BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

MUTYH-Associated Polyposis (MAP) Cancer Risks and Management

Overview

MUTYH-associated polyposis (MAP) is an inherited colorectal cancer syndrome caused by inheritance of **two** pathogenic variants in *MUTYH* (one from each parent).

People who inherit a single pathogenic variant in the *MUTYH* gene are carriers for MAP and may have a low to moderate increase in colorectal cancer risk dependent on their family history.

This document summarizes the cancer risks and management recommendations for people with a confirmed monoallelic or biallelic *MUTYH* variant(s).

MUTYH Carriers – One/Monoallelic Variant

Cancer risks:

People with a single pathogenic variant in *MUTYH* are not expected to have a higher chance to get cancer. Screening should be guided by the family history of cancer.

Inheritance

MAP is inherited in an autosomal recessive manner, meaning that an affected person inherited a pathogenic *MUTYH* gene variant from each parent.

For someone confirmed to be a *MUTYH* carrier (one, monoallelic *MUTYH* variant):

- Parents: 50% chance to have a single *MUTYH* variant.
- Siblings: 50% chance to have a single *MUTYH* variant. Risk for MAP dependent on carrier status of parents (which is estimated to be 0.5-1% in the absence of contributing medical history or consanguinity [e.g. parents are first cousins]).
- Children: 50% chance to have a single *MUTYH* variant. Risk for MAP dependent on carrier status of their other parent (which is estimated to be 0.5-1% in the absence of contributing medical history or consanguinity [e.g. parents are first cousins]).

Genetic testing for a single *MUTYH* variant is not available through the Hereditary Cancer Program at this time.

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Family members at risk for MAP are encouraged to contact their local genetics clinic to learn more about whether genetic testing or cancer screening may be helpful for them. Family members who live in British Columbia or the Yukon can contact our program directly at hereditarycancer@bccancer.bc.ca. In BC/Yukon, genetic testing is generally available starting at age 19.

MUTYH-Associated Polyposis (MAP) – Two/Biallelic Variants

Cancer risks:

MAP is characterized by the development of multiple colorectal polyps, typically ranging from tens to a few hundred but most often less than 100. In some cases, colorectal cancer may occur even in the absence of polyposis. The number of polyps does not appear to correlate with colorectal cancer risk. The polyps seen in MAP are most often adenomatous, although hyperplastic, sessile serrated, traditional serrated and mixed (hyperplastic and adenomatous) adenoma types have also been reported. Duodenal adenomas are common and there is an increased risk of duodenal cancer.

Additional reported features include jawbone cysts, thyroid nodules, benign adrenal lesions and congenital hypertrophy of the retinal pigment epithelium (CHRPE, a benign freckle of the retina that does not affect vision). Data for extraintestinal malignancies is preliminary and may be conflicting; further research is required to clarify these risks.

Current estimates of the risks for an individual with MAP are as follows:

By Age	Colorectal Cancer Risk*	Extraintestinal Malignancies Risk **	Duodenal Adenomas and Cancer Risk (Lifetime)
40 years	12%		10-40% duodenal adenoma risk
50 years	20 to 40%	20%	Y179C_Y179C genotype: 42% duodenal adenoma risk
60 years	43 to 63%	38%	G396D_G396D genotype: 13% duodenal adenoma risk
70 years	86%		4% duodenal cancer risk

* If polyposis left untreated.
** Bladder, ovarian, skin, breast and endometrium cancers have been reported. Absolute risks have not been confirmed and management should be guided by family history alone.

Colorectal Cancer Screening

- Colonoscopy every 1-2 years is recommended starting from age 18.
- Subsequent screening post-polypectomy should be guided by the polyp burden (number, size, histology, location/amenability to removal).

Colorectal Cancer Prevention

- There is no data for aspirin use for colorectal cancer prevention in MAP, but chemoprevention recommendations from Lynch syndrome (a hereditary colorectal cancer predisposition) can be considered, if not contraindicated: **daily low-dose aspirin** (81 mg; double dose if BMI ≥30) starting 5 years before colonoscopy screening and stopping by age 70 if used solely for colorectal cancer prevention. H. pylori testing and eradication as well as blood pressure control reduce the risk of aspirin-related adverse effects.
- Prophylactic colectomy is generally not recommended in the absence of polyposis. Colectomy may be considered depending on polyp burden, degree of dysplasia, age, co-morbidities, patient's views, and compliance with endoscopic surveillance as appropriate. Surveillance of all remaining colonic mucosa should continue every 1–2 years, even after surgery.

Upper Gastrointestinal Screening

- High-quality esophagogastroduodenoscopy (including complete visualization of the ampulla of Vater) every 1-3 years, preferably at time of colonoscopy, beginning from age 30-35.
- Polypectomy is recommended regardless of polyp size or Spigelman staging.

Pancreatic Cancer

- There is no clear data to recommend pancreatic cancer surveillance in individuals with MAP who do not have a family history of pancreatic cancer in a first or second degree relative.
- Begin screening for type 2 diabetes at age 40, repeat every 3 years.
- Investigate new onset of diabetes or unexplained changes in diabetic control carefully, with consideration of pancreatic imaging (CT pancreatic protocol or contrast-enhanced MRI/MRCP); refer to GI specialist if any abnormalities are found.

Additional pancreatic screening may be recommended to people who have MAP and a close relative with pancreatic cancer. There is more information here: HCP_GuidelinesManuals_FamilialPancreaticCancer.pdf

Note: In the information above, male/female refers to sex assigned at birth.

Inheritance

MAP is inherited in an autosomal recessive manner, meaning that an affected person inherited a pathogenic *MUTYH* gene variant from each parent.

For someone confirmed to have MAP (two biallelic *MUTYH* variants):

- Parents: considered obligate carriers of a single *MUTYH* variant.
- Siblings: 25% chance to have MAP, 50% chance to have a single *MUTYH* variant.
- Children: considered obligate carriers of a single *MUTYH* variant. Their risk for MAP is dependent on the carrier status of their other parent (which is estimated to be 0.5-1% in the absence of contributing medical history or consanguinity [e.g. parents are first cousins]).

Family members at risk for MAP are encouraged to contact their local genetics clinic to learn more about whether genetic testing or cancer screening may be helpful for them. Family members who live in British Columbia or the Yukon can contact our program directly at hereditarycancer@bccancer.bc.ca. In BC/Yukon, genetic testing is generally available starting at age 19.