riscover®
HEREDITARY CANCER

Result Navigator

Positive Test Result: *MUTYH*

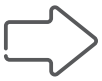
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic variant is a change in a gene that is known to cause increased risk for cancer. A likely pathogenic variant is a change in a gene that is very likely to cause increased risk for cancer.

After a positive test result, there can be many questions about what to do next.

This guide is a supplement to Riscover® Hereditary Cancer test results, helping patients and healthcare providers understand the results and together determine the best path forward.

Navigate Your Results

Learn* | *page 2
Review the test results along with this guide, and discuss the meaning of these results with your healthcare provider.



Plan* | *page 2
Develop a healthcare plan for early detection and prevention of specific cancers.

Share* | *page 3
Understand the risks for other family members, and consider how to inform relatives of their risks.

Connect* | *page 4
Reach out to medical experts and find local and national groups that can provide more information and support.

Glossary of Terms

Colonoscopy: Visual exam of the inside of the colon with a flexible, lighted tube inserted through the rectum.

Gene: A section of DNA with a specific job.

Pathogenic: Causing or capable of causing disease.

Risk: The chance, or possibility, of developing a disease.

Variant: A change, or "misspelling," in the DNA sequence. Variants can be benign (not associated with disease), pathogenic (associated with disease), or of uncertain significance.

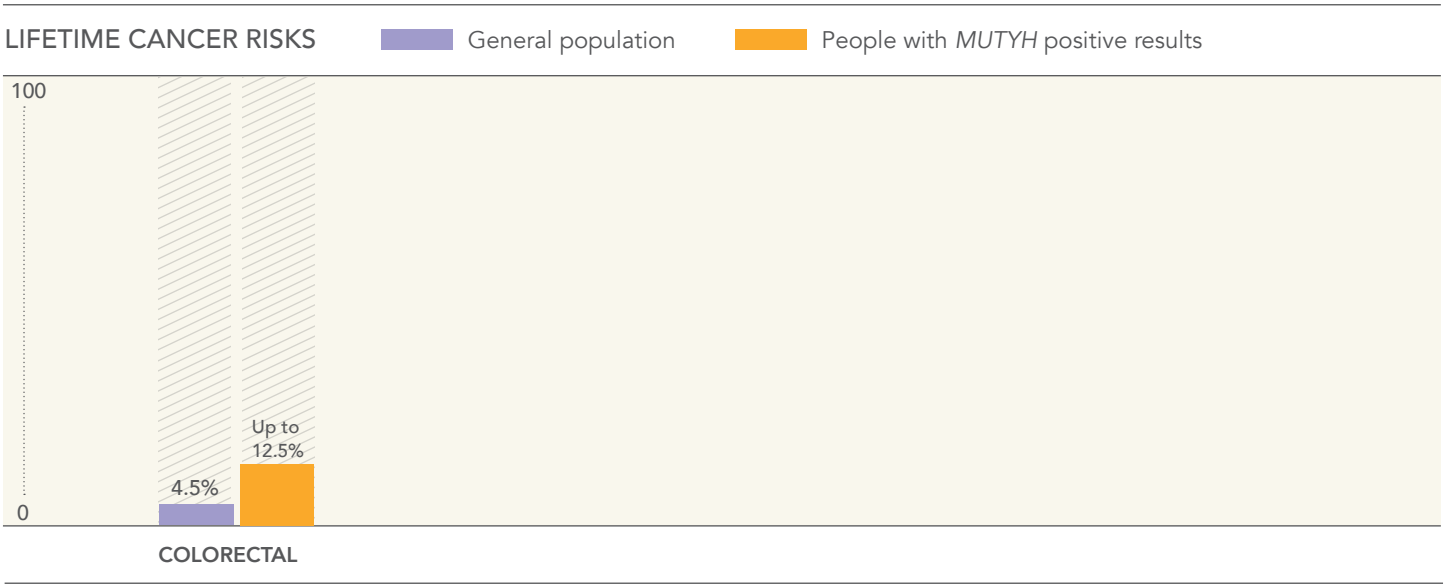
Your Diagnosis

MUTYH is a gene that helps in repairing DNA. People with a pathogenic/likely pathogenic variant in one copy of the *MUTYH* gene have an increased risk of colorectal cancer. About 1 – 2% of the general population are carriers of a *MUTYH* pathogenic variant.

