Genetic Counseling Graduate Program

Arizona Telemedicine Program

Southwest Telehealth Resource Center TRC

Improving Access to Quality Medical Care Webinar Series

Presented by

The UArizona Health Sciences Genetic Counseling Graduate Program, the Southwest Telehealth Resource Center, & Arizona Telemedicine Program

Welcome

- SWTRC region - AZ, UT, CO, NM & NV
- Fellow HRSA Grantees
- All other participants from the US & abroad

The **University of Arizona Health Sciences Genetic Counseling Graduate Program, the Arizona Telemedicine Program,** and **Southwest Telehealth Resource Center** welcome you to this free webinar series!

The series will discuss the the use of telegenetics to improve access to genetics services for patients & providers.

Telemedicine can help you achieve these goals!

Webinar Tips & Notes

- When you joined the webinar your phone &/or computer microphone was muted
- Time is reserved at the end for Q&A
- Please use the **Chat function** to ask questions
- Please complete the post-webinar survey
- Webinar is being recorded
- Recordings will be posted on the ATP website
    - http://telemedicine.arizona.edu/webinars/previous

Consumer-Initiated Genetic Testing

Shannon Kieran, MS, LCGC, MBA

Head of Clinical, Ambry Genetics

Genetic Counselor Senior, University of Arizona Health Sciences Genetic Counseling Graduate Program

COI Disclosures

- Currently employed at the University of Arizona and Ambry Genetics
- Shareholder, founder or formerly employed at:
  - Life Technologies
  - Thermo Fisher Scientific
  - Helix
  - Vinome
  - Exploragen
  - Color Genomics
  - Genome Medical
  - Intelliger Consulting
  - Bethesda Group

…. Which may have or have had something to do with CIGT or DTC or some other perceived COI at some point some where.

Consumer-Initiated Genetic Testing (CIGT)

Learning Objectives

- Contrast consumer-initiated and physician-initiated genetic testing
- Define the strengths and weaknesses of consumer-initiated genetic testing
- Discuss the role of telegenetics in consumer initiated genetic testing

Defining consumer-initiated genetic testing.

CIGT is the process of the average person ordering a genetic test, independently collecting a DNA sample and receiving the result interpretation report, all on their own.


I GOT THIS!
meme-arsenal.ru

CIGT- A user experience

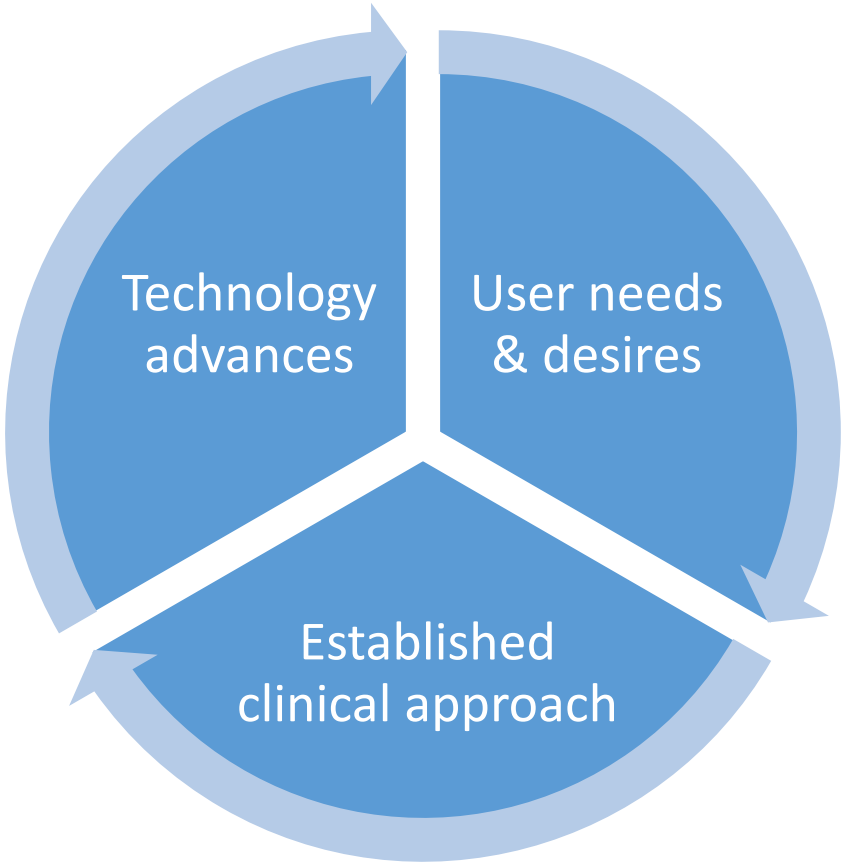


Image credit: Elissa Levin, MS, CGC

Landscape of CIGT*

Non-health related — **Health related**

Ancestry
(composition, haplogroups, relatives)
Traits
(hair color, taste)
Paternity

Nutrigenomics
(diet supplementation)
Sports/fitness
(performance, injury)
Skin
(sun damage, skin type)

Carrier screening
Pharmacogenomics
Hereditary cancer
Adult onset disease
(Mendelian and multifactorial)

