Exploring the Current Landscape of Consumer Genomics:

Integration with Scientific and Medical Communities

Danielle Bonadies, MS, CGC
Co-Founder and Director of Genetics
My Gene Counsel
Danielle@MyGeneCounsel.com

Conflicts of Interest

- Danielle Bonadies is Co-Founder and current Director of Genetics at My Gene Counsel.

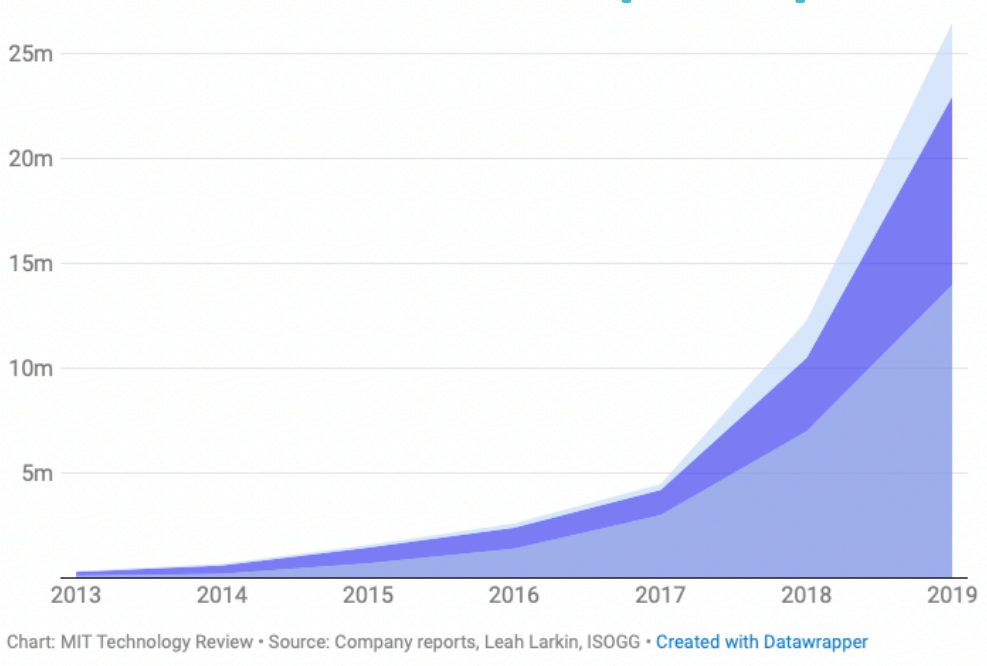
Biotechnology / DNA Testing

More than 26 million people have taken an at-home ancestry test

The genetic genie is out of the bottle. And it's not going back.

by **Antonio Regalado** Feb 11, 2019

Over 42,000 People per Day



Total number of people tested by consumer genomics companies through January 2019 (in millions)

Khan and Mittelman *Genome Biology* (2018) 19:120
https://doi.org/10.1186/s13059-018-1506-1

Genome Biology

COMMENT Open Access

Consumer genomics will change your life, whether you get tested or not

Razib Khan[1] and David Mittelman[2*]

100,000,000 genotyped individuals by 2021

Impact to Patients

Impact to Patients

The Online Gene Test Finds a Dangerous Mutation. It May Well Be Wrong.

Third-party analysis of raw DNA is not as rigorous as that done in a certified laboratory. But many consumers don't understand that their results are not conclusive.

By Gina Kolata

July 2, 2018

YOUR HEALTH

Results Of At-Home Genetic Tests For Health Can Be Hard To Interpret

June 18, 2018 · 4:58 AM ET
Heard on Morning Edition

ROB STEIN

npr

Home / *The Scientist*

Study Finds Inaccuracies in 40 Percent of DTC Genetic Testing Results

An analysis of 49 patient samples finds high proportions of false positives and misinterpretation.

