riscover®
HEREDITARY CANCER

Result Navigator

Positive Test Result: *STK11*

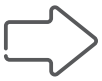
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic variant is a change in a gene that is known to cause increased risk for cancer. A likely pathogenic variant is a change in a gene that is very likely to cause increased risk for cancer.

After a positive test result, there can be many questions about what to do next.

This guide is a supplement to Riscover® Hereditary Cancer test results, helping patients and healthcare providers understand the results and together determine the best path forward.

Navigate Your Results

Learn | *page 2*
Review the test results along with this guide, and discuss the meaning of these results with your healthcare provider.



Plan | *page 3*
Develop a healthcare plan for early detection and prevention of specific cancers.

Share | *page 4*
Understand the risks for other family members, and consider how to inform relatives of their risks.

Connect | *page 5*
Reach out to medical experts and find local and national groups that can provide more information and support.

Glossary of Terms

Breast tomosynthesis: Advanced three-dimensional (3-D) breast imaging.

Colonoscopy: Visual exam of the inside of the colon with a flexible, lighted tube inserted through the rectum.

Gene: A section of DNA with a specific job.

Mastectomy: Surgical removal of the breast tissue.

MRI: An abbreviation for magnetic resonance imaging, a test that provides detailed pictures of a specific part of the body.

Pathogenic: Causing or capable of causing disease.

Risk: The chance, or possibility, of developing a disease.

Variant: A change, or "misspelling," in the DNA sequence. Variants can be benign (not associated with disease), pathogenic (associated with disease), or of uncertain significance.

Your Diagnosis: Peutz-Jeghers Syndrome

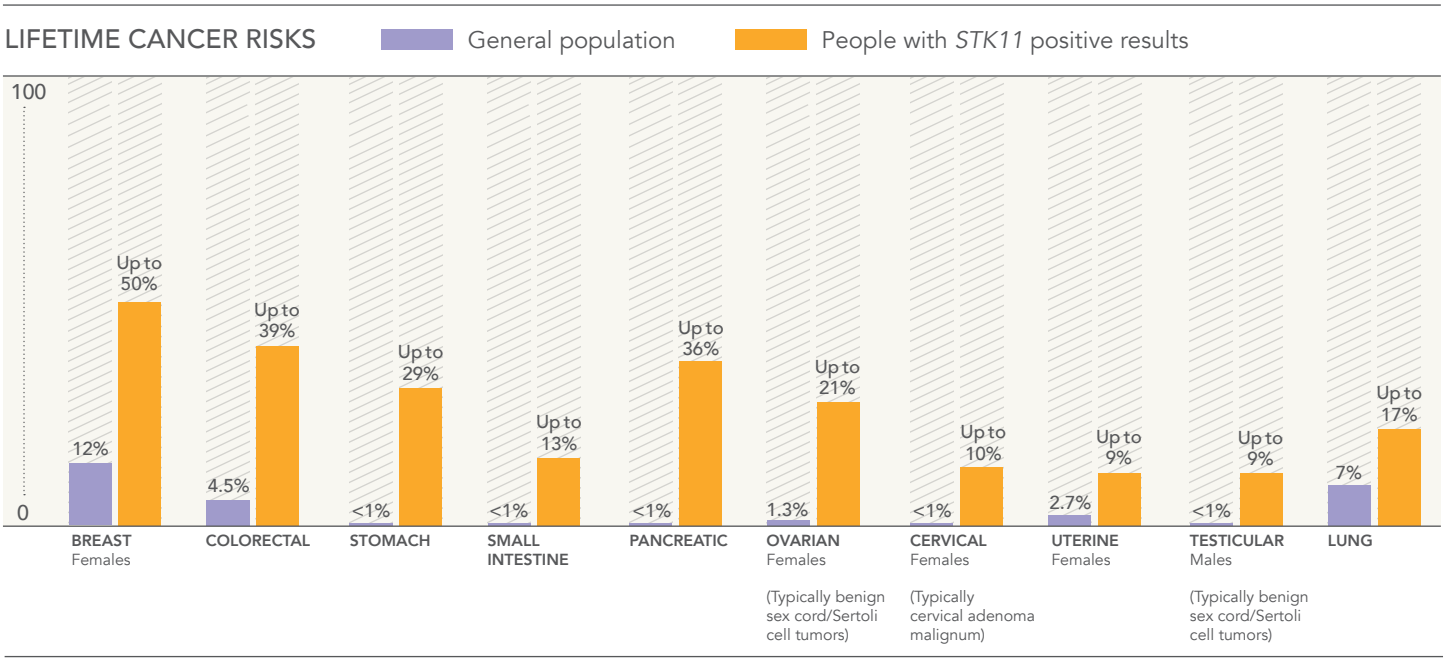
Pathogenic/likely pathogenic variants in the *STK11* gene cause an inherited cancer disorder called Peutz-Jeghers syndrome. People with Peutz-Jeghers syndrome (PJS) have an increased lifetime risk of breast, colon, stomach, small intestine, pancreatic, cervical, uterine, and lung cancers/tumors. Females with this syndrome are at risk for sex cord tumors (tumors that originate from the ovaries). Males occasionally develop tumors of the testes that secrete estrogen, and can lead to gynecomastia (development of breast tissue), advanced skeletal age, and short stature, if untreated.