*Not a comprehensive list

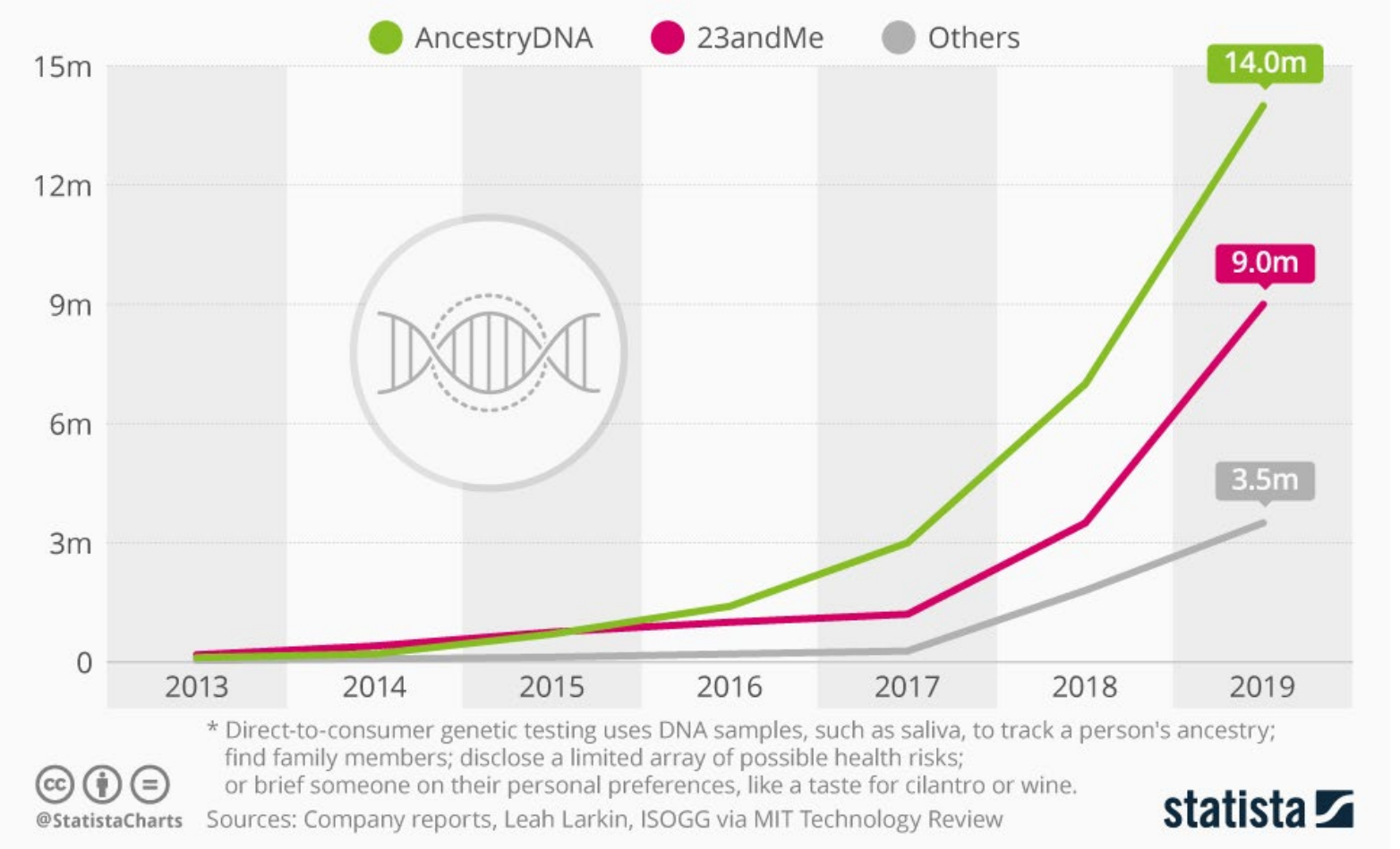
Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

CIGT vs. physician-mediated genetic testing

Strict Consumer-Initiated Genetic Testing	Hybrid Testing Models (Physician-Mediated)	Physician-Iniiated Genetic Testing
• Initiation to test 100% on the person/patient • No provider involved • Typically genotyping for particular variants/SNPs • Patient self-pay • Provider not involved in result disclosure • Entertainment, ancestry, wellness/lifestyle and health focused	• Non-affiliated provider “involved” in ordering • Typically sequencing, may include del/dup • May be covered by health insurance or self-pay options • Ordering provider likely not involved in result disclosure • Typically health focused (predisposition testing, pharmacogenomics)	• Initiation to test starts with physician • Patient’s personal provider “involved” in ordering • Typically sequencing, may include del/dup • May be covered by health insurance • Results typically disclosed by provider • Medically relevant, action focused

Who is using CIGT and why?

Over 25 million people have tested



Why people might pursue CDGT and what can it actually deliver?

- What might it deliver?
  - Fun, entertaining and educational insights for those who are curious
  - Find distant/lost family members (adoptees, ART conceived)
  - Disease risk factors (may have not family history and/or don't meet traditional testing guidelines)
  - Convenience (given at-home use)
- What won't it deliver (but people think that it can)
  - An answer to those on a diagnostic odyssey
  - The complete picture (limitation of genetic test and limitation given the role non-genetic factors play)
  - Risk information for every health condition

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

How it works.

The testing process

1. Person orders a kit online or purchases at a retail store
    - Test will be ordered/authorized by patient's own physician *or* a physician as facilitated by the lab
2. Register kit online
    - Customer may complete a health history questionnaire to allow for completion of the physician order*
3. Sample (likely saliva or buccal swab) mailed to the lab
    - Can be completed in the doctor's office*
4. DNA analysis and report generation typically take 2-4 weeks
5. Customer accesses results online
    - Results sent to consumer
    - May include access to genetic counseling

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

CIGT Technologies

Genotyping

Typically enabling DTC genetic tests

- Looks for common mutations or variations associated/linked to a disease, trait or ancestry
- Typically looking at single letter changes (called Single Nucleotide Polymorphisms or SNPs)
- Can look at 100s-1000s of known genetic mutations/variants
- The results
  - Variant is present (1 or 2 copies)
  - Variant is absent

Sequencing

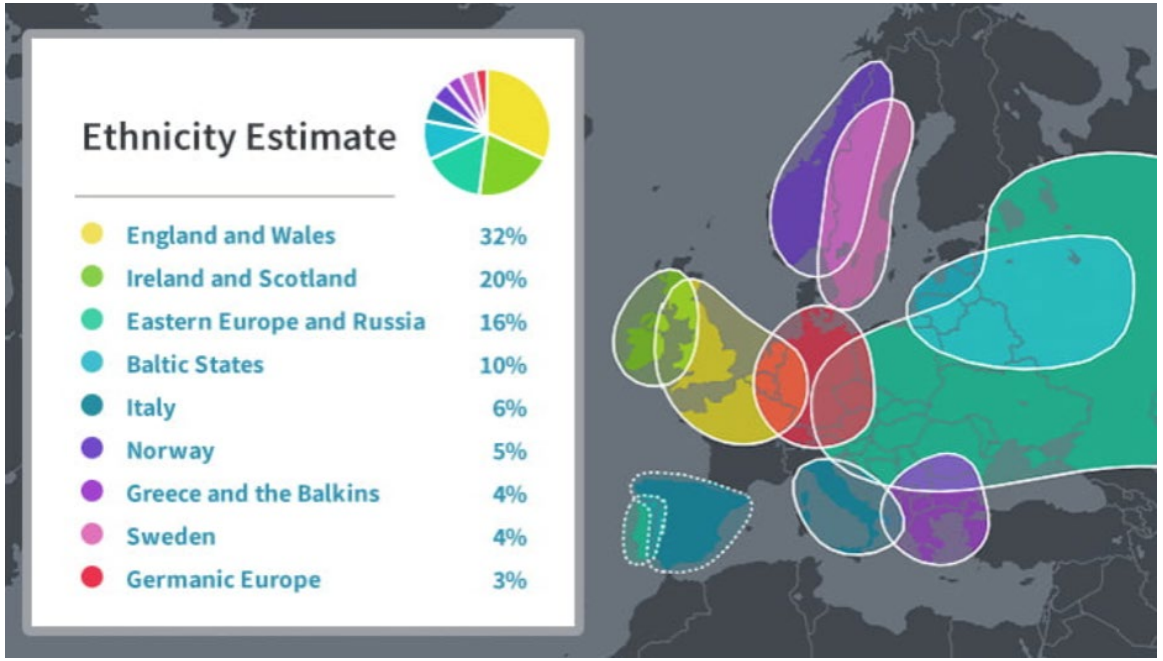
Typically enabling physician-mediated genetic tests

