riscover®
HEREDITARY CANCER

Result Navigator

Positive Test Result: *RAD51C*

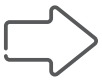
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic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

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.

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

Salpingo-oophorectomy: Surgical removal of the ovaries and fallopian tubes.

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

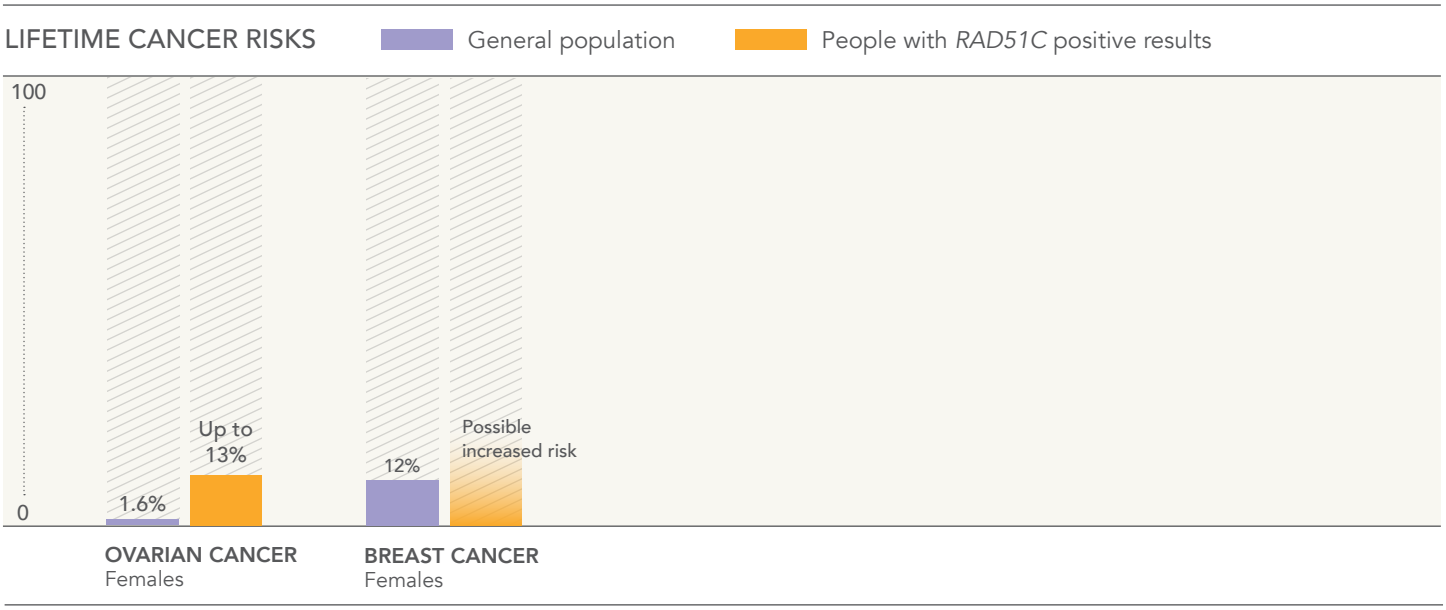
Women with pathogenic variants in the *RAD51C* gene have an increased lifetime risk of ovarian cancer. Also, several families with pathogenic variants in the *RAD51C* gene have been reported with a family history of breast cancer in women.

RAD51C is a relatively newly discovered cancer predisposition gene, and the frequency of individuals with pathogenic variants in the *RAD51C* gene is unknown. Management guidelines and associated cancers may change with the identification of more individuals with pathogenic variants in this gene. As with any individual that has a strong family history of cancer, surveillance should be tailored based on their personal and family history in addition to established guidelines.

Prior to being identified as a cancer predisposition gene, *RAD51C* was identified as the cause of Fanconi Anemia Type O. This disorder is diagnosed when an individual inherits pathogenic variants in the *RAD51C* gene from both parents, and is a rare complex disorder with multiple medical concerns including various early onset cancer risks. The risks described below are for a person with one *RAD51C* pathogenic variant, not a person with Fanconi Anemia Type O.

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.

OVARIAN CANCER (FEMALES)

Risk-reducing salpingo-oophorectomy (RRSO)	Consider removal of the ovaries and fallopian tubes, typically performed between 45 – 50 years of age, or earlier based on family history.

