A Patient's Guide to Lynch Syndrome

It Takes Guts™

HEREDITARY COLON CANCER FOUNDATION

Dear Reader,

"A Patient's Guide to Lynch Syndrome" was created by the Hereditary Colon Cancer Foundation and was authored by Travis H. Bray, PhD (Hereditary Colon Cancer Foundation), Reagan Barnett, PhD (Alive and Kickn and The University of Texas MD Anderson Cancer Clinic), C. Richard Boland, MD (Baylor University Medical Center [retired] and Baylor Research Institute), Dave Dubin (Alive and Kickn and Icahn School of Medicine at Mt. Sinai), Heather Hampel, MS, CGC (The Ohio State University Wexner Medical Center), Karen Lu, MD (The University of Texas MD Anderson Cancer Clinic), Sharon Perlman (Colon Cancer Alliance Research and Education for Lynch Syndrome). The content is based on the approved recommendations in the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology "Genetic/Familial High-Risk Assessment: Colorectal" (2015) and the American College of Obstetricians and Gynecologist's "Practice Bulletin - Clinical management guidelines for obstetrician-gynecologists: Lynch syndrome."

This guide is intended to provide information for those affected by Lynch syndrome and should not replace discussions or advice from your medical provider. We suggest you read this Guide in the order in which it is written, as each section builds upon information in previous sections. Medical terms in blue are explained in the glossary.

Be well and stay strong!

Travis H. Bray, PhD
Previvor, Founder, and Executive Director
Hereditary Colon Cancer Foundation

This Guide was Made Possible Through a Generous Grant From:

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If you or your loved one has just been diagnosed with Lynch syndrome,

Don't panic...

Lynch syndrome affects as many as 1 out of every 280 people. Think about that... there are over 7 billion people on the earth. Over 25 million of them have Lynch syndrome just like you. And many of them are living long, fulfilling lives!

In other words, YOU are not alone!

Knowing that you have Lynch syndrome is the most important first step towards living a healthy life. It empowers you to manage your care and reduce your risk of cancer. It allows you and your doctor to form a care plan to prevent cancer, or catch and treat it early.

HEREDITARY COLON CANCER FOUNDATION
It Takes Guts

What is Lynch Syndrome?

Lynch syndrome is named after Henry T. Lynch, MD, who wanted to understand why some families seem to have a higher risk of cancer. He was the first to describe what he called 'Cancer Family Syndrome' in 1966. Lynch syndrome was originally called 'Hereditary Non-Polyposis Colorectal Cancer (HNPCC).' The name 'HNPCC' is rarely used now because people with Lynch syndrome:

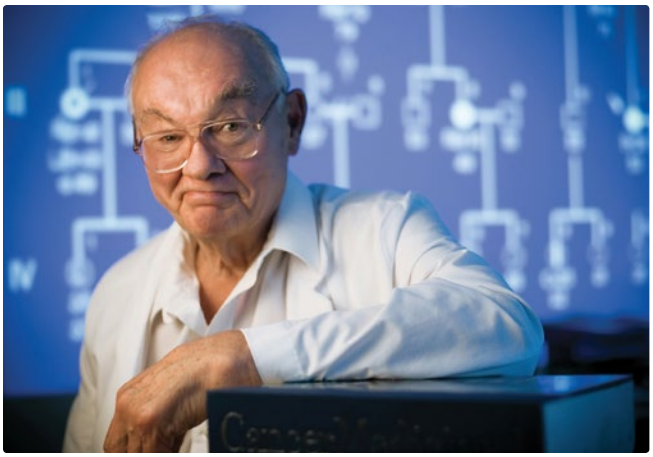
1. can have **polyps**, AND
2. have an increased risk of other cancers in addition to **colorectal cancer** (See Table 3: Cancer Risks Associated with Lynch Syndrome on page 14).

While most cancers are due to environmental or lifestyle factors, as much as 10% of cancer may be due to an **inherited** condition. Lynch syndrome is the most common form of **hereditary colon** cancer and causes 3–5% of all **colorectal cancer**.

