23andMe Information Connecticut Legislative Forum on DNA Testing and Genomic Medicine

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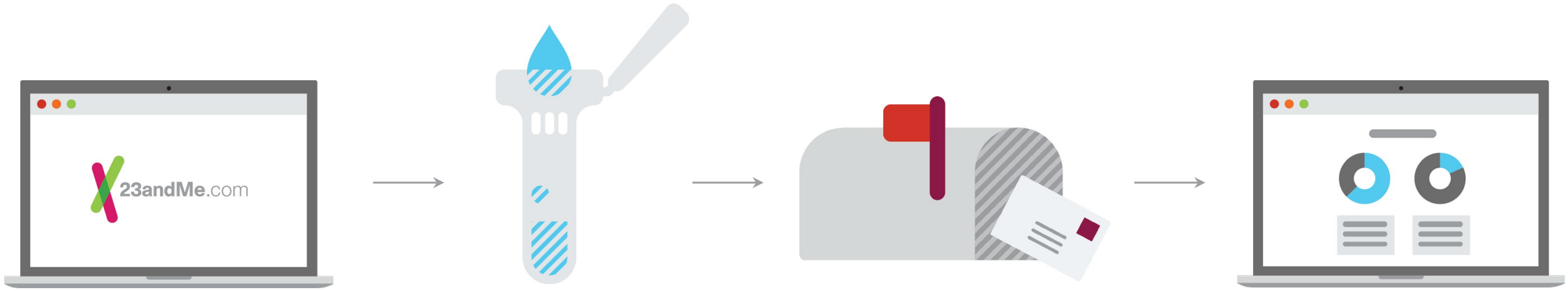
Agenda/Objectives

- Review of benefits of 23andMe OTC Genetic Testing
- Review of Federal Regulations of OTC Genetic Tests and 23andMe's five FDA Authorizations
- Review of standard of care and applicable Connecticut Prescriber Laws not being met by majority of labs and other third parties selling RX services to consumers

23andMe –
The Only FDA Authorized Consumer Genetic Health Test

Our mission is to help people access , understand and benefit from the human genome.

