: 000000 |

ORDERING PHYSICIAN: Physician Name, MD

**RESULT: POSITIVE—CLINICALLY SIGNIFICANT MUTATION IDENTIFIED**

Note: "CLINICALLY SIGNIFICANT," as defined in this report, is a genetic change that is associated with the potential to alter medical intervention.

| GENE | MUTATION | INTERPRETATION |
|---|---|---|
| *BRCA1* | c.68_69del (p.Glu23Valfs*17)<br>Heterozygous | HIGH CANCER RISK<br>This patient has Hereditary Breast and Ovarian Cancer (HBOC) syndrome. |

DETAILS ABOUT: *BRCA1* c.68_69del (p.Glu23Valfs*17): NM_007294.3; AKA: 187delAG

**Functional Significance: Deleterious – Abnormal Protein Production and/or Function**
The heterozygous germline *BRCA1* mutation c.68_69del is predicted to result in the premature truncation of the *BRCA1* protein at amino acid position 39 (p.Glu23Valfs*17).

**Clinical Significance: High Cancer Risk**
This mutation is associated with increased cancer risk and should be regarded as clinically significant.

**ADDITIONAL FINDINGS: VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED**

| GENE | VARIANT(S) OF UNCERTAIN SIGNIFICANCE | INTERPRETATION |
|---|---|---|
| *CDKN2A (p16INK4a)* | c.2T>A | UNCERTAIN CLINICAL SIGNIFICANCE<br>There are currently insufficient data to determine if these variants cause increased cancer risk. |

**Additional Details About *CDKN2A* (p16INK4a):** The heterozygous germline *CDKN2A* (p16INK4a) variant c.2T>A is located within the *CDKN2A* (p16INK4a) gene translation start codon and is predicted to result in abnormal protein translation. Start codon mutations are known to disrupt normal initiation of protein synthesis and are interpreted as pathogenic according to the recommendations of the American College of Medical Genetics (Richards CS et al, Genet Med, 10:294-300, 2008). However, an alternative in-frame methionine is located 9 amino acids downstream of the normal start codon. If this methionine were to be utilized as an alternative initiation codon, it would result in the deletion of the first 8 amino acids of the *CDKN2A* (p16INK4a) protein. At this time, there is insufficient information to determine whether or not this alternative methionine is utilized, and if the resulting shortened protein would be fully functional.

**Details About Non-Clinically Significant Variants:** All individuals carry DNA changes (i.e., variants) and most variants do not increase an individual's risk of cancer or other diseases. When identified, variants of uncertain significance (VUS) are reported. Likely benign variants (Favor Polymorphisms) and benign variants (Polymorphisms) are not reported and available data indicate that these variants most likely do not cause increased cancer risk. Present evidence does not suggest that non-clinically significant variant findings be used to modify patient medical management beyond what is indicated by the personal and family history and any other significant clinical findings.

**Variant Classification:** Myriad's myVision™ Variant Reclassification Program continuously performs ongoing evaluations of variant classifications. In certain cases, healthcare providers may be contacted for more clinical information or to arrange family testing to aid in variant classification. When new evidence about a variant is identified and determined to result in clinical significance and management change, that information will automatically be made available to the healthcare provider through an amended report.

MYRIAD © 2014, Myriad Genetic Laboratories, Inc. | 320 Wakara Way, Salt Lake City, Utah 84108 | PH: 800-469-7423 FX: 801-584-3615

myRisk Genetic Result: Page 1 of 2

**The genetic test result**

The genetic test result indicates whether a clinically actionable mutation is identified from the 25 genes analyzed.

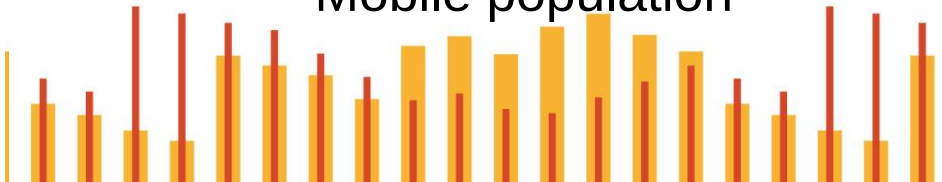
If positive, the genetic mutation is detailed with appropriate nomenclature, and its clinical and functional significance.

Presence of genetic variants of uncertain significance (VUS) that are not currently considered clinically actionable, are reported.

