

CENTER FOR INDIVIDUALIZED MEDICINE

Consumer Genomics @ Mayo
NASEM, September 29, 2019



Disclosures/Need to Know

Mayo Clinic GeneGuide™ is a Mayo Clinic laboratory operating within the Center for Individualized Medicine

Helix and PWN-Health are for profit companies

Mayo Clinic has an investment in the sequencing laboratory, Helix

No Mayo Clinic GeneGuide™ team members have a financial interest in any part of the product(s)

How Many People Have Had DTC?

Everybody's doing DNA tests

Total number of people tested by consumer genetics companies through January 2019, in millions

■ AncestryDNA ■ 23andMe ■ Others

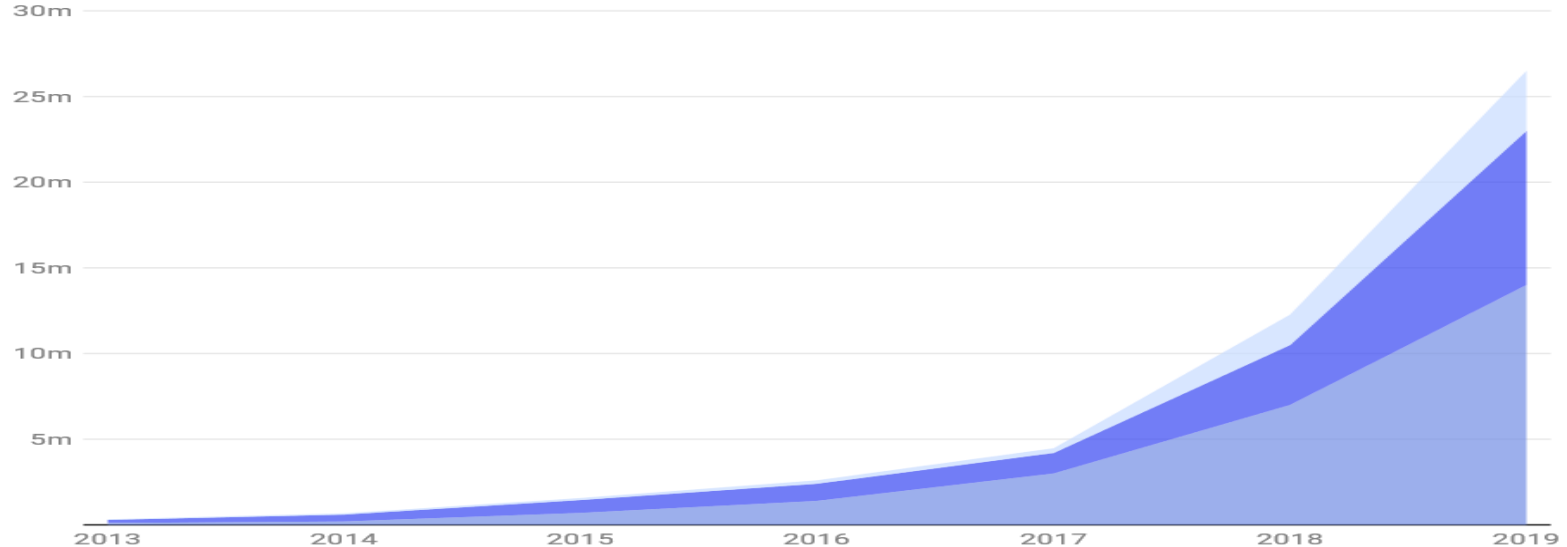


Chart: MIT Technology Review • Source: Company reports, Leah Larkin, ISOGG • Created with Datawrapper

<https://www.technologyreview.com/s/612880/more-than-26-million-people-have-taken-an-at-home-ancestry-test/>

Why Do Consumers Want DNA Testing?