Mar 28, 2018
SHAWNA WILLIAMS

BUSINESS

Genetic tests ordered by doctors race to market, while 'direct-to-consumer' tests hinge on FDA approval

By IKE SWETLITZ @ikeswetlitz / MARCH 16, 2018

GENETICS

Another Reminder That Consumer DNA Tests Are Not 100% Accurate

Kristen V. Brown
3/28/18 3:55pm • Filed to: 23ANDME

78.5K 35

How Accurate Is Direct-To-Consumer Genetic Testing? From Gold(ish) To Garbage

Ellen Matloff Contributor ⓘ
May 28, 2018, 02:18pm • 10,551 views • #IfIOnlyKnew

my GENE COUNSEL

Impact to Patients

h. @hbl5_ Follow

Replying to @akaalison1

Here in the states 23 and Me will show you if you likely have the BRCA1 & 2. My bmom also had breast ca caught very early. I don't have the BRCA gene according to my dna test. I do go for yearly 3D mammo's.

7:14 PM - 2 Aug 2018

Lara Diamond @larasgenealogy Follow

Lots of talk about @23andMe being able to give results for the Ashkenazi #BRCA mutations. Well, this saved my life when I tested with #23andMe in 2013 when they previously gave these results. Here's the story: larasgenealogy.blogspot.com/2013/11/how-ge ... #genetics #genealogy #FDA

8:56 PM - 7 Mar 2018

Erica Goldberg @GoldbergPrime Follow

Using services like 23andMe provides a wealth of important genetic and health information, such as whether you are a BRCA carrier, and whether you are likely to consume caffeine (I was less likely and consume almost none!). (3)

12:03 PM - 10 Aug 2018

Ken Deutsch @KDeutsch Follow

According to @23andme I am 97% Ashkenazi (AJ) & #BRCA - . I am BRCA+ w/ metastatic cancer. Your marketing convinced 1 of my relatives that as an AJ your test would be enough. What will you do to avoid false negatives that put peoples lives at risk? #GenCSM #gcchat

1:06 PM - 19 Jun 2018

Amy Byer Shainman @BRCAresponder Follow

Replying to @GoldbergPrime

Impt. to note: #23andme only tests for 3 out of over 1000 #BRCA 1 & 2 mutations & is not a diagnostic test. Test must be repeated in clinical setting. Many are not understanding this. Ideal to speak with a certified genetic counselor @GeneticCouns Happy to connect you to one.

11:36 AM - 12 Aug 2018

Alexander (Sasha) Wait Zaranek @wait_sasha Follow

Replying to @chrissyfarr

A negative result from the 23andMe test is not a negative result for BRCA.

7:53 PM - 9 Jul 2018

no more music not takes @quidditch424 Follow

There's over a 1000 variations of BRCA and 23 and Me only tests for 3. What's the benefit to the consumer?

12:30 PM - 6 Mar 2018

my GENE COUNSEL

Current: Transactional

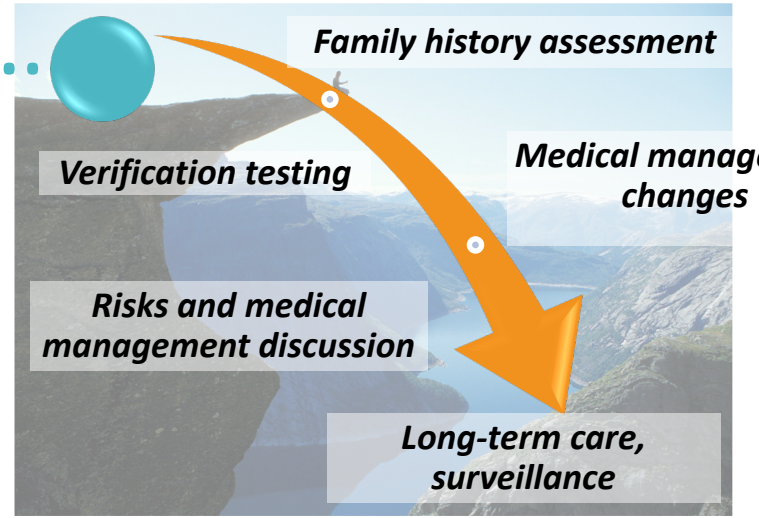
Marketing Efforts

Saliva Collection

Genetic Testing

Online Results

? ? ?



