Mass General Brigham
Mass General Cancer Center

MUTYH-Associated Polyposis Syndrome: Information for individuals with a pathogenic variant in both *MUTYH* genes

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 MUTYH 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 pathogenic variants in both copies of the *MUTYH* gene. This means you have *MUTYH*-Associated Polyposis syndrome (also known as **MAP 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, individuals and families with MAP syndrome have one or more of the following features:
    - Multiple colon polyps, often diagnosed at a young age.
    - Colon cancer, possibly diagnosed at a young age.

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 MAP syndrome cause an increased risk for cancer?

- The job of the *MUTYH* gene is to prevent cancer. When working correctly, *MUTYH* helps to prevent cancer by repairing DNA damage in our cells.

- People born with MAP syndrome have no working copy of the *MUTYH* gene, so their risk for cancer is higher than average.

What are the cancer risks linked to MAP syndrome?

People born with MAP syndrome also have a higher risk for developing pre-cancerous polyps in the colon, called adenomas. An adenoma is a pre-cancerous growth, and if it is not removed it can grow into a colon cancer. The cancer risks linked to MAP syndrome are outlined in the table below.

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

	People who do not have MAP syndrome	People who have MAP syndrome
Colon cancer	4-5%	70-90%*
Small intestinal cancer	<1%	4%

GeneReviews.org; National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Colorectal Guideline, Version 1.2023
*These risks are based on people who did not have regular screening and/or other treatments such as risk-reducing surgery.

- 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.

Is it possible to fix the pathogenic variants?

Unfortunately, it is not yet possible to fix pathogenic variants in the *MUTYH* 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 MAP syndrome 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 MAP syndrome (adapted from the National Comprehensive Cancer Network Genetic/Familial High-Risk Assessment: Colorectal Guideline, Version 1.2023). *Please note that these are general guidelines. Specific guidelines for individual patients and families may differ.*

Cancer type	Surveillance recommendations
Colon cancer	Colonoscopy beginning no later than age 25-30 (or earlier based on family history); repeat every 1-2 years. Consider colectomy when >20 polyps and/or polyps are difficult to remove by colonoscopy
Small intestine	Periodic upper endoscopy, beginning at age 30-35

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.

- **Colectomy:** This surgery removes all or part of the colon (large intestine) to lower the risk of colon cancer. Colectomy is usually necessary once a person develops a large number of polyps that cannot be managed through colonoscopy alone. The timing of a colectomy depends upon age, number of polyps, and other factors. This surgery may also be recommended in patients that have developed colon cancer and have MAP syndrome. There are different types of procedures for removal of the colon and/or rectum which should be discussed with a gastroenterologist and specially trained surgeon. Most colectomy operations do not require a permanent external bag.

Medications (Chemoprevention):

- **Sulindac:** Some research shows that an NSAID called sulindac may stop colon polyps from growing. However, there is still much to be learned about the use of sulindac in people with MAP syndrome, and it may or may not be right for you. **The use of sulindac is not appropriate for everyone and should not be taken without talking to your healthcare providers first.**

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:** If you have MAP syndrome, all of your children will inherit one of your *MUTYH* pathogenic variants. Your children can have MAP syndrome only if their other biological parent is also a carrier of a *MUTYH* pathogenic variant. MAP syndrome is 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 MAP syndrome is not recommended.

- **Your siblings and other relatives:** In most cases, siblings of an individual with MAP syndrome have a 25% chance of also having MAP syndrome. Additionally, other family members (such as parents, cousins, aunts, uncles) may also be at risk for MAP syndrome.

- **Family planning:** People with MAP syndrome may have concerns about passing a *MUTYH* pathogenic variant to a child. Some patients may be interested in reproductive options that can lower the chance of having a child with MAP syndrome. 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.

What are the risks of carrying one *MUTYH* pathogenic variant?

Some of your relatives may learn that they have a single *MUTYH* pathogenic variant (carriers). These individuals do not have MAP syndrome. However, depending upon the family history of cancer, *MUTYH* carriers may have a slightly increased risk for colon cancer compared to the general population.

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 MAP syndrome 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

Colorectal Cancer Alliance
www.ccalliance.org
(877) 422-2030 for Patient and Family support

National Cancer Institute's Cancer Information Service
www.cancer.gov/aboutnci/cis
(800) 4-CANCER

Glossary of cancer genetics terms:

- **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 their 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.
    - Mismatch repair (MMR) genes: There are many types of tumor suppressor genes and MMR genes are just one type. As new DNA is being made in a cell, the MMR genes help proofread the new DNA strands to detect and correct mistakes.