How it works



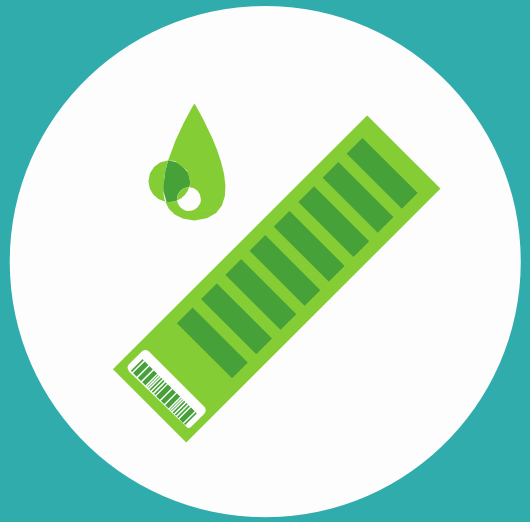
DNA Extraction and Amplification

1 Saliva sample arrives at a CLIA-certified lab

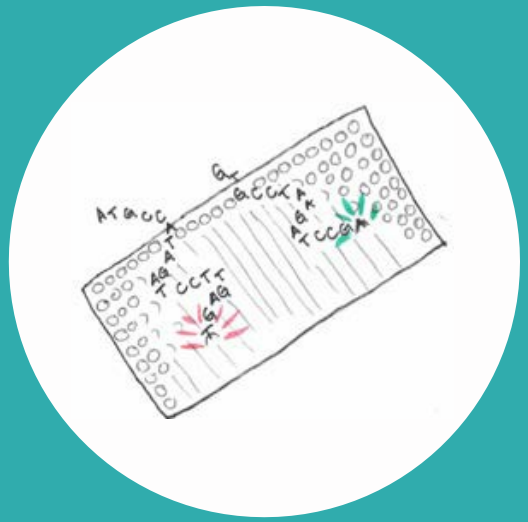
2 DNA is extracted from saliva sample

3 The DNA is amplified many times so that it can be analyzed

Hybridization and SNP Detection



1 The amplified DNA is cut into smaller pieces and washed over a custom Illumina microarray chip



2 The tiny probes on the chip detect specific bits of DNA and glow in a way that indicates the SNP version

3 That fluorescent signal is read by a computer, and the data uploaded to the customer's 23andMe account

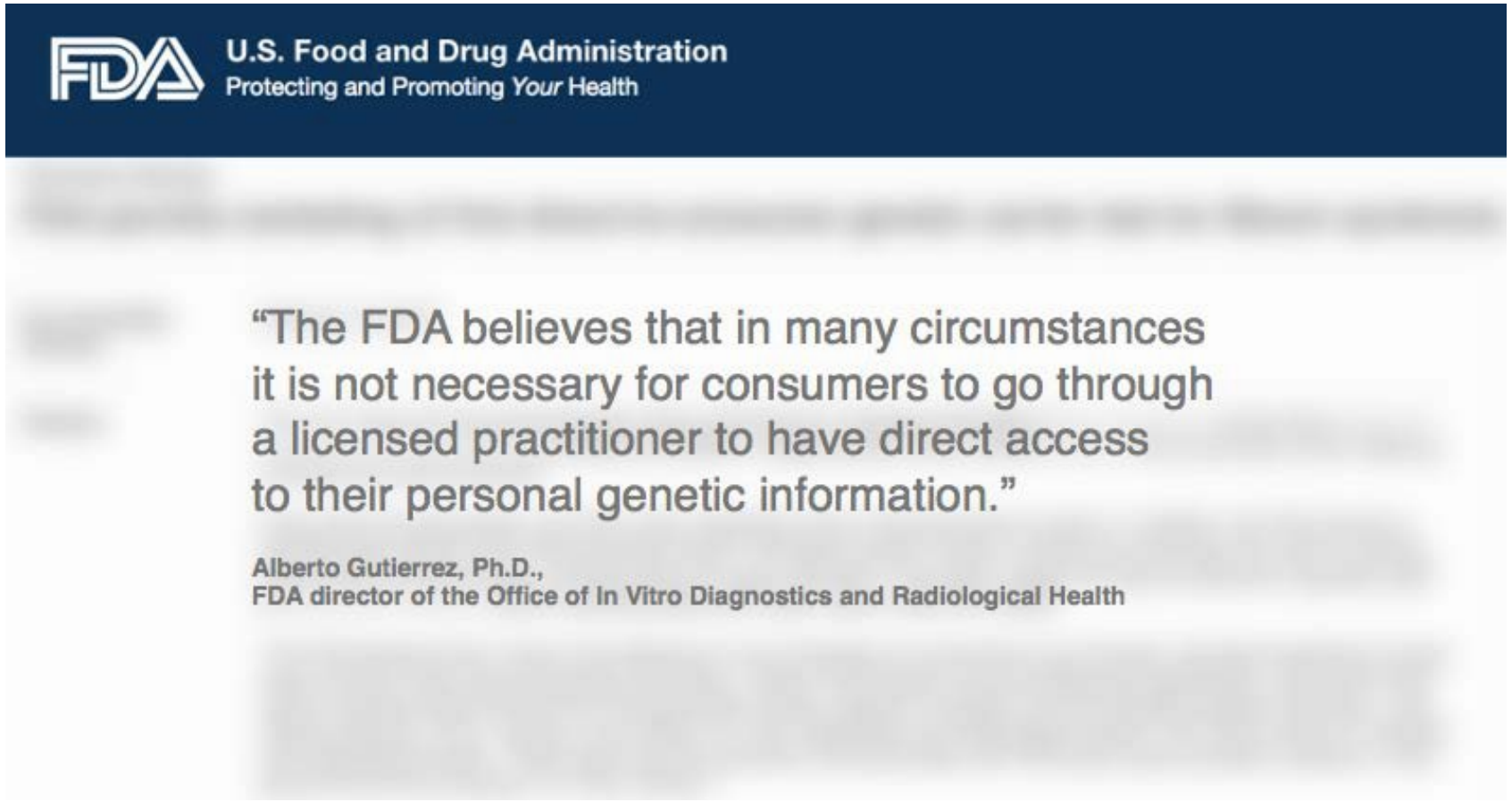
23andMe's FDA Authorizations for OTC Use

23andMe is the ***only*** company authorized to ***legally*** market OTC genetic health tests 5 FDA pre-market reviews- including for Carrier status, Genetic Health Risks, BRCA and Pharmacogenetic information, all held by FDA to have:

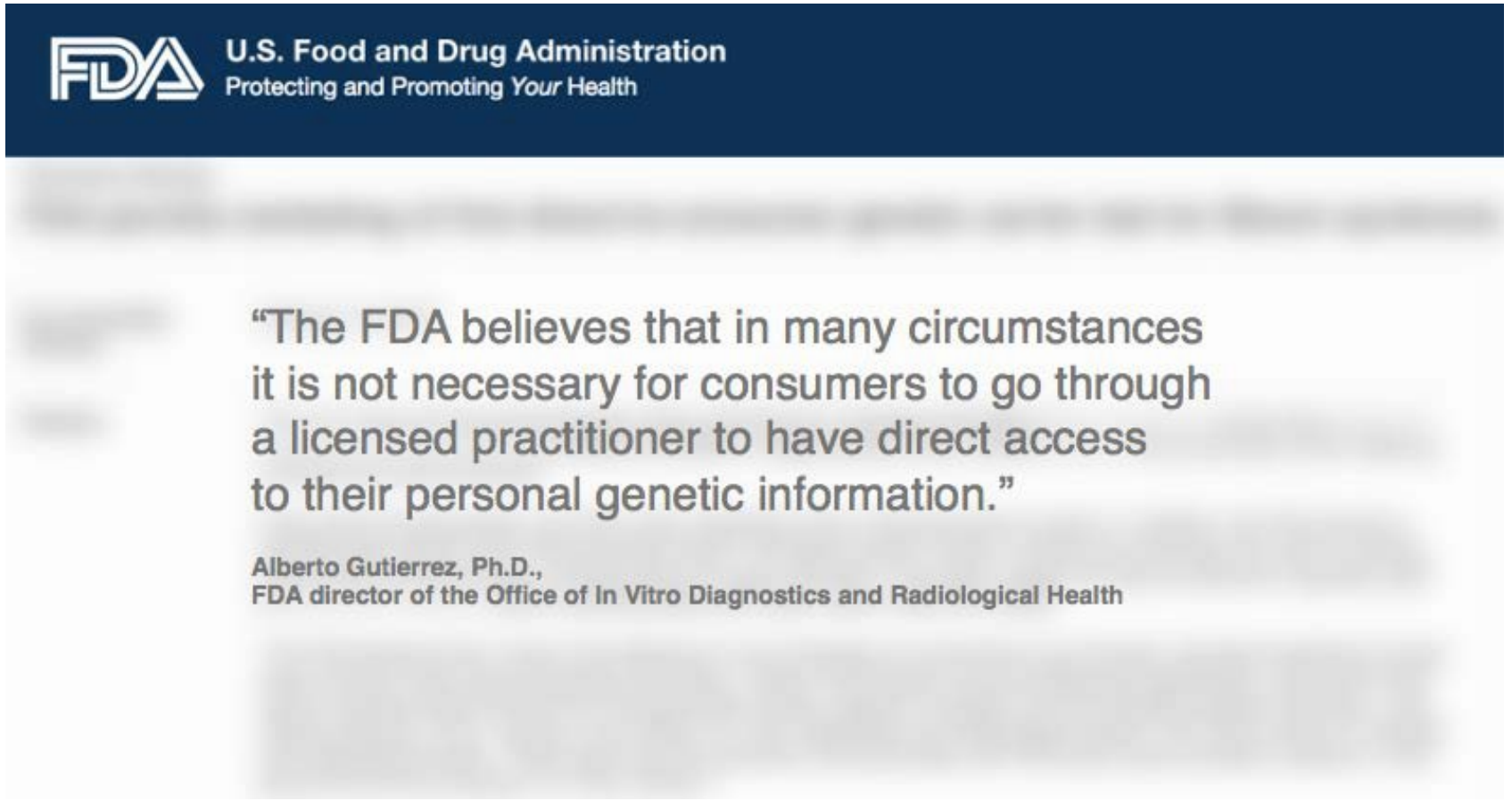
- **>99% Accuracy, > 99% Precision** in statistically robust studies
- **> 90% User Comprehension** of report labeling
- Scientific and Clinical Validity
- Robust and compliant post market quality system