- Traditionally focused on variants linked to genetic conditions but can be used for traits, ancestry and disease predisposition
- Reads the entire sequence of a gene, the whole exome or the whole genome
- May detect larger deletions or duplications
- Can find rare variants or previously unknown variants
- The results
  - Positive
  - Negative
  - Variant of uncertain significance

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

Direct-to-consumer genetic testing: ancestry results

- Typically compares large numbers of SNPs with database to estimate ethnic background
  - Can also include Neanderthal, mitochondrial, and Y chromosome testing
- Different companies use different databases
  - Results can vary
  - Populations reported based on available databases

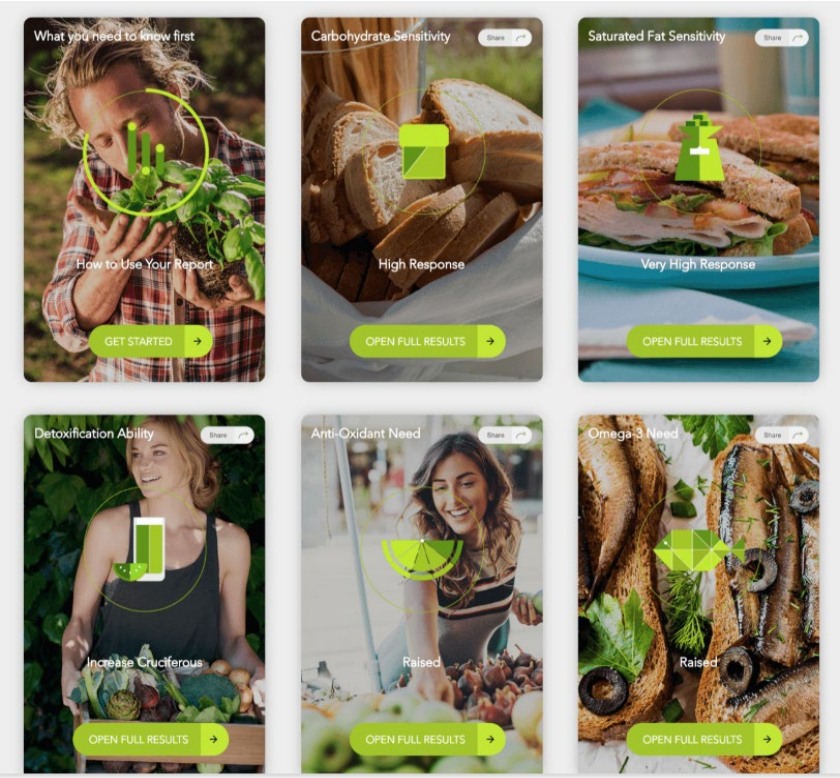


www.ancestry.com/dna

https://ghr.nlm.nih.gov/primer/testing/ancestrytesting

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

Direct-to-consumer genetic testing: lifestyle reports



https://www.helix.com/products/dnafit-diet-fitness-pro-360

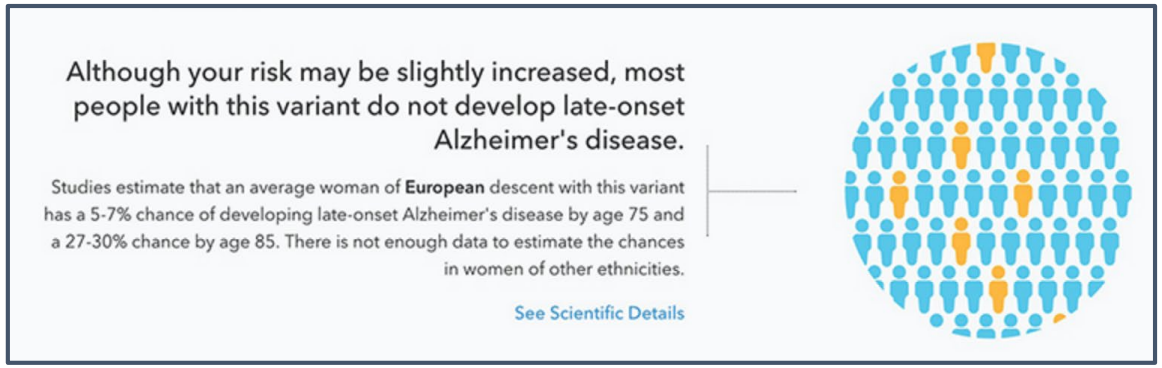
- Provide information based on specific variants associated with a trait impacting lifestyle
  - Ex. weight, sleep, athletic performance, food sensitivity, taste preference
- Need to be cautious around recommendations of specific products or lifestyle changes based solely on genetic result
  - Typically complex traits so both genetic and non-genetic factors need to be taken into account

https://ghr.nlm.nih.gov/primer/dtcgenetictesting/dtcresults

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

Direct-to-consumer genetic testing: health risk results

- Report on genetic variants associated with an increase in risk for certain diseases
  - Cannot diagnose disease or determine whether someone will or will not develop the disease
  - Result should not be used to make medical management decision - confirmatory clinical testing needed
  - Reports may be authorized by the FDA
- Level of risk presented in these reports can vary
  - A variant identified may not always result in disease risk
  - Some variants will present higher disease risk than others
  - Genetics may play larger or smaller role for certain diseases



https://ghr.nlm.nih.gov/primer/dtcgenetictesting/dtcalzheimer

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

Consumer-initiated, physician mediated, hereditary cancer testing examples

Direct-to-Consumer	Physician-Mediated	Physician-Directed
• 3 particular mutations out of >1000 within the BRCA1 and BRCA2 genes • Highly specific test most relevant to Ashkenazi Jewish ancestry • FDA recommends confirmatory testing through clinical lab if positive • Concerns re: false reassurance with “negative” results	• Full gene analysis of BRCA1/2 or multi-gene panel • May or may not include del/dups or VUS • Patient initiated, but must have MD sign off • Lab will provide MD, by request • Affordable self-pay options • Post-test counseling offered by genetic counselor if positive.	• Full gene analysis of BRCA1/2 or multigene panel • Test must be ordered by healthcare provider • Must meet insurance criteria for coverage • Pre-test counseling recommended • Post-test counseling recommended

Image credit: Precision Medicine SIG’s Consumer-Driven Genetic Testing subcommittee