HEALTH WELLNESS
Ancestry
Curiosity Entertainment
Paternity

Types of Genetic Testing

Diagnostic

Consumer facing

GoodStart Genetics

23andMe

Counsyl

Arivale

GENE BY LifeNome
Enhancing Personalized Wellbeing

SURE GENOMICS

Edu-Tainment

Understand Your Genome



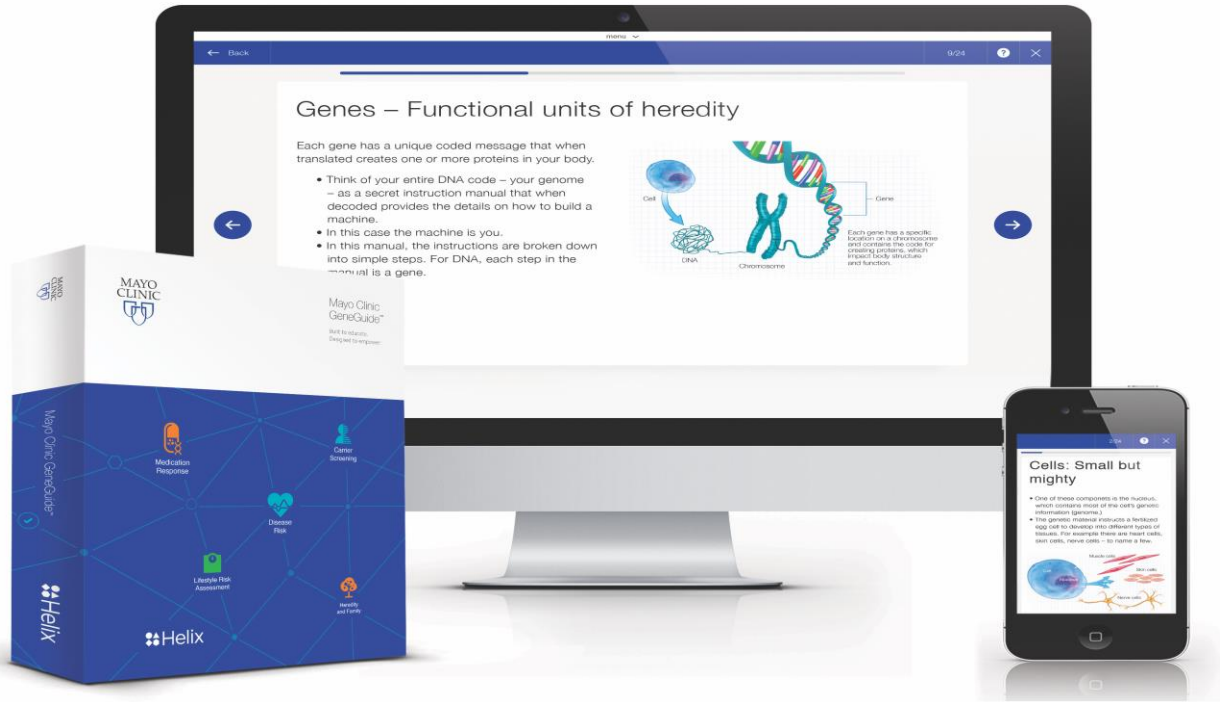
PATHWAY GENOMICS®

INVITAE



Provider ordered





What is Mayo Clinic GeneGuide™?

A genetic testing experience

- Educates consumers and helps them understand how genetics can affect their health

Consumer-initiated, physician-ordered product

Includes results for 15 conditions in categories:

- Carrier screening > Medication Response
- Disease risk > Health traits

Includes 4 health learning tools:

- Health ancestry results > Lifestyle questionnaire
- Pedigree tool > Breast cancer risk screening tool

Includes a robust education section: 15 topics

Why is Mayo Clinic pursuing this initiative?

Allows Mayo Clinic to educate consumers before they present as sick patients

Share Mayo Clinic knowledge to an eager audience in a balanced way

Setting realistic expectations

Prepare OURSELVES for the management of DTC results

Potential benefits

May provide ***meaningful health information*** to individuals who might otherwise not qualify to receive testing through current medical guidelines.

Availability of this testing may ***increase the genetic literacy*** of the general population at a time when genetics is becoming an integrated part of the medical practice.

