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 (broken) gene 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.

*Other cancers include uterine/endometrial, ovarian, stomach/gastric, ureter/renal pelvis, biliary tract, small bowel, pancreas, brain, and sebaceous adenomas.

**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

†Colon, endometrial, ovarian, stomach/kidney, biliary tract, small bowel, pancreas, brain, and sebaceous adenoma/carcinoma.
Cancer Risks for Lynch Syndrome Mutation Carriers

<table>
<thead>
<tr>
<th>Lynch Syndrome</th>
<th>Mutation Carrier Risk</th>
<th>General Population Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>up to 82%</td>
<td>2%</td>
</tr>
<tr>
<td>Endometrial (uterine)</td>
<td>up to 71%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Stomach</td>
<td>up to 13%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Ovarian</td>
<td>up to 12%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Second cancer within 10 years</td>
<td>30%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Second cancer within 15 years</td>
<td>50%</td>
<td>5%</td>
</tr>
</tbody>
</table>

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.
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

<table>
<thead>
<tr>
<th>Site</th>
<th>Procedure</th>
<th>Age to Begin</th>
<th>Repeat Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>Colonoscopy</td>
<td>20-25 years (or 2-5 years prior to the earliest colorectal cancer if it is diagnosed under age 25)</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Endometrium (Uterus)/Ovaries</td>
<td>Gynecologic exam Transvaginal ultrasound Endometrial tissue sample CA-125</td>
<td>25-35 years</td>
<td>1-2 years</td>
</tr>
</tbody>
</table>

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
Cancer Risks Associated With MAP

*MYH*-associated polyposis (MAP) is a syndrome that was discovered fairly recently. MAP causes an increased risk for developing colon polyps (adenomas). Because of the numerous colorectal polyps (adenomas) that occur in MAP, the colorectal cancer risk is known to be significantly increased. Additionally, it is possible that risks of other cancers, such as small bowel, may be increased as well. More detailed information about cancer risks in MAP will likely be available in the future. Contact your healthcare provider on a regular basis for up-to-date information on MAP.

Patients who test positive for a single *MYH* mutation do not have MAP, but they may have a slightly increased risk of developing colorectal cancer.

Notes:
Managing Your MAP Cancer Risks*

Options for reducing cancer risk are available whether or not you have already had a diagnosis of cancer and/or polyps (adenomas). 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.

INCREASED SURVEILLANCE

<table>
<thead>
<tr>
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<th>PROCEDURE</th>
<th>AGE TO BEGIN</th>
<th>REPEAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon—Small polyp (adenoma) burden, manageable by colonoscopy</td>
<td>Colonoscopy</td>
<td>25-30 years</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Colon—Large polyp (adenoma) burden</td>
<td>Counseling regarding surgical options</td>
<td>Varies based upon polyp (adenoma) burden</td>
<td>N/A</td>
</tr>
<tr>
<td>Colon—After colon surgery</td>
<td>Endoscopy of any remaining colon and rectum</td>
<td>After colon surgery</td>
<td>1-2 years</td>
</tr>
<tr>
<td>Duodenum and stomach†</td>
<td>Upper endoscopy and side viewing duodenoscopy</td>
<td>30-35 years</td>
<td>3-5 years</td>
</tr>
</tbody>
</table>

†Patients who have small bowel polyps (adenomas) should follow FAP small bowel screening guidelines.

SURGICAL MANAGEMENT

• Preventive removal of the colon and rectum may be recommended depending on the number of polyps (adenomas).

*For references and supporting data on risk factors and medical management, visit www.MyriadPro.com/references
### Cancer Risks for People Who Have AFAP or FAP

<table>
<thead>
<tr>
<th></th>
<th>Gene Mutation Carrier Risk</th>
<th>General Population Risk¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal cancer in FAP</td>
<td>approximately 100%</td>
<td>2%</td>
</tr>
<tr>
<td>Colorectal cancer in AFAP</td>
<td>80%-100%</td>
<td>2%</td>
</tr>
<tr>
<td>Small bowel cancer</td>
<td>5%-12%</td>
<td>NA²</td>
</tr>
</tbody>
</table>

*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.