Note 1

Lynch syndrome has also been called Turcot syndrome and Muir-Torre syndrome. These were thought to be specific types of Lynch syndrome and were based on a certain set of symptoms. These names are rarely used today.

What is Cancer?



Henry T. Lynch, MD

For your body to grow and/or repair itself, **cells** have to create new **cells**. If you cut yourself, your skin **cells** continue to divide until the wound is healed. Normal, healthy **cells** know when to stop dividing. They have sensors in their walls that say "Stop… that's enough!"

Having cancer means you have **cells** that do not know when to stop creating new **cells**. This can happen anywhere but, with Lynch syndrome, this happens most often in the **colon** and uterus. As cancer **cells** continue to grow and multiply out of control, they begin to crowd out normal **cells** and may eventually form a lump. A lump of cancer **cells** is called a **tumor**.

Medical professionals rank how serious the cancer is and/or how far it has spread by 'stages.' Cancer stages use roman numerals instead of normal numbers. In roman numerals, the number 1 is 'I', 2 is II, 3 is III, and 4 is IV. As cancer grows, spreads, and becomes more life-threatening, it progresses from Stage I to Stage IV.

The most common cancer stages are listed below.

Stage I, also called early-stage cancer: The cancer or **tumor** is still small. It has not grown in to nearby tissues very much and has not spread to the lymph nodes or other parts of the body.

Stage II–Stage III: The cancer is larger and has grown deeper into nearby tissue. It has not spread to other parts of the body, but may have spread to the lymph nodes.

Stage IV, also called advanced or metastatic. Metastatic cancer is cancer that has spread to other organs or other parts of the body.

Knowing the stage of cancer helps your medical team decide what type of treatment will likely work best.

Why Does Lynch Syndrome Cause Cancer?

Lynch syndrome is usually caused by a change in one of the **Mismatch Repair (MMR) genes**. Learning how **MMR genes** work will help you understand how Lynch syndrome causes cancer.

Mismatch Repair Genes

The human body produces nearly two trillion (2,000,000,000,000) **cells** per day. That is 23,000,000 **cells** every second of every day! Each new **cell** gets a copy of **DNA**. **Mismatch Repair (MMR) genes** check each new copy of **DNA** for errors (mismatches). If a mismatch is found, it must be repaired by the **MMR genes**.

MMR genes are **inherited** from your parents. If you **inherit** an **MMR gene** with a mistake (**mutation**) in it, that gene cannot proofread **DNA**. Luckily, the copy from your other parent may work just fine.

However, there is a chance that, one day, your working **MMR gene** will make a mistake in one of the organs affected by Lynch syndrome. When both **MMR genes** are no longer working, the **cell** can not repair **DNA** mistakes. The mistakes remain as the **cell** continues to divide. When one **cell** accumulates too many mistakes, it can start growing too fast and not die when it should. This can lead to cancer.

The **MMR genes** that cause Lynch syndrome include **MLH1, MSH2**, **MSH6**, **PMS2**. A fifth **gene** called the **EPCAM gene** has also been shown to cause Lynch syndrome by turning off the **MSH2 gene**. It only takes a change in ONE of these **genes** to have Lynch syndrome.

Table 1: Genes Associated with Lynch Syndrome

MLH1	MutL Homolog 1
MSH2	MutS Homolog 2
MSH6	MutS Homolog 6
PMS2	Postmeiotic Segregation Increased 2
EPCAM	Epithelial Cell Adhesion Molecule

EPCAM Gene

The **EPCAM gene** is not involved in **DNA** repair. **Mutations** that ONLY affect the **EPCAM gene** do not cause Lynch syndrome.

However, certain **mutations** at the end of the **EPCAM gene** can turn off the neighboring **MSH2 gene** and cause Lynch syndrome. This causes up to 6% of Lynch syndrome cases.

Note 2

Genes are like a set of instructions. They provide information for cells to divide, **proteins** to be produced, and our body to grow and heal itself. The **proteins** made by MMR genes make sure that the **DNA** has been copied properly when cells divide.

Do I Have Lynch Syndrome?