Limitations

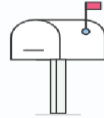
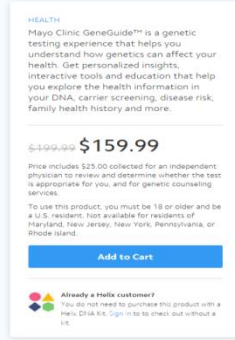
Results may be informative, but ***should not be considered diagnostic.***

- A positive result may suggest further medical evaluations and/or confirmatory testing.

Assesses ***limited number of variants***, or changes, in a specific set of genes.

- A negative test result will reduce, but cannot eliminate risk of having a variant in a gene. i.e., BRCA1/2.

Consumer-initiated ordering process



Consumer orders
product on
Helix.com

Helix sends kit to
the consumer's
home

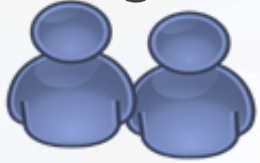
Consumer
registers with
Helix and
provides health
history

PWNHealth
physician
reviews the
consumer's
health history

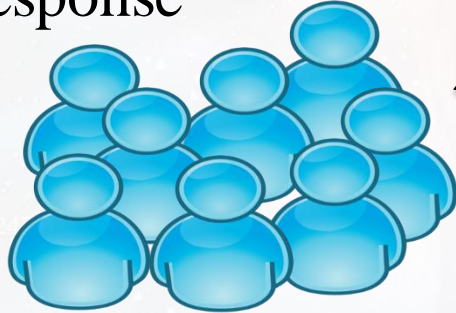
Consumer
receives an email
when the
physician has
approved their
order

What is pharmacogenomics?

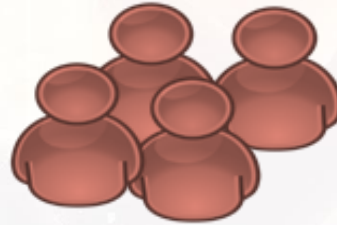
Study of genetic variations that influence individual response to drugs



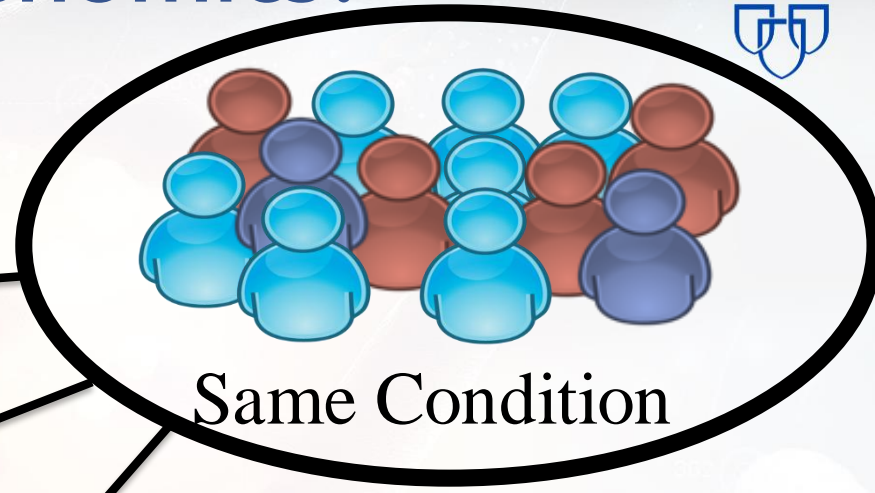
No Response



Desired Response



Toxic Side Effects



Pharmacogenomic Testing at Mayo Clinic

Mayo Medical Labs

- Single gene tests
- Nine gene panel

AssureRx Health

- GeneSight®

OneOme

- RightMed®

Summary Labs Medications Vital Signs Intake / Output Documents / Images Assessments / Cares Allergies/Immunizations/Devices Patient Facts Clinical Problem List Orders Patient's Messages Viewers / Reports

Labs (155) Microbiology Pathology (0) Pending Labs (0) Transfusion/Blood Bank Genetics (1) Genotype (1)

