

GREM1 gene

Associated Syndrome Name: Hereditary mixed polyposis syndrome (HMPS)

GREM1 Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Colorectal	Elevated Risk

GREM1 gene Overview

Hereditary mixed polyposis syndrome (HMPS) ^{1,2,3}

- Mutations in *GREM1* have been found in some individuals with hereditary mixed polyposis syndrome (HMPS), a rare condition which has to date only been identified in a small number of families.
- Individuals with HMPS develop colorectal polyps of varied types including adenomatous polyps, hamartomatous polyps, hyperplastic polyps, and polyps of mixed histology. These polyps may develop in large numbers, and in individuals at young ages, i.e., in their teens. The clinical features of HMPS are not yet well defined, due to the rarity of the condition.
- Individuals with HMPS are believed to have a significantly increased risk for colorectal cancer.
- Although there is an increased risk for colorectal cancer in individuals with HMPS due to mutations in *GREM1*, it may be possible to reduce this risk with appropriate medical management. Guidelines for the medical management of patients with HMPS have been developed by the National Comprehensive Cancer Network (NCCN). These are listed below. These guidelines will evolve as we learn more about HMPS, and it is recommended that patients with a *GREM1* mutation and a diagnosis of HMPS be managed by a multidisciplinary team with expertise in medical genetics and the care of patients with hereditary cancer syndromes.

GREM1 gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Colorectal	To age 80 ^{2,3,4}	Elevated risk	2.8%

GREM1 Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Colorectal	Colonoscopy ³	25 to 30 years	Every 2 to 3 years
	Colorectal surgical evaluation and counseling. ³	Based on cancer diagnosis and/or polyp number, size and histology	NA

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the GREM1 gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and

sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

References

1. Jaeger E, et al. Hereditary mixed polyposis syndrome is caused by a 40-kb upstream duplication that leads to increased and ectopic expression of the BMP antagonist *GREM1*. *Nat Genet.* 2012 44:699-703. PMID: 22561515.
2. Rozen P, et al. A prospective study of the clinical, genetic, screening, and pathologic features of a family with hereditary mixed polyposis syndrome. *Am J Gastroenterol.* 2003 98:2317-20. PMID: 14572586.
3. Gupta S, et al. NCCN Clinical Practice Guidelines in Oncology® Genetic/Familial High-Risk Assessment: Colorectal, Endometrial, and Gastric. V 1.2025. Jun 13. Available at <https://www.nccn.org>.
4. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. [Cited 2025 Aug 12]. Available from <https://seer.cancer.gov/explorer/>.

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