- No "LDT" competitors meet ***any*** of the above and all ***are intended for Physician use only***

February 2015 – First OTC FDA Authorization for 23andMe Autosomal Recessive Carrier tests



April 2017 – OTC FDA Authorization for 23andMe Genetic Health Risk Reports



March 2018 – OTC FDA Authorization for 23andMe BRCA1/BRCA2 (Selected Variants)

FDA authorizes, with special controls, direct-to-consumer test that reports three mutations in the BRCA breast cancer genes

Test only reports 3 out of more than 1,000 known BRCA mutations and negative result doesn't rule out increased cancer risk

There Have Been NO Reportable Events Related to 23andMe's Results

- **Millions of 23andMe customers** have received their health reports
  - no reports of erroneous or misuse of health results
- 23andMe has a robust FDA and ISO 13485 compliant post market quality system:
  - must investigate all customer complaints
  - must rapidly and publicly report malfunctions which do or could cause serious harm
- 23andMe conducted a 1 year post market surveillance program with UK Medicines and Health Regulatory Agency (MHRA) –there were **no reportable events**
- 23andMe was inspected by FDA in June of 2019 and **received a rating of no deficiencies**

Benefit of 23andMe Testing is to Identify People Who Are Unlikely to Be Clinically Tested

The list of criteria in the NCCN guidelines for detection has limitations

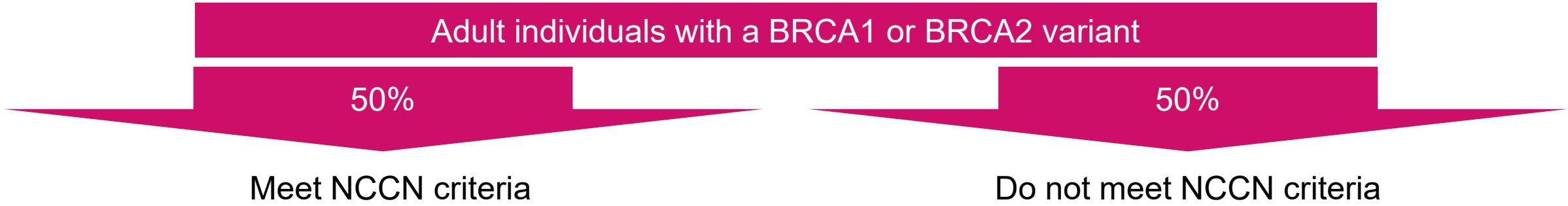
BRCA1/2 testing criteria are predicated on specific combinations of the following factors:

A. Personal history of cancer (conditions apply)
B. Known BRCA1/BRCA2 mutation via tumor profiling
C. Known family history of deleterious BRCA1/BRCA2 mutation
D. Known family history of cancer (conditions apply)
E. Ashkenazi Jewish ancestry*

*NOTE: Ashkenazi Jewish ancestry is not a stand-alone criteria, but it does help qualify certain individuals when factored together with a personal history of certain cancers

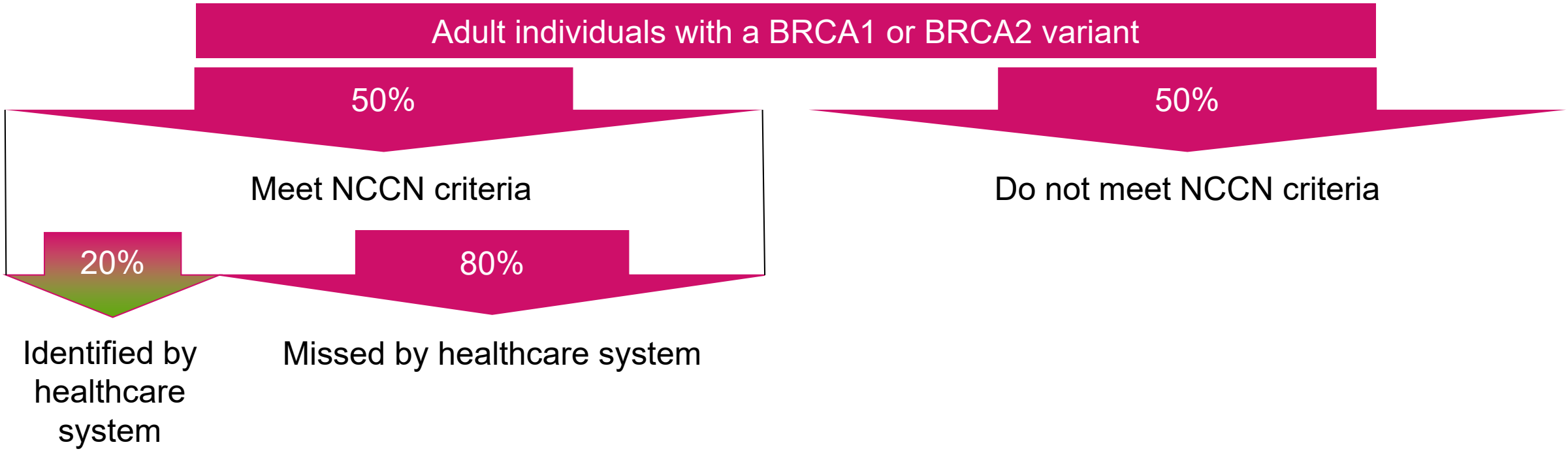
1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Genetic/Familial High-Risk Assessment: Breast and Ovarian. Version 2.2019 https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf

