CT Genomics Forum

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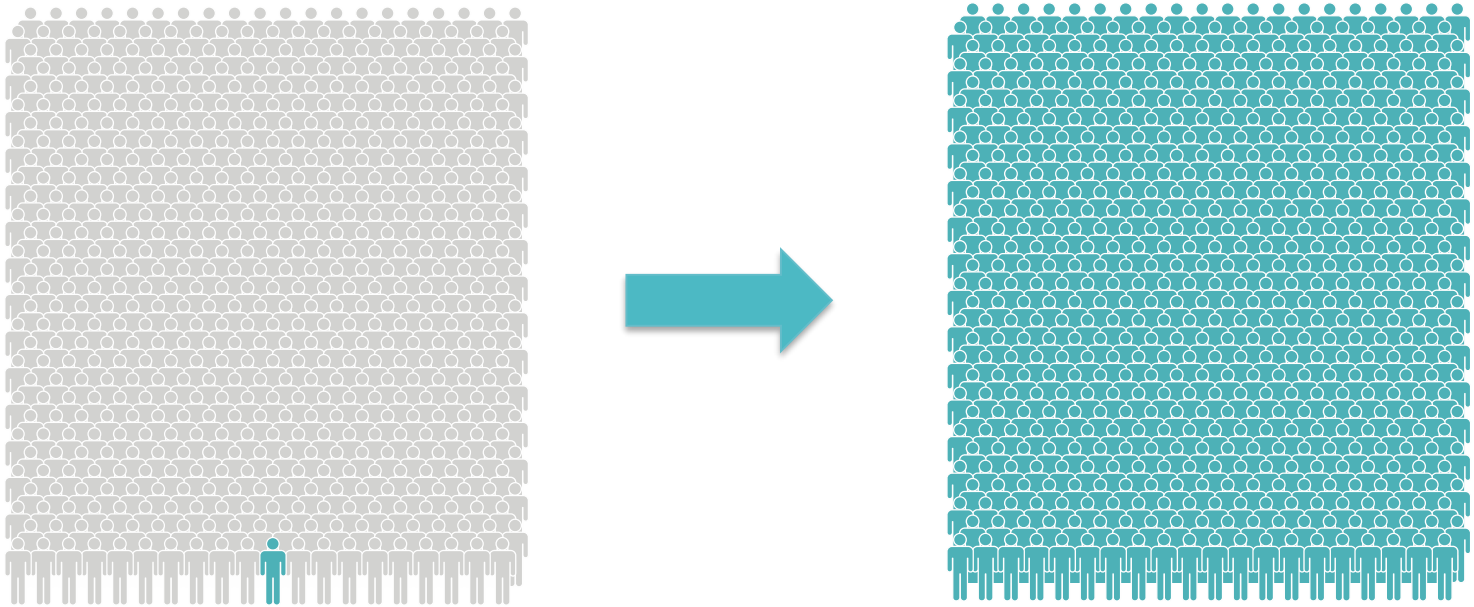
Overview

1. Genetics in Medicine
2. What Tests Are Available?
3. How Does It Work?
4. Avenues of Testing
5. Who is Involved?
6. Regulation and Protections
7. Opportunities

Rare to Common



What Tests Are Available?

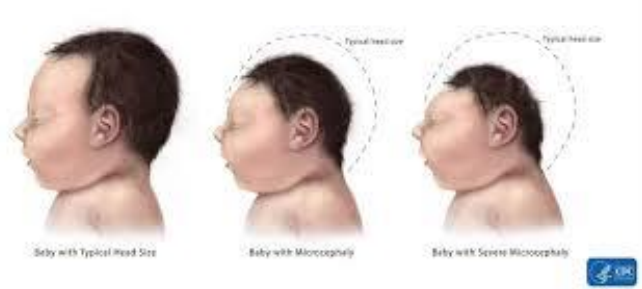
Prenatal

Newborn Screening

- Heel stick
- Most states screen for at least 35 genetic conditions
- CT screens for 65+ genetic conditions
- Early treatment