Paths to Integration

1. Verification Testing
2. DTC Medical Grade Testing
3. Other Trends

Verification Testing

- 49 patient samples
- 43 variants sent for confirmatory testing
- 40% (17/43) were false positives
- 19% (8/43) were confirmed but classified inaccurately
  - Classified as pathogenic by DTC
  - Benign or VUS by clinical lab

Genetics in Medicine

Original Research Article | OPEN | Published: 22 March 2018

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 & Brigette Tippin Davis PhD, FACMG

Verification Testing

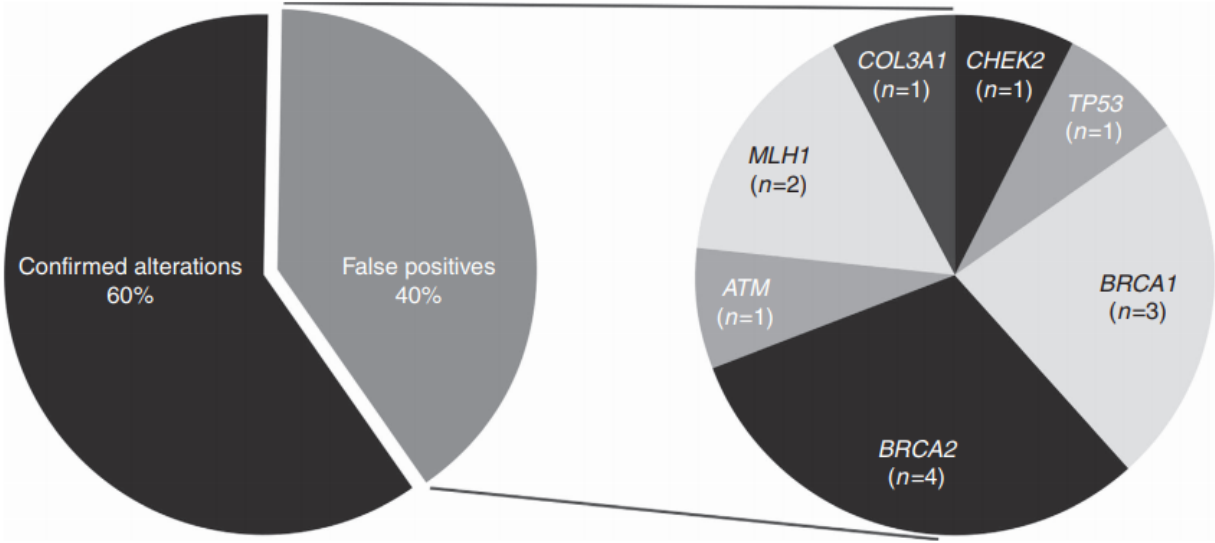


Figure 1 False-positive variants in clinically actionable genes. The pie chart on the left indicates of the variants analyzed, 60% were confirmed and 40% were false positives. The pie chart on the right shows which genes were involved with the false-positive cases and how often those false calls were detected in this study.

Table 2 Concordance of DTC and confirmatory results from our clinical diagnostic laboratory

Confirmed variants	Variant frequency	Ambry[a]	False positives	Variant frequency	Ambry[a]
BRCA1 c.68_69delAG (p.E23Vfs*17)	3	PV	CHEK2 c.1100delC (p.T367Mfs*15)	2	PV
BRCA1 c.5266dupC (p.Q1756Pfs*74)	1	PV	TP53 p.R175H (c.524G > A)	3	PV
BRCA2 c.5946delT (p.S1982Rfs*22)	9	PV	BRCA1 p.E1250* (c.3748G > T)	1	PV
CHEK2 c.1100delC (p.T367Mfs*15)	2	PV	BRCA1 p.A1708E (c.5123C > A)	1	PV
CFTR p.F508del (c.1521_1523delCTT)	4	PV	BRCA1 p.R1699W (c.5095C > T)	1	PV
BRCA1 p.Q356R (c.1067A > G)	1	Benign	BRCA2 p.S1955* (c.5864C > A)	1	PV
BRCA2 p.N372H (c.1114A > C)	3	Benign	BRCA2 c.9026_9030delATCAT (p.Y3009Sfs*7)	2	PV
CHEK2 p.I157T (c.470T > C)	1	MPPV	BRCA2 p.R2336H (c.7007G > A)	1	PV
MEFV p.A744S (c.2230G > T)	1	VUS	BRCA2 c.1813dupA (p.I605Nfs*11)	1	PV
MEFV p.V726A (c.2177T > C)	1	PV	ATM p.M1040V (c.3118A > G)	1	Benign
	26 Total[b]		MLH1 p.H329P (c.986A > C)	1	PV
			MLH1 c.1101delC (p.S368Rfs*33)	1	PV
			COL3A1 p.A698T (c.2092G > A)	1	Benign
				17 Total[b]	

DTC, direct to consumer.