Go Back: 10 Years Refresh Interval: Continuous View: Default Show reference ranges Hide 'Most Recent' column

LABS	Continuous	Most Recent	MCR	MCR	MCR	MCR	MCR	MCR	MCR	MCR	MCR	MCR	MCR
LABS	Continuous	Most Recent	24-Feb-15	07-Jan-15	29-Aug-14	24-Feb-14	01-May-13	29-Apr-13	25-Feb-13	15-Jan-13	02-Mar-12	01-Jun-11	
Enzymes Genotype Results 2													
CYP2C19 Phenotype, B		See comments	29-Aug-14		See comments								
2C19 Genotype Star Alleles		17/17	29-Aug-14		17/17								
2C19 Interpretation		See comments	29-Aug-14		See comments								
2C19 Reviewed by		See comments	29-Aug-14		See comments								
CYP2C9 Phenotype		See comments	29-Aug-14		See comments								
CYP2C9 Genotype Star Alleles		1/1	29-Aug-14		1/1								
CYP2C9 Phenotype Interpret...		See comments	29-Aug-14		See comments								
CYP2C9 Reviewed by		See comments	29-Aug-14		See comments								
Enzymes Genotype Results 3													
CYP3A4 Genotype Result		See comments	29-Aug-14		See comments								
CYP3A4 Interpretation													
Reviewed by (w/C)													
3A5 Phenotype, B													
3A5 Star Alleles, B													
3A5 Interpretation													
Reviewed By (w/C)													
Transporters Ge													
SLC01B1 Genotyp													
SLC01B1 Interpre													
Reviewed by (w/SI													
Hypersensitivity													
HLA-B*5801 Resu													
HLA-B*5801 Inter													
HLA-B*5801 Revie													
Anticoagulation													
Warfarin Sensitiv													
CYP2C9 Star Allele													
VKORC1-1639 Res													
Warfarin Sensitiv													
Warfarin SensRev													

Service Description Date/Time Status Subtype Dept Fac

Pharmacogenomics Gene Panel, B 29-Aug-2014 12:31 A LAB MCR

Zoom In 150% Zoom Out

CYP2C19 Phenotype, B Ultrarapid metabolizer MCR

2C19 Genotype Star Alleles 17/17 MCR

2C19 Interpretation MCR

This individual is expected to be an ultrarapid (increased) CYP2C19 metabolizer due to the presence of the homozygous *17 variant which results in increased expression of CYP2C19 enzyme. Caution should be exercised when treating with drugs metabolized by CYP2C19 as follows:

If this patient is taking a prodrug that is activated by CYP2C19, such as clopidogrel, increased activation of the drug is expected to occur which may result in increased activity of the drug and side effects such as bleeding.

If this patient is taking a drug that is inactivated by CYP2C19, such as citalopram or phenytoin, increased inactivation is expected which may result in lower blood levels of the parent drug and poorer response.

-----ADDITIONAL INFORMATION-----

A Luminex assay using Polymerase Chain Reaction (PCR) with Allele-Specific Primer Extension (ASPE) was used to test for the presence or absence of variants in the promoter and exons 1, 3, 4, 5 and 9 of the CYP2C19 gene. Specifically, the reactions detect the presence or absence of c.-806C>T (*17), c.1A>G (*4), c.358T>C (*8), c.395G>A (*6), c.431G>A (*9), c.636G>A (*3), c.680C>T (*10), c.681G>A (*2), c.819A>T (*7), and c.1297C>T (*5).

This Luminex assay will not detect all the known variants that result in altered CYP2C19 activity. Therefore, absence of a detectable gene variant does not rule out the possibility that a patient has an altered CYP2C19 metabolism status due to other CYP2C19 variants that cannot be detected with this method. Furthermore, when two or more gene variants are identified, the cis-trans status (whether the variants are on the same or opposite chromosomes) is not always known.

In addition to a genetic basis for CYP2C19 altered enzymatic activity, CYP2C19 enzyme activity can be inhibited by a variety of medications or their metabolites. The following is a partial listing of drugs known to affect CYP2C19 activity as of the date of this report.