**Personal report**
via snail mail


**but**

Not easily scalable
Expensive (?)
Mobile population



# Return of Curated Research Genetic Results

Through your healthcare provider

but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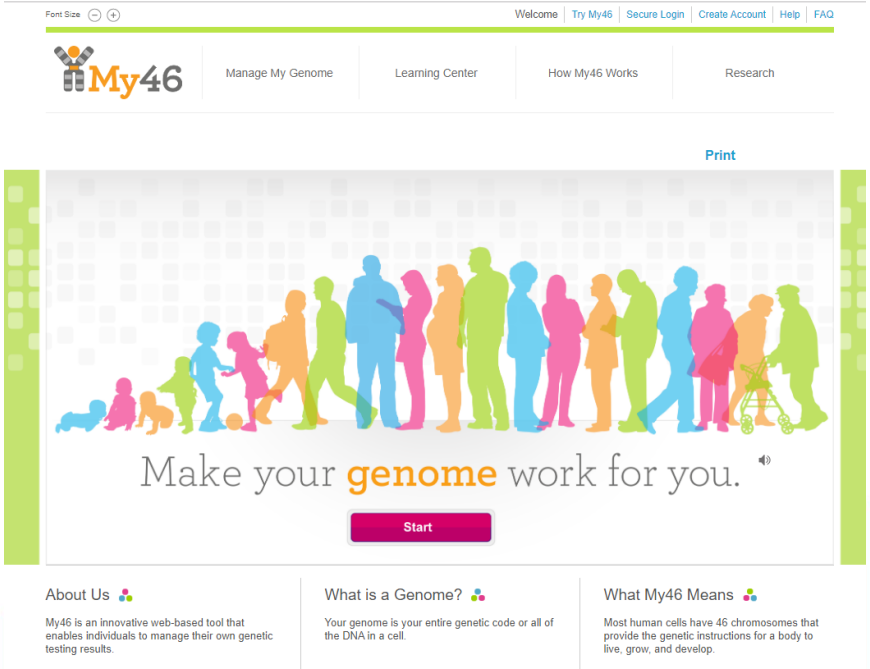
# Return of Curated Research Genetic Results

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



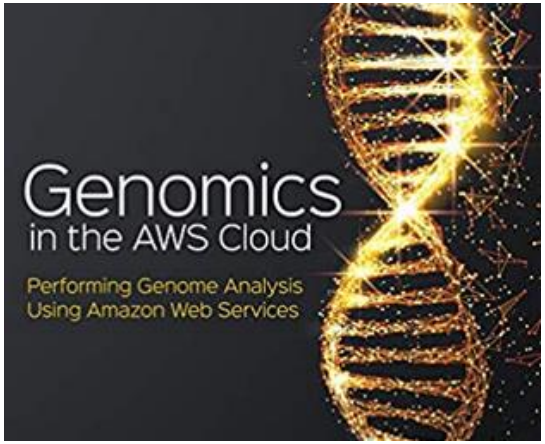

Through a Web-based tool

**but**

www.my46.org

# Return of LARGE Genetic Data Files


Other private storage tools




**but**

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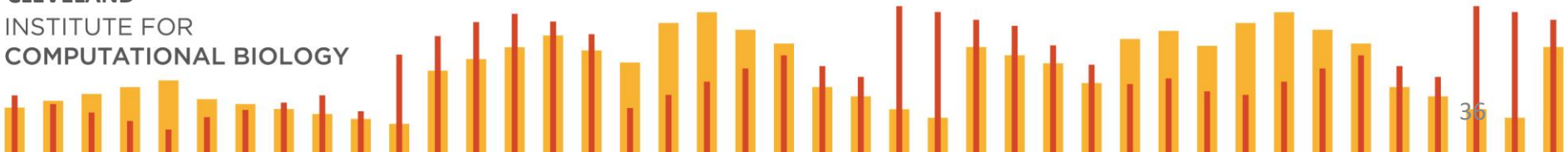
# What to Do with LARGE Genetic Data Files?





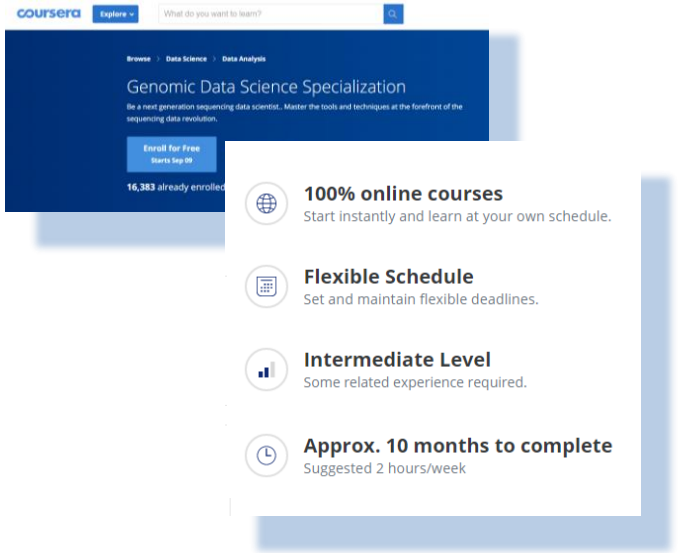
# RETURNING RAW SEQUENCE DATA
## VCF FORMAT

```
##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
```