In addition to cancer, PJS is associated with mucocutaneous hyperpigmentations (dark blue to dark brown spots around the mouth, eyes, nostrils, fingers, and/or perianal area). These spots typically fade as a person gets older, and may not be noticed at all. Gastrointestinal polyps are also common in people with PJS, and can result in chronic bleeding, anemia (low red blood cell count), and recurrent bowel obstructions.

About 1 in 25,000 to 1 in 280,000 people in the general population are estimated to have a *STK11* pathogenic variant, and a diagnosis of PJS.

Your Risk

Not all people with positive test results will develop cancer, but the chance for cancer is higher than the general population risk. The graphs below show how much the risk for cancer increases when a pathogenic variant is found. The cancer risks are presented in ranges based on multiple studies of families who have a pathogenic variant. There is not enough evidence available to give a specific risk to a person or family.



Your Screening and Management Options

Listed below are the intervention options that are recommended by medical experts for individuals who carry this cancer gene variant. Your healthcare provider can explain these options in more detail, and together you can make a plan for cancer prevention and/or early detection.

BREAST CANCER (FEMALES)	
Breast self-exams	Periodic, consistent breast self-exams at the end of your period may be considered.
Clinical breast exam	A clinical breast exam performed by your healthcare provider is recommended every 6 months, starting at age 25.
Breast MRI	An annual breast MRI is recommended starting at age 25, or earlier if you have a family history of breast cancer diagnosed before age 30.
Mammogram	Annual mammograms with consideration for breast tomosynthesis are recommended starting at age 30 or earlier based on your family history of breast cancer.
Risk-reducing mastectomy	There is not enough evidence for risk-reducing mastectomy to be routinely recommended. Managed based on family history.
COLORECTAL CANCER	
Colonoscopy	A colonoscopy is recommended every 2 – 3 years beginning during the late teenage years.
STOMACH CANCER	
Upper endoscopy	An upper endoscopy is recommended every 2 – 3 years beginning during the late teenage years.
SMALL INTESTINE CANCER	
A CT or MRI enterography	A CT or MRI enterography or video endoscopy baseline is recommended at age 8 – 10 with follow up interval based on findings but at least by age 18, then every 2 – 3 years based on individual symptoms.
PANCREATIC CANCER	
Magnetic resonance cholangiopancreatography or endoscopic ultrasound	Magnetic resonance cholangiopancreatography or endoscopic ultrasound is recommended every 1 – 2 years beginning between 30 – 35 years of age or 10 years prior to the earliest diagnosis in the family (both ideally performed at a center of expertise).
OVARIAN, CERVICAL, AND UTERINE CANCERS/TUMORS (FEMALES)	
Annual pelvic examination and Pap smear	Annual pelvic examination and Pap smear are recommended beginning between 18 – 20 years of age.
TESTICULAR CANCER/TUMOR (MALES)	
Annual testicular exam and observation for feminization changes	An annual testicular exam and observation for feminization changes is recommended beginning at age 10.
LUNG CANCER	
Provide education about symptoms and smoking cessation.	Your healthcare provider can recommend screening options based on your personal and family history of lung cancer.