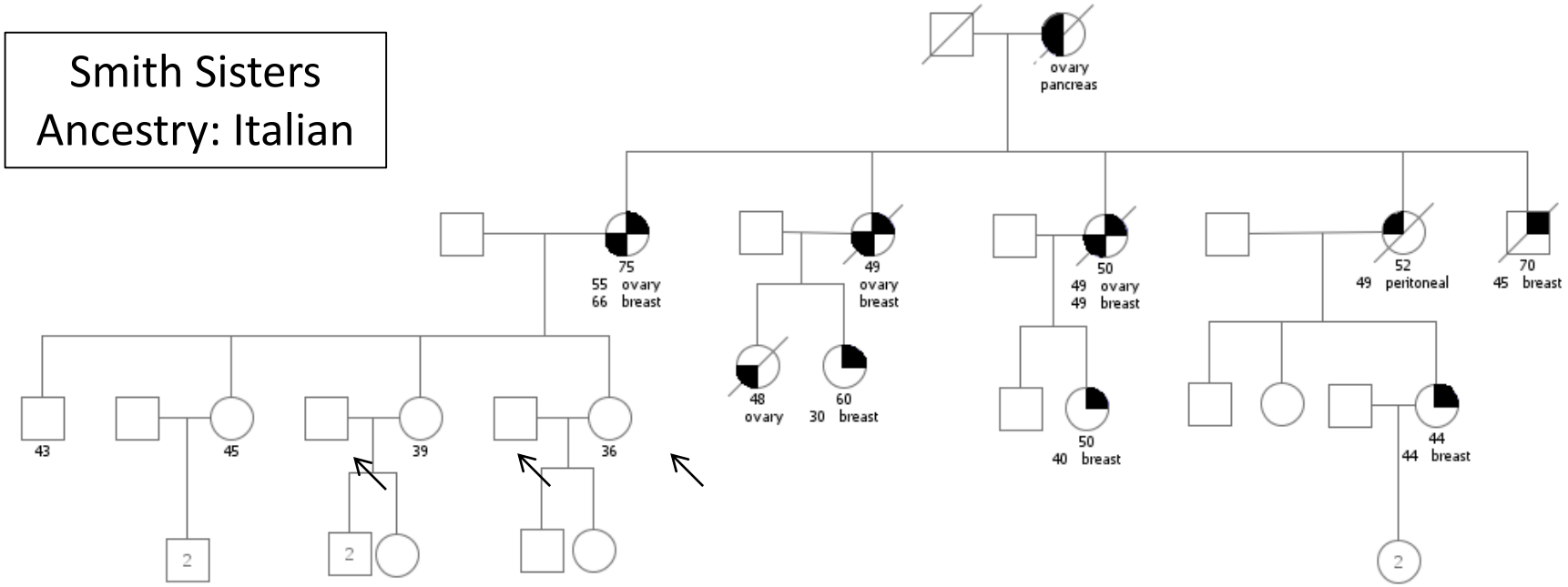
Pediatrics

AGE-APPROPRIATE SKILLS TO LOOK FOR	4 - 5 months	9 - 12 months	18 - 23 months	3 years	4 years
Movement (physical development)	Does Baby do push-ups or bring hands and toys to his or her mouth?	Does child sit independently, crawl, creep or scoot forward?	Does child climb into chairs, walk forward, turn pages in a book?	Does child run easily, falling rarely, or kick a ball forward?	Does child run easily, or copy a circle and a square?
Thinking and Learning (cognitive development)	Does Baby listen to conversations or follows conversations with eyes?	Does child explore with hands and mouth or find hidden objects?	Does child put small toys into a cup, basket or box?	Can child tell his first name (or nickname) and last name?	Does child know the difference between boys and girls?
Communication (receptive and expressive language development)	Does Baby imitate some sounds you make (like a cough)?	Does child respond to own name (for example, look up when called)?	Does child point to objects or people to express a need?	Does child use words that describe things (like "It's icky" or "I'm hungry")?	Does child refer to self as "me" or "I" in addition to name?
The Senses: Vision, Hearing and Touch (sensory development)	Does Baby turn head or eyes toward a sound?	Does child enjoy or put up with different types of touch?	Does child respond when name is called?	Does child move to or hum along with music?	Is child mostly comfortable with change or going from one activity to another?
Relating to Self and Others (social and emotional development)	Does Baby usually quiet or calm down when talked to, held or rocked?	Does child enjoy watching (and may play) games like "peek-a-boo"?	Does child approach other children?	Does child take turns in games?	Does child enjoy humor (for example, laughs at silly faces or voices)?
Self Care (daily living skills)	Does Baby sleep regularly for three to four hours at a time?	Does child feed self with fingers?	Does child pull off simple clothes (such as socks)?	Does child wash his hands without help?	Does child brush his teeth by self or with help?



