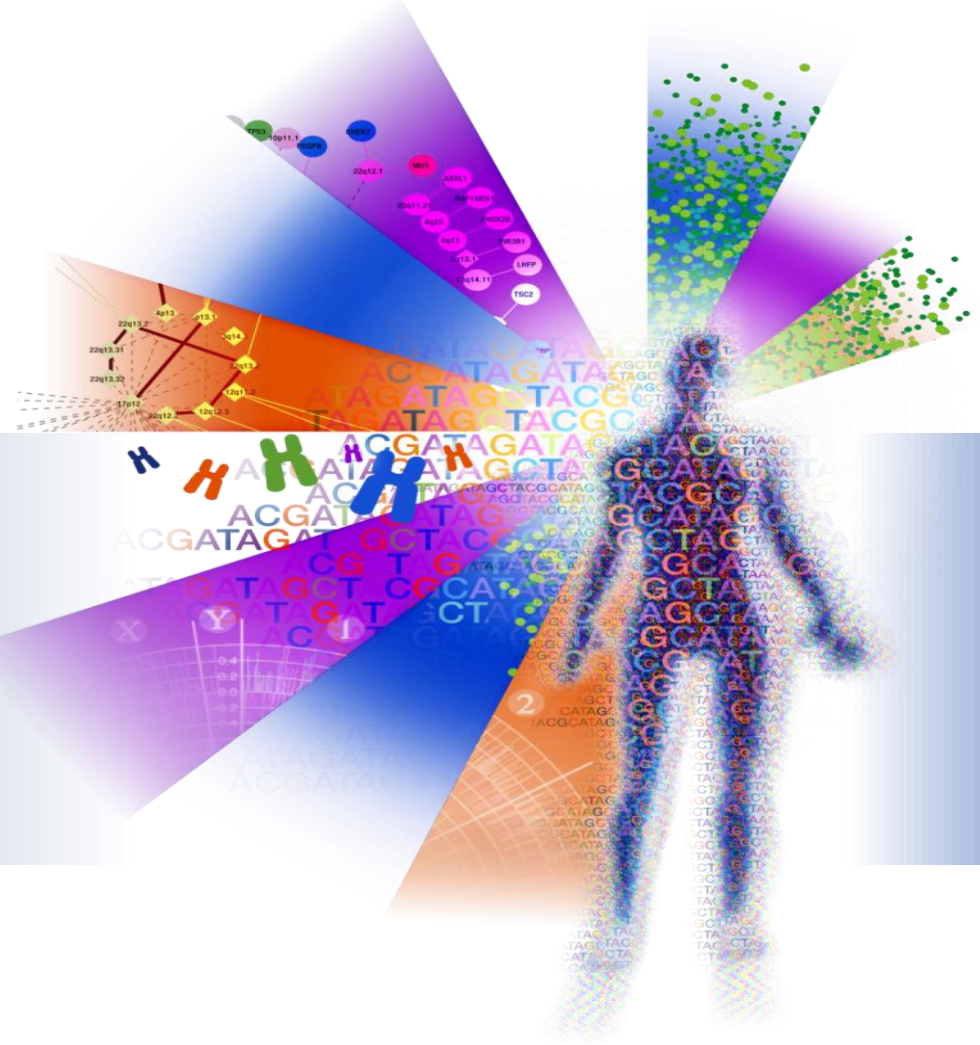
MAYO CLINIC



CENTER FOR INDIVIDUALIZED MEDICINE

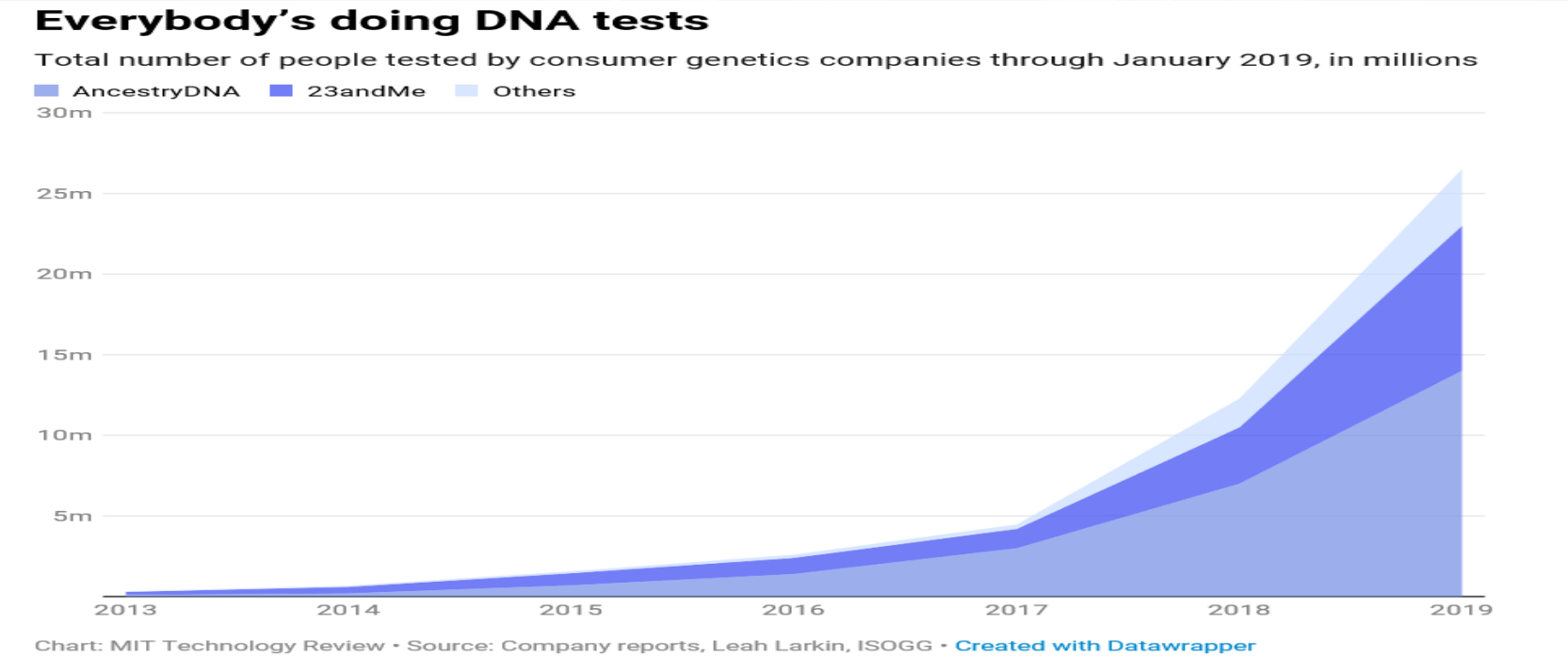
Consumer Genomics @ Mayo

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?



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

Why Do Consumers Want DNA Testing?

