

# Result Navigator

## ⊕ Positive Test Result: SMAD4

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 3

Develop a healthcare plan for early detection and prevention of specific cancers.



### Share | page 4

Understand the risks for other family members, and consider how to inform relatives of their risks.



### Connect | page 5

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.

**Endoscopy:** Using an endoscope (a tube-shaped tool that includes a light, camera, and small tools to remove polyps or other tissues) to look in the body at the inside of organs such as the stomach or intestines.

**Gene:** A section of DNA with a specific job.

**Hereditary hemorrhagic telangiectasia:** An inherited disorder that results in development of multiple abnormalities in blood vessels.

**Juvenile polyposis:** The presence of multiple juvenile polyps in the GI tract. The term juvenile refers to how the polyp looks under the microscope, does not refer to children/age of onset.

**Pathogenic:** Causing or capable of causing disease.

**Polyp:** An abnormal growth of cells that can become a cancer tumor.

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

**Upper endoscopy:** Test that uses a scope to look at the esophagus (part of the GI tract that connects the throat to the stomach), stomach, and upper part of the small intestine.

**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.



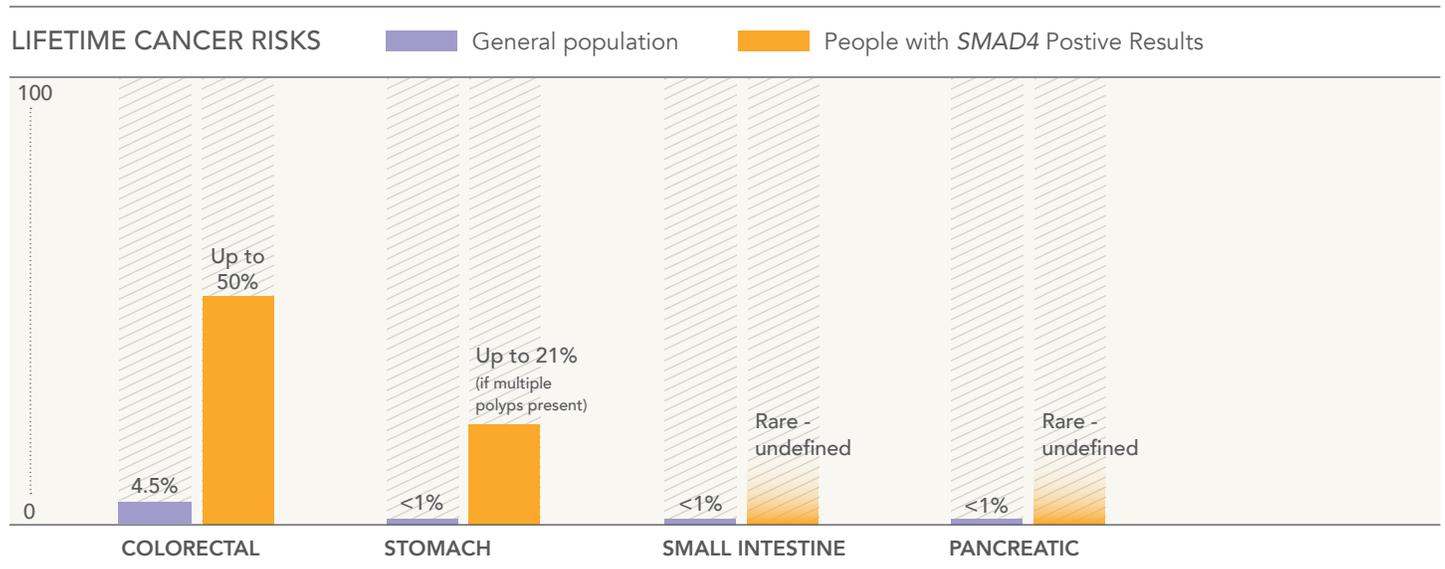
## Your Diagnosis: Juvenile Polyposis Syndrome

Pathogenic/likely pathogenic variants in the *SMAD4* gene are associated with an inherited disorder called Juvenile Polyposis Syndrome (JPS). JPS can also be caused by pathogenic variants in another gene called *BMPR1A*. JPS is associated with an increased lifetime risk of gastrointestinal (GI) polyps, colorectal and stomach cancers, and possibly small intestine and pancreatic cancers. Up to 10% of cases of GI polyposis are due to JPS. People who have a *SMAD4* pathogenic variant are also at increased risk to develop hereditary hemorrhagic telangiectasia (HHT).

About 1 in 100,000 people in the general population has JPS caused by a pathogenic variant in either *SMAD4* or *BMPR1A*. Some people with JPS have a family history consistent with the diagnosis, while others are the first in their family to be affected.

## 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.



## 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

A colonoscopy is recommended every 2 – 3 years beginning at age 15. If polyps are found, annual colonoscopies should be performed.

### STOMACH CANCER

Upper endoscopy

An upper endoscopy is recommended every 2 – 3 years beginning at age 15. If polyps are found, annual upper endoscopies should be performed.