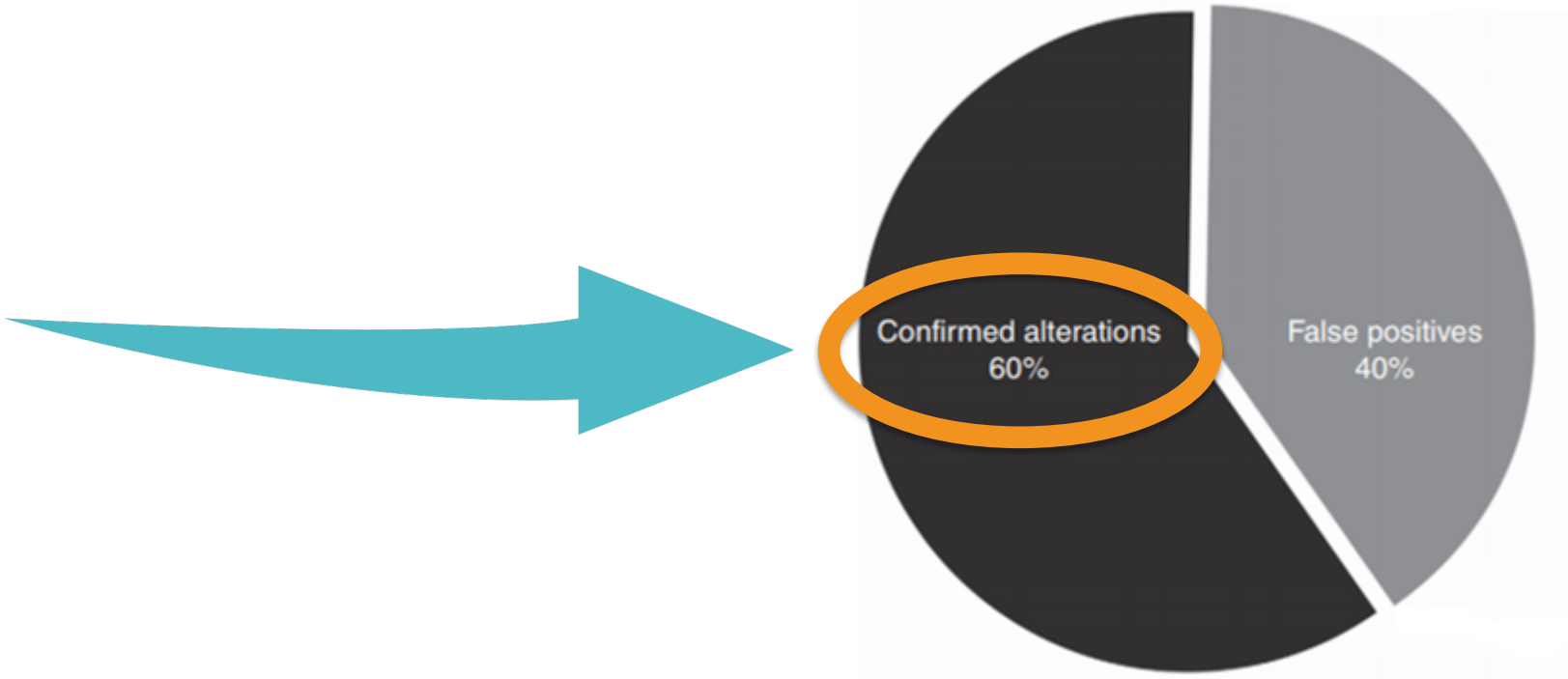
[a]Ambry variant classification: PV, pathogenic variant; MPPV, moderate penetrance pathogenic variant; VUS, variant of unknown significance. [b]The combined number of variants analyzed does not equal the total number of individuals in this study (n = 49) because some individuals had overlapping variants in question. In addition, four variants in question were out of our reporting range and therefore not analyzed.

