Quest Advanced Oncology

Hereditary Cancer Genetic Test Results

This report is intended to facilitate a discussion between providers and their patients.

INFORMATION FOR INDIVIDUALS WITH ONE OR TWO PATHOGENIC OR LIKELY PATHOGENIC VARIANT(S) IN THE *MUTYH* GENE

What this result means

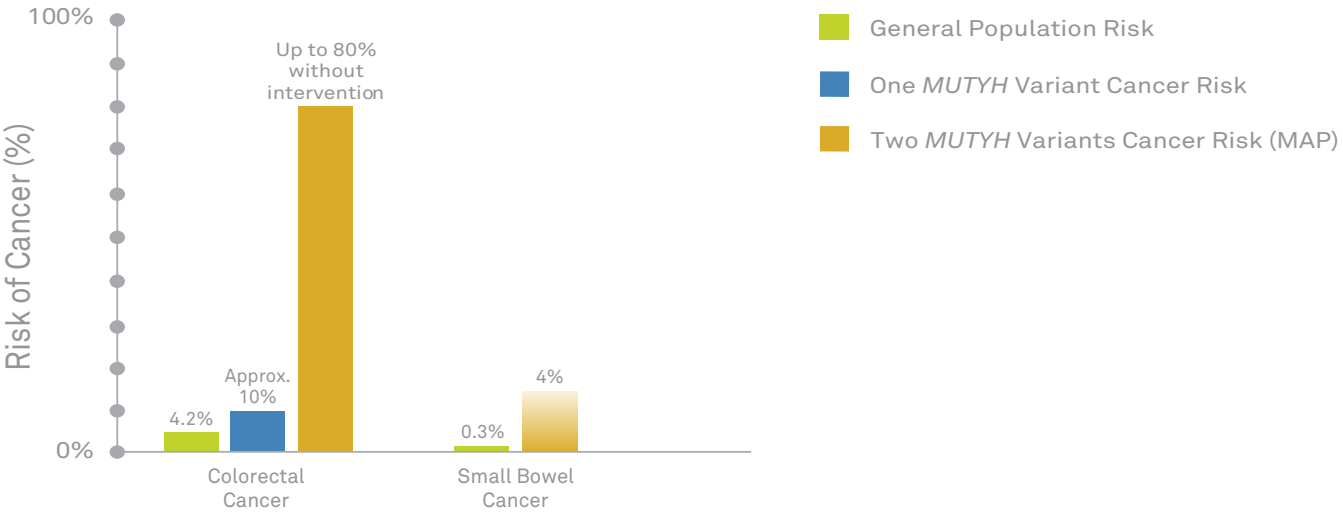
Individuals who have **two** (one in each copy of *MUTYH*) pathogenic or likely pathogenic variants (sometimes called mutations) in the *MUTYH* gene have *MUTYH*-Associated Polyposis (MAP). Individuals with MAP have a higher-than-average chance to develop adenomatous colorectal polyps, colorectal cancer, small bowel cancer, duodenal adenomas, and fundic gland polyps.

People with only **one** pathogenic or likely pathogenic variant in *MUTYH* do not have MAP, but may have an elevated risk of colorectal cancer.

Cancer risk

The graph below compares the general population cancer risks to the potential cancer risks associated with pathogenic variants in *MUTYH*. Individual cancer risks may be higher or lower depending on the specific variant identified in addition to each individual's gender, age, medical history, and family history. Not everyone with a pathogenic or likely pathogenic variant will develop cancer.

Information about cancer risks related to pathogenic variants in *MUTYH* may change over time, so it is important for the ordering healthcare provider, genetic counselor, and patient to keep in contact regarding this result.



*Data on file.

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Options for managing cancer risk

There are options for cancer prevention and early detection. The following are general guidelines for individuals who have either one or two pathogenic *MUTYH* variants. These guidelines are evolving and not specific to any one individual. Each individual's gender, age, medical history, family history, quality of life goals, reproductive desires, general health status, and other medical information should be taken into account when developing a medical management plan.