A partial list of commonly prescribed drugs that undergo metabolism by CYP2C19:

Anticoagulants: clopidogrel, R-warfarin (less active isomer)

Anticonvulsants: mephenytoin, phenobarbitone, phenytoin, primidone

Antidepressants: amitriptyline, citalopram, S-citalopram, clomipramine,

The RIGHT Study: Right Drug, Right Dose, Right Time

Goals:

- Improve health care by utilizing **clinical decision support (CDS) alerts**
- Evaluate the clinical and fiscal impact of alerts.
- Retrospectively analyze EHR data to determine how the presence of genetic information might have altered patient outcomes.

The Journal of Molecular Diagnostics, Vol. 18, No. 3, May 2016



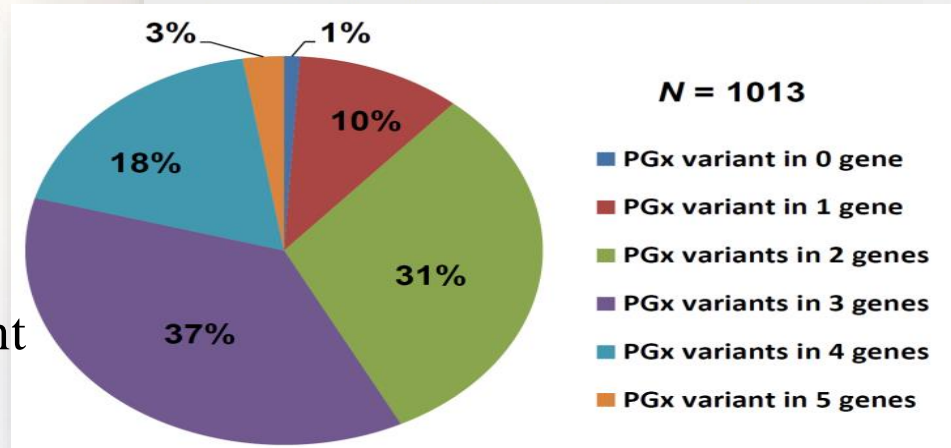
the Journal of
Molecular
Diagnostics

jmd.amjpathol.org



Preemptive Pharmacogenomic Testing for Precision Medicine

*A Comprehensive Analysis of Five Actionable
Pharmacogenomic Genes Using Next-Generation DNA
Sequencing and a Customized CYP2D6 Genotyping Cascade*



Pharmacogenomic CDS at Mayo Clinic

CYP2C19

- Clopidogrel (2014)
- Citalopram (2015)
- Escitalopram (2015)

SLCO1B1

Simvastatin (2014)

TPMT/NUDT15

(phenotype & genotype)

- Mercaptopurine (2013)
- Thioguanine (2013)
- Azathioprine (2013)

CYP2D6

- Codeine (2013)
- Tramadol (2013)
- Tamoxifen (2013)
- Paroxetine (2015)
- Fluoxetine (2015)
- Fluvoxamine (2015)
- Venlafaxine (2015)

CYP2C9/VKORC1

- Warfarin (2014)

CYP3A5

- Tacrolimus (2016)

DPYD

- 5-fluorouracil (2017)
- Capecitabine (2017)

HLA-B*15:02/HLA-A*31:01

Carbamazepine (2013)

HLA-B*57:01

Abacavir (2013)

HLA-B*58:01

Allopurinol (2014)

EPIC CDS or Best Practice Advisory

BestPractice Advisory - Cdstesting,Adt


High Priority (1)

 **PHARMACOGENOMICS ALERT:** This patient is a CYP2D6 Ultra Rapid metabolizer. Avoid codeine due to potential for toxicity. 


Remove the following orders? _____

Remove

Keep

 **butalbital-aspirin-caff-codeine 30-50-325-40 mg per capsule 1 capsule (FIORINAL WITH CODEINE)**
1 capsule, oral, Every 4 hours PRN, headaches, Starting Today at 1714

[Genomic Indicators](#) 

[For more information go to AskMayoExpert \(codeine\)](#) 

Acknowledge Reason _____


Benefit outweighs risk

Patient previously tolerated

Therapeutically appropriate

Will cancel order

Other reason

 **Accept**

Over 22,000 CDS alerts fired to date

We can run – but we can not hide!