You may have Lynch syndrome if any of the following statements are true:

1. If a parent or sibling has Lynch syndrome AND the **mutation** is known, a genetic test can be quick, inexpensive, and highly reliable. This is the only way to confirm that you do or do not have Lynch syndrome (see "Genetic Testing" on page 9).

2. A parent or sibling has had colorectal or endometrial cancer AND another Lynch-related cancer, with one of the cancers developing before age 50,

OR

Two relatives, including a parent, sibling, aunt, uncle, or cousin, have had colorectal or endometrial cancer AND another Lynch-related cancer at any age (see Note 3).

If either of these are true for your family, and if tissue from the colorectal or endometrial cancer is available, it may be sent for **tumor** testing. (See "Tumor Testing" on page 8)

If not, there are computer programs that can predict your risk of having Lynch syndrome. These programs consider your family's history of cancer.

If you receive a positive result from any of the above, you should be referred for genetic testing (see "Genetic Testing" on page 9).

If you receive a negative result, your doctor or genetic counselor should continue searching for the cause of your family's history of cancer.

3. You developed any of the following:
   A. Colorectal or endometrial cancer before the age of 50
   B. Colorectal or endometrial cancer AND another Lynch-related cancer* at any age
   C. Colorectal cancer with tumor features linked to Lynch syndrome at an age younger than 60
   D. Colorectal or endometrial cancer AND a first degree relative developed a Lynch-related cancer* before age 50
   E. Colorectal or endometrial cancer AND two or more first- or second-degree relatives developed a Lynch-related cancer* at any age.

If you have had colorectal and/or endometrial cancer and answered 'Yes' to any of these, you meet the requirements for tumor testing (See "Tumor Testing" on page 8).

Note 3

Lynch-related cancers include colorectal, endometrial, ovarian, renal pelvis, gastric, small intestine, and/or ureter cancer.

How Did I Get Lynch Syndrome?

If you have Lynch syndrome, there is a 99% chance that you have inherited it from your mother OR your father. One of your parents could have Lynch syndrome and not know it. It is also possible that your brothers and sisters have Lynch syndrome too.

There is no such thing as being a "carrier" of Lynch syndrome. You either have it or you do not have it. If you do not have Lynch syndrome, you can not pass it on to your children.

It is possible to have Lynch syndrome without inheriting it from a parent, but this is extremely rare. This is called a "de Novo" mutation. The brothers or sisters of a de Novo person are unlikely to have Lynch syndrome.

Lynch syndrome is a "dominant" genetic disease. If you have Lynch syndrome, there is a 50% that each of your children could inherit it. Even if you are the first person in your family to have it, you still have a 50% chance of passing it along to each child you have. This risk is the same for each pregnancy.

Your doctor may suspect you have Lynch syndrome based on your personal or family history of cancer. A tumor test can identify those who should be genetically tested, but only genetic testing can confirm and diagnose Lynch syndrome.

How Is Lynch Syndrome Diagnosed?

Tumor Testing

When Lynch syndrome causes colorectal or endometrial cancer, it leaves certain characteristics, similar to fingerprints, on the tumor. While a genetic test is the best way to find out if you have Lynch syndrome, tumor testing is often the first step in identifying the syndrome.

There are two types of tumor testing commonly used: Microsatellite Instability (MSI) and Immunohistochemistry (IHC).

Microsatellite Instability (MSI)

Microsatellites are short sections of DNA that repeat over and over. Microsatellite instability (MSI) is when these short sections of DNA repeat much more frequently because the MMR system is not working. Tumors with a lot of these changes are called MSI high or MSI positive. Having a tumor that is MSI high does not necessarily mean that you have Lynch syndrome. It means that the MMR system is defective. It is possible for a person who does not have Lynch syndrome to have a tumor that is MSI high.