Direct-to-consumer genetic testing: medically actionable results

- Report on genetic variants associated with an increase in risk for certain diseases
  - Cannot diagnose disease or determine whether someone will or will not develop the disease
  - Result should not be used to make medical management decision - confirmatory clinical testing needed
  - Reports may be authorized by the FDA
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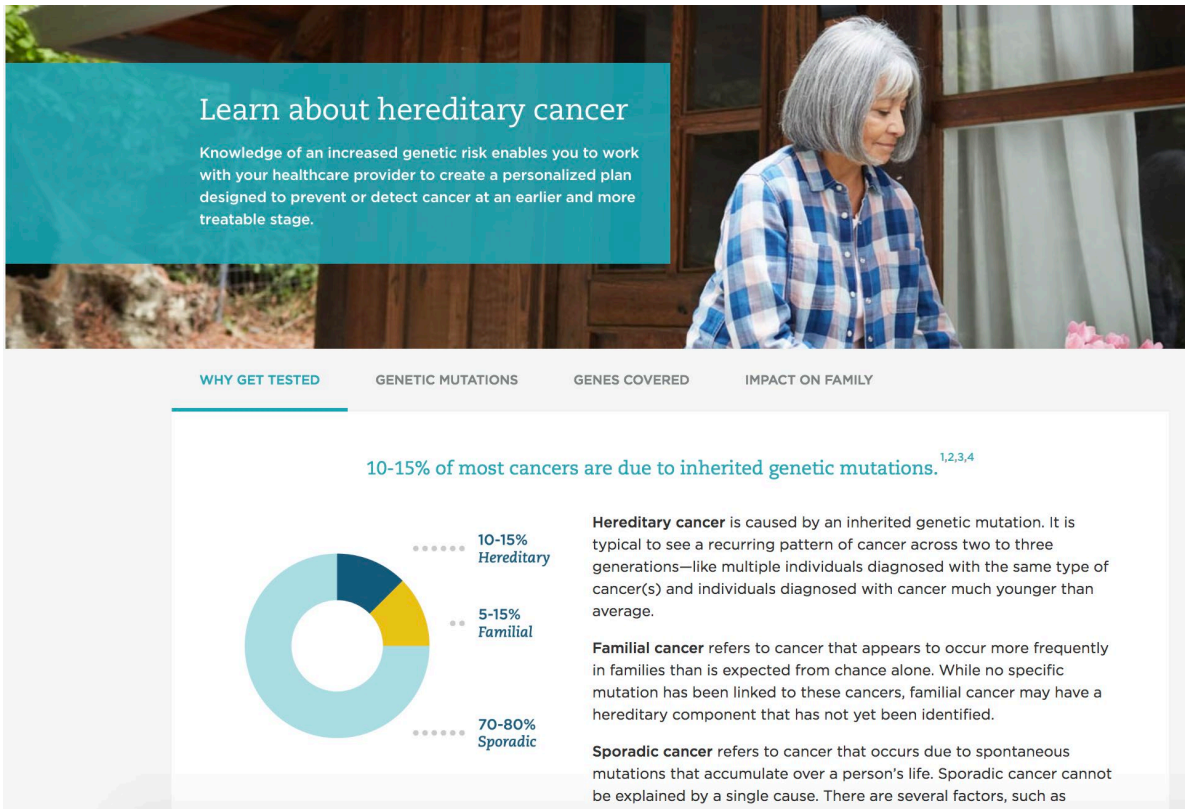
https://ghr.nlm.nih.gov/primer/dtcgenetictesting/dtcalzheimer

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

http://www.medicalgenome.com/wp-content/uploads/2017/09/Alzheimer_one_e4_female.pdf

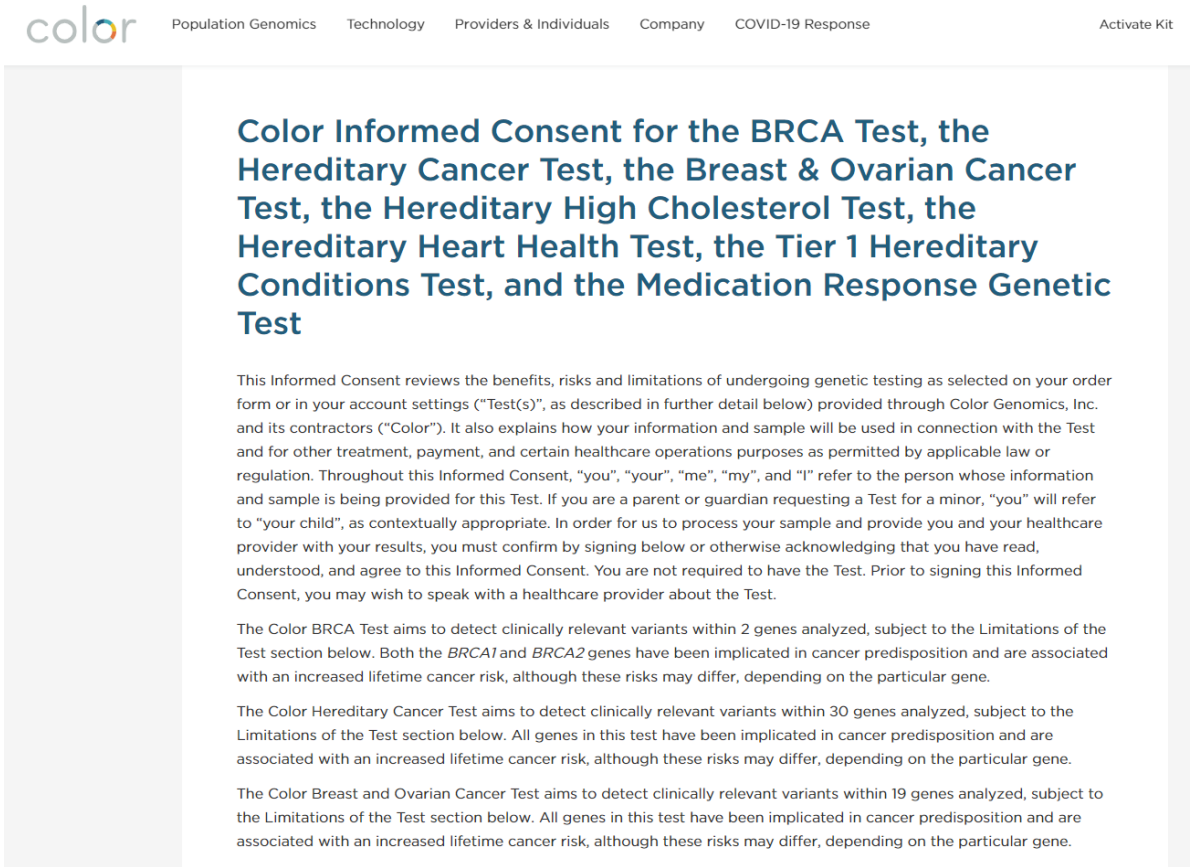
The journey- One example

- Pre-purchase information gathering and education



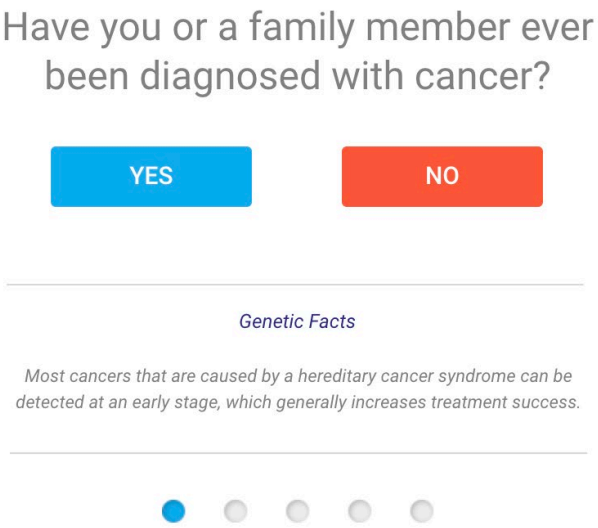
The journey- One example

- Pre-purchase informed consent



The journey- One example

- Post-purchase health history information collection through streamlined questions
- Purpose
  - Pre-test qualification (is this test appropriate for this person?)
  - Context for results interpretation