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

# What to Do with Raw Sequence 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

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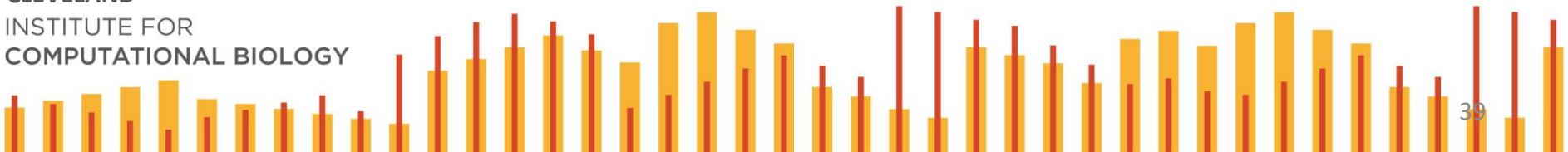
# How to Interpret Genetic Data?



# 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

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# 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?

As Findings Improve and Change…

### Who bears the onus?

Participant, Researcher, Funding Agency, Government?

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# Presenters and Topics

Electronic Health Records: Not Your Parents' Paper Charts

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

Annotating Genomics Sequence for Human Health

The intersection of bioethics and genomics in precision medicine

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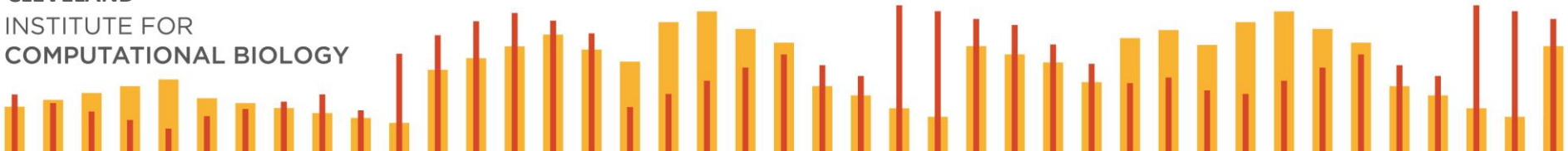

# BIOETHICS?

"the ethical implications and applications of health-related life sciences"

https://www.nlm.nih.gov/bsd/bioethics.html

https://bioethics.msu.edu/about/what-is-bioethics

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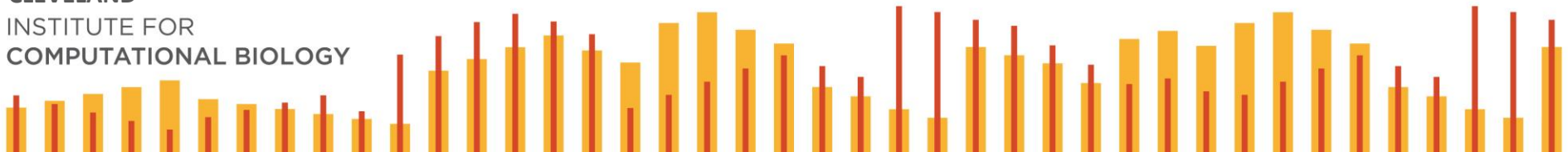
Illustration by Stephanie Dalton Cowan:
https://www.hopkinsmedicine.org/news/publications/hopkins_medicine_magazine/features/fall-2018/bioethics-gets-practical

# Research Ethics History Overview

- Early 20th Century
  - No national or international regulations on human participants in research
  - No research ethics committees, institutional review boards
  - No consumer regulations
  - No Food and Drug Administration (FDA)





# What were some of the ethical, legal, and social implications addressed by the Human Genome Project?

The Ethical, Legal, and Social Implications (ELSI) program was founded in 1990 as an integral part of the Human Genome Project. The mission of the ELSI program was to identify and address issues raised by genomic research that would affect individuals, families, and society. A percentage of the Human Genome Project budget at the National Institutes of Health and the U.S. Department of Energy was devoted to ELSI research.

The ELSI program focused on the possible consequences of genomic research in four main areas:

- Privacy and fairness in the use of genetic information, including the potential for genetic discrimination in employment and insurance.
- The integration of new genetic technologies, such as genetic testing, into the practice of clinical medicine.
- Ethical issues surrounding the design and conduct of genetic research with people, including the process of informed consent.
- The education of healthcare professionals, policy makers, students, and the public about genetics and the complex issues that result from genomic research.