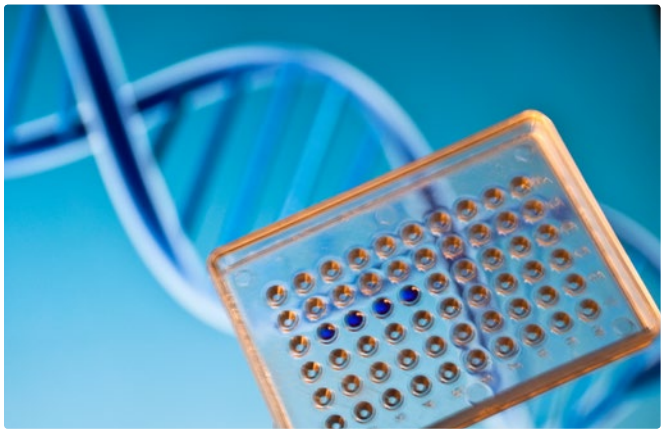
If the MSI test shows that the tumor cells have no microsatellite instability, then it is unlikely that the person has Lynch syndrome. If the MSI shows that tumor cells has microsatellite instability, then Lynch syndrome is more likely.

If the tumor test shows a high amounts of microsatellite instability, the patient is usually referred for genetic testing.

Immunohistochemistry (IHC)

Immunohistochemistry is a process that can look for certain proteins in tumors. These proteins can be stained and made easy to see. IHC is used to detect whether the proteins produced by the MMR genes were produced correctly. When the MMR system is not working properly, a protein is missing. The missing protein suggests which Lynch syndrome gene is mutated.

If the IHC staining does not come back normal, the situation becomes a bit more complicated. Your medical team may run further tests and/or recommend genetic testing.



Genetic Testing

Genetic testing is a medical test that identifies changes in your **DNA**. If there is a chance you have Lynch syndrome, genetic testing may confirm it. This can help you learn more about your risks and possibly avoid cancer. It can help you and your doctors make better decisions about your health care, and create a prevention, screening, and treatment plan just for you. Family members may avoid unnecessary cancer screening if genetic testing confirms that they do not have Lynch syndrome.

The **cells** needed for a genetic test are most easily obtained from blood, a mouth rinse or an inner cheek swab. The sample is sent to a laboratory where your **DNA** is analyzed to see if you have Lynch syndrome. This process can take 2–12 weeks. The genetic tests will look for mistakes in the genes related to Lynch syndrome.

If you know which gene is mutated in your family, then you will likely be tested for that specific **mutation** only. Testing for one specific gene is less expensive and very reliable.

Genetic tests can be expensive and special training is required to understand the results. Receiving a **false-positive** result could lead to unnecessary stress, tests, and, surgeries. A **false-negative** result could mean not getting the screening you need to avoid advanced cancer.

For these reasons, we recommend you work with a genetic counselor, geneticist, or a doctor who is experienced with Lynch syndrome. They will choose the right test for you, explain the results, and help figure out what to do next.

Note 4: At Home Genetic Testing

Genetics is a fast growing field. The science is constantly changing and new companies seem to join the market daily. It is important that you work with a genetic counselor or a doctor who knows how to choose a high quality genetic test. We do not recommend that you order a genetic test on your own.

Genetic Testing Results

If genetic testing confirms that you have Lynch syndrome, a screening plan can be found in the section titled “How Should I Manage Lynch Syndrome?” on page 13.

If you know which Lynch syndrome **gene** is mutated in your family and genetic testing confirms that you have NOT **inherited** it, then you do not have Lynch syndrome. You do not need intensive screening, and your children can not **inherit** Lynch syndrome from you.

It is not always possible to be certain if you have Lynch syndrome. When this happens, screening should be based on your personal and family

medical history. A genetic counselor or a doctor who specializes in Lynch syndrome can create a personal screening plan for you. (See "Watching for Symptoms and Screening for Cancer" on page 15)

Risks and Limitations

It is important to understand the risks and limitations of genetic testing before you have a genetic test. Most of the risks associated with genetic testing are emotional, social, and/or financial in nature. The risks include:

- **Emotional Risks**: Undergoing genetic testing may change someone's self-identity. Emotional risks can include feelings of isolation, anger, depression, anxiety, or guilt. Emotional risks are not limited to those who discover they have Lynch syndrome. Other family members who discover they do not have the condition may also be affected by "survivor's guilt."

- **Family Dynamics**: Genetic testing can reveal information about other family members. The results may create tension within a family.

- **Genetic Discrimination**: Genetic discrimination means being treated differently by employers or insurance providers. Fear of genetic discrimination is common.