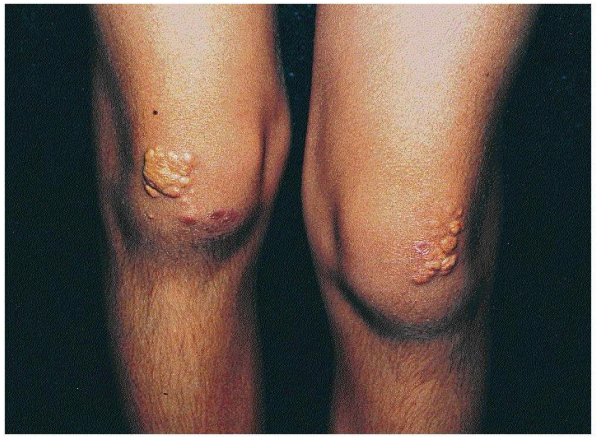
Hereditary Cancer

Smith Sisters
Ancestry: Italian

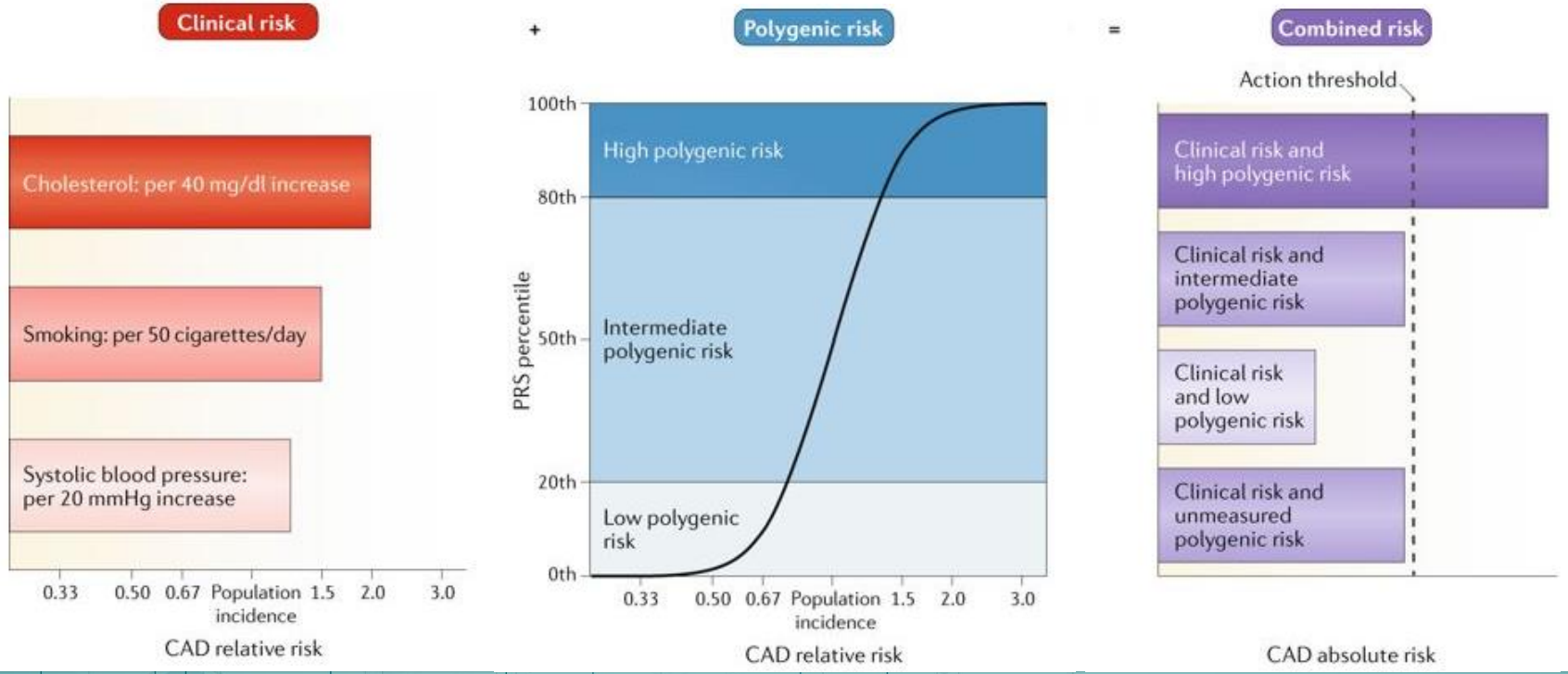


Cardiovascular

- Familial Hypercholesterolemia
  - Markedly elevated LDL cholesterol levels beginning at birth
  - In males, heart attacks often occur in 40s-50s
  - 85% of men have an MI by age 60
  - In females, onset of heart attacks generally occur a decade later