**For more information about the ELSI program:**

Information about the ELSI program at the National Institutes of Health, including program goals and activities, is available in the fact sheet The Ethical, Legal and Social Implications (ELSI) Research Program from the National Human Genome Research Institute. The ELSI Planning and Evaluation History web page provides a more detailed discussion of the program.

More discussion about ethical issues in human genetics, including genetic

# The Importance of Engagement

## "Hands-off" research study

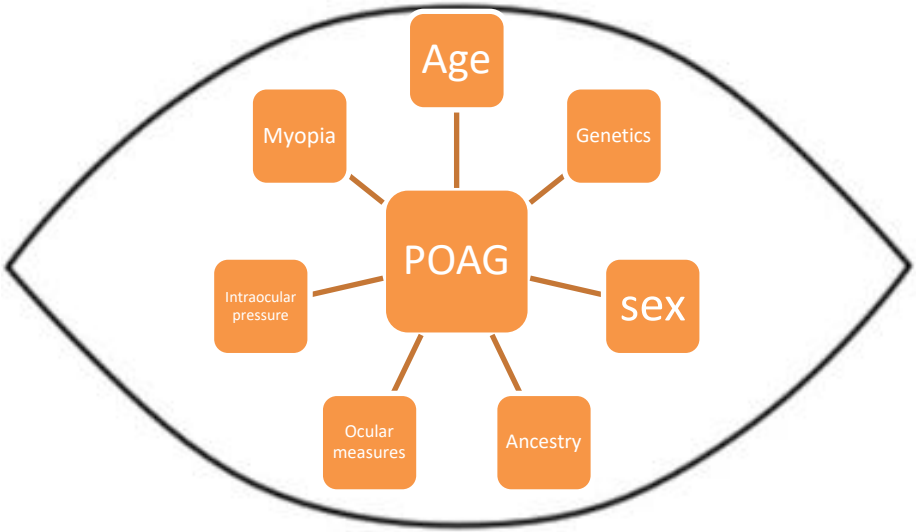
- Researchers get the data they want, and publish to the scientific community
- Possible translational/health impact

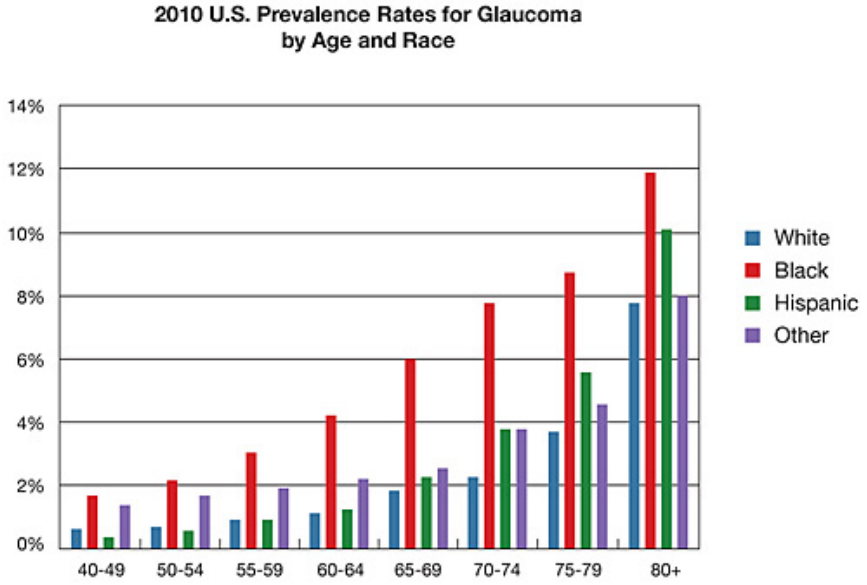
## Engaged research study

- Greater research impact
- Improved research quality
- New research questions generated or fresh insights into research challenges
- Increased accountability and transparency of research
- Increased responsiveness of research to societal needs
- The potential to build trust between research institutions and society
- Increased visibility, both of the research and the researcher's profile
- Addressing increased public interest in research and raising awareness of the outputs arising from the funding of research

