We have over 20,000 different genes in the body, and those genes are located in our DNA. These genes are like instruction manuals for how to build a protein, and each protein has an important function that helps to keep our body working how it should. The *BRCA2* gene makes a protein called the BRCA2 protein. As we go through life, our DNA can get damaged in many different ways, including exposures in the environment, or when our cells are dividing to make new cells. Sometimes this damage happens due to causes that we do not yet know about. As this damage builds up, it can cause a cell to grow out of control. This can lead to a tumor, which can then lead to cancer. The BRCA2 protein works with other proteins to fix this damage that happens in the DNA, thus preventing the cells from growing out of control. Repairing this damaged DNA helps to prevent tumors from forming.

If someone has a harmful change (called a pathogenic variant) in one of their *BRCA2* genes, then their body does not make as much BRCA2 protein as it should. Without enough BRCA2 protein, our body can not repair our damaged DNA as well as it should be able to. This can allow the damage to build up in cells more quickly, which causes the increased risk for BRCA-related cancers. Someone with HBOC is not producing enough BRCA2 protein from birth, which is also why people with HBOC can be diagnosed with these cancers at an earlier age than would normally be expected.

BRCA2-related cancer risks

There are increased risks for certain types of cancer in individuals who have a pathogenic variant in the *BRCA2* gene, although the associated cancers and lifetime risks are different between men and women:

Cancer type	**General population risk**	**Risk with pathogenic variant in *BRCA2***
Female breast	12%	50-70%
Second female breast	1.5% per year	Up to 12% within 5 years
Ovarian	1-2%	12-20%
Male breast	0.1%	7%
Prostate	16%	20-30%
Pancreatic	0.9%	3-5%
Melanoma	1-2%	3-5%

Inheritance

Pathogenic variants in the *BRCA2* gene are inherited in an autosomal dominant pattern, meaning that children of someone who has a pathogenic variant in *BRCA2* have a 50% chance to inherit the variant and associated cancer risks. Notably, women and men both have the *BRCA2* gene and have the same chances to inherit and pass down pathogenic variants. Therefore, both sides of the family are important when assessing inherited risk. Almost all people who have a pathogenic variant in *BRCA2* will have a parent who also carries it.

If someone inherits a pathogenic variant in **both** of their *BRCA2* genes (one from each parent), then they have a genetic condition called Fanconi anemia, which primarily affects the bone marrow. People with Fanconi anemia can have physical signs, including patches of skin that are different colors, skeletal problems, issues with their kidneys and urinary tract, heart defects, eye and ear malformations, and hearing loss. There is also an increased risk for a blood cancer called acute myeloid leukemia, or tumors in the head, neck, skin, gastrointestinal system, or genital tract.

Genetic Testing for *BRCA2*

Genetic testing for pathogenic variants in *BRCA2* has been available for many years, and the testing methods have changed and improved over time. There are several different ways to approach to testing depending on the medical and family history, and any prior testing that may have been done. Different approaches include:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- *Full gene sequencing and rearrangement analysis*: Comprehensive testing to search for all currently detectable pathogenic variants in the genes. If past testing included full gene sequencing but not the rearrangement analysis, this additional testing can be ordered to evaluate for these types of variants that would have been missed on older testing.
- *Founder variant testing*: Testing specific to the three common pathogenic variants found in the Ashkenazi Jewish population
- *Gene panels*: Newer, more broadly based gene tests that would include not only the *BRCA2* gene, but other genes known or suspected to be associated with increased cancer risks

Click here to learn more about scheduling a genetic counseling appointment for questions

about hereditary cancer predisposition.