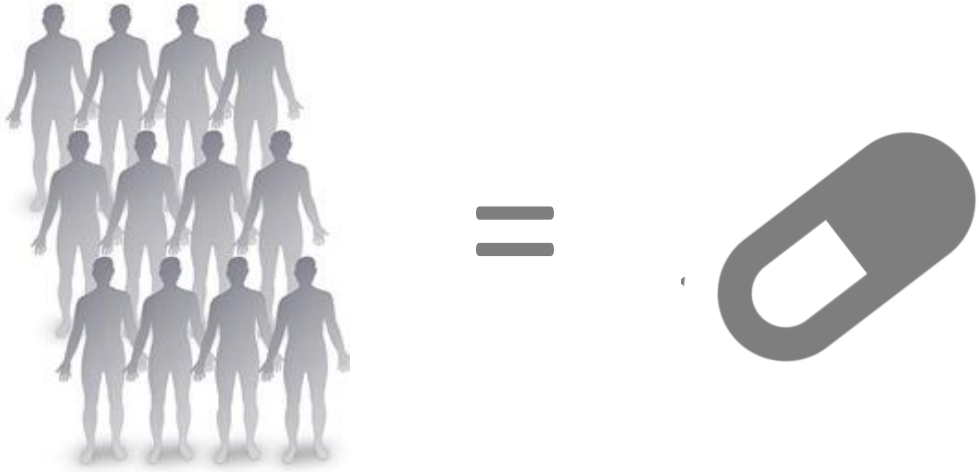


Polygenic: Coronary Artery Disease



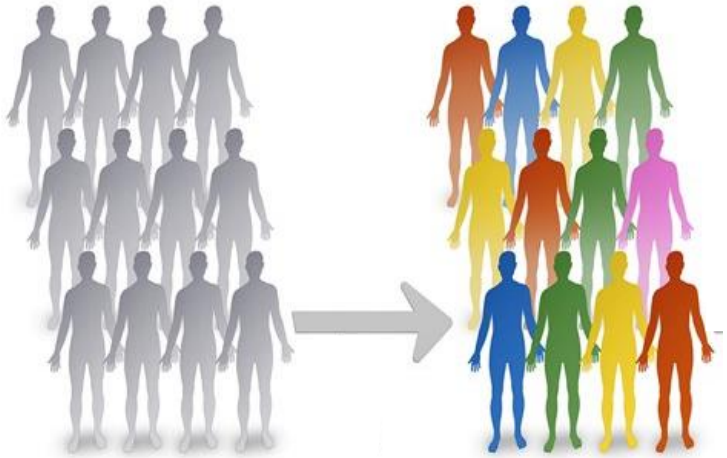
https://www.nature.com/articles/s41576-018-0018-x

Pharmacogenetics