Unfortunately, NCCN criteria only capture ~50% of all adults with BRCA1 or BRCA2 variants



1. Gabai-Kapara, E. et al. Population-based screening for breast and ovarian cancer risk due to BRCA1 and BRCA2. Proc. Natl. Acad. Sci. U.S.A. (2014).
2. Manchanda, R. et al. Population Testing for Cancer Predisposing BRCA1/BRCA2 Mutations in the Ashkenazi-Jewish Community: A Randomized Controlled Trial. JNCI J. Natl. Cancer Inst. 107, (2014).
3. Metcalfe, K. A. et al. A comparison of the detection of BRCA mutation carriers through the provision of Jewish population-based genetic testing compared with clinic-based genetic testing. Br. J. Cancer 109, 777–779 (2013).
4. Manickam, K. et al. Exome Sequencing–Based Screening for BRCA1/2 Expected Pathogenic Variants Among Adult Biobank Participants.

To compound the problem, only ~10% of all adults with BRCA1/2 variants are identified by the healthcare system



1. Childers CP et al. [2017]. “National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer” J Clin Oncol. 35(34):3800-8806

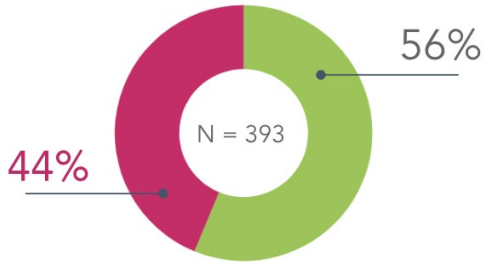
23andMe Research Reveals Additional Concerns

Goal: To characterize 23andMe's cohort of BRCA carriers with respect to ancestry and family cancer history (two factors considered in recommending healthy individuals for BRCA testing)

Participants: 2,853 consented research participants with at least one BRCA variant 23andMe tests for

Findings:

44% with an Ashkenazi Jewish BRCA variant don't report a family history of a BRCA-related cancer

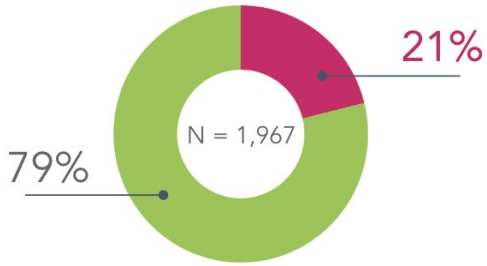


First-degree family history of a BRCA-related cancer

No first-degree family history of a BRCA-related cancer

21% with an Ashkenazi Jewish BRCA variant didn't self-report having Jewish ancestry

(Though 62% do have detectable (≥1%) Ashkenazi genetic ancestry)



Self-reported having Jewish ancestry

Did not self-report having Jewish ancestry

1. Identifying Ashkenazi Jewish BRCA1/2 founder variants in individuals who do not self-report Jewish ancestry. Ruth I Tennen, Sarah B Laskey, Bertram L Koelsch, Matthew H McIntyre, The 23andMe Health Team, Joyce Y Tung

23andMe Research Reveals Additional Concerns

The findings suggests that these individuals (and those like them in the community) are **unlikely to qualify** for clinical genetic testing **until they develop cancer.** This is a missed opportunity for cancer prevention.

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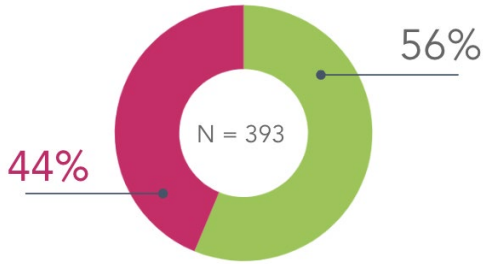

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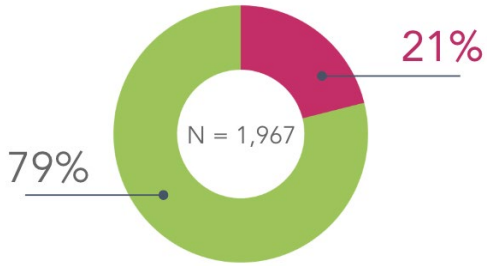

