

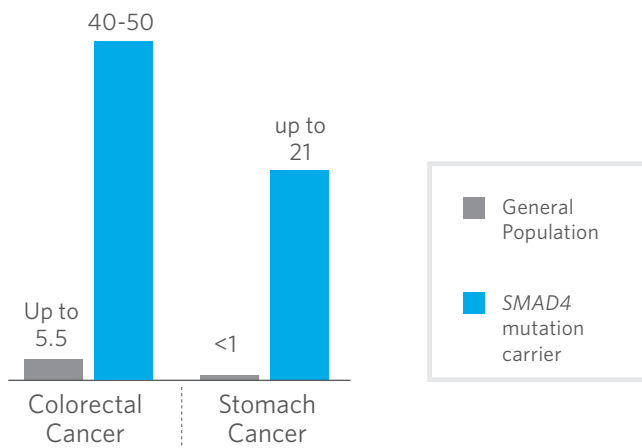
Understanding Your Positive *SMAD4* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION** OR **VARIANT, LIKELY PATHOGENIC**

5 Things To Know

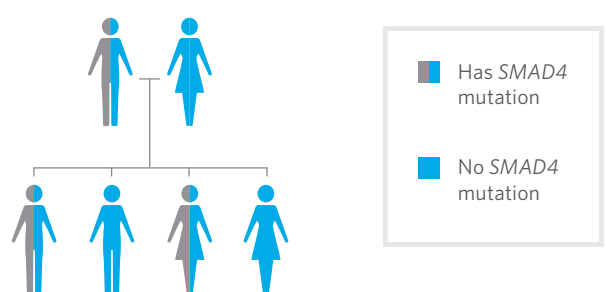
1	<i>SMAD4</i> mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the <i>SMAD4</i> gene.
2	Juvenile polyposis syndrome	People with <i>SMAD4</i> mutations have juvenile polyposis syndrome (JPS).
3	Cancer risks and other medical concerns	You have an increased chance to develop non-cancerous gastrointestinal polyps, as well as colorectal and possibly stomach cancer. In addition, you may be at risk for hereditary hemorrhagic telangiectasia (HHT) and the associated characteristics.
4	What you can do	There are risk management options to detect cancer early or lower your risk to develop cancer. It is important to discuss these options with your doctor, and decide on a plan that best manages your cancer risks.
5	Family	Family members may also be at risk - they can be tested for the <i>SMAD4</i> mutation that was found in you.

SMAD4 Mutation Lifetime Cancer Risks (%)*



SMAD4 Mutations in the Family

There is a 50/50 random chance to pass on a *SMAD4* mutation to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations.



*The above cancer risks represent the typical range for individuals with a mutation in this gene. If available, cancer risks specific to the mutation found in you will be provided in your results report.

Understanding Your Positive *SMAD4* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION OR VARIANT, LIKELY PATHOGENIC**

Result	MUTATION	Your testing shows that you have a pathogenic mutation (a disease-causing change in the gene, like a spelling mistake) or a variant that is likely pathogenic in the <i>SMAD4</i> gene. Both of these results should be considered positive.
Gene	<i>SMAD4</i>	Everyone has two copies of the <i>SMAD4</i> gene, which we randomly inherit from each of our parents. Mutations in one copy of the <i>SMAD4</i> gene are associated with an increased chance to develop cancer, gastrointestinal polyps and possibly characteristics of HHT.
Condition	JUVENILE POLYPOSIS SYNDROME	People with a <i>SMAD4</i> mutation have juvenile polyposis syndrome (JPS).
Cancer Risks	INCREASED	You have an increased chance to develop multiple gastrointestinal polyps, colorectal cancer, and possibly stomach cancer, if you have stomach polyps.
Other Medical Concerns	MAY BE PRESENT	Those with JPS may also have hereditary hemorrhagic telangiectasia (HHT). This may include malformations of your arteries and/or veins, frequent nosebleeds, and/or telangiectasias (small gatherings of blood vessels), which may be visible under your skin. Those with HHT may also be at-risk for tearing (dissection) or expansion (dilation) of the aorta, the large blood vessel branching from the heart.
Management Options	FOR MEN & WOMEN	Options for screening and early detection for men and women may include: colonoscopy, upper endoscopy, and screening for malformations in your arteries and veins. Talk to your doctor about which options may be right for you.
Risk Management	VARIES	Risk management decisions are very personal, and the best option depends on many factors. Screening typically begins earlier than in the general population, and is often more frequently done. It is important to discuss these options with your doctor.
Family Members	50/50 CHANCE	Your close relatives (like your parents, brothers, sisters, children) have a 50/50 random chance of inheriting the <i>SMAD4</i> mutation that you carry, and other family members (like your aunts, uncles, cousins) may also inherit it. Your relatives can be tested for this same mutation. Depending on the family history, those who DO NOT have it may not have an increased lifetime chance (above the general population) to develop cancer.
Next Steps	DISCUSS	It is recommended that you share this information with family members so they can learn more and discuss this with their healthcare providers.
Reach Out	RESOURCES	<ul style="list-style-type: none">• Ambry's Hereditary Cancer Site for Families patients.ambrygen.com/cancer• Hereditary Colon Cancer Foundation hcctakesguts.org• Genetic Information Nondiscrimination Act (GINA) ginahelp.org• National Society of Genetic Counselors nsgc.org• Canadian Association of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *SMAD4* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.