Same Diagnosis = Same Treatment

Genetic Testing Is NOT Precision Medicine



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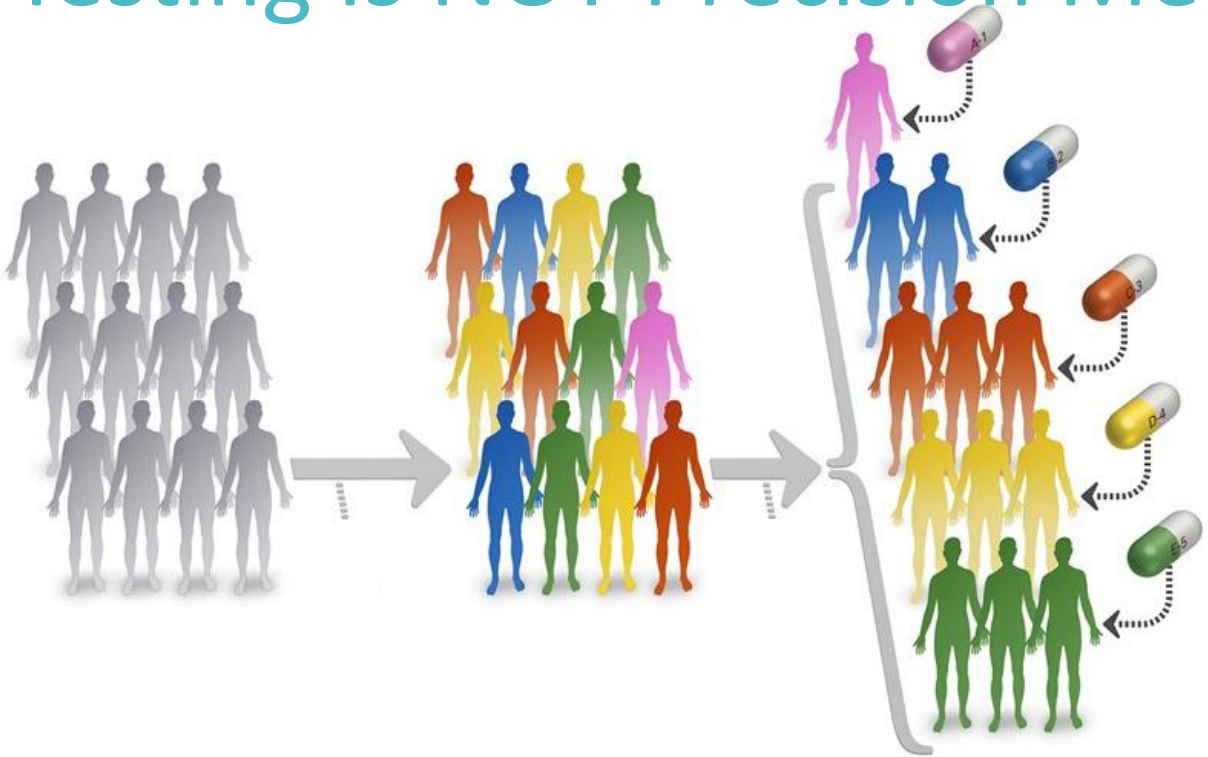
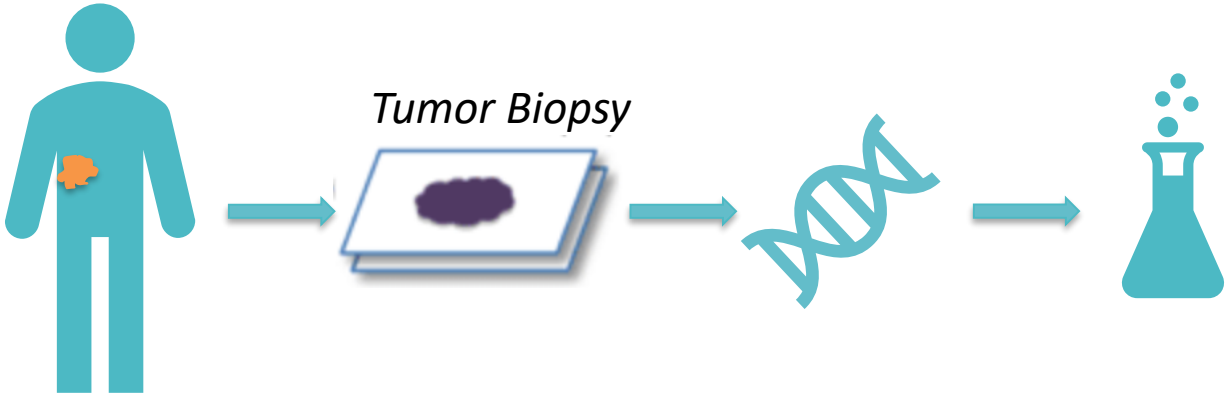


