riscover®
HEREDITARY CANCER

Result Navigator

Inconclusive (VUS) Test Result: *APC* (I1307K or c.3920T>A)

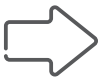
An inconclusive result happens when testing identifies a change in your DNA that is not clearly positive or negative. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. Inconclusive results can change over time as new evidence becomes available from research. For now, there is limited clinical evidence suggesting an increased cancer risk associated with this variant.

After an inconclusive test result, there can be 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 2*
Develop a healthcare plan for early detection and prevention of specific cancers.

Share | *page 3*
Understand the risks for other family members, and consider how to inform relatives of their risks.

Connect | *page 4*
Reach out to medical experts and find local and national groups that can provide more information and support.

Glossary of Terms

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.

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.

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.

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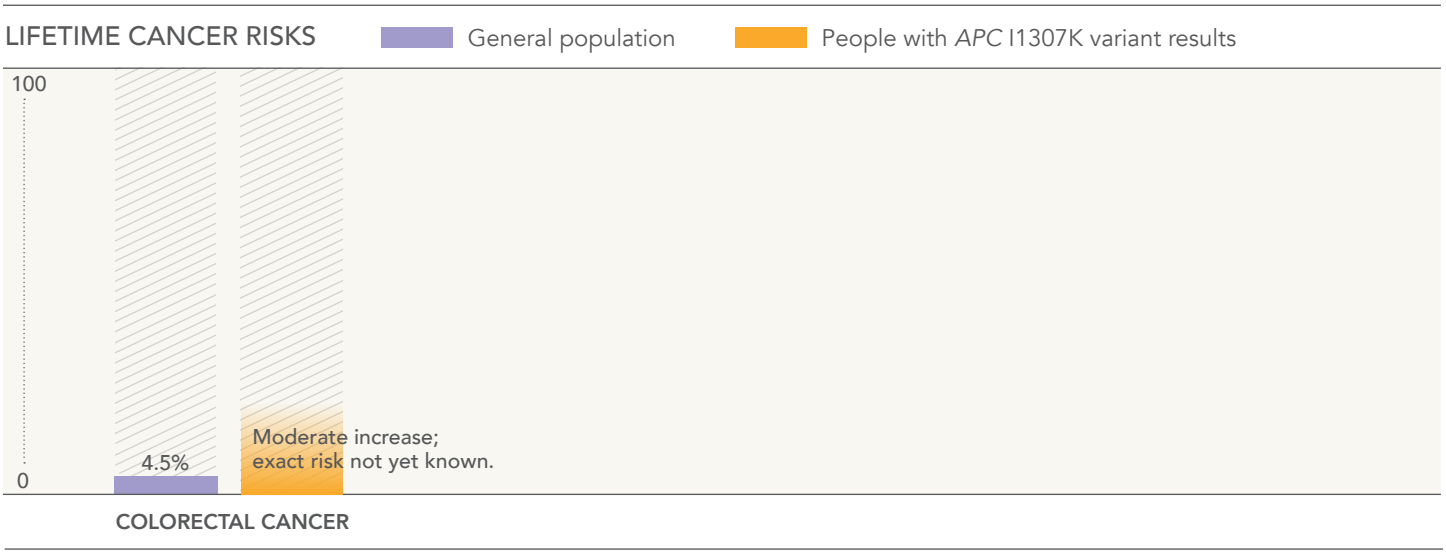
Your Diagnosis: *APC* I1307K Variant

The *APC* I1307K (c. 3920T>A) variant is considered a variant of uncertain significance (VUS) result at this time. It may be associated with a moderately increased risk for colorectal cancer. More research is ongoing to help learn more about this variant and its potential cancer risks. This particular variant is found in 6 – 7% of the Ashkenazi Jewish population.

Your Risk

For people with the *APC* I1307K variant, the chance for cancer may be higher than the general population risk. The graphs below show how much the risk for cancer increases when this variant is found. The cancer risks are presented in ranges based on multiple studies of families who have this *APC* variant. There is not enough evidence available to give a specific risk to a person or family.



Plan

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 CANCER	
Colonoscopy	A colonoscopy every 5 years is recommended starting at age 40, or 10 years prior to the age of the first colorectal cancer diagnosis in an affected first-degree relative.

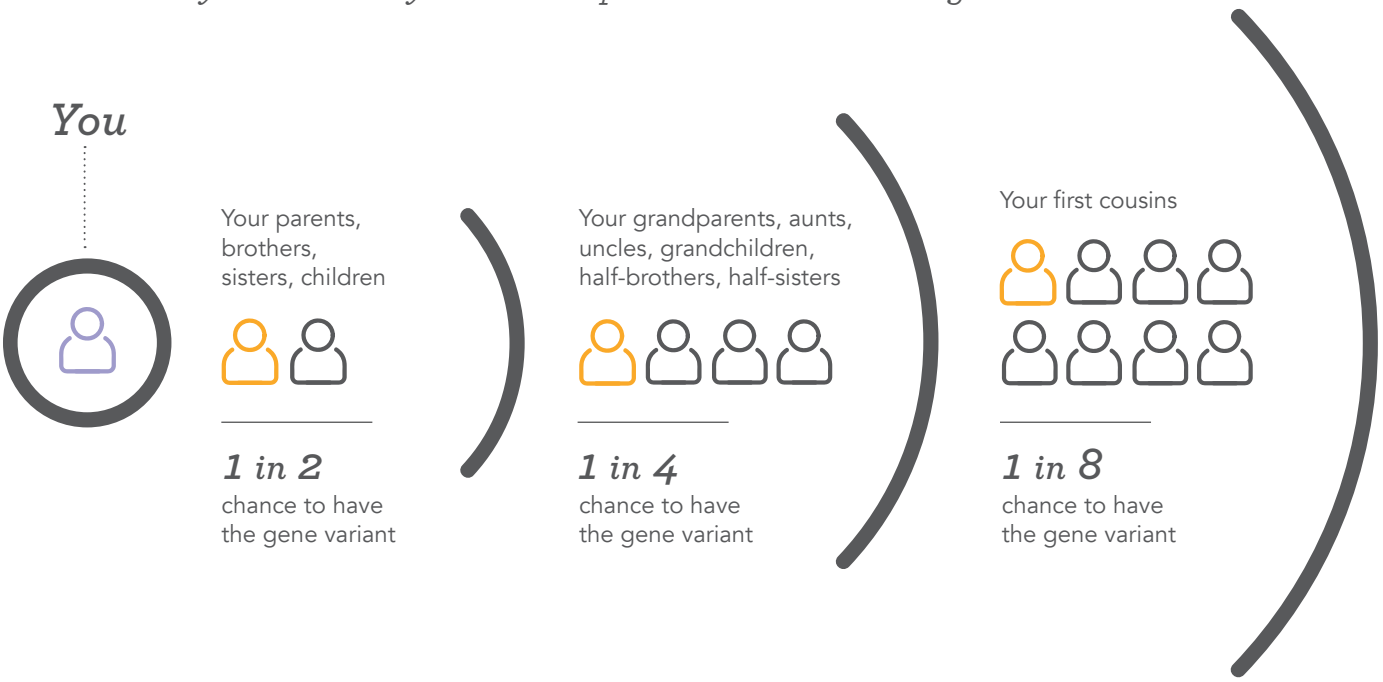
Your Family Matters

Cancer gene variants are inherited in an autosomal dominant manner. This means that when a parent has this variant, 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 this variant 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.



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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. Information available for both healthcare 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 3.2017). 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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