Table 3 Classification discrepancies

Gene	Variant	DTC/third party[a]	Ambry[b]	ClinVar[c]	ESP[d]	1000 Genomes[e]	dbSNP[f]
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%
COL5A1	c.655-8689C > T	Increased risk	Deep intronic—benign	N/A	N/A	N/A	N/A
COL5A1	c.654+2749A > G	Increased risk	Deep intronic—benign	N/A	N/A	N/A	N/A
COL5A1	c.1827+399C > T	Increased risk	Deep intronic—VUS	N/A	N/A	N/A	N/A
COL5A1	c.1827+1142T > C	Increased risk	Deep intronic—benign	N/A	N/A	N/A	N/A

DTC, direct to consumer; N/A, not available; VUS, variant of unknown significance.
aVariant classification provided by the DTC company or a third-party interpretation service. bVariant classification provided by Ambry. cVariant classification provided in ClinVar (clinical laboratory submissions only). dExome Sequencing Project population frequency database. e1000 Genomes population frequency database. fdbSNP population frequency database.

Verification Testing



Don’t throw the baby out with the bath water

Building a Bridge from DTC to Medicine

Direct-to-Consumer
Test Kits

Verified Through
Medical-Grade Testing

My Gene Counsel turns your family history into health information for your future

Inside your body, your DNA holds centuries of information about your health. Outside in the world of science, new discoveries are made everyday. My Gene Counsel decodes complex genetic information bringing you a new generation of health advice.

my GENE COUNSEL.

Be one step ahead

my GENE COUNSEL

Insurers

- Recognizing the power of genetic testing
- Verification testing for BRCA1 and BRCA2 DTC findings now covered by:
  - Blue Shield of California
  - Anthem
  - Aetna
- Allows patients to take advantage of genomic data they already have in their hands

DTC Medical Grade Testing

- Opportunities
- Trends
- Research
- Providers still left to evaluate

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:

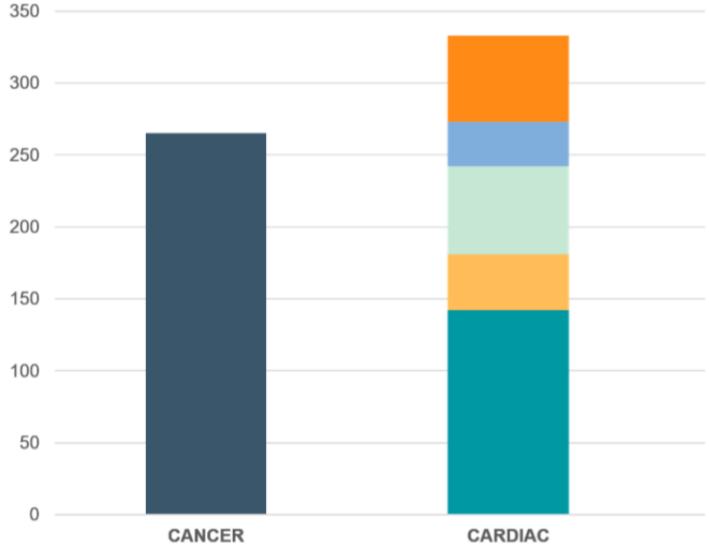
<5,000

genetic counselors in US

my GENE COUNSEL

Continuous Medical Management Changes

600+ changes within the ACMG59 genes



Within 5 Years

Future: Long-Term Engagement

- Verification programs
- Tools for healthcare providers
- Accessible, scalable information
- Gene and variant specific reports
- Updating reports with notifications
  - Variant reclassifications
  - Medical management updates

- Comprehensive, searchable resources
  - Patient experience
  - Provider experience
- Engagement and retention
  - Outcome data
  - Feedback
  - Clinical trial info

Thank You

Danielle Bonadies, MS, CGC
Co-Founder and Director of Genetics
My Gene Counsel
Danielle@MyGeneCounsel.com