Treatment of Cancer



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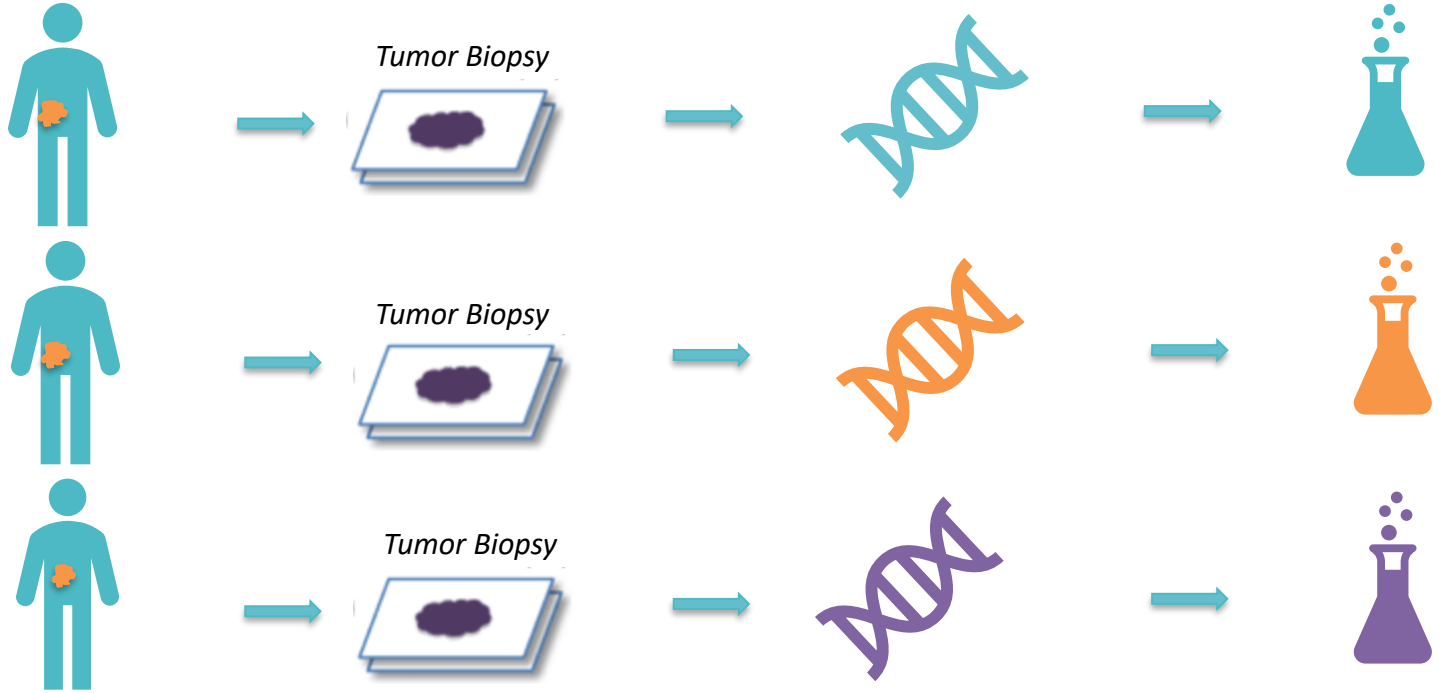
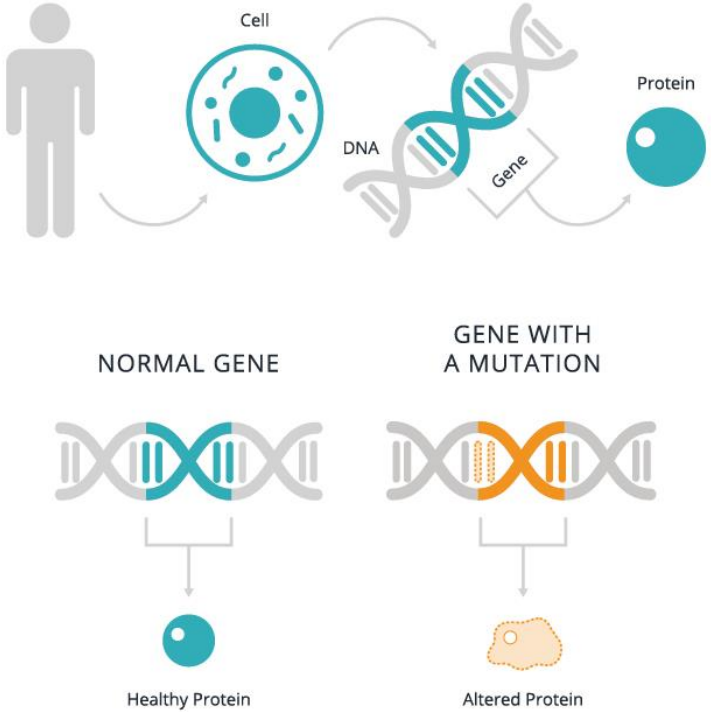
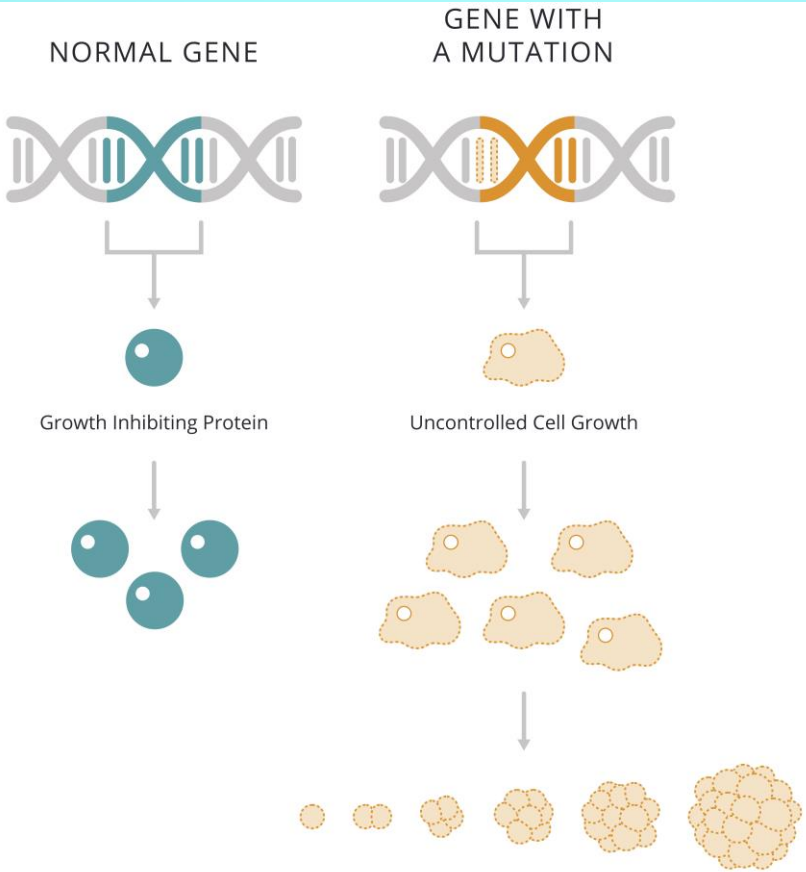


Person to Protein




NORMAL GENE
GENE WITH
A MUTATION
Growth Inhibiting Protein
Uncontrolled Cell Growth

How Does It Work?

How Does It Work?

