Mass General Brigham
Mass General Cancer Center

Information for families with a pathogenic variant in the *CHEK2* 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 CHEK2 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.)

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 his or her 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.
- Because *CHEK2* is linked to a moderately increased risk for cancer, some families with a *CHEK2* pathogenic variant may not show typical features of a hereditary cancer syndrome. Other families may have a history that includes breast cancer in women and/or colon cancer.

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 *CHEK2* 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 *CHEK2* pathogenic variant have only one working copy of the *CHEK2* gene, so their risk for certain types of cancer is higher than average.

What are the cancer risks linked to this pathogenic variant?

- People born with a *CHEK2* pathogenic variant 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 *CHEK2* pathogenic variant
Breast cancer (assigned female at birth)	10-12%	20-40%
Colon cancer	4-5%	5-10%

National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment Breast, Ovarian and Pancreatic Guideline, Version 3.2023

- 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, personal medical history, family cancer history, and other genetic or unknown factors.

- *CHEK2* pathogenic variants may also be linked to other cancer risks. Some that are under study include ovarian, breast (in people assigned male at birth), endometrial, thyroid, prostate, and melanoma.

- Certain pathogenic variants in the *CHEK2* gene, such as p.I157T (p.Ile570Thr), are associated with a lower risk of breast cancer in people assigned female at birth than typically reported for *CHEK2* pathogenic variants. (Please review your test report to learn which *CHEK2* pathogenic variant you carry.)

Is it possible to fix the pathogenic variant?

Unfortunately, it is not yet possible to fix a pathogenic variant in the *CHEK2* 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?

Current medical care recommendations for people with *CHEK2* pathogenic variants focus on cancer surveillance (also referred to as 'screening'). The purpose of surveillance 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 most individuals with a *CHEK2* pathogenic variants (adapted from the National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Breast, Ovarian and Pancreatic Guideline, Version 3.2023). *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)	Mammograms yearly starting at age 40 and consider breast MRI with contrast, beginning at age 30-35 years.
Colon cancer	Colonoscopy screening every 5 years, beginning at age 40, or 10 years prior to first-degree relative's age at colorectal cancer diagnosis.

It is important to note that cancer risk information related to *CHEK2* is an area of ongoing research. Over time, the cancer risk information and medical care recommendations for individuals with *CHEK2* pathogenic variants may change.

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 *CHEK2* gene and a 50% chance to inherit the *CHEK2* pathogenic variant (the non-working copy). *CHEK2* pathogenic variants are not linked to childhood cancers and will not change a person's medical care plan until the age of 30. Therefore, testing children (minors, under the age of 18) for *CHEK2* pathogenic variants is not recommended.

- **Your siblings and other relatives:** In most cases, siblings of a person with a *CHEK2* 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 *CHEK2* pathogenic variants may have concerns about passing a *CHEK2* pathogenic variant to a child. There are reproductive options that can be used to lower the chance of passing a *CHEK2* 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 *CHEK2* 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

Hereditary Colon Cancer Takes Guts
www.hcctakesguts.org

info@HCCTakesGuts.org
Facing Our Risk of Cancer Empowered (FORCE)
www.facingourrisk.org
(866) 288-RISK

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 a 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.