

Result Navigator

⊕ Positive Test Result: BRCA2

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

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

CA-125: A substance that can indicate the development of ovarian cancer. Testing for CA-125 is performed on a blood sample.

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.

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.

Transvaginal ultrasound: An imaging test performed by inserting an ultrasound probe into the vagina to take detailed images 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.



Your Diagnosis: Hereditary Breast and Ovarian Cancer Syndrome

Hereditary breast and ovarian cancer syndrome (HBOC) is caused by a pathogenic variant in the *BRCA1* or the *BRCA2* gene. HBOC is an inherited disorder associated with an increased lifetime risk of breast, ovarian, pancreatic, prostate, and other types of cancer. Of all the genes associated with hereditary breast and ovarian cancer, *BRCA1* and *BRCA2* are the most common.

About 1 in 400 people in the general population will test positive for a *BRCA1* or *BRCA2* variant. About 1 in 40 people of Ashkenazi Jewish ancestry will test positive for a *BRCA1* or *BRCA2* variant. Three specific variants (called *BRCA1* c.68_69delAG, *BRCA1* c.5266dupC, and *BRCA2* c.5946delT) account for >98% of pathogenic variants in the Ashkenazi Jewish population.

People who have two pathogenic variants (one inherited from each parent) are affected with a condition called Fanconi anemia. This condition has different signs and symptoms. The cancer risks discussed here apply only to people with one pathogenic variant.

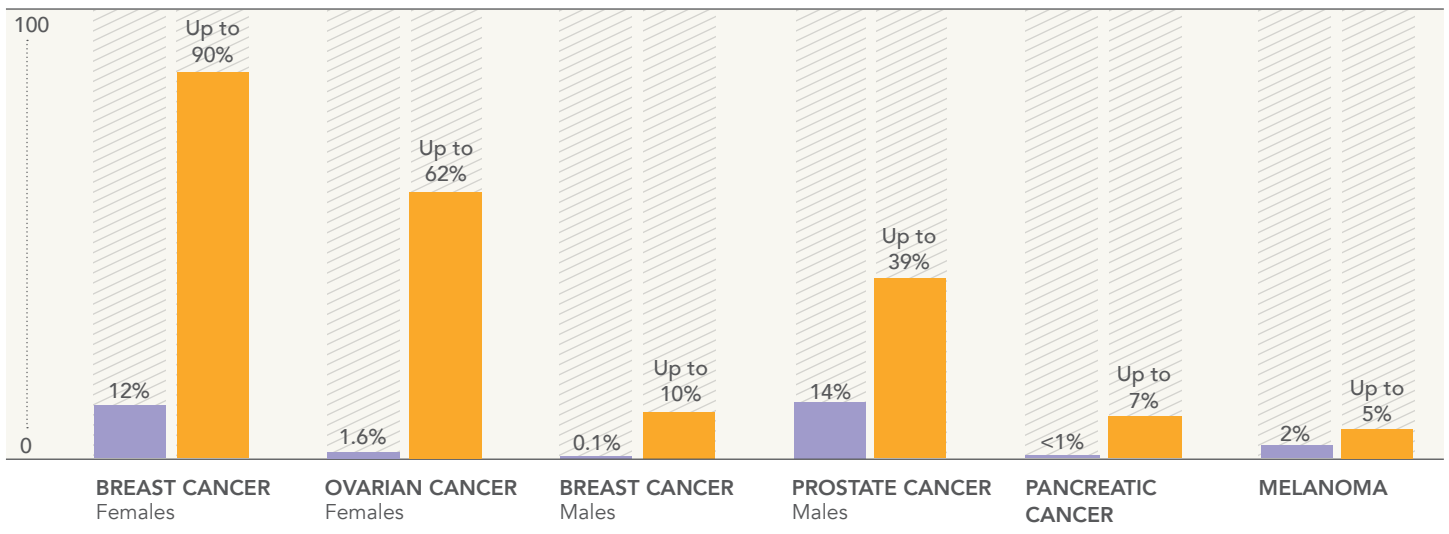
Your Risk

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.

LIFETIME CANCER RISKS

General population

People with *BRCA2* positive results



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)

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| 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 | 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. These are usually performed until age 75, and can be considered on an individual basis after that. |
| Mammogram | Annual mammograms with consideration for breast tomosynthesis are recommended starting at age 30 or earlier based on family history. These are usually performed until age 75, and can be considered on an individual basis after that. |
| Chemoprevention (i.e., tamoxifen) | Your healthcare provider may prescribe a medication to help prevent breast cancer, based on your individual situation. |
| Risk-reducing mastectomy | Risk-reducing mastectomy can be considered on an individual basis. |

OVARIAN CANCER (FEMALES)