DNA Sequencing

Full gene analysis for many different types of mutations

Looks throughout the gene for both common and rare disease-causing changes in your DNA

Genotyping

Focuses on specific areas; may miss known genetic markers

Looks for specific common disease-causing changes in your DNA

Image from www.sbivf.com

Avenues of Testing

Provider Initiated

- Traditional medical test
- Most comprehensive
- Provider recommends and coordinates testing
- Diagnostic tests
- Often covered by health insurance when certain criteria are met

Patient Initiated

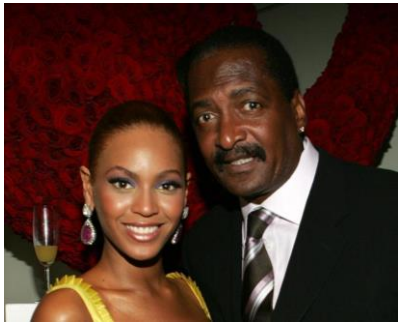
- Patient initiated, but…
- Doctor “approved”
- Typically full genetic analysis/sequencing
- Generally self-pay

Direct-to-Consumer

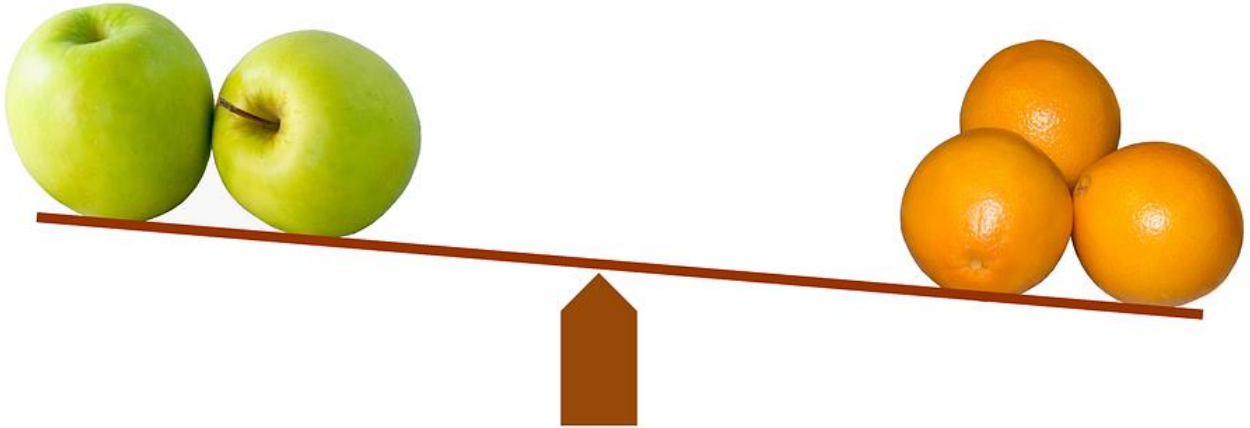
- Initiated by consumer
- No MD/clinician involved
- Often ordered online
- Genotyping for particular variants/SNPs
- Patient self-pay

BRCA1/2: Breast and Ovarian Cancer Syndrome

CANCER	AVG RISK	BRCA1+ RISK	BRCA2+ RISK
Female Breast	12-13%	50-85%	40-70%
Ovarian	1-2%	25-60%	10-20%
Prostate	11%	increased	20-30%
Male Breast	<1%	1-2%	7%
Pancreatic	<1%	2-3%	2-5%
Melanoma	1-2%	increased	3-5%



Entertainment vs. Health



Who Is Involved?

- Genetic counselors
  - Specialized graduate degrees and experience in the areas of medical genetics and counseling
  - Certified by the American Board of Genetic Counseling
  - Licensure by state
  - Several insurers now only pay for testing after being seen for genetic counseling
  - Adoption of H.R. 3235, the “Access to Genetic Counselor Services Act of 2019” needed for field growth
- Medical genetics
- Other health care providers
- The patient/consumer

Testing Without Guidance = Misinterpretation

ORIGINAL ARTICLE

Errors in Genetic Testing: The Fourth Case Series

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Purpose: In this ongoing national case series, we document 25 new genetic testing cases in which tests were recommended, ordered, interpreted, or used incorrectly.

Methods: An invitation to submit cases of adverse events in genetic testing was issued to the general National Society of Genetic Counselors Listserv, the National Society of Genetic Counselors Cancer Special Interest Group members, private genetic counselor laboratory groups, and via social media platforms (i.e., Facebook, Twitter, LinkedIn). Examples highlighted in the invitation included errors in ordering, counseling, and/or interpretation of genetic testing and did not limit submissions to cases involving genetic testing for hereditary cancer predisposition. Clinical documentation, including pedigree, was requested. Twenty-five cases were accepted, and a thematic analysis was performed. Submitters were asked to approve the representation of their cases before manuscript submission.