### SMALL INTESTINE CANCER

No specific guidelines

Your healthcare provider can recommend screening options based on your personal and family history of small intestine cancer.

### PANCREATIC CANCER

No specific guidelines

Your healthcare provider can recommend screening options based on your personal and family history of pancreatic cancer.

### HEREDITARY HEMORRHAGIC TELANGIECTASIA

Screen for vascular lesions

Screening for vascular lesions is recommended within the first 6 months of life, and then as determined by your healthcare provider depending on your individual situation.

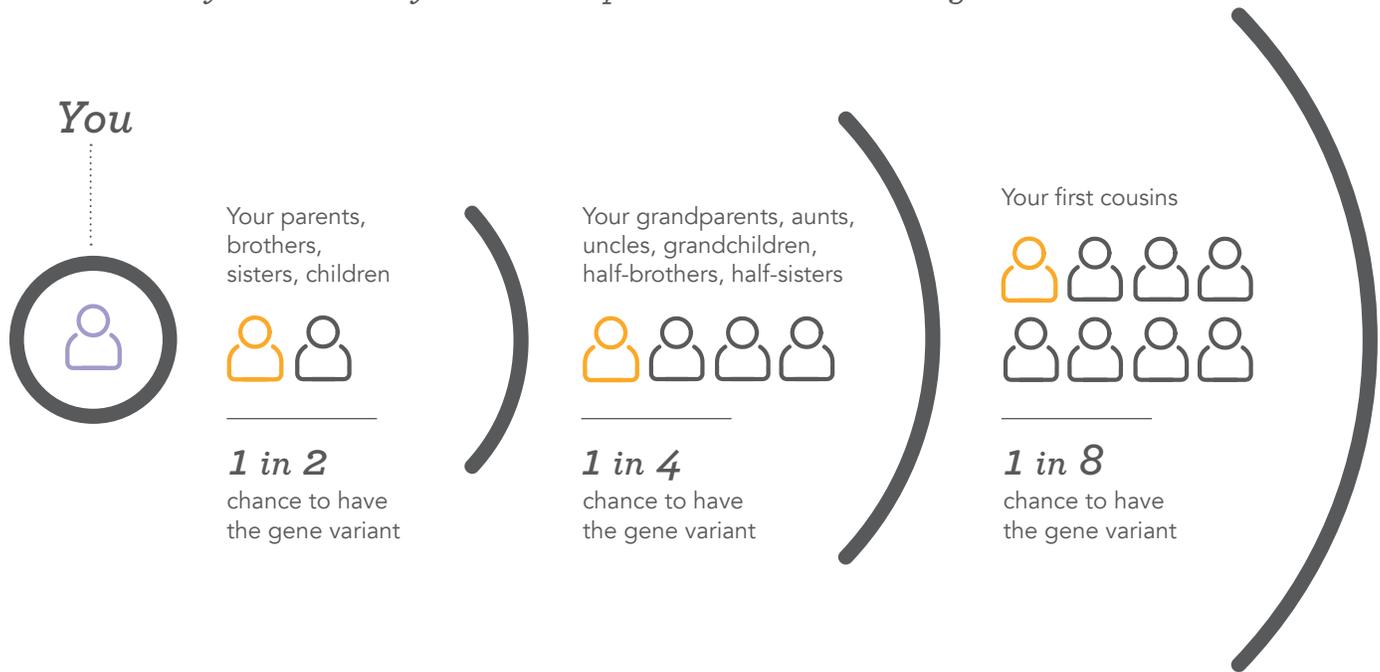
## Your Family Matters

Cancer gene variants are inherited in an autosomal dominant manner. This means that when a parent tests positive, each child has a 1 in 2 chance to inherit the variant. Some people who inherit the variant will develop cancer, and some will not, but the risks are significantly increased compared to the average person. People in the same family may develop different types of cancers at varying ages, and the pattern of cancer and age of onset can differ from family to family.

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](http://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/NBK1469](http://ncbi.nlm.nih.gov/books/NBK1469)

A detailed clinical summary of juvenile polyposis syndrome (JPS) written for healthcare providers.

### National Comprehensive Cancer Network (NCCN)

[nccn.org](http://nccn.org)

Expert guidelines for cancer screening and treatment. Versions available for both providers and patients.

### Genetics Home Reference

[ghr.nlm.nih.gov/condition/juvenile-polyposis-syndrome](http://ghr.nlm.nih.gov/condition/juvenile-polyposis-syndrome)

A detailed summary of Juvenile polyposis syndrome (JPS) written for patients and their families that includes links to additional resources.

### Hereditary Colon Cancer Takes Guts

[hcctakesguts.org](http://hcctakesguts.org)

Patient support group whose mission is to improve the lives of individuals with hereditary colon cancer syndrome.

### Cure HHT

[curehht.org](http://curehht.org)

Formerly known as the HHT Foundation, this patient support group aims to educate families and physicians about HHT and link patients with each other and the medical and research communities.

## REFERENCES

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