Table 2: Understanding Genetic Testing Results

If this...	Then...
Negative Result **and** the family's Lynch syndrome gene has been identified...	The person does not have Lynch syndrome. People who do not have Lynch syndrome do not need to follow the screening recommendations provided in this guide.
Negative Result and the family's Lynch syndrome gene has **NOT** been identified...	The presence of Lynch syndrome could not be confirmed at this time. Screening should be based on medical history and a family risk assessment performed by a genetic counselor or other genetics expert.
Uncertain Result	An uncertain result occurs because the genetic test reported a "variant of uncertain significance" (VUS). A VUS does not confirm or deny Lynch syndrome and should NOT be used to make medical decisions.
Positive	Lynch syndrome was identified. This helps you and your medical team manage your cancer risks and allows for testing of family members.

The Genetic Information Nondiscrimination Act (GINA) is a federal law protecting people from genetic discrimination based on genetic test results and family history information.

GINA has two parts:

Title I says that health insurance providers:

- Cannot use the fact that you have Lynch syndrome to determine eligibility or to set rates for health insurance.
- Cannot require you or a family member to take a genetic test.

Title II prohibits genetic discrimination in employment and says:

- Genetic information may not be used for hiring, firing, promoting, determining pay or assigning jobs, except in the US military.
- Employers cannot require you to take a genetic test.

There are important limitations to this law. GINA does not apply to:

- Small businesses (fewer than 15 employees),
- The Federal Employees Health Benefits Program,
- The U.S. military / TRICARE,
- The Veterans Health Administration,
- The Indian Health Service,
- Other types of insurance including life, disability, or long-term care insurance

As a result, consider obtaining disability or life insurance BEFORE you undergo genetic testing.

Cost of Genetic Testing

The cost of genetic testing can depend on the number of **genes** being tested and if more than one test is needed. The doctor who orders the test should provide information about the cost of the test.

Most health insurance plans cover genetic testing if it is "medically necessary" and recommended by your doctor. The doctor who orders the test, or a genetic counselor, will work with your insurance to verify coverage.

Many genetic testing laboratories may also help to verify your insurance coverage for a test. If you have difficulty getting your insurance to cover your test, or if you do not have insurance, ask your doctor to contact the genetic testing laboratory on your behalf. These laboratories often provide patient support.

Decide if Testing is Right for You and Your Family

Genetic testing is a personal choice. Before you have a genetic test, you should meet with a genetic counselor or other genetics expert. They will explain how the testing will be done and the pros and cons of being tested. This is the best way to learn what testing can and cannot do for you.

Lynch syndrome does not usually increase your risk of cancer until after your teens. As such, genetic testing is usually not ordered until a person is at least 18.

If you decide to have a genetic test, the following people can order it:

- Gastroenterologists (GI)
- Medical geneticists
- Nurse practitioners
- Oncologists
- Obstetricians and Gynecologists (Ob/Gyn)
- Primary care doctors
- Surgeons

Genetic counselors cannot order genetic tests. They can recommend the correct test, help work with your insurance company to cover all or part of the costs, and interpret the results.

Genetic Counseling

Genetic counselors are experts at explaining how a genetic condition, like Lynch syndrome might affect your physical and mental health, as well as the health of your family. They can answer many questions to help you make important decisions. Here are some questions that are commonly answered in a genetic counseling appointment:

"Lynch syndrome runs in my family. What does this mean for me?"

"I've had cancer. What does that mean for my children?"

"What does this mean about future children?"

"My partner and I are planning a pregnancy. What types of genetic testing are available to us?"

"Could I pass Lynch syndrome on to my children?"

"Would genetic testing be useful for me or my family?"

"What can I do to manage my own care?"

"How do I talk to my relatives or my doctors about Lynch syndrome?"

Individuals, couples, or families can visit a genetic counselor. During your appointment, the genetic counselor may:

- Review your personal and family medical history
- Explain your options for genetic testing
- Identify your cancer risks and discuss ways to stay ahead of cancer
- Give you information on Lynch syndrome
- Discuss family planning

You may speak with a genetic counselor once or several times. Meeting with a genetic counselor does not always mean that you will have a genetic test.