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| Risk-reducing salpingo-oophorectomy (RRSO) | Removal of the ovaries and fallopian tubes, typically performed between 35 – 40 years of age, but could delay until age 40 – 45 or after a woman has had her last child. |
| Transvaginal ultrasound and serum CA-125 (at clinician discretion) | If RRSO is not performed, your healthcare provider may consider a transvaginal ultrasound to screen for ovarian cancer along with a blood test for cancer antigen 125 (CA-125) starting at age 30 – 35 years of age. |
| Risk-reducing medications (birth control pills) | Your healthcare provider may prescribe medication such as hormonal birth control pills to reduce risk for ovarian cancer, based on your individual situation. |

BREAST CANCER (MALES)

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| Breast self-exam | Regular self-exams are recommended starting at age 35. |
| Clinical breast exam | A physical exam performed by your healthcare provider is recommended every 12 months, starting at age 35. |

PROSTATE CANCER (MALES)

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| PSA blood test and digital rectal exam | A regular blood test for prostate-specific antigen (PSA) along with a digital rectal exam performed by your healthcare provider is recommended starting at age 45. |
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PANCREATIC CANCER

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| No specific guidelines | Your healthcare provider can recommend screening options based on your personal and family history of pancreatic cancer. |
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MELANOMA

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|------------------------|---|
| No specific guidelines | Your healthcare provider can recommend screening options based on your personal and family history of melanoma. |
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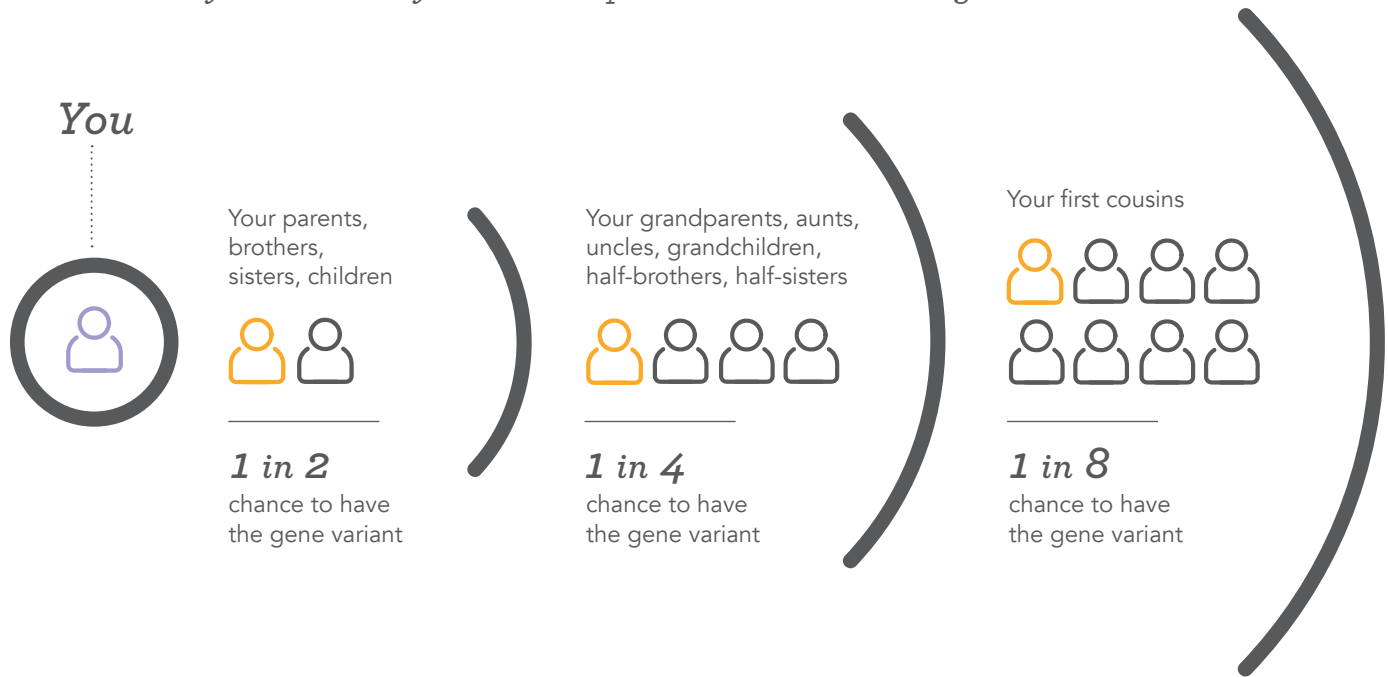
Your Family Matters

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/NBK1247

A detailed clinical summary of hereditary breast and ovarian cancer 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.

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.

Bright Pink

brightpink.org

An organization targeting young women with a mission to save lives from breast and ovarian cancers.

Sharsheret

sharsheret.org

An organization supporting Jewish women who are diagnosed with breast cancer or at increased risk to develop breast cancer due to their genetics.

BRCAn't Stop Me

brcantstopme.wixsite.com/brcantstopme

An organization targeting young adults whose mission is to raise awareness and provide support for people affected by BRCA gene mutations.

REFERENCES

Hereditary Cancer. FORCE. <http://www.facingourrisk.org/understanding-brca-and-hboc/index.php>.

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