BREAST CANCER (FEMALES)

Breast self-exams	Periodic breast self-exams at the end of your period are suggested starting at age 18.
Clinical breast exam	A physical breast exam performed by your healthcare provider is recommended every 6 to 12 months, starting at age 25.
Breast MRI	Your healthcare provider may consider a breast MRI based on your personal and family history.
Mammogram	Your healthcare provider can recommend mammography options based on your personal and family history.

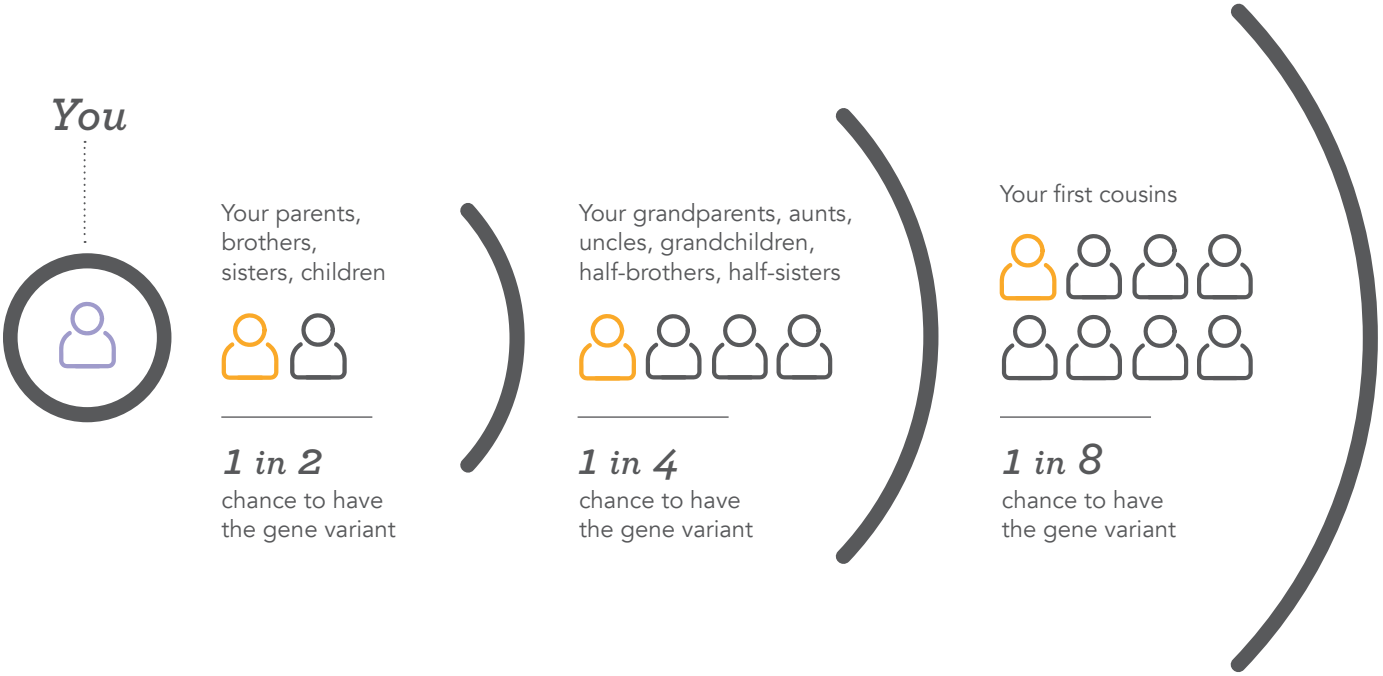
Your Family Matters

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.



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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

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.

REFERENCES

Alter BP, Kupfer G. Fanconi Anemia. 2002 Feb 14 [Updated 2013 Feb 7]. 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/NBK1401

National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian (Version 1.2018). Available from: http://www.nccn.org/.

Song H, Dicks E, Ramus SJ, et al. Contribution of Germline Mutations in the RAD51B, RAD51C, and RAD51D Genes to Ovarian Cancer in the Population. J Clin Oncol. 2015 Sep 10;33(26):2901-7.

Toss A, Tomasello C, Razzaboni, et al. Hereditary Ovarian Cancer: Not Only BRCA 1 and 2 Genes. Biomed Res Int. 2015;2015:341723.

Tung N, Domchek SM, Stadler Z, et al. Nat Rev Clin Oncol. 2016 Sep; 13(9):581–8. DOI: 10.1038/nrclinonc.2016.90. Epub 2016 Jun 14

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