https://www.ox.ac.uk/research/

# PRIMARY OPEN-ANGLE GLAUCOMA




https://nei.nih.gov/eyedata/glaucoma

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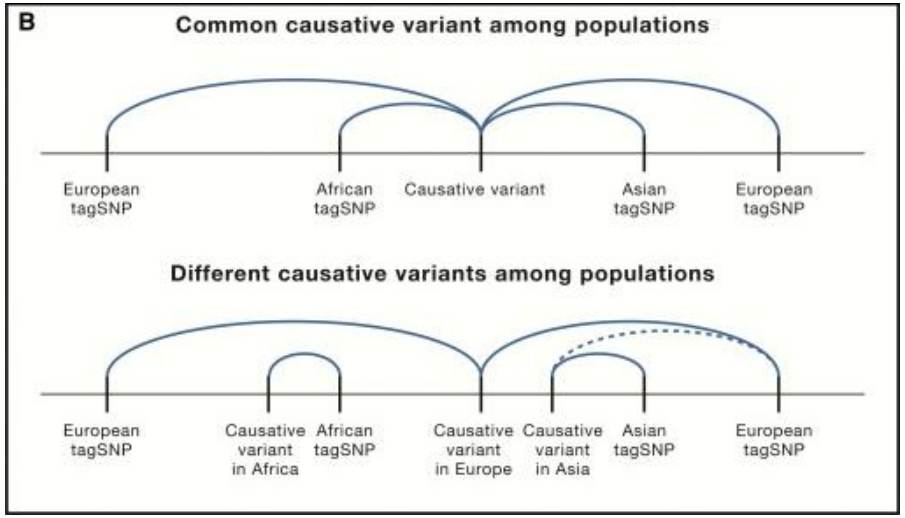
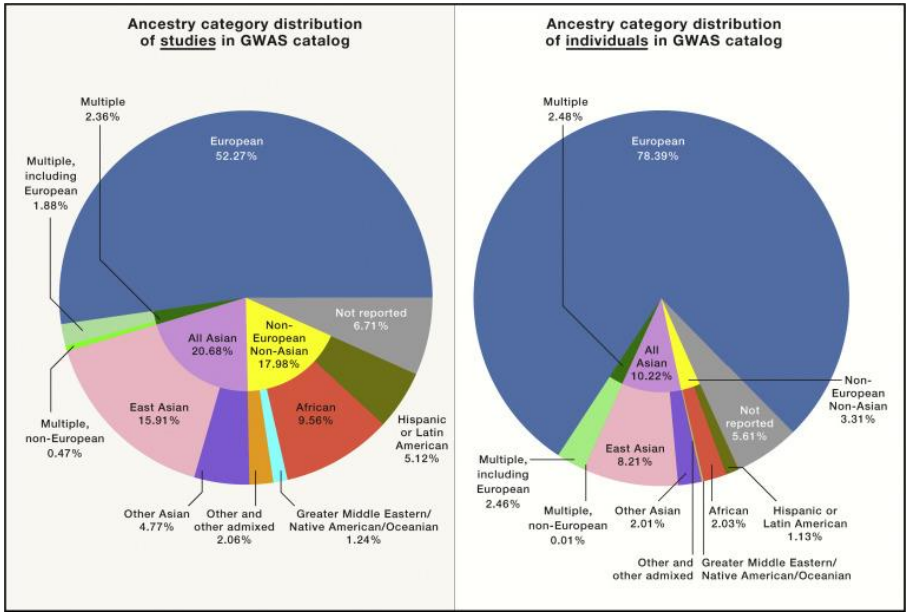
# GENETIC STUDIES LACK DIVERSITY




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

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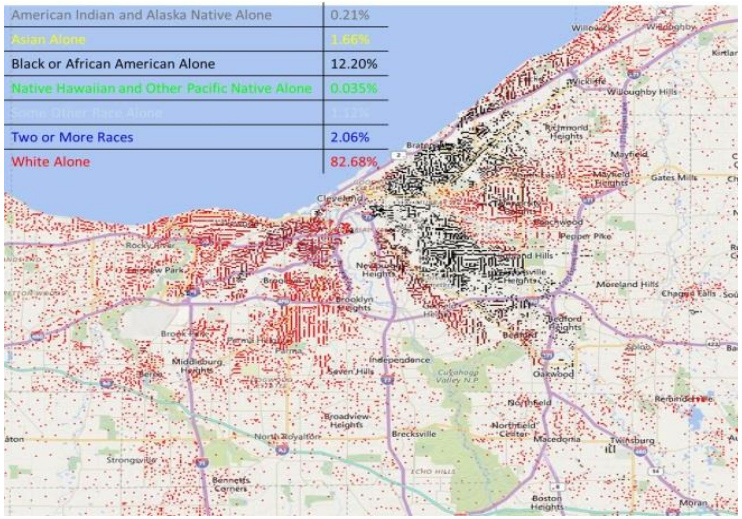
# COMMUNITY ENGAGEMENT EXAMPLE

Distribution of Race/Ethnicity in Greater Cleveland, Ohio.

http://ohio.us.censusviewer.com/client




https://www.atsdr.cdc.gov/communityengagement/

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https://www.universitysettlement.net/