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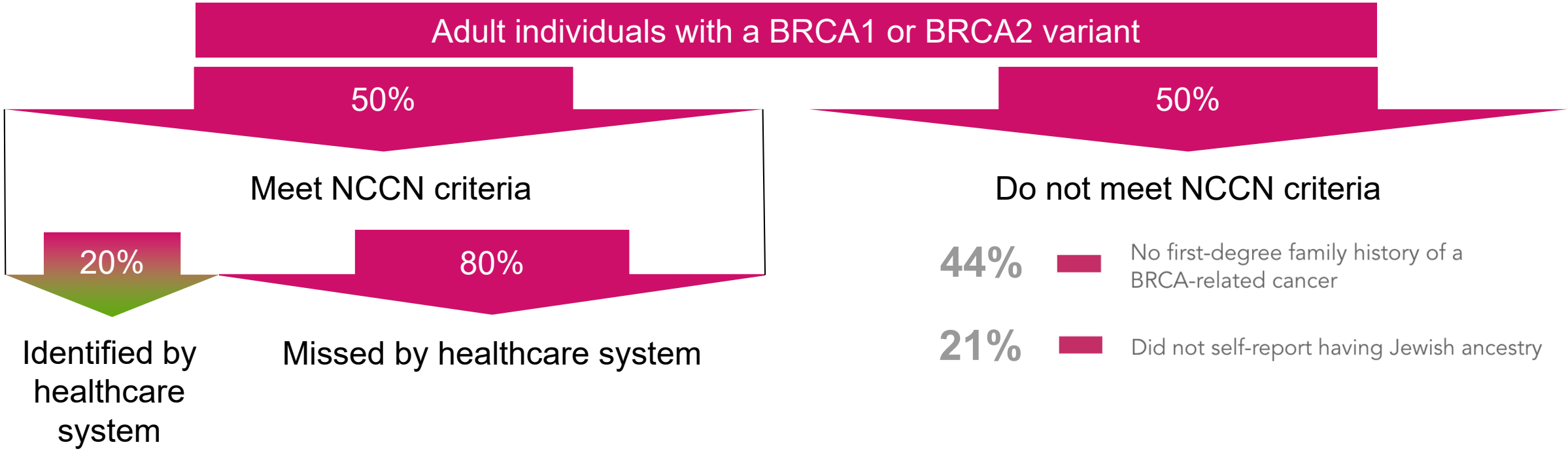
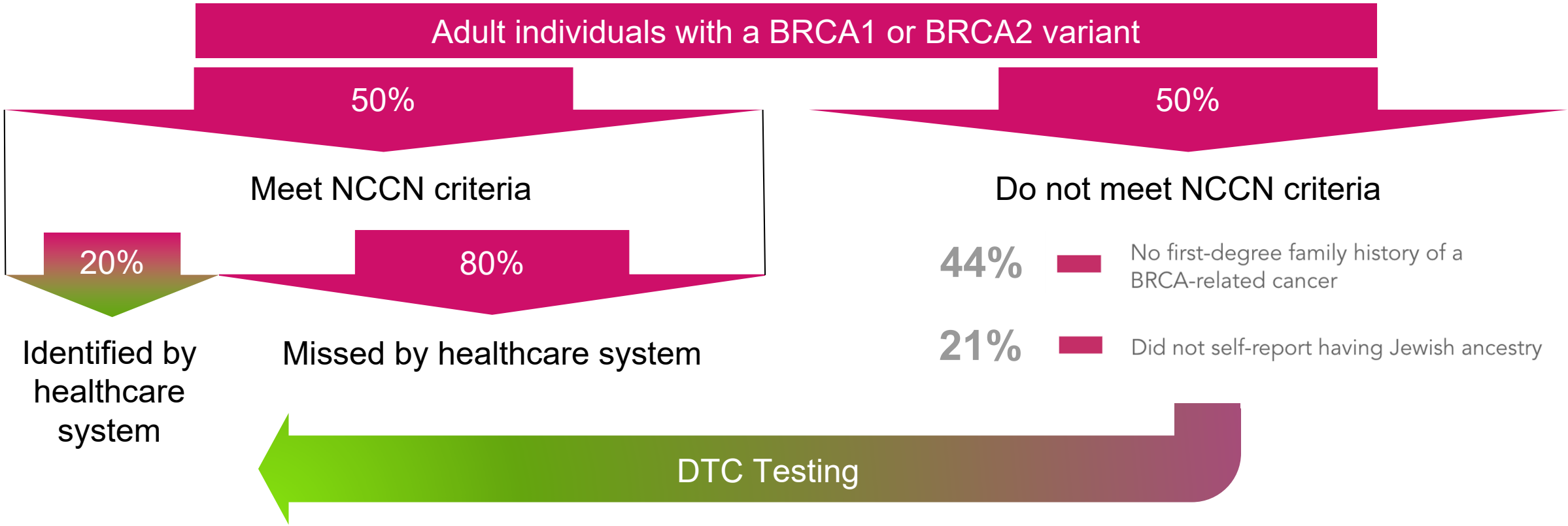
Individuals like those highlighted in the 23andMe study have a strong chance of falling through the cracks



1. Childers CP et al. [2017]. “National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer” J Clin Oncol. 35(34):3800-8806

DTC testing creates an opportunity to capture those in the community and guide them into the healthcare system



1. Childers CP et al. [2017]. "National Estimates of Genetic Testing in Women With a History of Breast or Ovarian Cancer" J Clin Oncol. 35(34):3800-8806

There is a clear FDA path for OTC Genetic Tests – Why is only 23andMe following regulations?

Home / Medical Devices / Products and Medical Procedures / In Vitro Diagnostics / Direct-to-Consumer Tests

As a matter of policy, the FDA generally does not review some types of tests, called laboratory developed tests (LDTs), that are created and performed in a single laboratory, if they are offered to patients only when prescribed by a health care provider. These tests typically do not have the FDA's independent assurance of the analytical validity, clinical validity, or clear communication of test results.

See https://www.fda.gov/medical-devices/vitro-diagnostics/direct-consumer-tests

There is a clear FDA path for OTC Genetic Tests – Why is only 23andMe following regulations? (continued)

"... if they are offered to patients ***only when prescribed by a health care provider*** ..."

The key to understanding why there are so many DTC genetic tests flooding the market when only 23andMe is legally cleared for OTC indications is recognizing that unscrupulous labs are ***selling RX tests to consumers and frequently paying for prescriptions in order to get around FDA regulations*** and sell tests to consumers that do no meet FDA's standards for analytical accuracy, clinical validity and clear results appropriate for non prescription use

Connecticut State Statutes Relevant to Practice of Labs Selling Rx Genetic Tests Direct - to-consumers

Connecticut Laws Likely Violated By Labs Selling Rx Tests Direct -To-Consumers

Like many states Connecticut has enacted statutes to ensure high quality medical services for it citizens. A review of websites of numerous "Lab DTC" offerors indicate that they use "Doc in the Box" or "Sham RX" prescriptions which do not appear to comply with Connecticut laws.

Key Statutes-

Conn. Public Act. No 15-88 *An Act Concerning The Facilitation Of Telehealth*

– and –

CGS Sec 20-7 *et seq.* relating to required financial disclosures by physicians to patients

Conn. Public Act No. 15 -88
(Act Concerning the Facilitation of Telehealth)

In 2015 the State enacted a law to enable quality telemedicine and ensure that telehealth medical services would meet the same standard of care as in person medical services.