The journey- One example

- FDA-approved testing does not require physician authorization and review
- All other health-related (”clinical”) testing does
- Physicians with appropriate state licenses and qualifications for remote test review/approval

The journey- One example

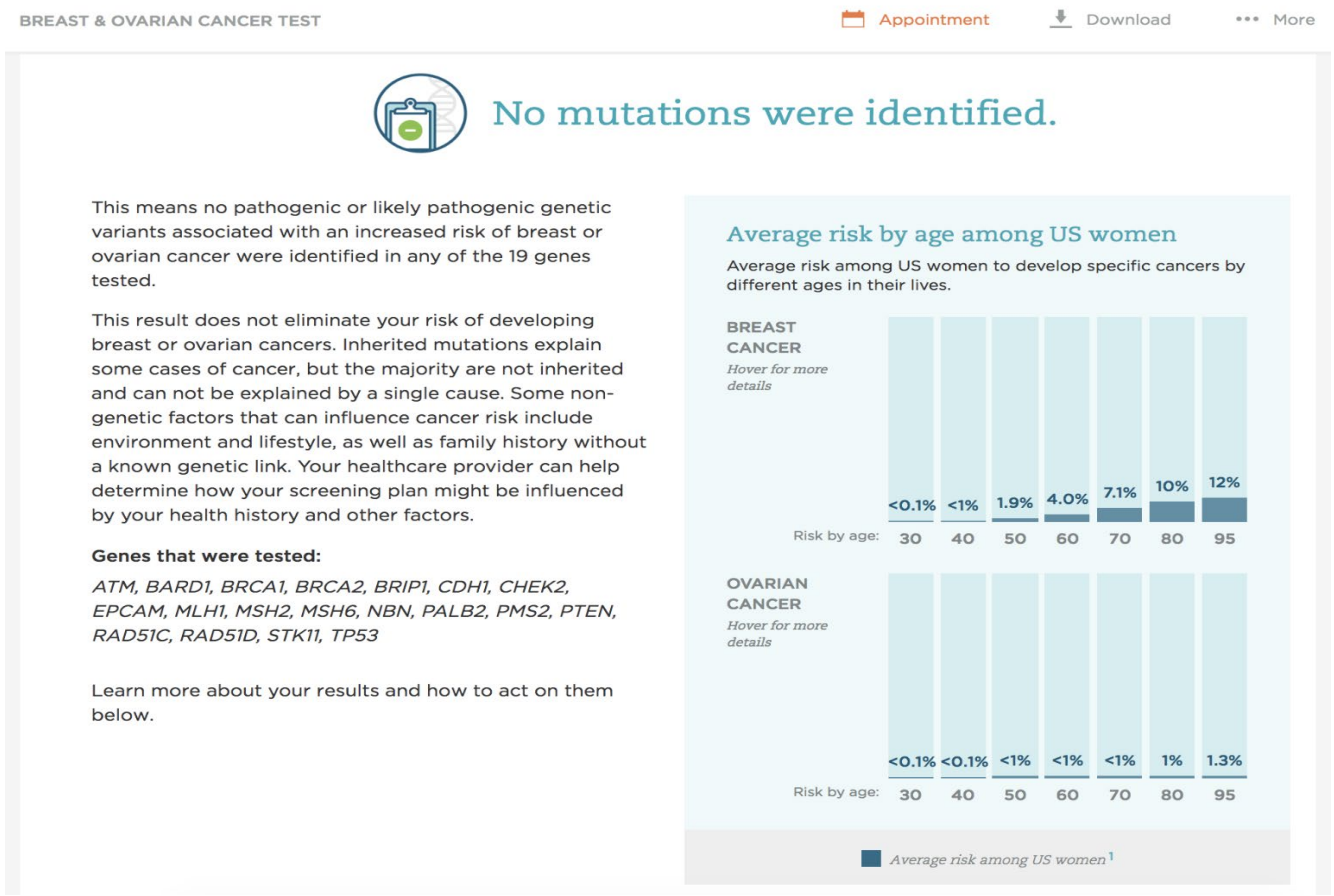
Growing industry of independent, 3rd-party physician approval services

Process

1. Consumer initiates order
2. Physician reviews test request
   - Relevant history and demographic info
   - May reach out with questions
3. Physician authorizes or denies request
   - Based on established exclusion criteria
4. Physician reviews and releases results

