



A Patient's Guide to risk assessment

Hereditary Colorectal Cancer

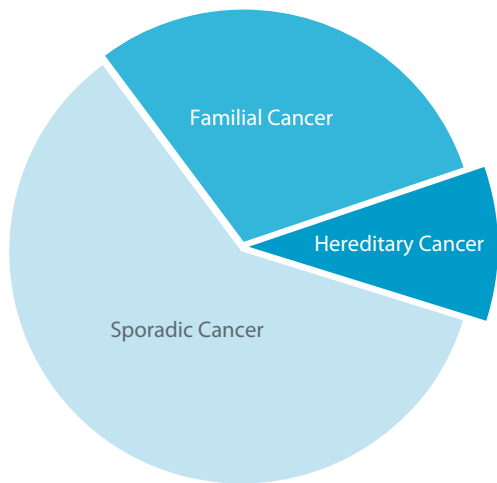


Hereditary Cancer Testing: Is it Right for You?

This workbook is designed to help you decide if hereditary cancer testing is right for you and testing should be completed with a trained healthcare provider.

Introduction

Most cancer occurs by chance. This is often called “sporadic cancer.” In some families we see more cancer than we would expect by chance alone. Determining which of these families have cancer related to an inherited gene mutation is important, as the cancer risks in hereditary cancer families are much higher than the general population.



Sporadic Cancer – Cancer which occurs by chance. People with sporadic cancer typically do not have relatives with the same type of cancer.

Familial Cancer – Cancer likely caused by a combination of genetic and environmental risk factors. People with familial cancer may have one or more relatives with the same type of cancer; however, there does not appear to be a specific pattern of inheritance (eg, the cancer risk is not clearly passed from parent to child).

Hereditary Cancer – Cancer occurs when an altered gene (gene change) is passed down in the family from parent to child. People with hereditary cancer are more likely to have relatives with the same type or a related type of cancer. They may develop more than one cancer and their cancer often occurs at an earlier than average age.

Overview of Syndromes

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC), is an inherited condition that causes an increased risk for colorectal cancer, gynecological cancers, as well as other related cancers.* The majority of Lynch syndrome is due to mutations in the *MLH1*, *MSH2*, *MSH6*, *PMS2*, or *EPCAM* (also known as TACSTD1) genes. These mutations can be inherited from either your mother or father.

MYH-associated polyposis (MAP) is a hereditary condition that causes an increased risk for colorectal cancer and colorectal polyps. Individuals with MAP often do not have a family history of colon cancer or colon polyps in family members (although siblings may be affected). MAP is caused by mutations in the *MYH* gene, and individuals with MAP have mutations in both of their *MYH* genes (one from each parent).

Familial adenomatous polyposis (FAP) or attenuated FAP (AFAP) is an inherited condition that is caused by a mutation in the *APC* gene. Patients who have a mutation in the *APC* gene can have tens to hundreds of colorectal polyps (adenomas), a greatly increased risk of colorectal cancer, and an increased risk for other associated cancers. An *APC* mutation can be inherited either from your mother or father.

Personal and Family History[†]

Check all that apply:

- ☐ Colon or rectal cancer before age 50.
- ☐ Endometrial cancer before age 50.
- ☐ One family member with colon or endometrial cancer before age 50.
- ☐ Two or more Lynch syndrome cancers* at any age in the same person.
- ☐ Two or more family members with a Lynch syndrome cancer* on the same side of the family, one under age 50.
- ☐ Three or more family members with a Lynch syndrome cancer* on the same side of the family.
- ☐ A previously identified Hereditary Colon Cancer mutation in the family.
- ☐ Personal or family history of 10 or more cumulative colorectal polyps (adenomas).

[†] Assessment criteria based on medical society guidelines. For these individual medical society guidelines go to www.myriadpro.com/professional-practice-guidelines

* Colon, endometrial, ovarian, stomach, kidney/urinary tract, biliary tract, small bowel, pancreas, brain, and sebaceous adenoma/carcinoma

Cancer Risks for Lynch Syndrome Mutation Carriers

Lynch Syndrome	Mutation Carrier Risk	General Population Risk
Colorectal	up to 82%	2%
Endometrial (uterine)	up to 71%	1.5%
Stomach	up to 13%	<1%
Ovarian	up to 12%	<1%
Second cancer within 10 years	30%	3.5%
Second cancer within 15 years	50%	5%

Lynch syndrome mutation carriers also have a slightly elevated risk over the general population of developing cancers of the kidney/urinary tract, brain, biliary tract, small bowel and pancreas.

Notes:

Managing Lynch Syndrome Risk*

It is recommended that you be managed according to these guidelines, depending on your personal and family history. Discuss these options with the appropriate medical professionals to determine how you will manage your cancer risks.