### 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:

1. Risk by age 70
2. Not available
### INCREASED SURVEILLANCE

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</tr>
</thead>
<tbody>
<tr>
<td>Colon—FAP</td>
<td>Sigmoidoscopy or colonoscopy</td>
<td>10-15 years</td>
<td>Annually</td>
</tr>
<tr>
<td>Colon—AFAP</td>
<td>Colonoscopy</td>
<td>Late teens (depending on age of polyp development in the family)</td>
<td>1-3 years</td>
</tr>
<tr>
<td>Colon—After colon surgery</td>
<td>Endoscopy of remaining rectum, ileal pouch, or ileostomy</td>
<td>After colon surgery</td>
<td>6 months to 3 years (depending on polyp number and type of surgery)</td>
</tr>
<tr>
<td>Duodenum and stomach</td>
<td>Baseline upper endoscopy (including side-viewing examination)</td>
<td>25-30 years</td>
<td>1-4 years</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Physical exam and consideration of ultrasound</td>
<td>Late teens</td>
<td>Annually</td>
</tr>
</tbody>
</table>

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](http://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.
Possible Test Results

Positive Result

Increased Cancer Risk
Medical management based on recommendations for mutation carriers

A mutation has been previously identified in the family (Single Site Analysis)

No Increased Cancer Risk
Medical management based on general population cancer screening recommendations

No mutation has been previously identified in the family (Comprehensive Analysis)

Negative Result

Cancer Risk Not Fully Defined
Medical management based on personal and family history of cancer and colon polyps (adenomas)

Uncertain Variant

Cancer Risk Not Fully Defined
Medical management based on personal and family history of cancer and colon polyps (adenomas)

*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.

Testing Options

- **COLARIS**PLUS® (Lynch Syndrome Plus MAP):
  Sequence and large rearrangement analysis of the MLH1, MSH2, MSH6, PMS2, and MYH genes, and large rearrangement analysis of EPCAM.

- **COLARIS AP**PLUS® (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.

Testing Options

- **COLARIS**PLUS® (Lynch Syndrome Plus MAP):
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- **Single Site Testing**:
  Mutation specific analysis for individuals with a known Lynch syndrome, AFAP, FAP, MAP mutation in the family.
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

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personalized risk assessment</td>
<td>Testing does not detect all causes of hereditary cancer</td>
</tr>
<tr>
<td>Appropriate medical management to help reduce cancer risk</td>
<td>A negative result is most helpful when there is a known mutation in the family</td>
</tr>
<tr>
<td>Important information for family members</td>
<td>Some variants are of unknown clinical significance</td>
</tr>
<tr>
<td>Reduced anxiety and stress</td>
<td></td>
</tr>
</tbody>
</table>

Health Care Coverage

- Insurance coverage for genetic testing of at-risk patients is excellent, with the majority of patients covered for testing. Although each case is unique, the average patient pays coinsurance of less than $100.*

Privacy

- Federal laws (HIPAA and GINA) and laws in most states prohibit discrimination regarding employment eligibility, benefits, or premiums based solely on genetic information. Additionally, it is Myriad’s policy that test results are disclosed only to the ordering healthcare professional or designee, unless the patient consents otherwise.

Next Steps:

- ☐ Pursue testing
  - ☐ Schedule follow-up appointment for results disclosure
    Date: ________________________ Time: ________________________
- ☐ Decline testing — Medical management based on personal and family history of cancer
- ☐ Undecided

Who to contact with questions: _____________________________________________

*Test prices may be confirmed by calling Myriad Customer Service at 800-469-7423. Unmet deductibles are always the responsibility of the patient.
Colorectal Cancer Network
A support network for individuals and families touched by colon cancer that promotes awareness, screening, and early detection programs as well as legislative actions.
www.colorectal-cancer.net

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

Myriad Genetic Laboratories, Inc.
www.MySupport360.com
800-4-MYRIAD (800-469-7423)
E-mail: helpmed@myriad.com

Colon Cancer Alliance
The Colon Cancer Alliance (CCA) is a national patient advocacy organization dedicated to ending the suffering caused by colorectal cancer.
www.ccalliance.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
FCC is the leading national colorectal cancer advocacy organization empowering survivors to raise their voices, training advocates around the country, and educating lawmakers and pushing them for better policies. FCC offers support for patients, family members and their caregivers, and serves as a resource for colorectal cancer advocates, policymakers, medical professionals, and healthcare providers. Additionally, they increase and improve research—at all stages of development and for all stages of cancer.
www.fightcolorectalcancer.org