Slide credit: Elissa Levin

The journey- One example

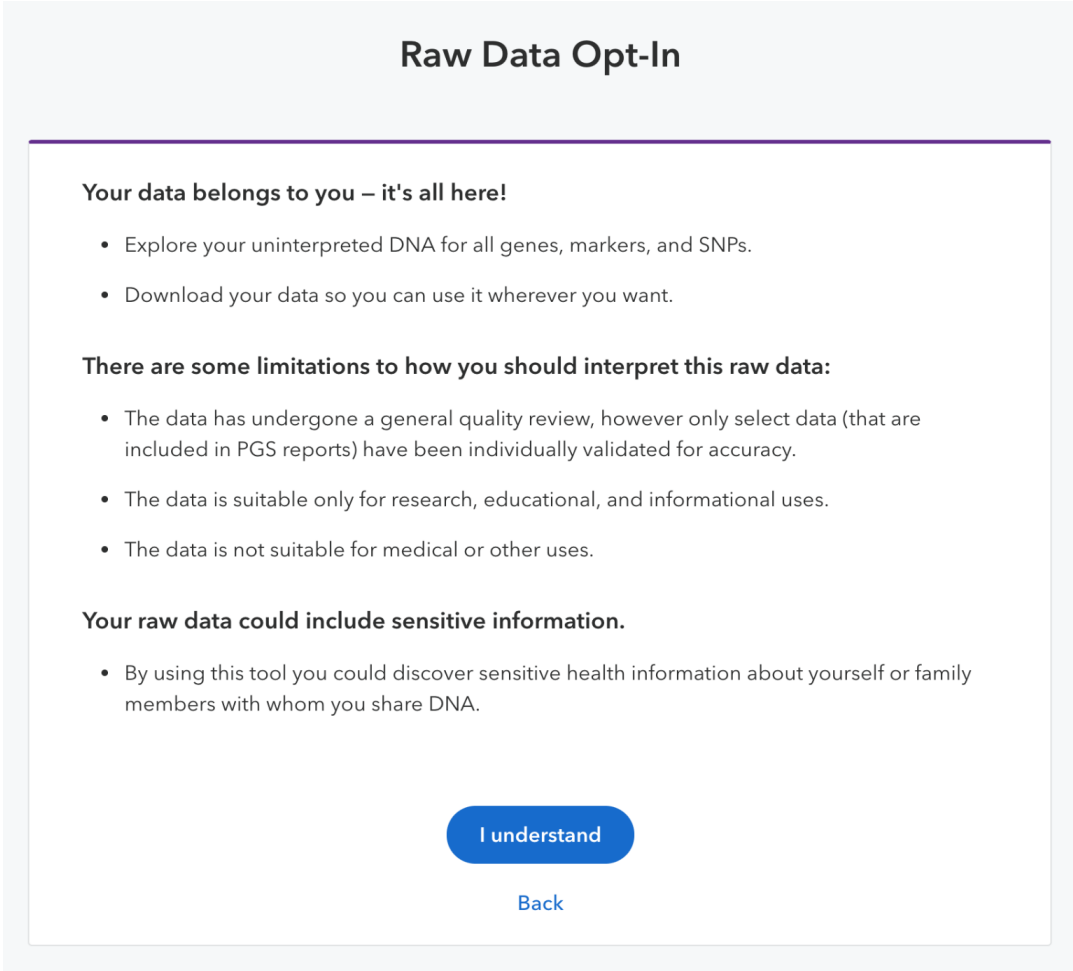


- Online results directly to the patient/consumer in tandem with the ordering provider (network)

Slide credit: Elissa Levin

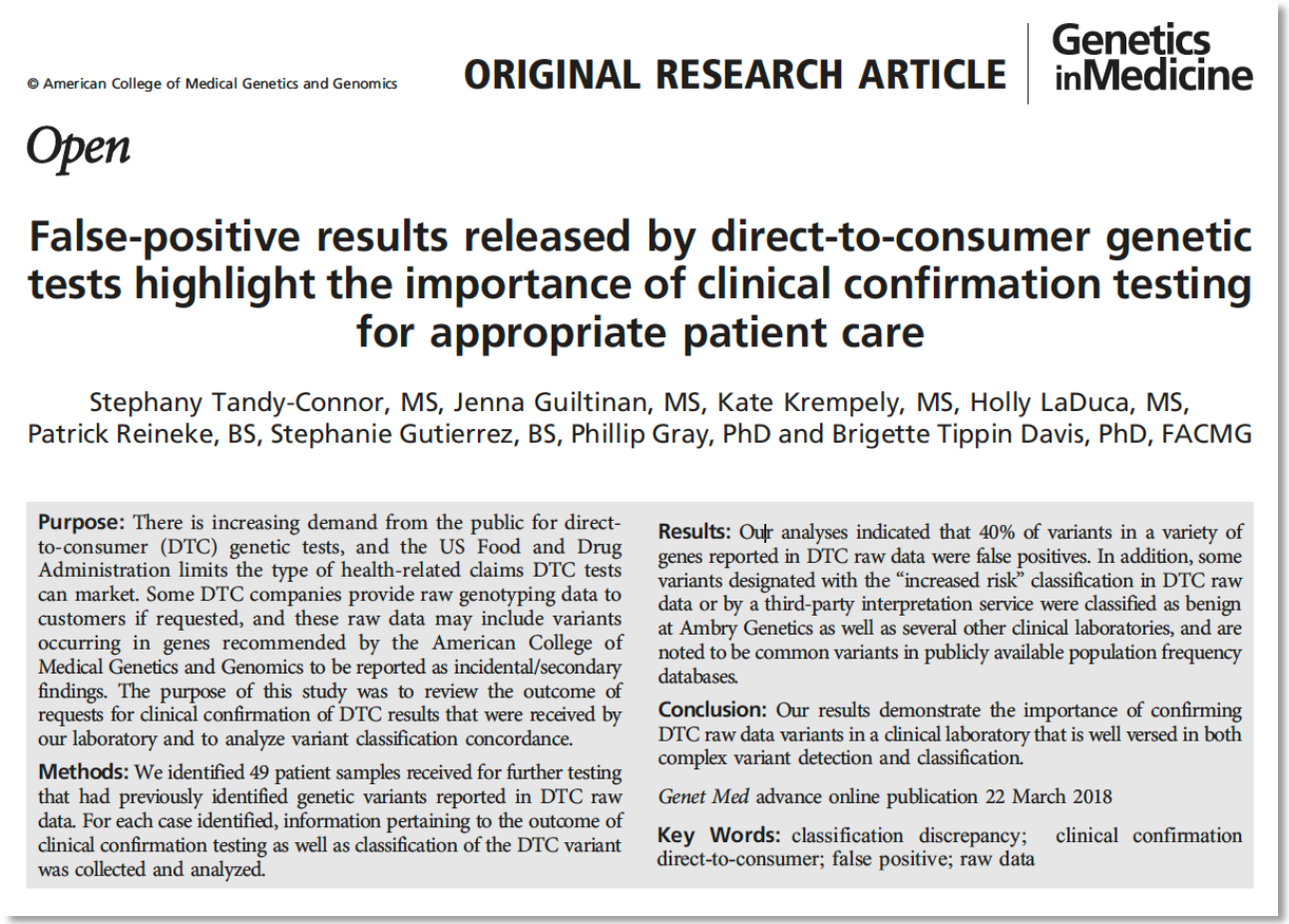
The journey- One example

- Some consumers may opt in to download their raw genetic data
- Problematic becausemany labs only validate the SNP's or genes that they provide reports on.
- Analytic validity may be poor/inaccurate



Slide credit: Elissa Levin

Confusion lurks in raw genomic data



ORIGINAL RESEARCH ARTICLE | Genetics inMedicine

Open

False-positive results released by direct-to-consumer genetic tests highlight the importance of clinical confirmation testing for appropriate patient care

Stephany Tandy-Connor, MS, Jenna Guiltinan, MS, Kate Krempely, MS, Holly LaDuca, MS, Patrick Reineke, BS, Stephanie Gutierrez, BS, Phillip Gray, PhD and Brigette Tippin Davis, PhD, FACMG

Purpose: There is increasing demand from the public for direct-to-consumer (DTC) genetic tests, and the US Food and Drug Administration limits the type of health-related claims DTC tests can market. Some DTC companies provide raw genotyping data to customers if requested, and these raw data may include variants occurring in genes recommended by the American College of Medical Genetics and Genomics to be reported as incidental/secondary findings. The purpose of this study was to review the outcome of requests for clinical confirmation of DTC results that were received by our laboratory and to analyze variant classification concordance.