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HEALTH

WELLNESS

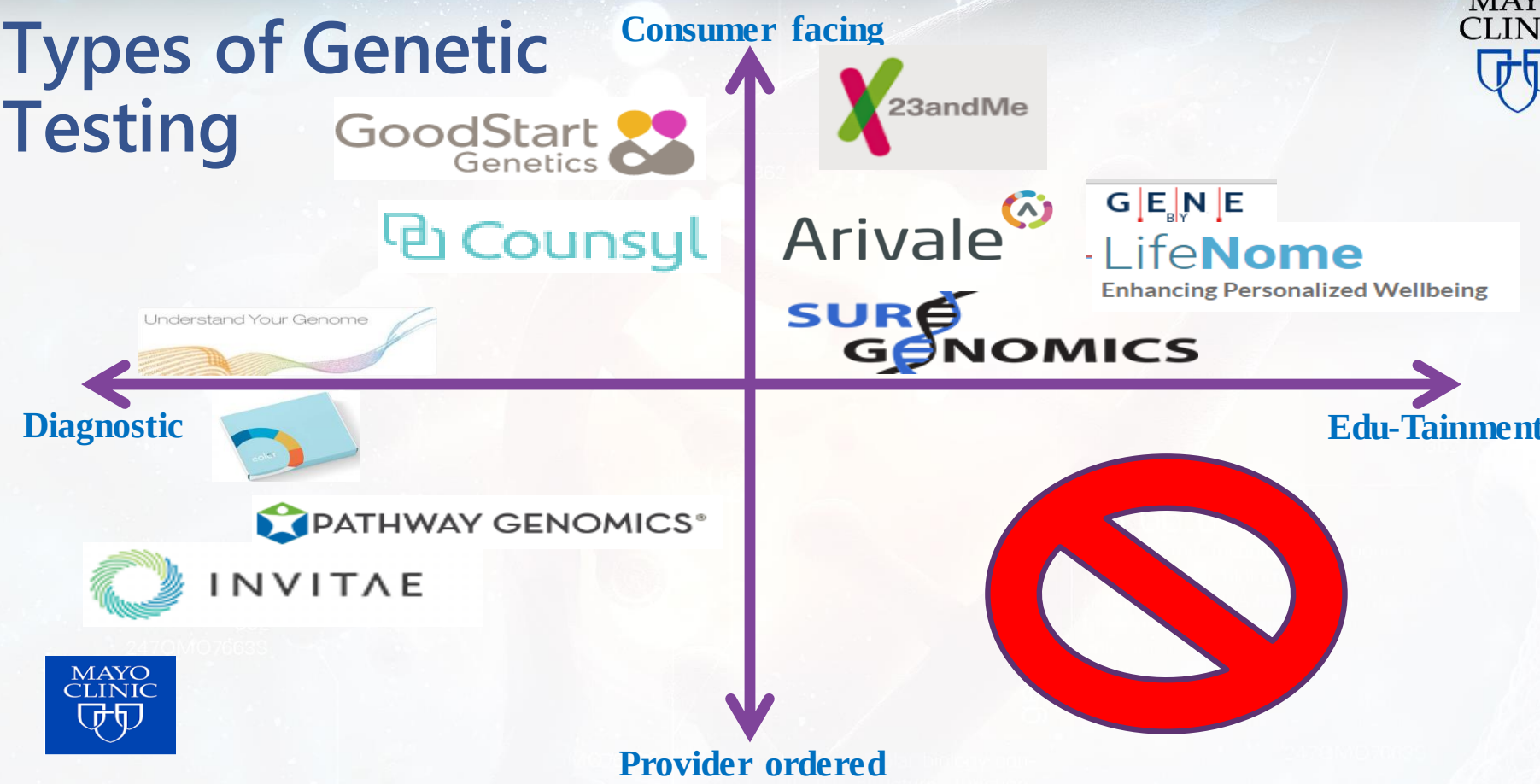
Ancestry

Curiosity

Entertainment