University Settlement

We Change Lives

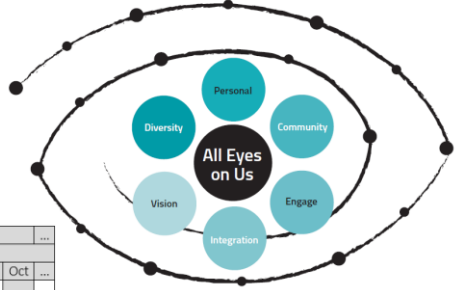
University Settlement is a 501(c)(3) nonprofit that has been providing much needed social services to the residents of the Broadway Slavic Village neighborhood since 1926. We are proud to be the premier social services provider and to continue our mission:

*"To offer the individuals and families we serve resources by which they can learn, grow, and thrive."*

## Our programs focus on:

Youth Seniors Families Community

# COMMUNITY ENGAGEMENT




CTSC Clinical and Translational Science Collaborative

SCHOOL OF MEDICINE CASE WESTERN RESERVE UNIVERSITY

University Settlement We Change Lives

**All Eyes on Us: Understanding Vision Disparities in Cleveland, OH**
**Memorandum of Understanding**
**(May 1, 2019 – April 30, 2020)**

- ***Purpose:*** This memorandum of understanding details the collaboration between the research team of Dr. Jessica Cooke Bailey, Principal Investigator, of Case Western Reserve University, and University Settlement for the period of time of May 1, 2019 through April 30, 2020. It is the hope of both parties that a new MOU will be established for the period of time beginning May 1, 2020.

- ***Study Overview:***

Blindness is understandably a major health fear, as sight is crucial for most activities of daily living. Globally, 36 million are blind. Among the leading contributors to blindness throughout the world, glaucoma is a disease that progressively damages the nerves connecting the eyes and brain. Glaucoma rates continue to increase with the growth of the aging population. In the United States, primary open-angle glaucoma (POAG), the most common glaucoma, is more prevalent and more aggressive in African Americans than other racial/ethnic groups. African Americans have been shown to have worse visual function and disproportionately higher burden of intervention-amenable blinding diseases than other racial/ethnic groups. Across all populations, lower SES is associated with greater severity of glaucoma at presentation. Research targeted at better understanding the mechanisms contributing to increased prevalence of glaucoma among poor and diverse groups of individuals is likely to improve understanding of health inequality and inform public health interventions.

To establish knowledge crucial to impacting these areas, we hypothesize that with this study we can identify perceptions of and barriers to vision care and health in an ethnically diverse neighborhood in Cleveland, Ohio with overall low socioeconomic status – the Broadway-Slavic Village Neighborhood. We *aim to identify perceptions of and barriers to vision care and health in an ethnically diverse neighborhood in Cleveland, Ohio with overall low socioeconomic status. In this exploratory, qualitative study, we will answer the following research questions: (1) How do lower SES individuals conceptualize and value their vision and prioritize vision care? (2) Are perceptions and values of vision care similar across whites and African Americans? (3) Do whites and African Americans of lower SES experience similar barriers to access to vision care?* Through understanding the significance of vision health and barriers to care, as expressed by the community, clearer points of intervention and access improvement will be illuminated.

| Year | 2019 | | | | | | | | 2020 | | | | | | | | ... |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Grant Year | 1 | | | | | | | | | | | | Post-award period | | | | | | | |
| Month | May | June | July | Aug | Sept | Oct | Nov | Dec | Jan | Feb | March | April | May | June | July | Aug | Sept | Oct | ... |
| Team Meetings | | | | | | | | | | | | | | | | | | | |
| Finalize data collection tools | | | | | | | | | | | | | | | | | | | |
| Establish CAB | | | | | | | | | | | | | | | | | | | |
| Meet with CAB | | | | | | | | | | | | | | | | | | | |
| *Update IRB* | | | | | | | | | | | | | | | | | | | |
| Conduct QI | | | | | | | | | | | | | | | | | | | |
| *Interview transcription* | | | | | | | | | | | | | | | | | | | |
| *Interview analysis* | | | | | | | | | | | | | | | | | | | |
| Community presentation | | | | | | | | | | | | | | | | | | | |
| Submit abstracts | | | | | | | | | | | | | | | | | | | |
| Draft manuscript(s) | | | | | | | | | | | | | | | | | | | |

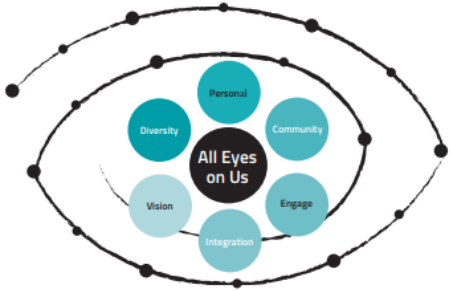
CAB=Community Advisory Board; IRB=internal review board; QI=qualitative interviews
*Italicized items are administrative*; **bold items will be joint efforts between University Settlement and CWRU**

We aim to identify perceptions of and barriers to vision care and health in an ethnically diverse neighborhood in Cleveland, Ohio with overall low socioeconomic status.