It mandates several specific requirements:

(b) (1) A telehealth provider shall only provide telehealth services to a patient when the telehealth provider: (A) Is communicating *through real-time, interactive, two-way communication technology* or store and forward technologies; (B) has access to, or knowledge of, the patient's medical history, as provided by the patient*, and the patient's health record, including the name and address of the patient's primary care provider, if any*; (C) conforms to the standard of care applicable to the telehealth provider's profession and expected for in-person care as appropriate to the patient's age and presenting condition, except when the standard of care requires the use of diagnostic testing and performance of a physical examination, such testing or examination may be carried out through the use of peripheral devices appropriate to the patient's condition; and (D) *provides the patient with the telehealth's provider license number and contact information .*

Conn. Public Act No. 15 -88 (Act Concerning the Facilitation of Telehealth) (cont.)

(2) At the time of the telehealth provider's first telehealth interaction with a patient, **the telehealth provider shall inform the patient concerning the treatment methods and limitations of treatment using a telehealth platform and**, after providing the patient with such information, **obtain the patient's consent to provide telehealth services. The telehealth provider shall document such notice and consent in the patient's health record.**

The ”Doc in a Box”/Sham Rx Mechanism Used By Labs Violates Public Law 15 -88

To facilitate sale of their tests Labs advertise that a physician “reviews” or “orders” the test for the customer. Most of the labs ask consumers to fill out a questionnaire, developed by the lab, which is provided to the “ordering physician,” after the consumer has purchased the test, who rubber stamps the order.

These ordering Physicians do not appear to have any opportunity to request the patient’s medical record or name and contact information of their usual treating physician as required.

These ordering Physicians do not appear to have any opportunity provide their provider license number or contact information to their patient as required.

These ordering Physicians do not appear to have any direct interaction with their “patient” and therefore no way to meet and document the consent prior to the performance of the telemedicine as required.

These ordering Physicians do not appear to even receive a copy of the test results for the tests they ordered for their patients and thus cannot meet the same standard practice of in person practice of medicine.

Connecticut General Statute Sec 20 -7

Sec. 20-7. Billing for clinical laboratory services. Cost of diagnostic tests. Financial disclosures to patients

(c) Each practitioner of the healing arts who (2) receives compensation or remuneration for referral of such patient to an entity which provides diagnostic or therapeutic services ***shall disclose such interest to any patient prior to referring such patient to such entity for diagnostic or therapeutic services*** . . . Such information shall be verbally disclosed to each patient or shall be posted in a conspicuous place visible to patients in the practitioner's office. ***The posted information shall list the . . . diagnostic services from which the practitioner receives compensation or remuneration for referrals ...***

The “Doc in a Box”/Sham Rx Mechanism Used By Labs Violates CGS 20 -7

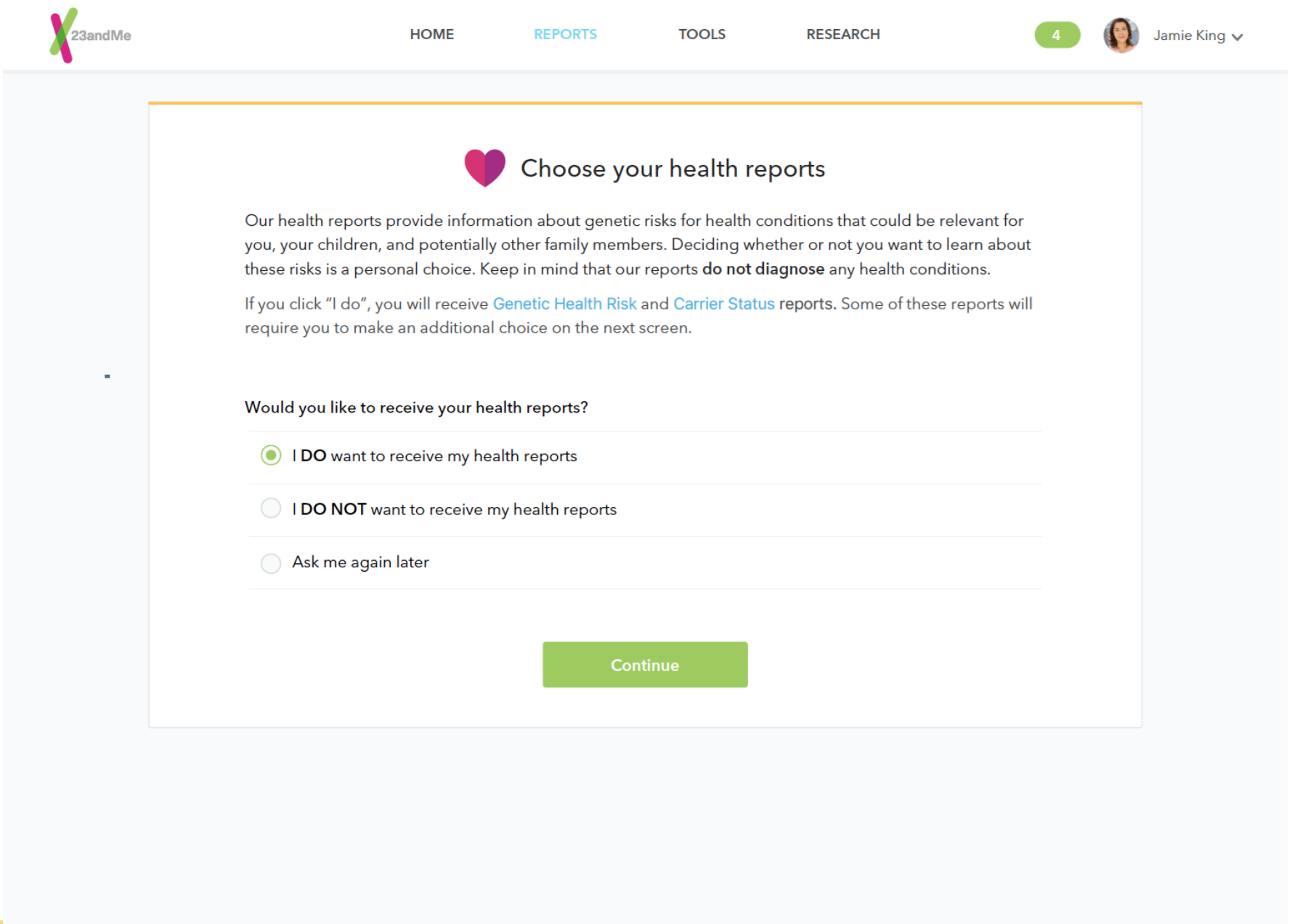
The financial disclosure requirements of CGS 20-7 are intended to alert patients to physician financial conflicts of interest prior to any prescription or order.