Methods: We identified 49 patient samples received for further testing that had previously identified genetic variants reported in DTC raw data. For each case identified, information pertaining to the outcome of clinical confirmation testing as well as classification of the DTC variant was collected and analyzed.

Results: Our analyses indicated that 40% of variants in a variety of genes reported in DTC raw data were false positives. In addition, some variants designated with the "increased risk" classification in DTC raw data or by a third-party interpretation service were classified as benign at Ambry Genetics as well as several other clinical laboratories, and are noted to be common variants in publicly available population frequency databases.

Conclusion: Our results demonstrate the importance of confirming DTC raw data variants in a clinical laboratory that is well versed in both complex variant detection and classification.

Genet Med advance online publication 22 March 2018

Key Words: classification discrepancy; clinical confirmation direct-to-consumer; false positive; raw data

- Identified 40% false positives (N=49)
- Issue is using genotype (SNP-based array) data inappropriately, not just about DTC results

- **Key take home**: Need for confirmatory testing especially if consumer test is based on:
  - Downloaded genotype data
  - ROU assays
  - Not performed in a CLIA/CAP lab

Slide credit: Elissa Levin

Confusion lurks in raw genomic data

Gene	Alteration	Classification Provided By DTC/3rd Party Service	Ambry's Classification	ClinVar Classification (Clincal Laboratory Submissions)	ESP Population Freq	1000 Genomes Population Freq	dbSNP Population Freq
ATM	p.M1040V (c.3118A>G)	Increased Risk	Benign	Benign	1.36%	0.95%	1.48%
BRCA1	p.Q356R (c.1067A>G)	Increased Risk	Benign	Benign	4.59%	2.81%	3.97%
BRCA2	p.N372H (c.1114A>C)	Increased Risk	Benign	Benign	23.32%	24.26%	24.44%
COL3A1	p.A698T (c.2092G>A)	Increased Risk	Benign	Benign	21.39%	21.16%	19.16%

Slide credit: Stephany Connor

Take-away? Play within the boundaries.

Benefits, Limitations & Risks of CIGT.

What are the potential benefits of CDGT?

- Ease of use
  - Simply online ordering process
  - Sample collection in the privacy of home or office
  - Option to have anonymity
- Affordable
  - Cash pay options, even for medically actionable CIGT are often far less than patient portion of bill when done through insurance
- Consumer-empowering

What are the limitations?

- There is no such thing as an all-encompassing comprehensive genetic test
- May not be diagnostic/will need confirmatory testing (will depend on the company)
- Possibility of inadequate analytical or clinical validity (will depend on the company)
- Informed consent may be lacking
- Ensuring chain of custody may not be the same as specimens collected in the clinic
- Genetics is typically just part of overall disease risk
- Some results may be seen as lacking clinical utility

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

What are the potential risks of CDGT?

- May not be the appropriate test for the individual's needs
- False positive or false negative results (risk of this will depend on the company)
- Misinterpretation of a result (by the company, by the consumer, by the HCP)
  - Big concern over false reassurance of a negative result
  - Current understanding of the risk associated with a variant may be an overestimation due to biased sampling in the literature or may not be applicable to a specific population
- Distress/anxiety risks
  - Identifying disease risk for severe disease which may not have a cure/treatment
  - Finding unexpected relative/non-paternity
  - Ancestry not what was expected
- Inappropriate action based on results
  - Changes diet, medication or other lifestyle habits without HCP involvement
  - May lead to screening tests (blood, imaging, genetic testing) that are inappropriate and expensive

Slide credit: Precision Medicine SIG's Consumer-Driven Genetic Testing subcommittee

The role of telegenetics in CIGT.

The clinical role in CIGT

- Unlike traditional patient visits, based in worry about a specific medical condition, CIGC patients are more likely to want their DNA decoded *out of general curiosity*.
  - Should genetic counselors and other clinicians have to be experts in the ins-and-outs of the validity and reports of every DTC company out there? Of course not!

The telemedicine role in CIGT

- Telemedicine can play an important role in helping patients determine if a CIGT is right for them, or if a different test may be more appropriate.
  - Collect personal and family medical history
  - Ascertain the patients underlying motivations for testing

What to do for patients wanting to do CDGT

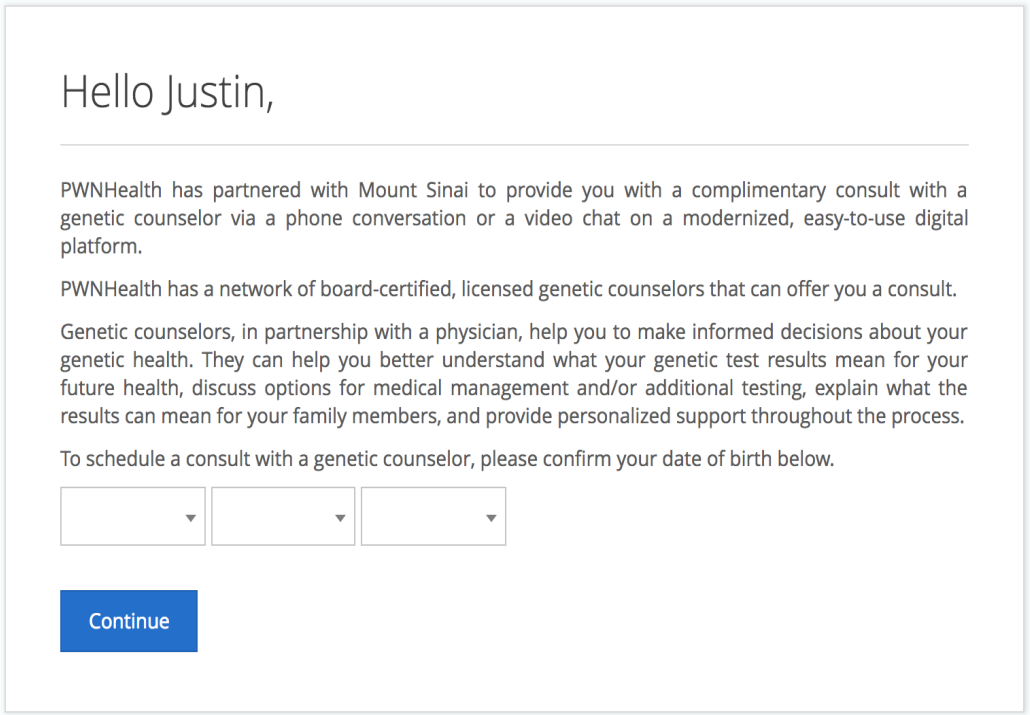
Understand their motivations	• Will this test address their needs?
Review personal and family history	• Is clinical genetic testing appropriate? • Will this test help address family/personal risk concerns?
Provide relevant education	• Risks, benefits and limitations of testing • General genetics concepts
Discuss implications of testing	• Possible test outcomes • Impact on family members
Refer	• Pre-test genetic counseling for CDGT • Genetic counseling if risk identified in personal/family history