1. How do lower SES individuals conceptualize and value their vision and prioritize vision care?
2. Are perceptions and values of vision care similar across whites and African Americans?
3. Do whites and African Americans of lower SES experience similar barriers to access to vision care?

**AEOU Study Team**
**Dr. Erika Trapl**
**Dr. Sarah Koopman-Gonzalez**
**Leah Cummings**
**Sara Kennedy**
**Leslie Castaneda**
**Leslie Richards**
**Bridget Croniger**
**University Settlement Partners**

**Aim 1:** Establish a Community Advisory Board comprised of Slavic Village neighborhood residents to facilitate discussion of vision health and construction of a qualitative interview guide.




CTSC
Clinical and Translational Science Collaborative

DEPARTMENT OF POPULATION AND QUANTITATIVE HEALTH SCIENCES

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

**All Eyes on Us: Understanding Vision Disparities in Cleveland, OH**
**The Community Advisory Board**
**Governing Guidelines**

Mission: The mission of the Community Advisory Board (CAB) is to provide guidance to the Case Western Reserve University All Eyes on Us (AEU) pilot study team by discussing intentional recruitment in the community and developing a semi structured interview protocol around vision health that is appropriately targeted to the population of interest.

The CAB/AEU collaboration benefits University Settlement and the AEU team by addressing and meeting their mission to foster partnerships within urban neighborhoods to better understand barriers, values, and perceptions surrounding vision health and care. Specifically, we will partner with neighborhood residents and leaders, and the community organizations that serve the neighborhoods, to address eye health concerns which are not particularly emphasized on a daily basis in the community (e.g., primary open-angle glaucoma (POAG), diabetic retinopathy, age-related macular degeneration (AMD)), but are influenced by the conditions, disparities and resources of the neighborhood itself.

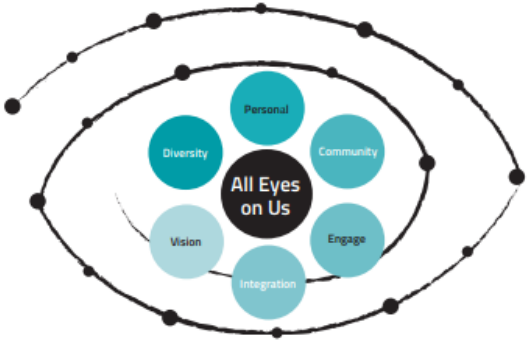
**Roles and Responsibilities**

The CAB will partner with leadership of the AEU to:

- Attend CAB meetings for the second, third, and fourth months of the study (refer to timeline on page 3);
- Recommend and brainstorm effective recruitment strategies;
- Identify community needs and concerns;
- Develop an interview protocol appropriate for community members;
- Provide a voice for their community regarding current and future eye health research;
- Set research priorities in the community and provide input as needed;
- Promote community support for, and involvement in, community-based research, including the specific research carried out by the AEU;
- Endorse, support and help to identify resources to implement and sustain local community-based research projects;
- Assist in planning and implementation of activities to educate community leaders and health professionals about the strengths and potential of community-based research.