Consumers and patients will increasingly drive genetic testing

Predictive Genomic Endeavors

Population Health – Mayo
Clinic GeneGuide™

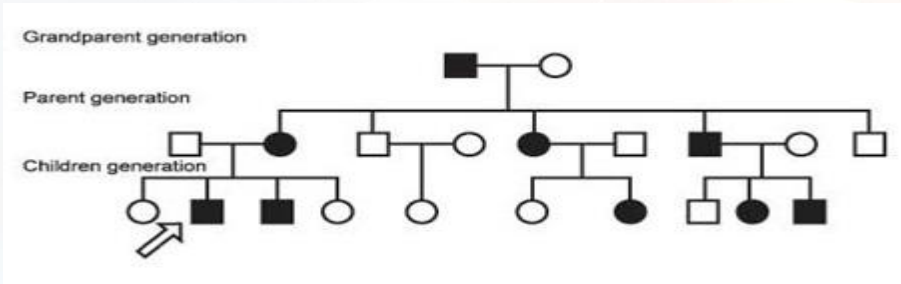
Sequencing of Mayo Clinic
Biobank (50K+)

Large Scale
Sequencing/Data
Repository



Do Genes Always Tell The Whole Story?

Emphasize: for many health related topics, genomics is just part of the equation



Environmental
lifestyle
social factors

Genetics



The End

247OM07663S

The branch of molecular biology concerned with the structure, function, evolution, and mapping of genomes

ACGT

73.66.6427

applying the techniques of genetics and molecular biology to the genetic mapping and DNA sequencing of sets of genes or the complete genomes of selected organisms, using high-speed methods; with organizing the results in databases, and with applications of the data (as in medicine or biology)

247OM07663S

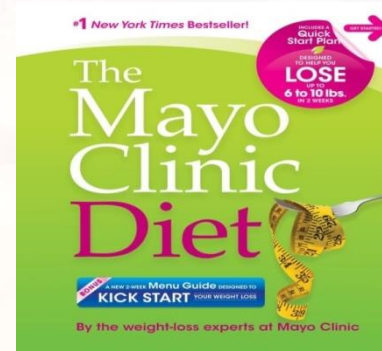
genomics

Mayo Clinic: Consumer Education

Worldwide leader in
medical care, research
and education

Rich history of health
care innovation

Mayo Clinic Books,
Newsletters, and many
other consumer goods



OUR **PURPOSE:**

**EDUCATE AND ENGAGE THE PUBLIC,
SHARING OUR KNOWLEDGE OF
GENOMIC DATA AND IMPLICATIONS
FOR HEALTH.**



**Patient Expresses
Interest or is Referred
for Consultation**



**Genetic Counseling
/ Pharmacist
Consult**



**Patient Test
Selection and
Sample Acquisition**



**Lab Sequencing and
Analysis**



**Clinical Analysis &
Genomic Board**



**Results Returned With
IM Counselor /
Pharmacist Support**

What have we found? (preliminary findings)

~300 patients that pursued predictive testing

11% Actionable Findings (34 patients)

- 13 were in hereditary cardiovascular genes
 - ~half had a suspicious personal or family history
 - All 3 patients with an FH gene had high cholesterol and were on statins
 - no other CV patient had manifest disease

- 15 were in hereditary cancer genes
 - ~ 50% of met NCCN guidelines for testing
 - One SDHA patient mutation w/bilateral carotid paragangliomas
 - otherwise no manifest cancer

Carriers and Disease Risk

40–75% of patients were found to be carriers of at least one AR condition

85.6% of WGS had at least one risk allele identified;

- APOE e4
- F5/F2
- Idiopathic pulmonary fibrosis
- MC1R/ MCM6 variants (melanoma)
- NAFLD (nonalcoholic fatty liver disease)