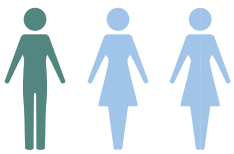
Ambry Genetics

WHITE PAPER

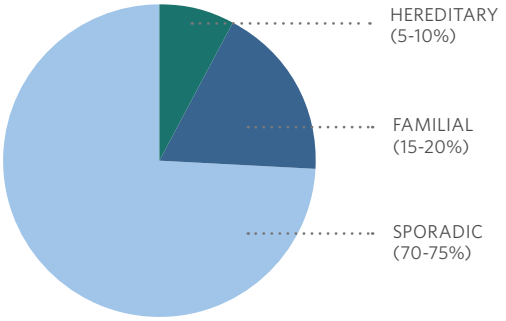
Why Test for Hereditary Cancer in Preventive Care?

Millions of people are sidelined by cancer. Wouldn't it be worth it for your patients to know their risk?

BACKGROUND



More than **1 in 3 men and women** in the United States will be diagnosed with cancer in their lifetime[1], making it a common concern in the primary care setting. 5-10% of cancer is hereditary; however most cancer is sporadic.



Sporadic Cancer	Familial Cancer	Hereditary Cancer
• Due to chance • Typically diagnosed at older ages (>50) • Occurs in one person (or two distantly related family members) • Little/no family history of cancer	• Due to genes and/or other shared factors (*e.g.* lifestyle, environment) • Often diagnosed at older ages • Some clustering of cancer in a family	• Due to inherited change (mutation) in a gene, which can run in families • Often diagnosed at younger ages (<50) • Strong clustering of cancer in a family, often in multiple generations

GENETIC TESTING FOR HEREDITARY CANCER

Germline genetic testing for hereditary cancer analyzes the DNA sequence within genes that are associated with cancer and can be passed from parent to child. The purpose is to look for small changes (mutations) within a gene, which may cause an increased risk for certain types of cancer. This testing is most often completed using a blood or a saliva sample.

WHO NEEDS GENETIC TESTING?

Genetic testing has the power to identify someone at increased risk for various cancers, allowing early steps for cancer prevention. Certain signs of hereditary cancer, listed below, can help identify patients who may benefit from genetic testing. Published guidelines (*e.g.* National Comprehensive Cancer Network® or NCCN®)[2,3] include clinical testing criteria helps, which can also guide you on when to offer testing to your patients.

Signs of Hereditary Cancer

If your patient or their family members have any of the following signs* for hereditary cancer, consider genetic testing:

MULTIPLE	• ≥3 cancers on the same side of the family • ≥2 primary cancers in the same person • ≥ 10 colorectal polyps
YOUNG	Any of the following cancers diagnosed <50y: Breast, colorectal, uterine
RARE	Personal or family history of any of the following: Male breast cancer, ovarian cancer

**Adapted from published genetic testing guidelines*

WHY DO GENETIC TESTING?

- **Early Detection:** Individualize your patient's cancer screening recommendations to his/her specific cancer risk
- **Prevention:** Offer preventive surgical options to reduce cancer risk
- **Treatment:** Tailor treatment recommendations to genetic test results, if your patient develops cancer
- **Family:** Access appropriate cancer screening by identifying those at increased risk for cancer

What about Genetic Counseling?

Genetic counseling helps people understand and manage the medical, psychological and familial implications of genetic contributions to disease.[4] If you are discussing genetic testing for hereditary cancer with your patient, genetic counseling may also be required by his/her insurance company. Your Ambry representative can give you information about third-party genetic counseling services. Ambry also has more than 100 genetic counselors on staff to help you throughout the testing process.

Things to Consider

Genetic testing has pros and cons and is a personal decision for your patient. Have a discussion with your patient before testing is done. Some things for your patient to consider may include: testing limitations (not every cancer gene is known or analyzed with a test), potential for genetic discrimination (available laws, like the Genetic Information Nondiscrimination Act (GINA)[5], may help), and impact on family dynamics.

How Does Genetic Testing Change Outcomes?

Genetic testing can increase survival rates because it allows individuals to make informed, personalized decisions about their medical management based on test results.

Breast and Ovarian Cancer Outcomes (*BRCA1/2* Mutation Carriers)

CANCER RISKS	• Up to 87% lifetime risk for breast cancer, up to 40% lifetime risk for ovarian cancer
MANAGEMENT RECOMMENDATIONS	• Increased breast cancer surveillance (mammogram, MRI) • Consider prophylactic mastectomy • Prophylactic salpingo-oophorectomy
RISK REDUCTION	• Several studies have shown that prophylactic mastectomy in *BRCA1/2* mutation carriers results in up to a 97% reduction in the risk for contralateral breast cancer.[6] • Salpingo-oophorectomy reduced ovarian cancer incidence by 69-100%[7]
SURVIVAL RATES	• Survival rates are significantly higher for *BRCA1/2* mutation carriers that chose prophylactic mastectomy (86-89%) compared to those who opt not to have surgery (66-71%).[6] • Salpingo-oophorectomy reduced all-cause mortality by 55-100%, respectively.[7]