Most, if not all, of the labs using the Doc in Box/Sham RX model provide no interaction between patient and prescriber at all and therefore do not provide any opportunity for the Physician to disclose their financial relationships with the lab.

APPENDIX

23andMe Customer Experience – BRCA Example

Step 1: Choose to Opt in / out



Choose your health reports (continued)

Some of the reports below are about serious diseases that may not currently have an effective treatment or cure. Others may have effective treatment or prevention options, but these actions may carry their own health risks. If you tend to feel anxious or have ever been diagnosed with anxiety or depression, you may have more emotional difficulty with these reports. Also consider:

- Having a risk variant does not mean that you will definitely develop the condition.
- If you receive a "variant not detected" result, you could still have a genetic variant not included in the test.
- Knowing or telling others about your genetic risks could affect your ability to get some kinds of **insurance**. (Learn more about privacy **here**.)
- Genetic testing for these conditions in the general population is not currently recommended by **any** healthcare professional organizations. The Alzheimer's Association, a patient advocacy group, also does not recommend genetic testing for Alzheimer's disease in the general population.

If you do decide to view these reports, your reports will provide information about resources that may be helpful, including support groups, genetic counseling, and how to discuss results with family.

Would you like to receive the following reports?

Late-Onset Alzheimer's Disease Report Learn more	● Yes	○ No	○ Ask me again later
Parkinson's Disease Report Learn more	● Yes	○ No	○ Ask me again later
BRCA1/BRCA2 (Selected Variants) Report Learn more	● Yes	○ No	○ Ask me again later
MUTYH-Associated Polyposis Report Learn more	● Yes	○ No	○ Ask me again later

BRCA1/BRCA2 (Selected Variants)

Specific genetic variants in the BRCA1 and BRCA2 genes are associated with an increased risk of developing certain cancers, including breast cancer (in women and men) and ovarian cancer. These variants may also be associated with an increased risk for prostate cancer. This test includes three genetic variants in the BRCA1 and BRCA2 genes that are most common in people of **Ashkenazi Jewish** descent.

Consider the following when deciding whether or not to view this report:

- Most cases of breast, ovarian, prostate, and other cancers are not caused by inherited genetic variants. Factors such as lifestyle, environment, and family history are also important.
- About 1 in 40 Ashkenazi Jewish individuals has one of the three variants in this report. **These three variants are much less common in people of other ethnicities.** In 23andMe customers of other ethnicities, between 0% and 0.1% of individuals has one of the three variants in this report.
- The report does **not** include all variants in the BRCA1 and BRCA2 genes linked to hereditary breast, ovarian, and prostate cancer. More than 1,000 variants in the BRCA1 and BRCA2 genes are known to increase cancer risk. Only three of those variants are included in this report. Furthermore, this report does not include variants in other genes linked to hereditary cancers. People with a personal or family history of cancer should talk with a genetic counselor to determine if additional genetic testing is appropriate.
- Many people will receive a test report indicating that no genetic variants were detected. If you receive this result, it does **not** mean your cancer risk is reduced. You could still have a variant that is not included in this test. In addition, most cases of cancer are not caused by inherited genetic variants, so factors such as lifestyle, environment, and family history are also important. If you have a family history of cancer, it is important to talk with your doctor or a genetic counselor to understand how all of these factors, along with the results of this test, may impact your cancer risk.

- **BRCA1 cancer risks:** Women with a BRCA1 variant have a 45-85% chance of developing breast cancer by age 70 and a 39-46% chance of developing ovarian cancer by age 70. Men with a BRCA1 variant have a 1-2% lifetime risk of developing male breast cancer and may also have an increased risk for prostate cancer, although increased risk was not observed in some studies. Women and men with a BRCA1 variant may also have an increased risk for pancreatic cancer, and more research is needed to determine whether they have an increased risk for melanoma.

- **BRCA2 cancer risks:** Women with a BRCA2 variant have a 45-85% chance of developing breast cancer by age 70 and a 10-27% chance of developing ovarian cancer by age 70. Men with a BRCA2 variant have a 7-8% lifetime risk of developing male breast cancer and an increased risk for prostate cancer. Women and men with a BRCA2 variant may also have an increased risk for pancreatic cancer and melanoma.

- Results from this test should not be used to make medical decisions and should be confirmed in a clinical setting before taking any medical action. For people with a variant detected, preventive measures such as increased cancer screening and risk-reducing surgery or medication may be considered, in consultation with your doctor or another healthcare professional. These interventions can be life-saving and have the potential to greatly reduce the risk of developing certain types of cancer. Always consult with a healthcare professional before taking any medical action.

Step 2: View Education Module

EDUCATIONAL TUTORIAL

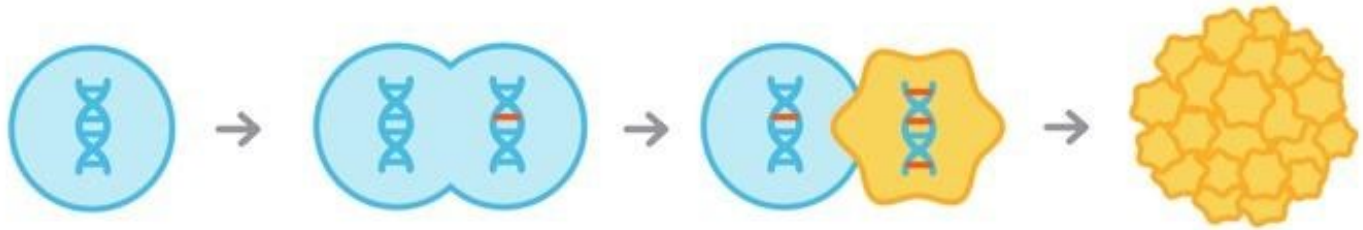
The **BRCA1/BRCA2 (Selected Variants)** report tests for genetic variants that increase a person's risk for cancer.