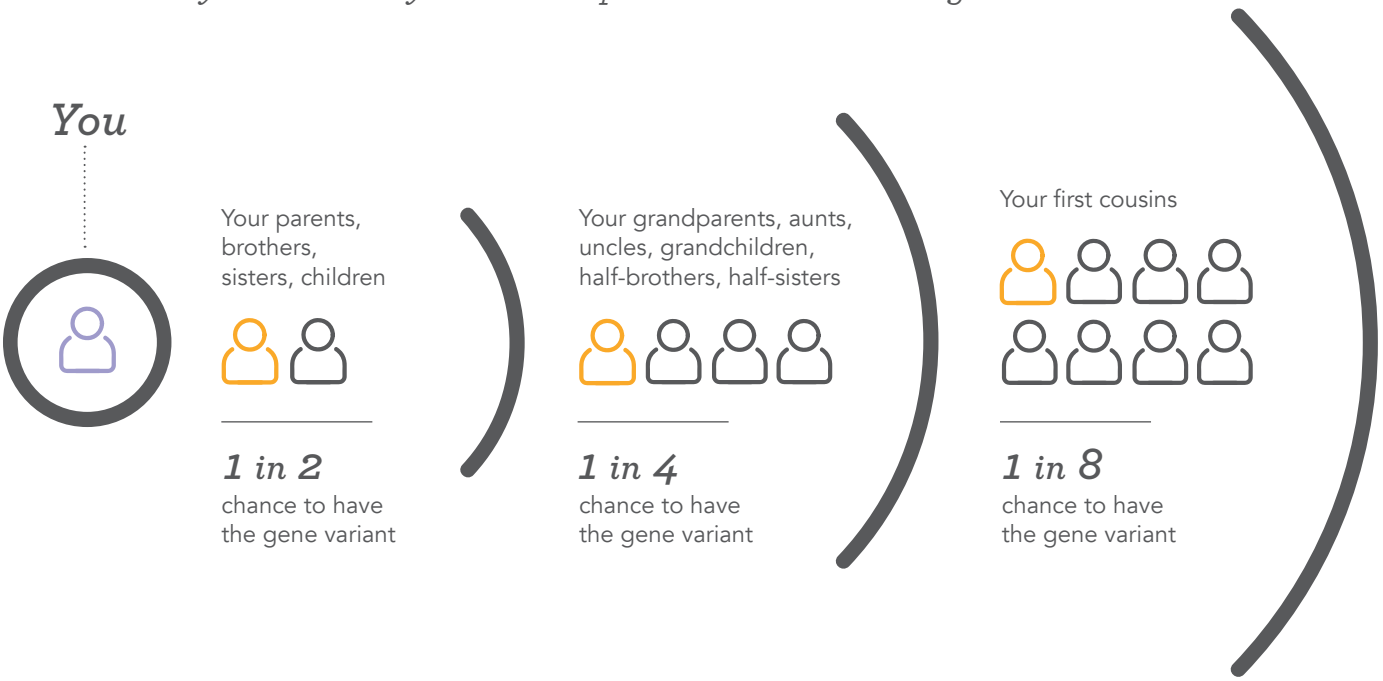
Your Family Matters

Cancer gene variants are inherited in an autosomal dominant manner. This means that when a parent tests positive, each child has a 1 in 2 chance to inherit the variant. Some people who inherit the variant will develop cancer, and some will not, but the risks are significantly increased compared to the average person. People in the same family may develop different types of cancers at varying ages, and the pattern of cancer and age of onset can differ from family to family.

Gene variants can be passed through families for many generations. When a gene variant is identified in one person in the family, relatives can be tested for just that variant. Sharing information about test results with family members is important, because it allows them to make informed choices about their healthcare and to decide whether they want genetic testing.

Some people who have pathogenic and likely pathogenic variants are interested in learning how to avoid passing these variants on to their children. If you are planning to have a child, you may wish to consult with a reproductive medicine specialist to discuss all of your reproductive options, including use of an egg or sperm donor, preimplantation genetic diagnosis, and prenatal genetic testing.

The likelihood for family members to carry the same gene variant depends on how closely related they are to the person with a known gene variant.



Your Expert Team

As you take your next steps, it can help to have a team of experts on your side. This team may include your primary care provider and a number of specialists who will help along the way.

If you haven't already done so, you may wish to speak with a genetic counselor. Genetic counselors are healthcare professionals with specialized training in medical genetics and counseling. They can help you understand your test results, discuss your healthcare plan, and connect to other resources in your area. Your healthcare provider may be able to provide a referral to a local genetic counselor. You can also find a genetic counselor through the National Society of Genetic Counselors at www.nsgc.org.

For questions about your test results, our genetic counseling team is available to help.
To reach a genetic counselor, call +1 855-293-2639 and select option 3.

Helpful Resources

GeneReviews
ncbi.nlm.nih.gov/books/NBK1266
A detailed clinical summary of Peutz-Jeghers syndrome written for healthcare providers.

National Comprehensive Cancer Network (NCCN)
nccn.org
Expert guidelines for cancer screening and treatment. Versions available for both providers and patients.

Facing Our Risk of Cancer Empowered (FORCE)
facingourrisk.org
A patient advocacy group whose mission is to improve the lives of individuals and families affected by hereditary breast, ovarian, and related cancers

Familial Adenomatous Polyposis Foundation
hcctakesguts.org
A nonprofit organization serving the hereditary colorectal cancer community that includes resources for patients and healthcare providers.

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