	Considerations for cancer prevention/early detection	Age to begin	Frequency
Options for Two *MUTYH* Pathogenic Variants (one in each copy of *MUTYH*): *MUTYH*-Associated Polyposis (MAP)			
Colorectal Cancer	Colonoscopy and Polypectomy	Individualized based on age, polyp burden, and clinical presentation but no later than 25-30 years	Every 1-2 years
	Surgical evaluation and counseling	Individualized based on age, polyp burden, and clinical presentation	—
	Post-colectomy surveillance	Following surgery	Based on surgery performed and polyp burden
	Post-colectomy chemoprevention	Individualized	Individualized
Small Bowel Cancer	Consider upper endoscopy, include ampulla of Vater	30-35 years	Every 4 years. If polyps are found, adjust frequency and surgical consideration based on polyp burden
Other Management	Physical examination	At diagnosis	Annual
	Refer to multidisciplinary team of specialists familiar with MAP for evaluation and management	—	—
Options for One *MUTYH* Pathogenic Variant			
Individuals with a first-degree relative with colorectal cancer	Colonoscopy	40 years or 10 years prior to the first-degree relative's colorectal cancer diagnosis	Every 5 years
Individuals with no first-degree relative with colorectal cancer	Colonoscopy	Insufficient evidence	—

Source: National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Colorectal. V1.2020. **www.NCCN.org**

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What this result means for family members

For individuals with two pathogenic or likely pathogenic variants in *MUTYH* (one in each copy of *MUTYH*), parents will likely each have one of the two *MUTYH* variants. Siblings have a 50% chance to have one of the variants and a 25% chance to have both of the variants and a diagnosis of MAP. Children will all have one of the *MUTYH* variants.

For individuals with one pathogenic or likely pathogenic variant in *MUTYH,* parents, brothers, sisters, and children may each have a 50% chance to have the same variant. Children of parents who both have an *MUTYH* variant are at risk for MAP.

Other blood relatives also have an increased risk for the variant(s). It is important to share these test results with family members to allow each of them to decide if they want to be tested. Some family members may only need testing for these *MUTYH* variants, while other relatives may need a more comprehensive test with multiple genes. A genetic counselor or other healthcare provider can help determine the most appropriate testing options.

Reproductive information

Individuals interested in family planning should speak to their doctor and/or genetic counselor to discuss reproductive options. This may include discussion of prenatal diagnosis or pre-implantation genetic testing.

Risk assessment and counseling: an important first step

A genetic counselor or other qualified healthcare professional can help explain test results and what they mean for a patient and family members. A team of specialized Quest genetic counselors or clinical geneticists is available to speak with healthcare providers about test results by calling 1.866.GENE.INFO. Patients can access a directory of independent genetic counselors at **FindAGeneticCounselor.com**.

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Creating a plan: a checklist for patients

- ☐ Get a copy of your genetic test results.
- ☐ Talk with your healthcare provider about what this result means and the things you can do to manage your risk.
- ☐ Ask your healthcare provider if additional genetic testing may benefit you.
- ☐ Share your test results with your family members and give them a copy. Their healthcare provider will need this information in order to provide them with the most accurate risk assessment.
- ☐ Talk with your healthcare provider regularly so that you know about any important changes in genetic testing and cancer screening options. Be sure to let him/her know of any changes in your family history, including family members' genetic test results.
- ☐ Consider talking to a genetic counselor about your results.

Research opportunities

Prospective Registry of MultiPlex Testing (PROMPT) PromptStudy.info

GenomeConnect: The ClinGen Patient Portal GenomeConnect.org

Additional resources

Hereditary Colon Cancer *Takes* Guts
hcctakesguts.org

Colorectal Cancer Alliance
ccalliance.org

National Colorectal Cancer Roundtable
nccrt.org

Quest Hereditary Cancer Testing Solutions
QuestHereditaryCancer.com

Genetic Information Nondiscrimination Act (GINA) GINAhelp.org

National Society of Genetic Counselors
FindAGeneticCounselor.com

This information is not a substitute for medical advice, diagnosis, or treatment. The diagnosis or treatment of any disease or condition may be based on personal history, family history, symptoms, a physical examination, laboratory test results, and other information considered important by a healthcare provider. Always talk with a healthcare provider about the meaning of genetic test results and before stopping, starting or changing any medication or treatment.

The classification and interpretation of the variant(s) identified reflect the current state of Quest Diagnostics' understanding at the time of this report. Variant classification and interpretation are subject to professional judgment, and may change for a variety of reasons, including but not limited to, updates in classification guidelines and availability of additional scientific and clinical information. This test result should be used in conjunction with the healthcare provider's clinical evaluation. Inquiry regarding potential changes to the classification of the variant is strongly recommended prior to making any clinical decision. For questions regarding variant classification updates, please call Quest Diagnostics at 1.866.GENE.INFO (1.866.436.3463) to speak to a genetic counselor or laboratory director, or visit **QuestDiagnostics.com/VariantIQ**.