Paternity

Types of Genetic Testing



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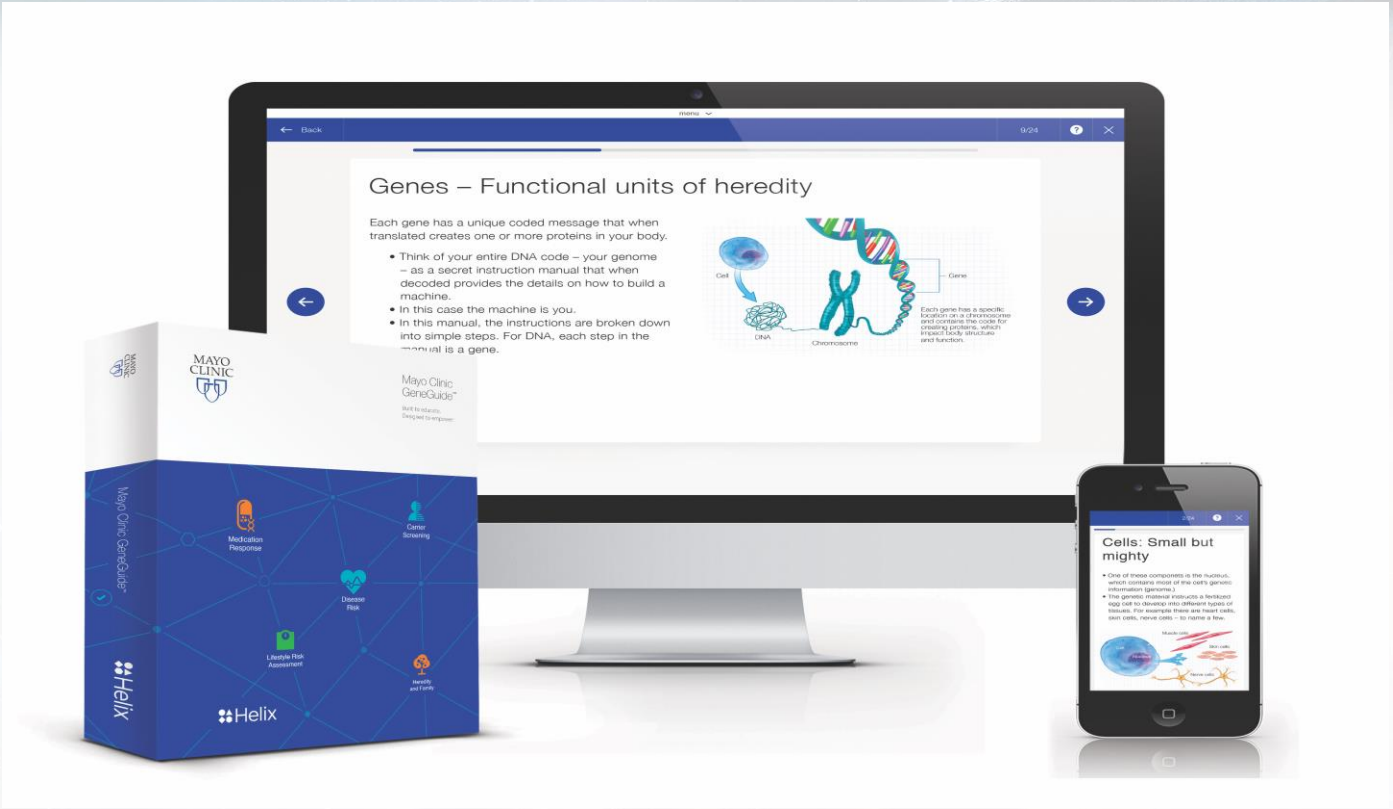