Is There a Cure?

While there is no 'cure' for Lynch syndrome, it can be managed. Proper care greatly increases your chances of living a normal number of years. It is important to follow the recommended screening and treatment plan created for you by a Lynch expert.

How Should I Manage Lynch Syndrome?

If you have Lynch syndrome, you may be at risk for several cancers. These cancers are listed by **gene** in Table 3 on page 14. It is important to find doctors who specialize in Lynch syndrome. They can help you put together a plan to manage your care. A growing list of experienced medical professionals can be found at www.HCCTakesGuts.org.

Note 5: Healthy Habits that Reduce Cancer Risk

Mayo Clinic recommends the following behaviors to reduce cancer risk:

1. Don't use tobacco
2. Eat a healthy diet
3. Maintain a healthy weight and be physically active
4. Drink alcohol in moderation, if you choose to drink

Table 3: Cancer Risks Associated with Lynch Syndrome

Cancer Risk Up to Age 70 Years in Individuals with Lynch Syndrome

Compared to the General Population

	MLH1, MSH2, EPCAM		MSH6		PMS2		General Population
Cancer Type	% Risk	Avg. Age of Onset	% Risk	Avg. Age of Onset	% Risk	Avg. Age of Onset	% Risk
Colon	40–80	44–61 years	10–22	54 years	15–20	61–66 years	5.5
Endometrium [1–5]	*MLH1:* 54 (20–80) *MSH2:* 21 (8–77) *EPCAM* up to 12	47.5 years	16 (8–32)	55 years	15 (6–35)	49 years	2.3
Ovary [1–5]	*MLH1:* 24 (1–65) *MSH2:* 24 (3–52) *EPCAM:* Very Low	42–48 years	1 (0–3)	46 years	The combined risk for renal pelvic, stomach, ovary, small intestine, ureter, and brain is 6% (1–33)	42 years	1.6
Urinary Tract	1–4	54–60 years	<1	65 years		Unknown	<1
Stomach	1–13	56 years	≤3	63 years		70–78 years	<1
Small Intestine	3–6	47–49 years	Unknown	54 years		59 years	<1
Liver, Gall Bladder, and Bile Ducts	1.4–4	50–57 years	Unknown	Unknown		Unknown	<1
Brain/CNS	1–3	~50 years	Unknown	Unknown		45 years	<1
Pancreas	1–6	Unknown	Unknown	Unknown	Unknown	Unknown	<1
Skin	1–9	Unknown	Unknown	Unknown	Unknown	Unknown	<1

*The risks of endometrial and ovarian cancer are based upon the American College of Obstetricians and Gynecologists November 2014 Practice Bulletin. All other cancer risks are based upon the NCCN Clinical Practice Guidelines in Oncology - Genetic/Familial High-Risk Assessment: Colorectal 2015.

Who is on my Medical Care Team?

It is common for people with Lynch syndrome to work with a genetic counselor, gastroenterologist, or gynecologist to help them put together a care team.

Here is a list of doctors you may need to include on your team and their speciality:

- **Colorectal Surgeon**: surgery of large intestines, including the colon and rectum
- **Dermatologist**: skin
- **Gastroenterologist**: stomach, small intestines, large intestines, liver, gall bladder, and bile ducts
- **Gastrointestinal Surgeon**: surgery of stomach, small intestines, large intestines, liver, gall bladder, and bile ducts
- **Genetic Counselor**: medical genetics and counseling
- **Geneticist:** medical genetics
- **Psychologist**: mental heath
- **Surgical Oncologists**: surgery of tumors, especially cancerous tumors
- **Urologist**: urinary tract, including the kidney, ureter, bladder, and urethra

In addition, women should include one or more of the following:

- **Gynecologist**: female reproductive system, including the breasts, uterus, and ovaries
- **Gynecological Oncologist**: cancer in the female reproductive system
- **Gynecological Surgeon**: surgery of female reproductive system

High risk cancer clinics usually include several of the doctors listed above. A high risk cancer clinic can help you understand your risk of cancer and work with you to reduce your risk. A growing list of high risk clinics and medical professionals with experience treating Lynch syndrome can be found at www.HCCTakesGuts.org.

