Mass General Brigham
Mass General Cancer Center

Hereditary Breast and Ovarian Cancer Syndrome: information for families with a pathogenic variant in the *BRCA2* gene

The purpose of this handout is to give you detailed information about your genetic test result which you may read and discuss with your medical providers. Researchers will continue to study the BRCA2 gene, so please check in with your medical providers once a year to learn of any new information that may be important for you and your family members. (Please see the last page for a glossary of medical terms which are underlined in this document.)

You have a pathogenic variant in the *BRCA2* gene. This means you have **hereditary breast and ovarian cancer syndrome** (also known as **HBOC syndrome**).

What is hereditary cancer?

- Cancer is a common disease. One out of every 3 people in the United States will develop some type of cancer in their lifetime.

- About 5-10% of cancers (up to 1 in 10) are hereditary. A hereditary cancer occurs when a person is born with a pathogenic variant (also known as a mutation) in a gene that increases the chance to develop certain types of cancer. A pathogenic variant can be passed on from one generation to the next.

- Typically, families with a *BRCA2* pathogenic variant have one or more of the following features:
    - Early-onset breast cancer (under the age of 45)
    - Ovarian cancer
    - Individuals with more than one cancer diagnosis (for example, two breast cancers, or breast and ovarian cancer)
    - Breast cancer in people assigned male at birth
    - Early-onset and aggressive prostate cancer
    - Multiple family members with breast or other HBOC-related cancers
    - Breast cancer in several generations of a family

What is a pathogenic variant?

- DNA is our genetic material which is passed on from parent to child. It contains the instructions for how our bodies develop, grow, and function. A gene is a small piece of DNA which has a specific job to do in the body. Some genes determine features like eye color or height, while other genes are involved with our health.

- We all have variations in our genes that make us different from one another. Most of these variations do not change the way our genes work. However, some variations do prevent a gene from working correctly. This type of variation is called a pathogenic variant or mutation.

Why does having this pathogenic variant cause an increased risk for cancer?

- The job of the *BRCA2* gene is to prevent cancer. It is called a tumor suppressor gene. When working correctly, tumor suppressor genes help to prevent cancer by controlling the growth and division of cells.

- People born with a *BRCA2* pathogenic variant have only one working copy of the *BRCA2* gene, so their risk for cancer is higher than average.

What are the cancer risks linked to this pathogenic variant?

- People born with a *BRCA2* pathogenic variant (who have HBOC syndrome) have higher risks for certain types of cancer which are outlined in the table below.

Table: **Lifetime Cancer Risk (chance to get cancer at any time during life)**

	People who do not have a pathogenic variant	People who have a *BRCA2* pathogenic variant
Breast cancer (assigned female at birth)	10-12%	>60%
Second primary breast cancer	up to 15%	26% (within 20 years)
Ovarian cancer	1-2%	13-29%
Breast cancer (assigned male at birth)	<1%	2-7%
Prostate cancer	11.6%	19-61%
Pancreatic cancer	1-2%	5-10%

National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic Guideline, v3.2023

- The numbers above are shown as a range. This is because not all families/individuals have the exact same degree of risk. Risks may be affected by the environmental factors, lifestyle, medical history, family cancer history, and other genetic or unknown factors.

Is it possible to fix the pathogenic variant?

Unfortunately, it is not yet possible to fix a pathogenic variant in the *BRCA2* gene. However, it is possible to change your medical care and certain things in your lifestyle. Your provider(s) will work with you to discuss these options and create a medical care plan that is right for you.

What are the medical care recommendations?

The medical care recommendations for people with a *BRCA2* pathogenic variant are divided into three categories: **surveillance**, **surgery**, and **medications**.

Surveillance:

The purpose of surveillance (also referred to as 'screening') is to diagnose cancer at as early a stage as possible. Although scientists and physicians can't prevent a cancer from developing, early detection is important. When a cancer is detected early, it is more likely to be treated successfully. There are very good surveillance methods for some, but not for all types of cancer.

The table below outlines surveillance recommendations for individuals with a *BRCA2* pathogenic variant (adapted from the National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic Guideline, v3.2023). *Please note that these are general guidelines. Specific guidelines for individual patients and families may differ.*

Cancer type	Surveillance recommendations
Breast cancer (assigned female at birth)	Breast awareness beginning at age 18 and report changes to your health care provider Clinical breast exams by a doctor or nurse every 6-12 months, beginning at age 25 Yearly breast MRI from age 25-29 or individualized based on family history (if MRI is unavailable, consider mammogram) Yearly mammogram and breast MRI from age 30-75 After age 75, management should be considered on an individual basis
Ovarian cancer	No proven benefit to screening. Pelvic examinations done at least yearly. For patients who have not had risk-reducing ovarian surgery, consider transvaginal ultrasound and CA-125 blood test, beginning at age 40-45
Breast cancer (assigned male at birth)	At age 35, monthly breast self-exam and clinical breast exam every 12 months Consider yearly mammogram from age 50 or individualized based on family history
Prostate cancer	Prostate cancer screening beginning at age 40
Pancreatic cancer	When applicable, discuss pancreatic cancer screening guidelines with your health care provider

Risk-reducing surgery options:

The goal of risk-reducing surgery is to reduce the risk of cancer by removing healthy tissue before cancer develops. This is also called prophylactic surgery. Risk-reducing surgery does not eliminate the chance to get cancer, but it does greatly lower the chance.

- **Risk-reducing bilateral salpingo-oophorectomy (RRBSO):** This surgery removes the ovaries and fallopian tubes to lower the risk of ovarian cancer. RRBSO is recommended for people with a *BRCA2* pathogenic variant when they have reached age 40 to 45 and are done having children. The timing of RRBSO may depend in part on family history and should be discussed with your doctors. Even after RRBSO, there is a still a small (1%-5%) risk of a rare cancer called primary peritoneal cancer (cancer of the abdominal lining which behaves like ovarian cancer).

