riscover®
HEREDITARY CANCER

Result Navigator

⊕ Positive Test Result: *APC*

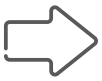
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic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

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

Colectomy: Surgery to remove the colon.

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

Endoscopy: Using an endoscope (a tube-shaped tool that includes a light, camera, and small tools to remove polyps or other tissues) to look in the body at the inside of organs such as the stomach or intestines.

Gene: A section of DNA with a specific job.

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

Mutation: A change in a gene that causes or is capable of causing disease. Another word for pathogenic/likely pathogenic variants.

Pathogenic: Causing or capable of causing disease.

Polyp: An abnormal growth of cells that can become a cancer tumor.

Polyposis: The growth of a large number of polyps.

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

Sigmoidoscopy: Visual exam of the last part of the colon and rectum using an endoscope.

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.

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Your Diagnosis: *APC*-Associated Polyposis

Positive *APC* results are associated with a group of inherited disorders called *APC*-associated polyposis conditions. These conditions are associated with a very high lifetime risk of colorectal cancer, most often due to having hundreds to thousands of colorectal polyps. People with *APC* pathogenic variants are also at increased risk for brain cancer (medulloblastoma), liver cancer (hepatoblastoma), stomach and small bowel cancer, thyroid cancer, and pancreatic cancer.

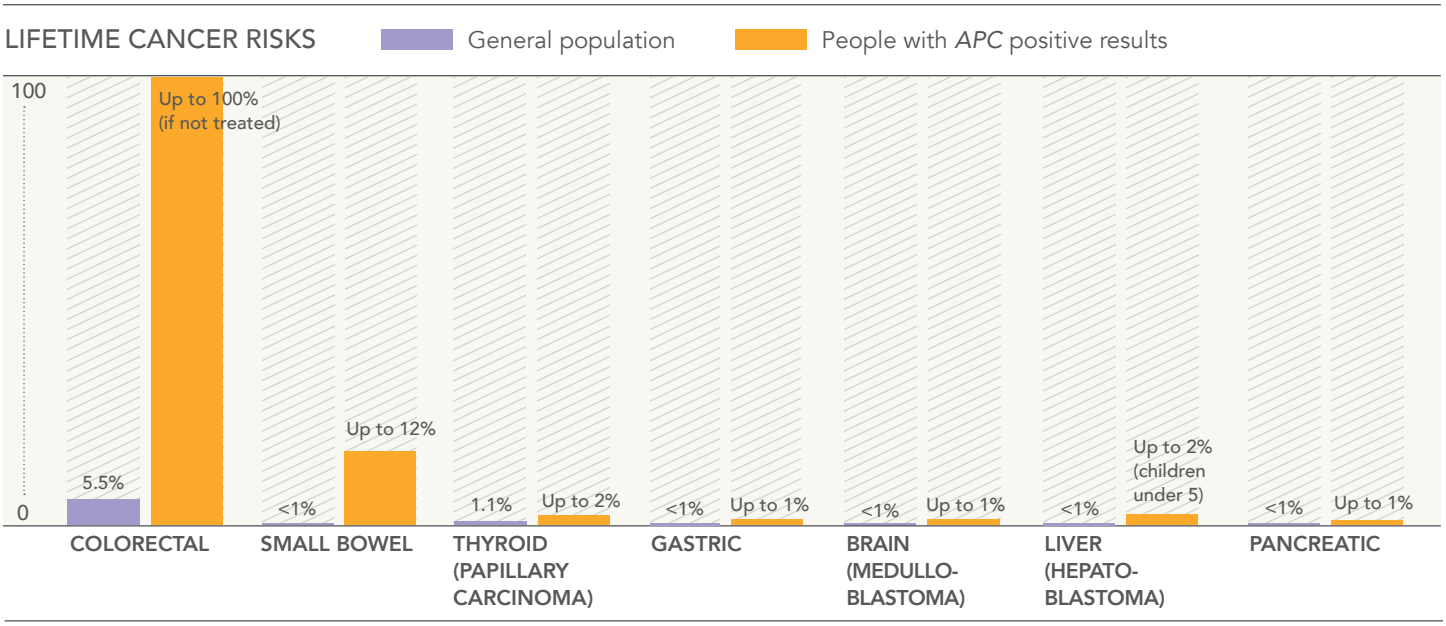
Some people with *APC* pathogenic variants have other clinical signs and symptoms unrelated to cancer. These include duodenal polyps, osteomas (bony growths), dental abnormalities (extra teeth, missing teeth, cysts), abnormalities on eye examination, thyroid disease, and other noncancerous growths (desmoid tumors, adrenal masses, epidermoid cysts/fibromas).

Depending on the combination of signs and symptoms, people may be given one of the following clinical diagnoses associated with an *APC* variant: familial adenomatous polyposis (FAP), attenuated FAP (a milder form), Gardner syndrome, or Turcot syndrome.

About 1 in 31,000 to 1 in 43,000 people have a positive *APC* result. Some people with pathogenic variants in the *APC* gene have a family history consistent with the disorder, but about 1 in 3 people are the first in their family to be affected.

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.



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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.