Watching for Symptoms and Screening for Cancer

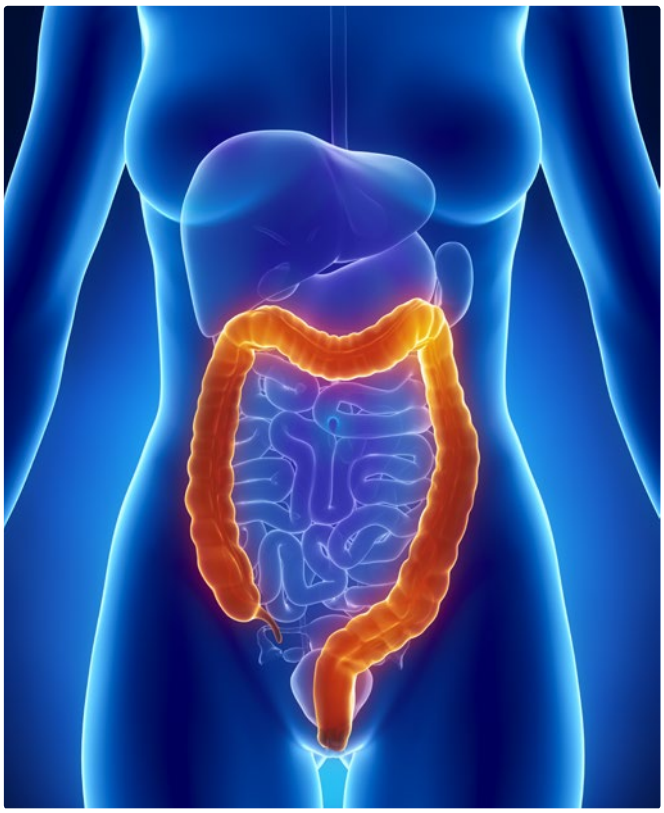
The following cancer risks, and the screening and treatment recommendations, are agreed upon by the National Comprehensive Cancer Network and/or the American College of Obstetricians and Gynecologists. As you read through these recommendations, remember that you may need to begin screening or treatment earlier than the age listed if you have a family history of cancer! (See "How Does Family History Affect My Care Plan?" on page 35.)

When deciding on a screening plan for Lynch syndrome, it is helpful to know:

1. Your family's cancer history.

2. Which gene mutation is causing Lynch. When the gene mutation is not known, a screening plan should be based on your personal and family history of cancer.

Colon and Rectum



Colorectal Cancer Risk

The average American has about a 5.5% chance of developing **colorectal cancer** in their lifetime. The risk of **colorectal cancer** is higher if you have Lynch syndrome and depends on which **gene mutation** you have.

Your risk of developing **colorectal cancer** is below:

- **MLH1** or **MSH2**/**EPCAM** is 40–80%. The average age is 44 to 61 years.
- **MSH6** is 10–22%. The average age is 54 years.
- **PMS2** is 15–20%. The average age is 61 to 66 years.

Symptoms of Colorectal Cancer

- A change in your bowel movements, such as diarrhea or constipation, that lasts more than a few days
- Bleeding during bowel movements
- Stool, or body waste, that is dark (black) or has blood in it
- Abdominal (gut) discomfort, such as cramps, gas, or pain, that lasts more than a few days
- A feeling that, when you need to 'go', you cannot, or you do not feel like you have emptied everything
- Stool, or body waste, that is more narrow than usual
- Feeling weak or very tired (fatigued)
- Unexplained weight loss
- Blood in your urine
- Unexpected vaginal bleeding

The American Cancer Society provides more detailed information on **colon** cancer symptoms.

Screening

If you have Lynch syndrome, colonoscopies to remove **polyps** and look for other potential problems, reduces the risk of **colorectal cancer**.

Colonoscopies should start between the ages of 20 to 25 and should be repeated every 1 to 2 years. If you have had **colon** surgery, any remaining large intestine and/or rectum should be examined every 1 to 2 years.

If you have a family history of **colorectal cancer**, find out the youngest age of the diagnosis. Your colonoscopies should start 2 to 5 years BEFORE that age.