The telemedicine role in CIGT

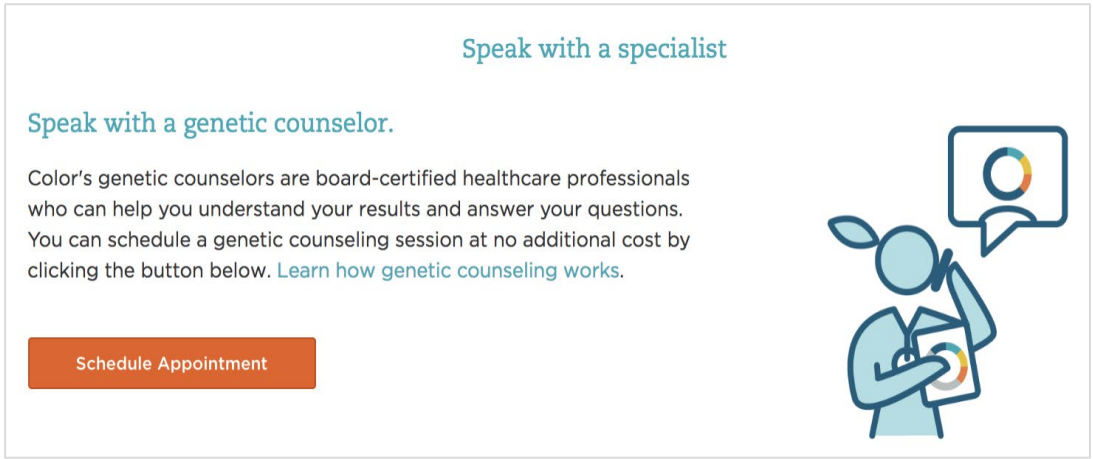
- Telemedicine can also play a huge role in helping the patient interpret their CIGT results

- Many companies have popped up in the past 5 years dedicated 100% to DTC/CIGT ordering and post-results genetic counsleing

Genetic counseling offered by DTC labs



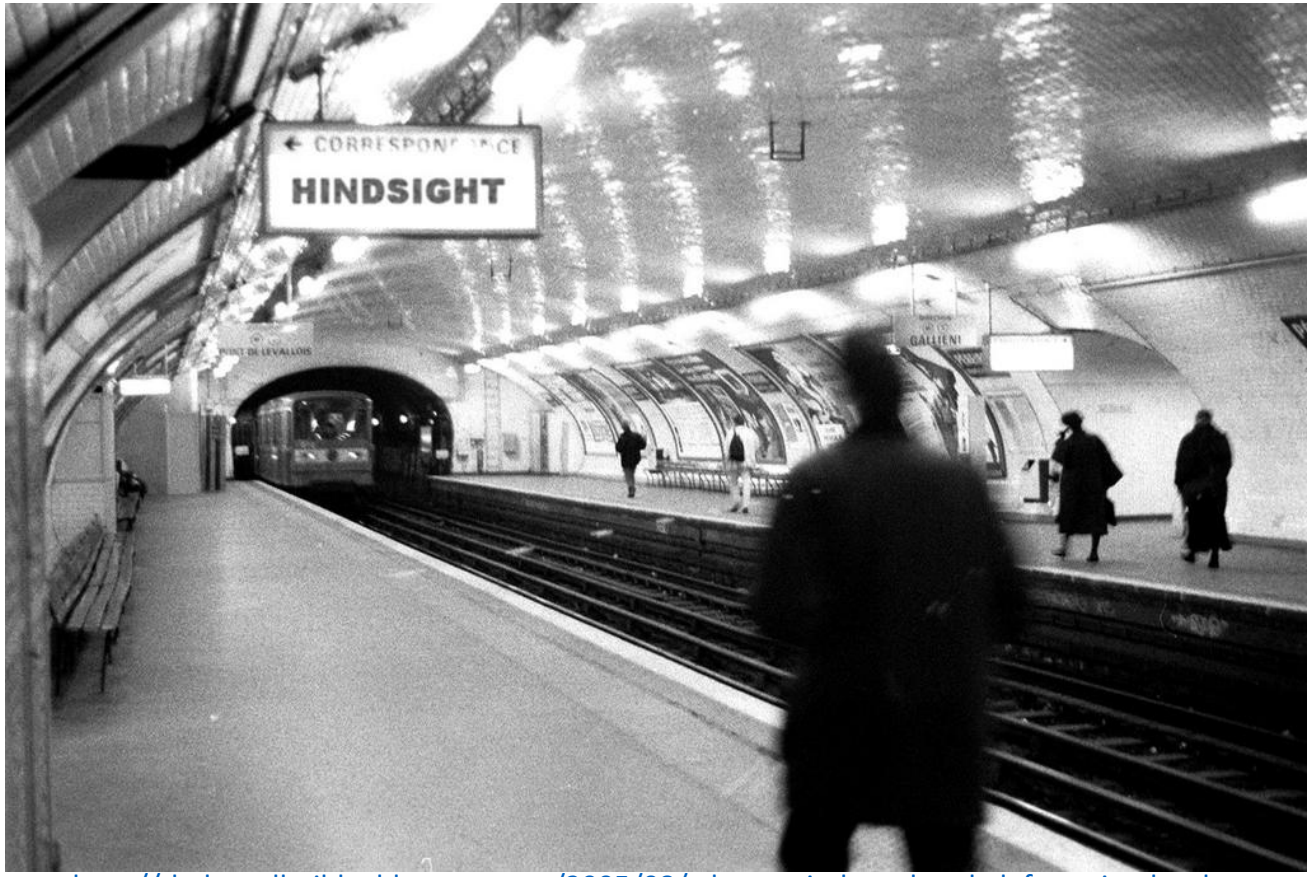
- GC is offered within the results experience
- A focused approach that allows the clinician to be the expert in the lab, test, and reuslts



What to do for patients who share their CDGT results

Understand their motivations	• Why do testing in the first place, what are their concerns? • Did doing this test address their needs?
Review personal and family history	• What risks are present in the personal/family history? • Is clinical genetic testing appropriate?
Provide relevant education	• General genetics, testing limitations, condition-specific information
Discuss CDGT results	• Review of test result • Clinical confirmation or diagnostic testing (if indicated)
Support	• Coping with unexpected or disappointing results • Sharing result with family members
Refer	• Genetic counseling to discuss CIGT result • Disease specialist depending on CDGT result

The CIGT train has left the station…will you be on it?



http://thebrandbuilder.blogspot.com/2005/08/when-train-has-already-left-station.html

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Improving Access to Quality Medical Care Webinar Series

May 14, 2020: Importance of Genetics Professionals in Clinical Care

Valerie Schaibley, PhD

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https://www.surveymonkey.com/r/SWTRCWebinar

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