- **Prophylactic bilateral mastectomy (PBM):** This surgery removes the healthy breast tissue to lower the chance for breast cancer by more than 90%. Those considering PBM may have questions about their options for breast reconstruction (the rebuilding of the breast mounds through implants or tissue) which can be discussed with a specially trained breast surgeon. Because there are effective breast cancer surveillance tools, those who carry *BRCA2* pathogenic variants may choose surveillance as an acceptable alternative to PBM. Deciding between PBM and surveillance is a very personal decision, so it is important to carefully consider the benefits and drawbacks of each option, which may be discussed with specially trained medical providers.

Medications (Chemoprevention):

In some cases, medication may be prescribed to lower the chance of developing cancer.

- **Tamoxifen:** This medication is effective at treating many types of breast cancer. Studies show that it also helps prevent breast cancer. However, there is still much to be learned about the use of tamoxifen to prevent breast cancer in people who carry *BRCA2* pathogenic variants. Your provider may discuss the option of tamoxifen and related medications with you.

- **Oral contraceptive pills (birth control pills):** Studies have shown that oral contraceptive (OC) use in people with *BRCA2* pathogenic variants is generally acceptable and can decrease the risk of ovarian cancer.

Who should I see for my medical care?

It is important to find health care providers you trust for long-term follow-up care. Your primary care providers may be able to provide some of this care. In some cases, you may need to see specially trained medical providers. We are happy to provide you with referrals to specialists at Mass General as needed.

How can I live a healthy lifestyle to lower my risk of developing cancer?

Everyone should follow a healthy lifestyle, but this may be even more important for someone with an increased risk of cancer. According to the American Cancer Society, a healthy lifestyle includes:

- Avoiding tobacco.
- Maintaining a healthy weight.
- Participating in regular physical activity.
- Keeping a healthy diet with plenty of fruits and vegetables.
- Limiting yourself to no more than 1-2 alcoholic drinks per day.
- Protecting your skin and eyes from the sun.
- Knowing your own body and medical history, your family history, and your risks.
- Having regular check-ups and cancer screening tests.

What are the chances that my family members also have the pathogenic variant?

- **Your children:** Each of your children has a 50% chance to inherit the normal (working) copy of the *BRCA2* gene and a 50% chance to inherit the *BRCA2* pathogenic variant (the non-working copy). *BRCA2* pathogenic variants are not linked to childhood cancers and will not change a person's medical care plan until the age of 20-25. Therefore, testing children (minors, under the age of 18) for *BRCA2* pathogenic variants is not recommended.
    - In rare circumstances, when both parents carry a *BRCA2* pathogenic variant, a child may inherit a disease called Fanconi Anemia (FA). Please contact your genetic counselor if you have questions or concerns about FA.

- **Your siblings and other relatives:** In most cases, siblings of a person with a *BRCA2* pathogenic variant have a 50% chance to have the same pathogenic variant. Additionally, other family members (such as parents, cousins, aunts, uncles) may also be at risk to have the pathogenic variant.

- **Family planning:** People with *BRCA2* pathogenic variants may have concerns about passing a *BRCA2* pathogenic variant to a child. There are reproductive options that can be used to lower the chance of passing a *BRCA2* pathogenic variant to a child. If you are interested in learning more about these options, please contact your genetic counselor for a referral.

The letter you received from your genetic counselor will give more specific recommendations about which relatives are candidates for genetic testing. However, please feel free to contact us with any further questions.

Where can I find additional information?

Feel free to contact us if you have any questions or would like additional resources. Some people find it useful to speak with other people with *BRCA2* pathogenic variants who have similar concerns. We would be happy to arrange this for you if you are interested.

The following is a list of additional sources of information:

Center for Cancer Risk Assessment Mass General Cancer Center www.massgeneral.org/ccra (617) 724-1971
American Cancer Society www.cancer.org (800) 227-2345
Facing Our Risk of Cancer Empowered (FORCE) www.facingourrisk.org (866) 288-RISK
Bright Pink www.brightpink.org (312) 787-4412
Sharsheret www.sharsheret.org (866) 474-2774

Glossary of cancer genetics terms:

- **Assigned female at birth/Assigned male at birth**: Refers to the sex that a doctor or midwife uses to describe a child at birth based on their external anatomy.

- **Cell**: The basic structural and functional unit of any living thing. Each cell is a small container of chemicals and water wrapped in a membrane. The human body is made up of 100 trillion cells forming all parts of the body such as the organs, bones, and blood.

- **DNA**: Deoxyribonucleic acid, or DNA, is the genetic material that is passed on from parent to child, which gives the instructions for how our bodies develop, grow, and function on a daily basis.

- **Early detection**: The process of finding cancer when it is just starting to develop.

- **Gene**: A gene is a small piece of DNA that gives instructions for a specific trait.

- **Inherited trait**: A character or feature that is passed on from a parent to a child.

- **Lifetime cancer risk**: The chance that a person will develop cancer in his or her life. This is sometimes defined as the chance of developing cancer by the age of 75 or 80.

- **Pathogenic variant**: A change in a gene that prevents it from working correctly. Also called mutation.

- **Risk-reducing surgery**: Surgery to remove healthy tissue or organs before cancer develops. Also called prophylactic surgery.

- **Surveillance**: Screening tests or procedures to look for early signs of cancer development or cancer returning (recurrence).

- **Syndrome**: A set of signs and symptoms that appear together and characterize a disease or medical condition.

- **Tumor suppressor gene**: When working correctly, tumor suppressor genes prevent cancers from developing by controlling the growth of cells.