Colorectal Cancer Outcomes (Patients with Lynch Syndrome)

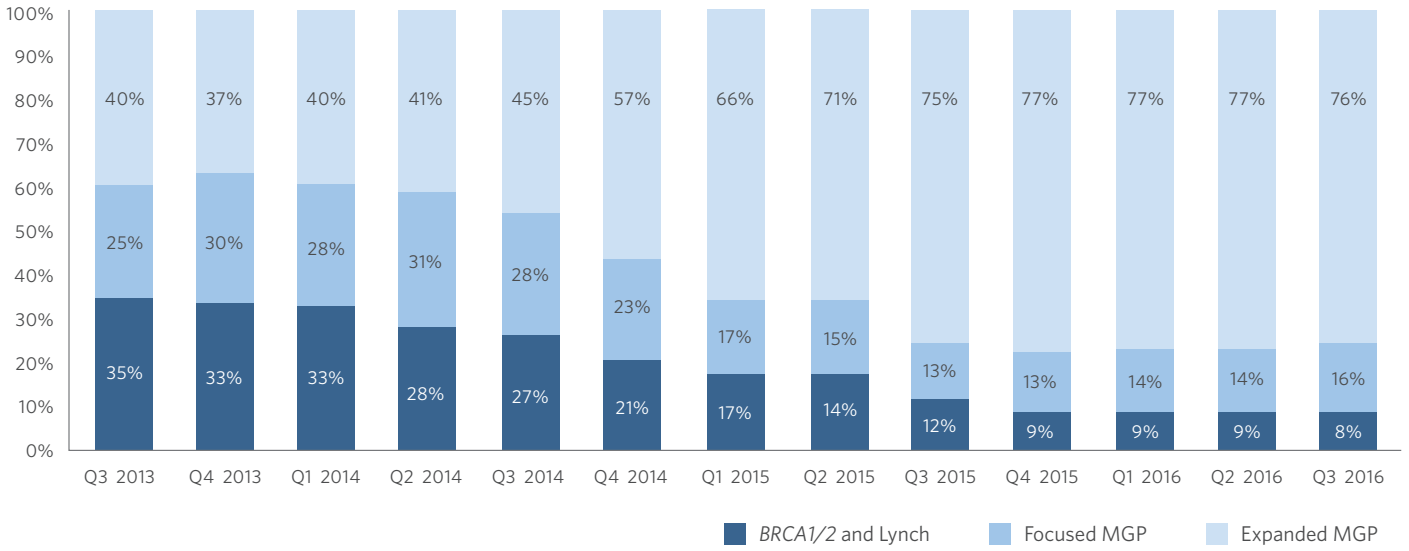
CANCER RISKS	• Up to 82% lifetime risk for colorectal cancer (as well as other cancers)
MANAGEMENT RECOMMENDATIONS	• Increased colorectal cancer surveillance (earlier and more frequent colonoscopies)
RISK REDUCTION	• A 15-year study found that colonoscopy screening at three year intervals in patients with Lynch syndrome reduces the risk for colorectal cancer by 62%[8]
SURVIVAL RATES	• The same study found that colonoscopy screening at three year intervals in patients with Lynch increases overall survival rates by about 65%[8]

Refer to NCCN® management guidelines for conditions beyond hereditary breast and ovarian cancer and Lynch syndrome. Testing beyond these genes via multigene panel testing may be critical for a complete risk assessment.

TRENDS SHOWING INCREASED USE OF MULTIGENE PANEL TESTING

Recent advancements have shifted clinical genetic testing from single gene testing to multigene panels (MGP), which cast a wider net to efficiently screen cancer susceptibility genes in high-risk families. Healthcare providers, including primary care physicians and OB/GYNs, are increasingly ordering multigene panel testing. An Ambry study looked at panel utilization over a three-year period based on submitted test orders from 2013-2016. Multiple specialties ordered focused and expanded multigene panels more frequently in 2016 (76%) compared to 2013 (40%), while single gene testing decreased.[9]

Hereditary Cancer Ordering Trends From 2013 to 2016



WHY MULTIGENE PANEL TESTING?

Multigene panels can capture unexpected mutations in other important genes that may not be clinically obvious, which can identify important cancer risks in a patient. Ambry collaborated in a study of >65,000 breast cancer patients who underwent multigene panel testing; mutations in genes other than *BRCA1* and *BRCA2* were identified in 6.2% of cases.[10] Other studies have supported these results, with one finding at least 7-11% of breast cancer patients without *BRCA1* and *BRCA2* mutations having a causative mutation in other high or moderate risk genes that would have been missed without multigene panel testing.[11-13]

Overall Benefits of Multigene Panels

- Efficient, cost-effective testing
- Can clarify a diagnosis when multiple cancer syndromes are suspected
- May identify a hereditary cancer syndrome in patients who do not clearly meet defined testing criteria
- May identify an unexpected, but clinically relevant gene mutation
- Helps to define the clinical spectrum of hereditary cancer syndromes

PRIMARY CARE: UNIQUELY POSITIONED FOR CANCER PREVENTION

A visit with their primary care physician or OB/GYN may be the only chance for a patient to be assessed for hereditary cancer and access genetic testing.