Increased surveillance

Site	Procedure	Age to begin	Repeat Test
Colon	Colonoscopy	20-25 years (or 2-5 years prior to the earliest colorectal cancer if it is diagnosed under age 25)	1-2 years
Endometrium (Uterus)/ Ovaries	Gynecologic exam Transvaginal ultrasound Endometrial tissue sample CA-125	20-25 years	1-2 years

Screening for other Lynch syndrome-related cancers (stomach, kidney/urinary tract, biliary tract, brain, small bowel, pancreatic) may be considered based on the presence of that cancer in a family member. Please speak to your healthcare provider.

Surgical Management

- Removal of the colon is often recommended in patients who develop colon cancer. The rectum is usually left in place.
- Preventive removal of the uterus (endometrium) and/or ovaries reduces the risk of uterine and/or ovarian cancer and may be an option when childbearing is complete.
- Unaffected mutation carriers not willing or unable to undergo screening colonoscopies may consider preventive removal of the colon.

* For reference and supporting data on risk factors and medical management visit www.MyriadPro.com/references

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Cancer Risks for People Who Have AFAP or FAP

	Gene Mutation Carrier Risk	General Population Risk ¹
Colorectal cancer in FAP	approximately 100%	2%
Colorectal cancer in AFAP	80%-100%	2%
Small bowel cancer	5%-12%	NA ²

APC gene mutation carriers have a slightly elevated risk over the general population of developing cancers of the pancreas, thyroid, stomach, and brain. Liver cancer risk in children is also increased.

¹ Risk by age 70
² Not available

Managing Your Risks for People Who Have AFAP or FAP*

Options for reducing cancer risk are available whether or not you have already had a diagnosis of cancer and/or polyps (adenomas). The following are medical management guidelines for individuals with FAP and AFAP. Discuss these options with the appropriate medical professionals to determine how you will manage your cancer risks.

It is recommended that you be managed according to these guidelines, depending on the number of colorectal polyps (adenomas) in you and your family members. Discuss these options with the appropriate medical professionals to determine how you will manage your cancer risks.

Notes:

Managing Your Risks for People Who Have AFAP or FAP

Increased surveillance

Site	Procedure	Age to begin	Repeat Test
Colon –FAP	Sigmoidoscopy or colonoscopy	10-15 years	Annually
Colon –AFAP	Colonoscopy	Late teens (depending on age of polyp development in the family)	1-3 years
Colon–After colon surgery	Endoscopy of remaining rectum, ileal pouch, or ileostomy	After colon surgery	6 months to 3 years (depending on polyp number and type of surgery)
Duodenum and stomach	Baseline upper endoscopy (including side-viewing examination)	25-30 years	1-4 years
Thyroid	Physical exam and consideration of ultrasound	Late teens	Annually

Screening for other related cancers (brain, pancreatic, hepatoblastoma, etc.) may be considered. Please speak to your healthcare provider about this option.

* For references and supporting data on risk factors and medical management, visit www.MyriadPro.com/references

Surgical Management

- FAP–Preventive removal of the colon and rectum is recommended. The timing of surgery is based on the number/size of polyps.
- AFAP–Preventive removal of the colon and rectum may be recommended depending on the number of polyps.

Chemoprevention

- Medications may be used to reduce the number of polyps in any rectum that remains after colon surgery.

Testing Options

COLARIS® (Lynch Syndrome Plus MAP):

Sequence and large rearrangement analysis of the *MLH1*, *MSH2*, *MSH6*, *PMS2*, *MYH* genes and large rearrangement analysis of *EPCAM*.

COLARIS AP® (AFAP, FAP, MAP):

Sequence and large rearrangement analysis of the *APC* and *MYH* genes.

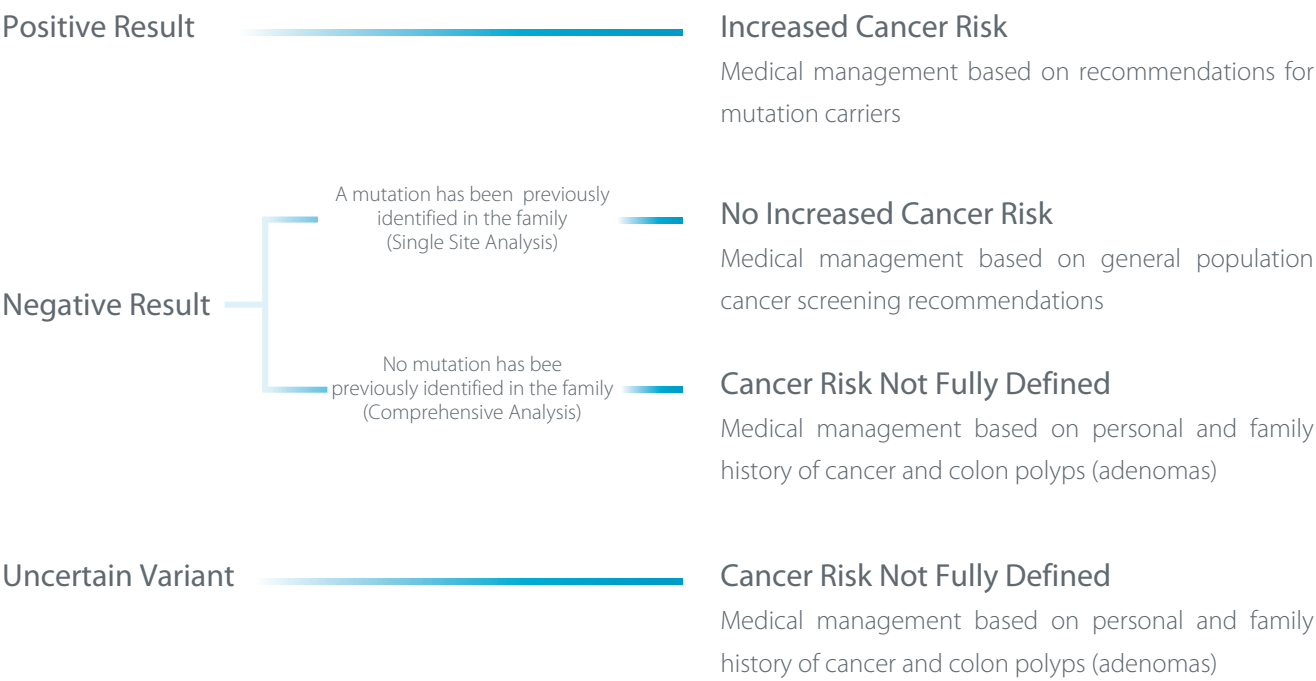
Single Gene Testing:

Sequence and large rearrangement analysis of one of the following genes: *MLH1*, *MSH2/EPCAM*, *MSH6*, *PMS2*, *MYH*, or *APC*

Single Site Testing:

Mutation specific analysis for individuals with a known Lynch syndrome, *AFAP*, *FAP*, *MAP* mutation in the family.

Possible Test Results



* Patients who test positive for one MYH gene mutation do not have MYH-associated polyposis (MAP), but may have a small increased risk for colon cancer.

It’s a Family Affair

- Hereditary Colon Cancer mutations can be passed on in a family.
 - If you have a mutation in one of these genes, your parents, your children, and your brothers and sisters have a chance that they have the same mutation.
 - Other relatives may be at risk to carry the same mutation.
- Testing is the only way to accurately identify mutation carriers.
- It is important to share test results with family members.
- Individuals may differ in their viewpoints and reactions to genetic testing.

Benefits and Limitations of Testing

BENEFITS

- Personalized risk assessment
- Appropriate medical management to help reduce cancer risk
- Important information for family members
- Reduced anxiety and stress

LIMITATIONS

- Testing does not detect all causes of hereditary cancer
- A negative result is most helpful when there is a known mutation in the family
- Some variants are of unknown clinical significance

Health Care Coverage

Health care reimbursement and coverage for genetic testing varies greatly throughout the world. Please check with your physician, insurance, Myriad affiliate or distribution partner in your country for additional information.

Privacy

- 1) Myriad is dedicated to offering high-quality laboratory services and is committed to securing your privacy through full compliance with federal and international regulations. Myriad has an active privacy program.
- (2) Myriad discloses test results only to the requesting healthcare provider/designee, and not to anyone else (including insurance carriers) without your written permission. Additionally, Myriad does not disclose results to patients directly, but only to their designated healthcare provider.
- (3) Myriad warrants that it has all necessary procedures and approvals, such as Safe Harbor, in place to transmit and protect the patient data received.

Next steps:

- ☐ Pursue testing
- ☐ Schedule follow-up appointment to discuss results
 - Date: _____ Time: _____
- ☐ Decline testing – Medical management based on personal and family history of cancer
- ☐ Undecided

Who to contact with questions: _____

Additional Resources:

Myriad Genetics GmbH

E-mail Medical Services with questions about testing:

helpmed-international@myriad.com

www.myriad.com

Tel. 0041 (0) 44 939 91 30

Gynecologic Cancers Foundation

This group aims to ensure public awareness of gynecologic cancer prevention, early diagnosis and proper treatment as well as supports research and training related to gynecologic cancers.

www.thegcf.org

Lynch Syndrome International

The primary mission of Lynch Syndrome International (LSI) is to serve global communities by focusing on providing support for individuals afflicted with Lynch syndrome, creating public awareness of the syndrome, educating members of the general public and health care professionals and providing support for Lynch syndrome research endeavors.

www.lynchcancers.org

Fight Colorectal Cancer

The Global Colon Cancer Alliance is committed to creating a Global Colon Cancer Community to ensure effective increased awareness, diagnosis and treatment of the disease.

<http://www.globalcoloncancer.com>

This information is provided to help answer some of your questions with respect to cancer risks, hereditary cancer risks and hereditary cancer testing. It is general in nature and is not intended to provide a definitive analysis of your specific risk factors for cancer or your hereditary cancer risks. You should not rely on the information provided herein; but rather, you should consult with your doctor or a qualified healthcare professional to review this information along with your individual health conditions and risk factors.



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