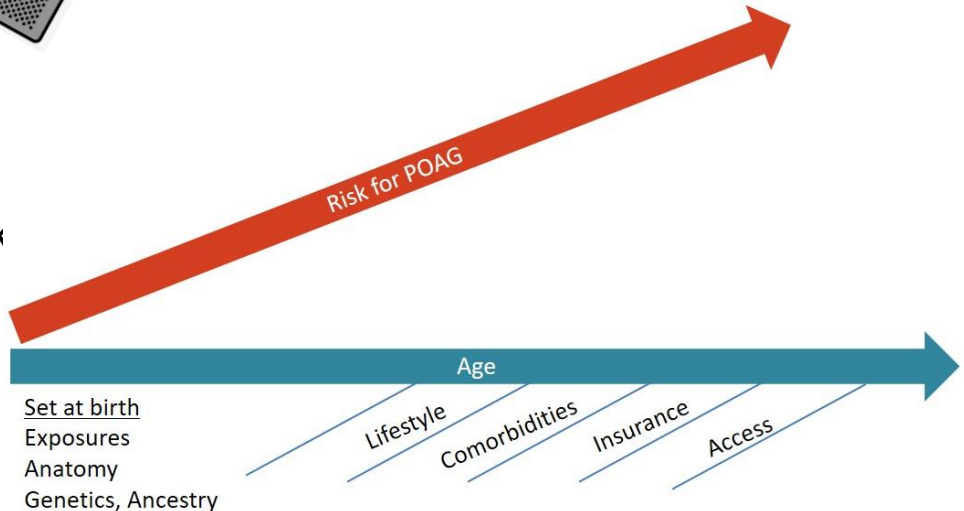
# All Eyes on Us

## Progress to date

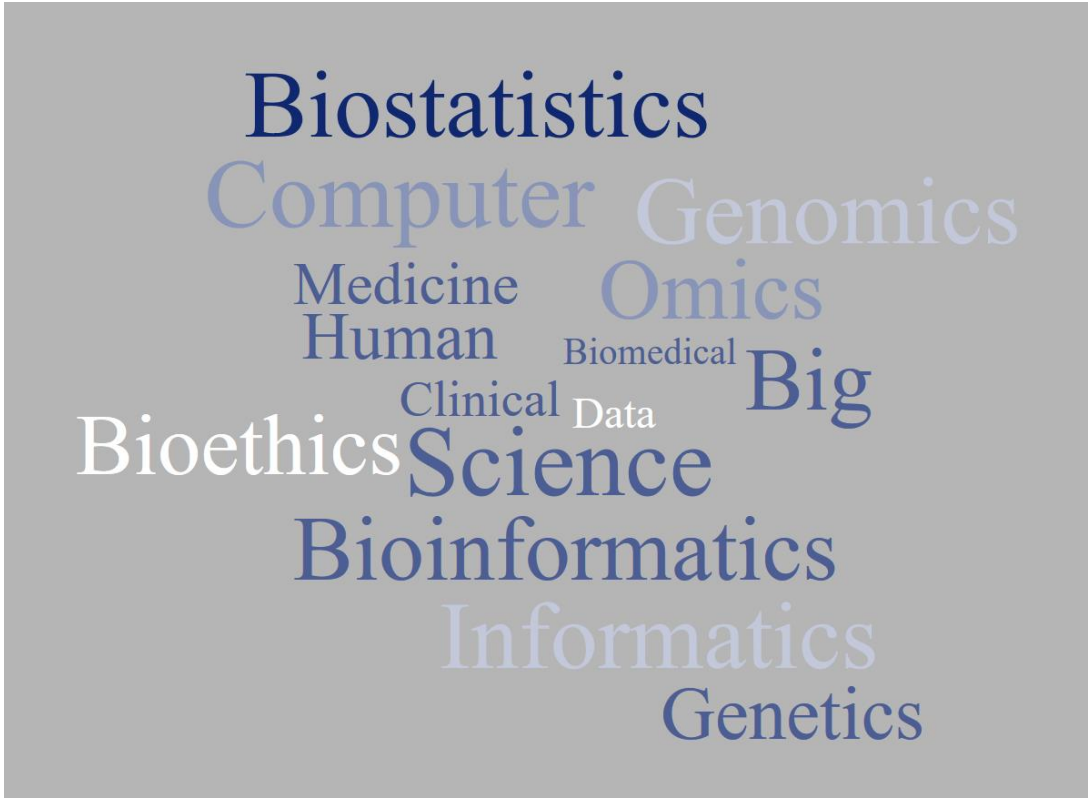



**Aim 2:** Assess perception, values, and barriers to vision health care among Slavic Village neighborhood residents.

- **60 audio-recorded interviews**
  - 30 self-identified African American
  - 30 self-identified White
- **Remuneration**
- **59 successfully recorded interviews transcribed**
- **Quality-control (double-check the transcription)**
- **Code for thematic elements**
- **Qualitative analyses ←preliminarily complete**
- **Dissemination ← on hold, thanks COVID-19**
- **Future grant funding for integrated model of glaucoma risk**
- **Expanding clinical study to Broadway Eye clinic (MetroHealth System)**
  - Surveys informed by our qualitative interview findings
  - Demographics
  - Clinical information
  - Blood for DNA



# PRECISION MEDICINE RESEARCH IS MULTIDISCIPLINARY

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# Presenters and Expertise

Dana Crawford, PhD
Human Genetics
Human Genomics

Will Bush, PhD, MS
Computer Science
Statistics
Bioinformatics
Human Genetics

Farren Briggs, PhD, ScM
Epidemiology
Genetic Epidemiology
Biostatistics

Jessica Cooke Bailey, PhD, MA
Human Genetics
Molecular Genetics
Bioethics

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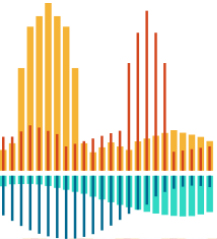
# QUESTIONS?

SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

# ¿PREGUNTAS?

DEPARTMENT OF POPULATION AND QUANTITATIVE HEALTH SCIENCES



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