Back
9/24
Genes – Functional units of heredity
Each gene has a unique coded message that when translated creates one or more proteins in your body.
• Think of your entire DNA code – your genome – as a secret instruction manual that when decoded provides the details on how to build a machine.
• In this case the machine is you.
• In this manual, the instructions are broken down into simple steps. For DNA, each step in the manual is a gene.
Cell
Gene
DNA
Chromosome
Each gene has a specific location on a chromosome and contains the code for creating proteins, which impact body structure and function.
Mayo Clinic GenesGuide™
MAYO CLINIC
Medication Response
Carrier Screening
Disease Risk
Lifestyle Risk Assessment
Helix
Helix
Cells: Small but mighty

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

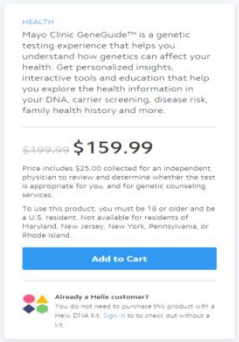
Results may informative, but ***should not be considered diagnostic***.

- 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



pwnhealth

POWERED BY Helix

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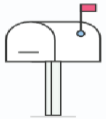
Consumer orders product on Helix.com



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?

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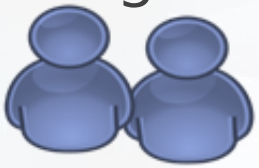
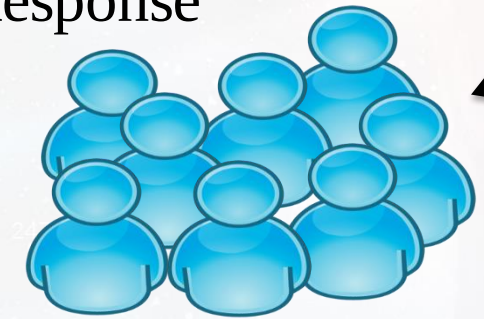
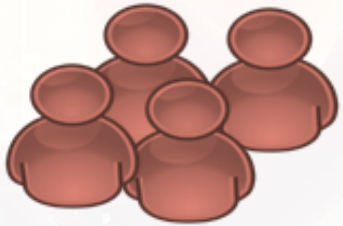
Study of genetic variations that influence individual response to drugs