COLORECTAL POLYPS/CANCER	
Classic FAP: Colonoscopy/flexible sigmoidoscopy	An annual colonoscopy (preferred) or flexible sigmoidoscopy is recommended starting between the ages of 10 – 15 years.
Attenuated FAP: Colonoscopy	A colonoscopy (preferred) is recommended every 2 – 3 years beginning at diagnosis or during the late teenage years. When polyps are present, screening frequency increases to every 1 – 2 years.
Medication	Your healthcare provider may recommend medication to decrease polyp burden, based on your individual situation.
Colectomy	Colectomy (surgical removal of the colon) is recommended based on your individual situation.
Endoscopic evaluation of the rectum	If a colectomy is performed, an endoscopic evaluation of the rectum is recommended every 6 – 12 months.
SMALL BOWEL AND GASTRIC CANCERS	
Upper endoscopy	An upper endoscopy is recommended every 4 years beginning between the ages of 20 – 25 years, or earlier if colectomy is performed before age 20. When polyps are present, screening frequency should increase depending on polyposis stage.
Surgery for fundic/non-fundic gland polyps	A surgery for fundic/non-fundic gland polyps may be considered in the event of high-grade dysplasia.
CT or MRI of small bowel	CT or MRI of the small bowel is recommended based on your individual situation in the case of advanced polyposis.
INTRA-ABDOMINAL DESMOIDS	
Abdominal palpation	An annual abdominal palpation performed by your healthcare provider is recommended.
Abdominal MRI or CT	If there is a family history of symptomatic desmoids, consider an abdominal MRI or CT within 1 – 3 years post-colectomy and then every 5 – 10 years.
THYROID CANCER	
Thyroid exam	An annual physical thyroid examination performed by your healthcare provider is recommended, beginning in the late teens.
Thyroid ultrasound	An annual thyroid ultrasound is considered on an individual basis.
BRAIN CANCER	
Physical examination	An annual physical exam by your healthcare provider to examine for any evidence of cancer is recommended.
LIVER CANCER	
Liver palpation, abdominal ultrasound, and measurement of AFP	Liver palpation, abdominal ultrasound, and measurement of AFP are recommended every 3 – 6 months until age 5 years, for children with an affected parent (50% risk) or known to have an inherited pathogenic variant.
PANCREATIC CANCER	
No specific guidelines	Your healthcare provider can recommend screening options based on your personal and family history of pancreatic cancer.

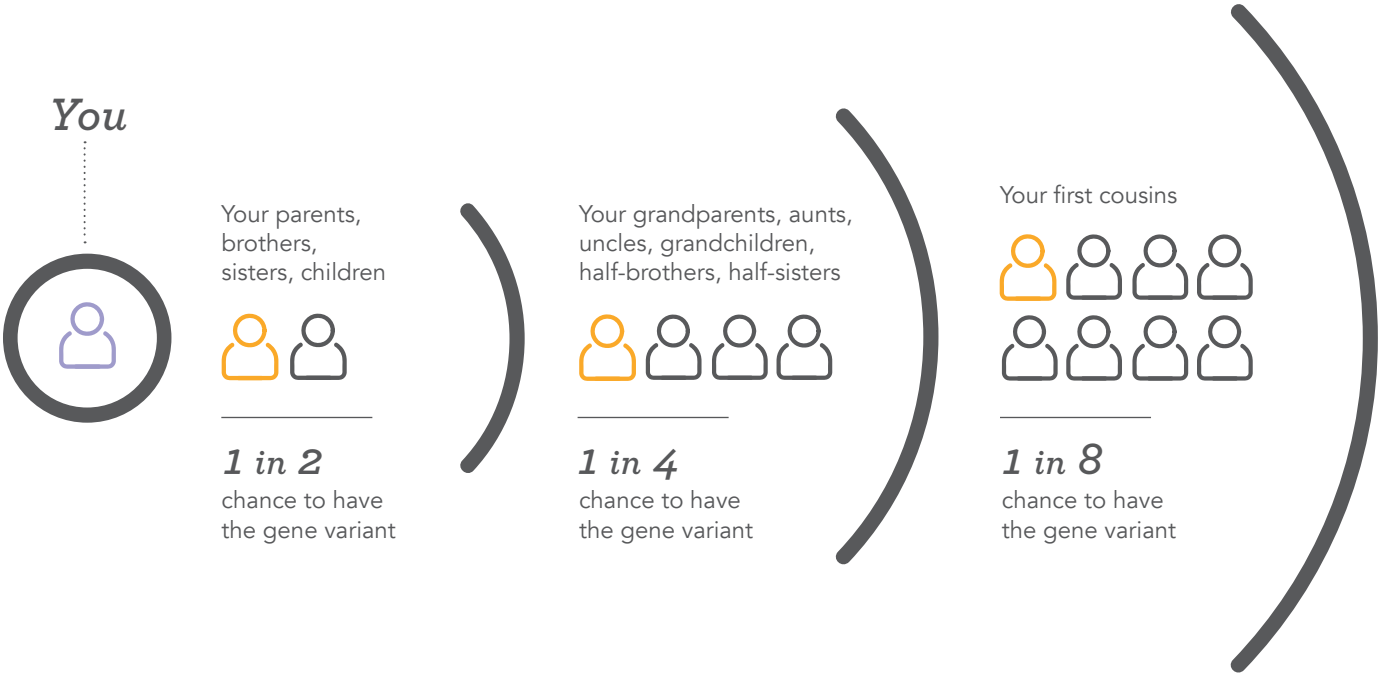
Your Family Matters

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, Progenity's 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/NBK1345
A detailed clinical summary of *APC*-associated polyposis conditions 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.

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

REFERENCES

National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal (Version 1.2017). Available from: http://www.nccn.org/.

Jasperson, K, Burt, R. APC-Associated Polyposis Conditions. 1998 December 18 [Updated 2014 March 2014]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1345/

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