This report has some limitations that are important to understand. The following information explains what you can expect from the report, and what different results mean. For some people, getting genetic results related to cancer risk can be upsetting or cause anxiety. We encourage you to talk with a healthcare professional, such as a genetic counselor, if you need more support.

Start tutorial

Cancer results when cells divide and grow in an uncontrolled way.

This can be caused by DNA changes that occur by chance as our cells divide over time. This is why everyone has some risk of developing cancer.

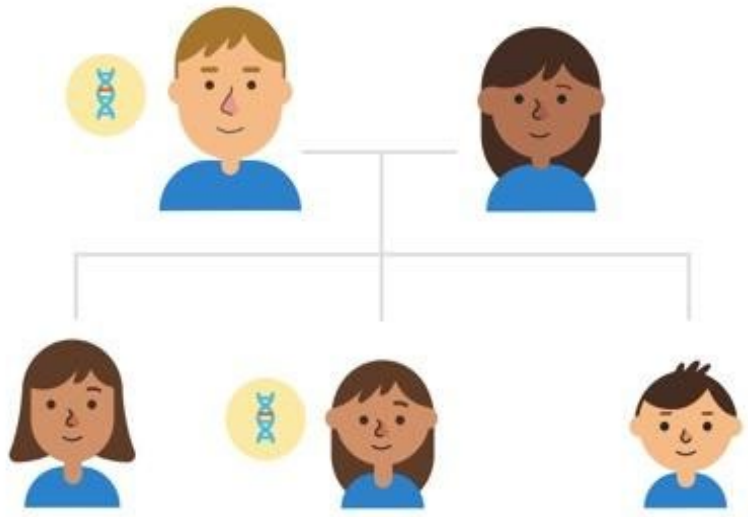


Back

Next

However, certain **inherited genetic variants** can also predispose cells to grow uncontrollably.

These variants increase a person's risk of developing cancer and can be passed down through families.



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If your report says you have a variant, it means you have an **increased risk** of developing certain cancers.

Women with these variants

have a greatly increased risk of developing breast and ovarian cancer. They may also have an increased risk for pancreatic cancer and melanoma.*

Men with these variants

have an increased risk of developing male breast cancer. They may also have an increased risk for prostate cancer, pancreatic cancer, and melanoma.*

* Learn more about these cancer risks

If you have this kind of result, it is important to follow up with a doctor or a genetic counselor, since there may be preventive options that are effective in reducing cancer risk. You should also think about sharing this information with your family members, since they may also have the risk variant.

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This report does **not** include all possible variants in the BRCA1 and BRCA2 genes.

More than 1,000 variants in the BRCA1 and BRCA2 genes are known to increase cancer risk. This report only includes three of those variants.

The three variants included in this report are most common in people of **Ashkenazi Jewish** descent.

This report does **not** include the majority of variants found in people of other ethnicities.

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Other factors also influence your risk of developing cancer.

Age

Environment

Weight

Lifestyle & behavior

Family history

Variants in other genes

Some of these factors have a small effect on cancer risk, and others can have a large effect.

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So if you don't have one of the variants we tested, you still have a risk of developing cancer.

In fact, **most** cases of cancer are not caused by the genetic variants in this report. A person could have a variant not included in this test, or could develop cancer due to other factors. A genetic counselor can help you understand how both genetic and non-genetic factors may influence your risk of developing cancer.

Example: Breast cancers

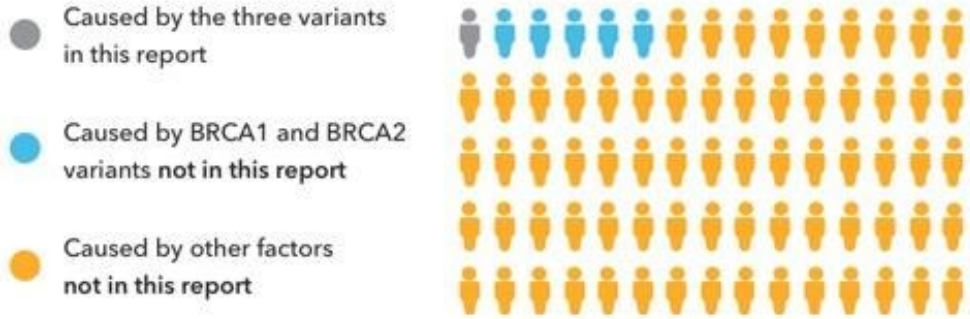

Image does not represent exact proportion of cancers

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Next

It's normal to have questions or concerns about your results.

Your doctor or a genetic counselor can help you understand what your results may mean for you, especially if you have a personal or family history of cancer. Your report will also provide information about resources and next steps.

Note that this test **does not diagnose cancer** or any other health conditions and is not a substitute for visits to a healthcare professional for recommended screenings. Results should not be used to make medical decisions. Results should be confirmed in a clinical setting before taking any medical action. Always consult with a healthcare professional before taking any medical action.

View Report

Step 3: Receive Report

BRCA1/BRCA2 (Selected Variants)

Specific genetic variants in the BRCA1 and BRCA2 genes are associated with an increased risk of developing certain cancers, including breast cancer (in women and men) and ovarian cancer. These variants may also be associated with an increased risk for prostate cancer and certain other cancers. This test includes three genetic variants in the BRCA1 and BRCA2 genes that are most common in people of Ashkenazi Jewish descent.

Overview | Scientific Details | Frequently Asked Questions

US, you do not have the three genetic variants we tested.

However, more than 1,000 variants in the BRCA1 and BRCA2 genes are known to increase cancer risk, so you could still have a variant not included in this test. In addition, most cases of breast and ovarian cancer are not caused by inherited variants, so women without a variant are still at risk of developing these cancers. It's important to continue with any cancer screenings your healthcare provider recommends.


23andMe®