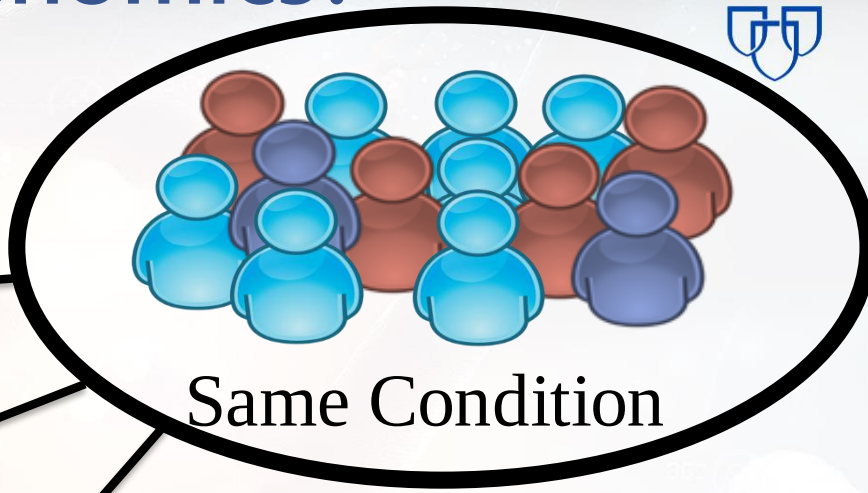
No Response



Desired Response



Toxic Side Effects



Pharmacogenomic Testing at Mayo Clinic

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Mayo Medical Labs

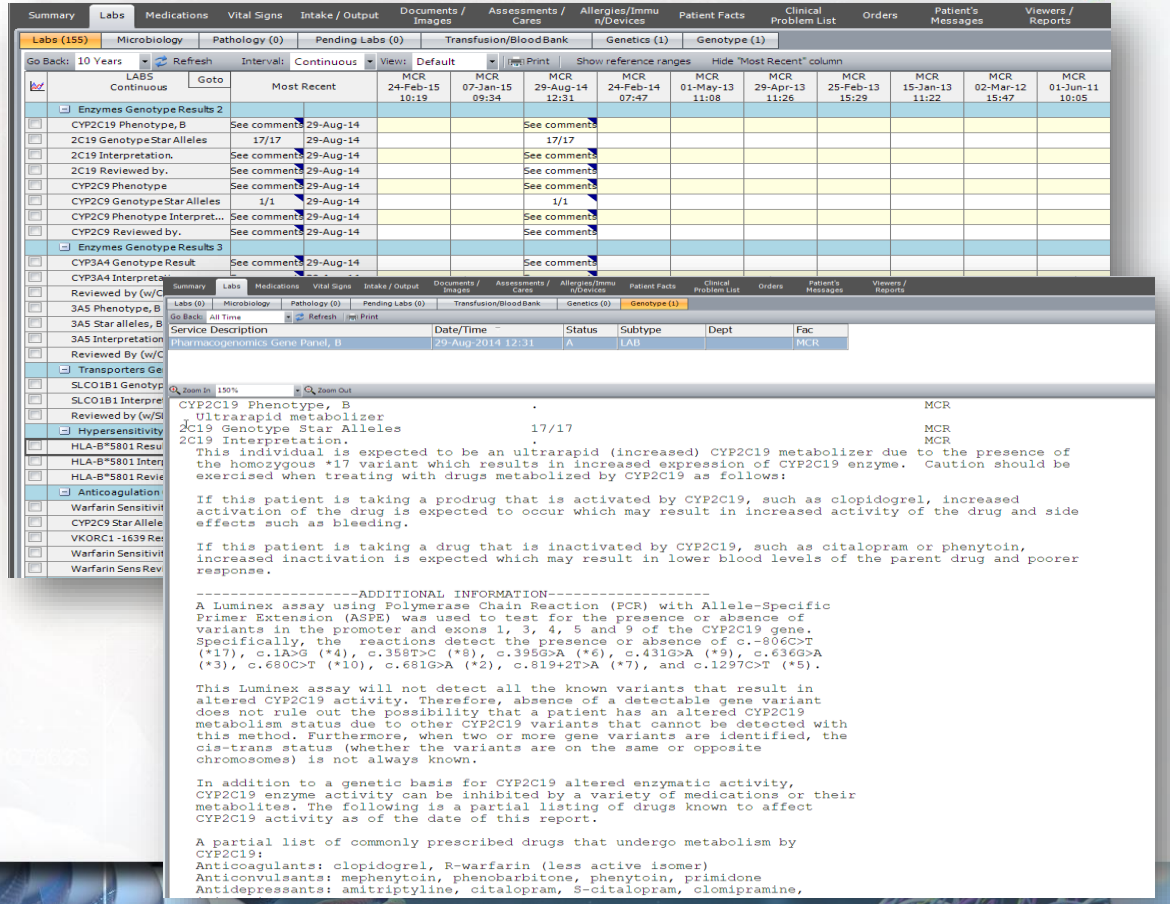
- Single gene tests
- Nine gene panel

AssureRx Health

- GeneSight®

OneOme

- RightMed®



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

