

MUTYH-Associated Polyposis (MAP)

Cancer Risks and General Management Recommendations

MUTYH-associated polyposis (MAP) is an adult-onset colorectal cancer predisposition syndrome characterized by the growth of tens to hundreds of adenomatous colorectal polyps.^{1,2} Features typically present at approximately 47 years of age.³ Polyp types can include conventional adenomas, as well as serrated adenomas, hyperplastic polyps, and mixed (hyperplastic and adenomatous) polyps.⁴ Occasionally, colon cancer may develop in the absence of polyposis.⁵⁻⁷

Cancer Type	MAP Cancer Risks	General Population Lifetime Cancer Risks	Surveillance/Management Recommendations ⁸
Colorectal ^{1,2}	43-100%	4.2%	<p>Surveillance</p> <ul style="list-style-type: none"> For unaffected individuals: <ul style="list-style-type: none"> Begin colonoscopy at age 25-30 years, and every 1-2 years if negative For individuals with polyps: <ul style="list-style-type: none"> Age <21 years with a small adenoma burden: Colonoscopy and polypectomy every 1-2 years; surgical evaluation and counseling if appropriate Age ≥21 years with small adenoma burden: Colonoscopy and polypectomy every 1-2 years; colectomy and ileorectal anastomosis (IRA) may be considered; surgical evaluation and counseling if appropriate <u>Small adenoma burden</u> is defined as <20 adenomas, all <1 cm in diameter, and none with advanced histology <p>Surgery</p> <ul style="list-style-type: none"> Colectomy may be indicated if colonoscopy is difficult and polyp control is uncertain. Surgery could be considered when polyp burden is >20 at any individual examination, when polyps have been previously ablated, when polyps have reach a size >1 cm, or when advance histology is encountered in any polyp. Extent of colectomy may be modified based on the burden and distribution of adenomas Colectomy with IRA if adenoma burden cannot be managed endoscopically <ul style="list-style-type: none"> If individual had colectomy with IRA, endoscopy evaluation of rectum every 6-12 months depending on polyp burden Consider proctocolectomy with ileal pouch-anal anastomosis (IPAA) if dense rectal polyposis not manageable with polypectomy <p>Chemoprevention</p>

			<ul style="list-style-type: none"> • The use of chemoprevention may facilitate management of the remaining rectum post-surgery • There are no known FDA-approved medications for this indication at present • There are data to suggest sulindac is the most potent polyp regression medication; however, it is not known if the decrease in polyp burden decreases the cancer risk
Upper GI tract ^{2,8}	<p>5%</p> <p>(Duodenal polyps found in 17-25% of individuals with MAP)</p>	0.3%	<p><i>Surveillance</i></p> <ul style="list-style-type: none"> • Annual physical examination • For unaffected individuals: <ul style="list-style-type: none"> ○ Consider upper endoscopy (including complete visualization of the ampulla of Vater) beginning at age 30-35 years • For individuals with polyps: <ul style="list-style-type: none"> ○ Baseline upper endoscopy beginning at age 30-35 years is recommended • Frequency of upper endoscopic surveillance should be based on duodenoscopic findings: <ul style="list-style-type: none"> ○ Stage 0, no polyposis: repeat every 4 years ○ Stage I, minimal polyposis (1-4 tubular adenomas, size 1-4mm): repeat every 2-3 years ○ Stage II, mild polyposis (5-19 tubular adenomas, size 5-9mm): repeat every 1-3 years ○ Stage III, moderate polyposis (>20 lesions, or size >1cm): repeat every 6-12 months ○ Stage IV, dense polyposis or high grade dysplasia: surgical evaluation, expert surveillance every 3-6 months, complete mucosectomy or duodenectomy, or Whipple procedure if duodenal papilla is involved • Recommended examination with side-viewing endoscope and use of Spigelman's or other standardized staging • More intensive surveillance and/or treatment is required in individuals with large or villous adenomas, and with advancing age >50 years <p><i>Surgery</i></p> <ul style="list-style-type: none"> • Surgery (as described above) is recommended for invasive carcinoma as well for dense polyposis or high-grade dysplasia that cannot be managed endoscopically

Other Clinical Features and Cancer Risks: Extra-gastrointestinal manifestations are uncommon, but may include jaw-bone cysts and congenital hypertrophy of the retinal pigment epithelium (CHRPE).⁹ There may be other cancer extra-intestinal cancer risks associated with MAP for which there is insufficient evidence to warrant intervention, including

ovarian, bladder, endometrial, skin, and thyroid cancers.^{2,9,10} Further research is needed to make conclusions about these risks.

Implications for Family Members/Reproductive Considerations

- MAP is an autosomal recessive condition caused by biallelic *MUTYH* mutations (i.e., two pathogenic mutations in *MUTYH*, one in each copy of the gene).
- Individuals with MAP will pass one *MUTYH* mutation to all of their children.
- Individuals with a single (monoallelic) *MUTYH* mutation are considered *carriers* of MAP.
 - If only one parent is a carrier, each of their children has a 50% chance to be a *carrier* of MAP
 - If both parents are carriers, each of their children has a 25% chance of having MAP.
- Individuals with a monoallelic *MUTYH* mutation are not affected with MAP, but may have moderately increased risks for colorectal cancer.^{5,11-13}
- Family members should have full *MUTYH* gene analysis rather than single-site testing for the known familial mutation(s), as 1-2% of the general Northern European population is a carrier of a monoallelic *MUTYH* mutation.^{5,14,15}
- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

References:

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