Results: All submitted cases took place in the United States and were from cancer, pediatric, preconception, and general adult settings and involved both medical-grade and direct-to-consumer genetic testing with raw data analysis. In 8 cases, providers ordered the wrong genetic test. In 2 cases, multiple errors were made when genetic testing was ordered. In 3 cases, patients received incorrect information from providers because genetic test results were misinterpreted or because of limitations in the provider's knowledge of genetics. In 3 cases, pathogenic genetic variants identified were incorrectly assumed to completely explain the suspicious genetic counseling delivery models, expanding the genetic counseling workforce, improving genetics and genomics education of nongenetics health care professionals, addressing health care policy barriers, and more. Genetic counselors have also positioned themselves in new roles to help patients and consumers as well as health care providers, systems, and payers adapt to new genetic testing technologies and models. The work to be done is significant, but so are the consequences of errors in genetic testing.

Key Words: Cancer genetic testing, direct-to-consumer screening and testing, genetic counseling, genetic counseling delivery models, genetic services, genetic testing, genetic testing adverse events, genetic test misinterpretation, genomics, multigene panel testing

(*Cancer J* 2019;25: 231–236)

ERRORS IN GENETIC TESTING: THE FOURTH CASE SERIES

The availability of genetic testing is growing at an exponential rate. In a 2018 study providing an overview of the current genetic testing landscape, authors estimated that there were approximately 75,000 genetic tests on the market, with 10 new tests being introduced daily.[1] Fourteen percent of these tests, and 2 to 3 of the new tests introduced per day, were panel tests, a category that includes

Volume & Complexity of Genetics Is Exploding

Demand for Results Exceeds Capacity to Process

- Direct-to-consumer testing going to 100 million people by 2021
- Global genetic testing market to exceed $22 billion by 2024
- Large population genome studies planned globally
- Gene panels more complex, requiring more interpretation
- Genetic research evolving at a rapid pace

Limited supply of experts who can provide proper guidance:

<5,000

genetic counselors in US

Regulation

Laboratory Performing Test

CMS pursuant to Clinical Laboratory Improvement Amendments (CLIA)

New York State Clinical Laboratory Evaluation Program (CLEP)

College of American Pathologists (CAP)

Laboratory Tools

(instruments, reagents)

FDA pursuant to the medical device authority under the Federal Food, Drug, and Cosmetic Act

Safety and effectiveness for intended use

Laboratory Developed Test

CLIA

NYS

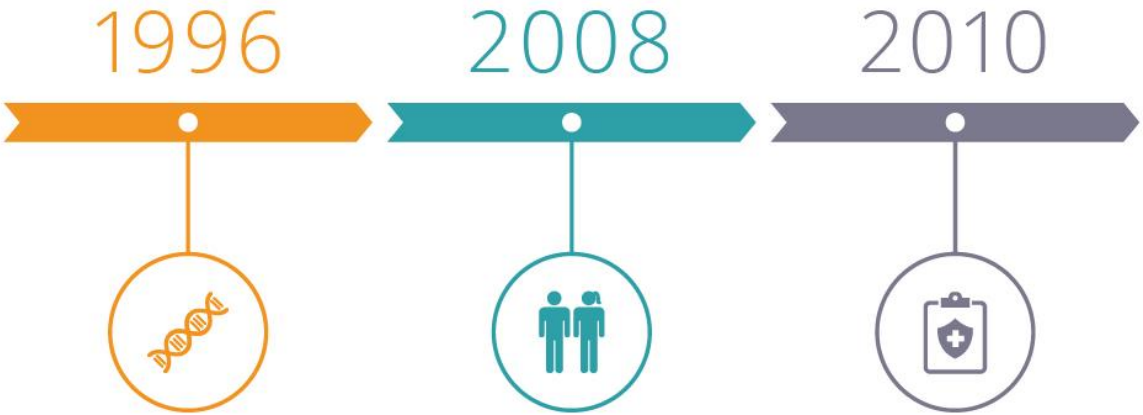
College of American Pathologists (CAP)

Advertising

Federal Trade Commission

Prohibits unfair trade practices, including false or misleading advertising

Protections



HIPAA

The Health Insurance Portability and Accountability Act

This law prohibits insurers from using genetic information as a preexisting condition.

GINA

The Genetic Information Nondiscrimination Act

This law protects individuals from discrimination by health insurance companies and employers based on genetic information.

ACA

Affordable Care Act

This law forbids group health plans from denying insurance or adjusting premiums based on any preexisting conditions.

Opportunities

- Genetic testing will be in every specialty, every disease
- Responsible testing and interpretation
- Access to genetics professionals
  - CT workforce studies
  - Grow the genetic counseling workforce
  - Support the UConn program
  - Support H.R. 3235, the “Access to Genetic Counselor Services Act of 2019”
- Tools for providers and patients
- Long-term follow-up

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