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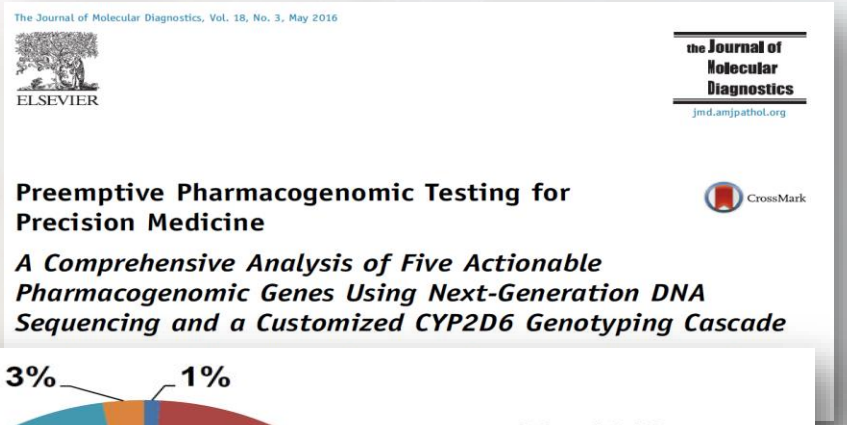
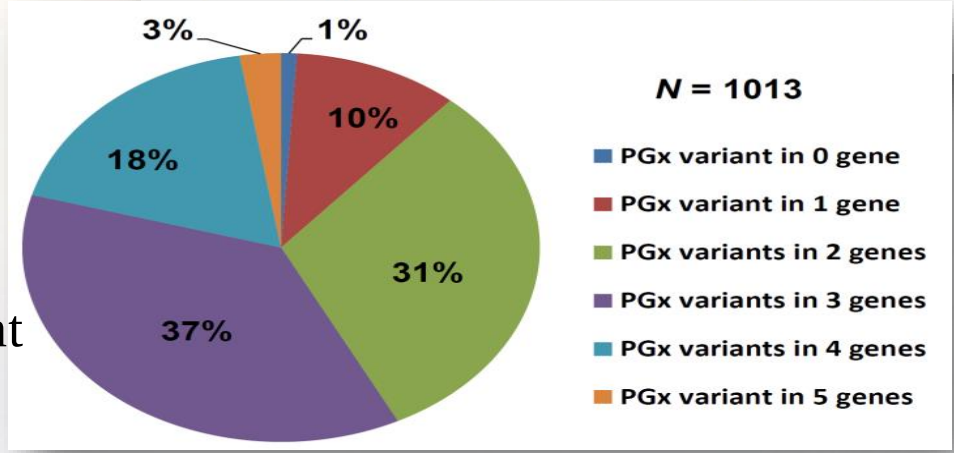
Goals:

- 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.





Pharmacogenomic CDS at Mayo Clinic

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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)