People who have a pathogenic variant in both copies of the *MUTYH* gene have a condition called *MUTYH*-Associated Polyposis (MAP), which has higher associated cancer risks. This occurs when an individual inherits a *MUTYH* pathogenic variant from each parent.

Your Risk

Not all people with positive test results will develop cancer, but the chance for cancer is higher than the general population risk. The graphs below show how much the risk for cancer increases when a pathogenic variant is found. The cancer risks are presented in ranges based on multiple studies of families who have a pathogenic variant. There is not enough evidence available to give a specific risk to a person or family.



Plan

Your Screening and Management Options

Listed below are the intervention options that are recommended by medical experts for individuals who carry this cancer gene variant. Your healthcare provider can explain these options in more detail, and together you can make a plan for cancer prevention and/or early detection.

COLORECTAL CANCER

Colonoscopy	If a parent, child, or sibling has had colorectal cancer, a colonoscopy every 5 years is recommended starting at age 40, or 10 years prior to the age that the affected relative was diagnosed. If there is no family history of colorectal cancer, the benefits of earlier screening are unclear, and screening protocols should be discussed with a healthcare provider.

Your Family Matters

MAP is inherited in an autosomal recessive manner. People who inherited only one pathogenic variant are carriers. Carriers have a moderately increased risk for colorectal cancer, but do not have other features associated with MAP. People who inherit two *MUTYH* pathogenic variants are affected with MAP.

Carriers can pass on their pathogenic variant to their children. Risks to your children depend on whether your partner is also a carrier. If your reproductive partner is not a carrier, then each child has a 1 in 2 chance to be a carrier. However, if your reproductive partner is also a carrier of a *MUTYH* pathogenic variant, then there is a 1 in 4 chance to have a child affected with MAP (and a 1 in 2 chance to be a carrier).

Gene variants can be passed through families for many generations. When a gene variant is identified in one person in the family, relatives can be tested for just that variant. Sharing information about test results with family members is important, because it allows them to make informed choices about their healthcare and to decide whether they want genetic testing.

Some people who have pathogenic and likely pathogenic variants are interested in learning how to avoid passing these variants on to their children. If you are planning to have a child, you may wish to consult with a reproductive medicine specialist to discuss all of your reproductive options, including use of an egg or sperm donor, preimplantation genetic diagnosis, and prenatal genetic testing.

The likelihood for family members to carry the same gene variant depends on how closely related they are to the person with a known gene variant.

Your Expert Team

As you take your next steps, it can help to have a team of experts on your side. This team may include your primary care provider and a number of specialists who will help along the way.

If you haven't already done so, you may wish to speak with a genetic counselor. Genetic counselors are healthcare professionals with specialized training in medical genetics and counseling. They can help you understand your test results, discuss your healthcare plan, and connect to other resources in your area. Your healthcare provider may be able to provide a referral to a local genetic counselor. You can also find a genetic counselor through the National Society of Genetic Counselors at www.nsgc.org.

For questions about your test results, our genetic counseling team is available to help.
To reach a genetic counselor, call +1 855-293-2639 and select option 3.

Helpful Resources

GeneReviews
ncbi.nlm.nih.gov/books/NBK107219
A detailed clinical summary of MUTYH-Associated polyposis written for healthcare providers.

National Comprehensive Cancer Network (NCCN)
nccn.org
Expert guidelines for cancer screening and treatment. Versions available for both providers and patients.

Hereditary Colon Cancer Takes Guts
hcctakesguts.org
A nonprofit organization serving the hereditary colorectal cancer community that includes resources for patients and healthcare providers.

REFERENCES

National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal (Version 1.2018). Available from: http://www.nccn.org/.

Win AK et al. Risk of Colorectal Cancer for Carriers of Mutations in MUTYH, with and without a Family History of Cancer. 2014. Gastroenterology, 146(5), 1208-1211.