Of the nearly 966 million visits that Americans made to office-based physicians, 495.6 million (51.3%) were to primary care physicians.

51.3%

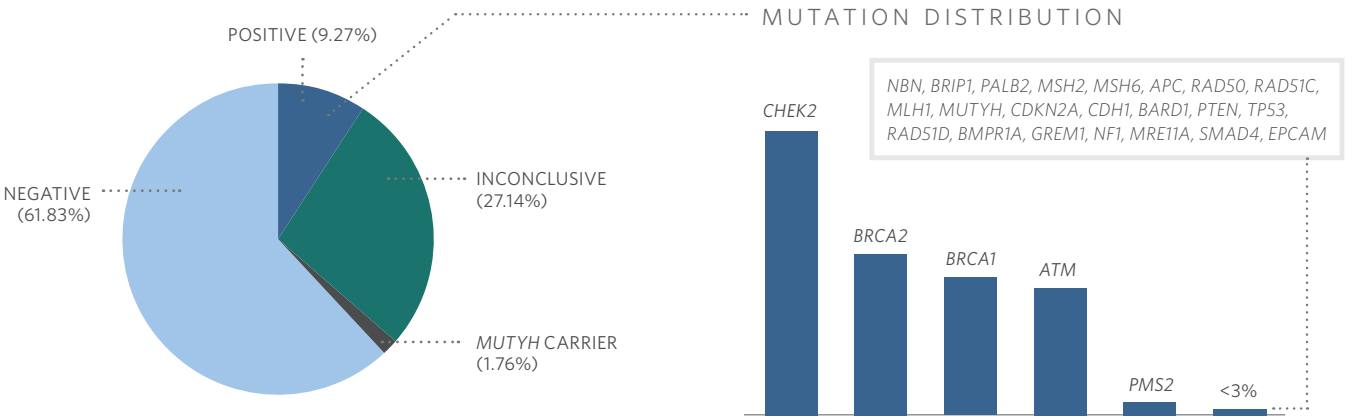
Women often visit only their OB/GYN for care, including general health checks.

Women between 45-64 years old[15]	12%	Women between 19-39 years old[16]	28.6%

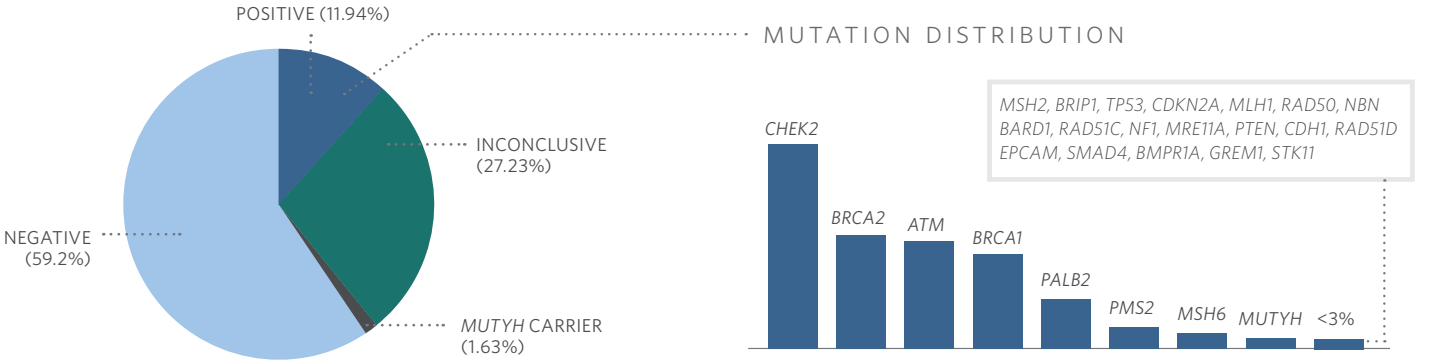
CANCERNEXT: GIVING YOU THE ANSWERS YOU NEED

Get ahead of disease with CancerNext, a quality, comprehensive genetic test for hereditary cancer that can help determine if your patients are at increased risk for various types of cancer. With more precise data to guide management, you can make timely, informed recommendations that promote early detection and cancer prevention for your at-risk patients.

CancerNext Data for Patients without a Personal History of Cancer



CancerNext Data for Patients with a Personal History of Cancer



ABOUT AMBRY

Ambry places value above all else through quality lab processes, confirmatory testing and advanced technology. We are constantly participating in numerous research studies and collaborations so we can better assess clinical validity of gene-disease relationships.[17] This is to ensure that the results healthcare providers receive are as accurate and informative as possible.

By identifying an inherited condition early on with genetic testing, we are given a chance to get in front of the disease with timely intervention, instead of treating it with expensive therapies after it has taken root, potentially impacting quality of life. The more information we have earlier on; the more choices we have to make timely actionable, value-based healthcare decisions.

Our mission is to get it right early on through our well-researched diagnostic tools and reporting processes. The more accurate reports we provide, the more insight healthcare professionals will have to better treat their patients.

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