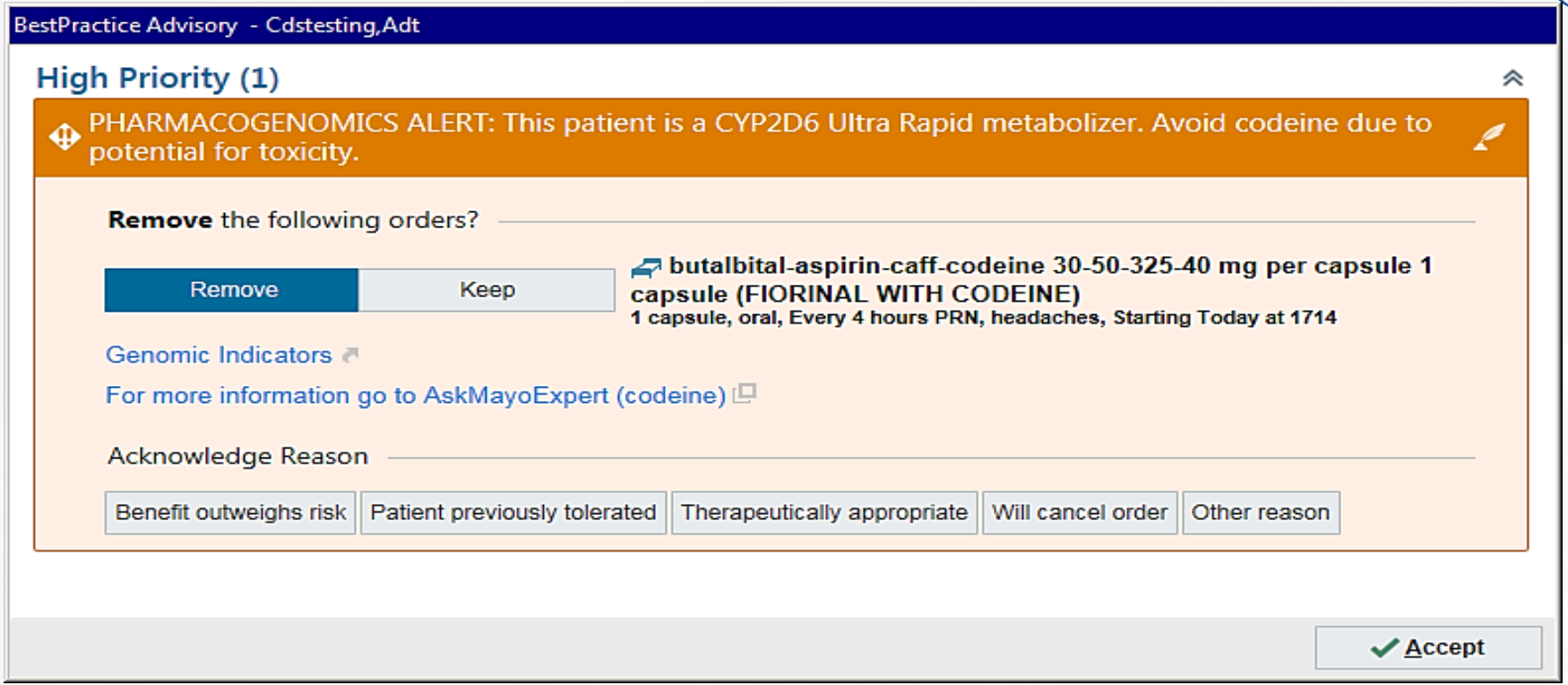
HLA-B*57:01

Abacavir (2013)

HLA-B*58:01

Allopurinol (2014)

EPIC CDS or Best Practice Advisory



Over 22,000 CDS alerts fired to date

We can run – but we can not hide!

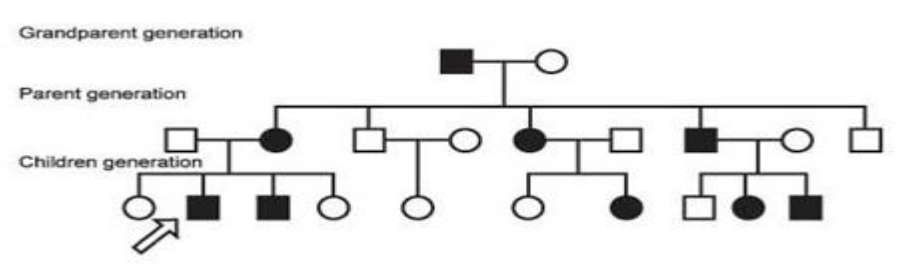
Consumers and patients will increasingly drive genetic testing

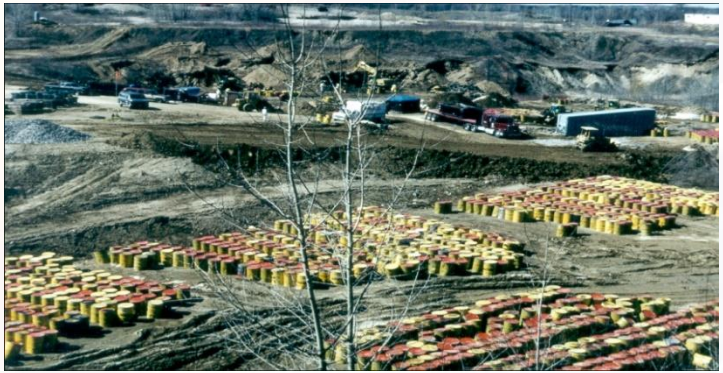
Predictive Genomic Endeavors

- 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



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The End
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362
ACGT
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genomics
The branch of molecular biology concerned with the structure, function, evolution, and mapping of genomes
362
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)
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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

MAYO CLINIC

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 (nonalc fatty liver disease)