Reducing Colorectal Cancer Risk

Pay Attention

Know the signs of **colorectal cancer**. Make an appointment as soon as possible if you experience any of the symptoms listed above. You know your body best. If something changes with your digestive system, contact your gastroenterologist, colorectal surgeon, or colorectal oncologist.

Colon Surgery

Surgery may be recommended if **polyps** cannot be managed through colonoscopies or if **precancerous cells** are found in the **colon**. Normally, only the part of the **colon** that may develop cancer is removed (**resection**). Sometimes surgeons have to remove the entire **colon** (total **colectomy**).

Advantages & Risks of Colon Surgery

The advantage of **colon** surgery is that it reduces the risk of **colorectal cancer**.

Possible complications of a **colon** surgery include:

- Bleeding and infection.
- Injury to nearby body parts, such as the **small intestine**, the **bladder**, **blood vessels**, and the **ureter**.
- A leak can occur where the intestine is reconnected.
- **Intestinal obstruction** from scar tissue. This can occur years after the surgery.
- Hernia at the surgical incisions.
- Blood clots can occur in the veins and can travel to the lungs. This is very rare.

You should discuss your risk of complications with your surgeon. Some people have a higher risk of complications. These include those:

- with other illnesses,
- who are overweight,
- who smoke, and/or
- who have had previous surgery.

Questions to Ask Your Surgeon

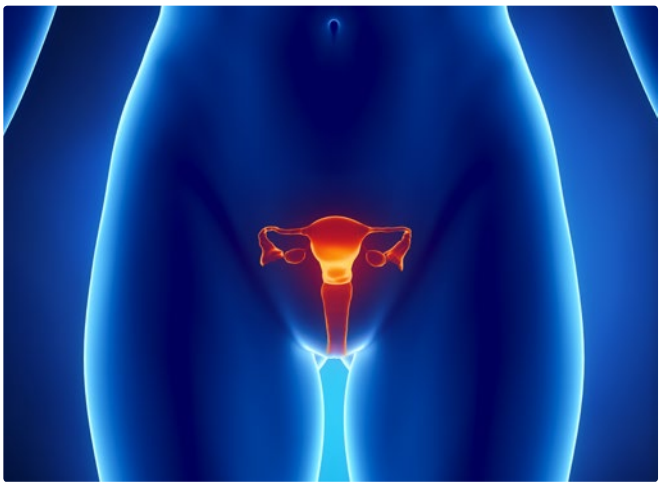
1. How many times have you performed this type of surgery?
2. How complex were the surgeries?
3. What is your surgical success rate?

Chemoprevention

Research suggests that aspirin can reduce your risk of cancer. A large dose (650 milligrams) for at least 2 years can significantly reduce the risk of colorectal and other Lynch syndrome-associated cancers. A smaller dose (75 milligrams) every day for 10 years may also reduce your risk of **colorectal cancer**.

If you are thinking about taking aspirin every day, please consult your doctor first. There are concerns about possible side effects, such as gastrointestinal bleeding. Your doctor may want to give you a general check up, take your blood pressure, and look for **H. pylori** (See "Stomach Surveillance" on page 29).

Uterus (Endometrium)



Endometrial Cancer Risk

Cancer in the lining of the uterus (womb) is called endometrial cancer. The average woman has about a 2% chance of developing endometrial cancer in her lifetime.

Average Endometrial Cancer Risk by Age 70 [1, 2]

- 54% for women with MLH1
- 21% for women with MSH2
- Up to 12% for women with EPCAM
- 16% for women with MSH6
- 15% for women with PMS2

If you are considering a hysterectomy before menopause, below are the estimated risks of endometrial cancer by age 40 and 50: [3-5]

Table 4: Average Endometrial Cancer Risk by Ages 40 and 50

	40 years	50 years
MLH1	1 (0–4)%	9 (3–19)%
MSH2	2 (0–7)%	8 (3–21)%
MSH6	1 (0–2)%	3 (1–8)%
PMS2	<2%	3 (1–8)%
EPCAM	The risk of endometrial cancer at these ages has not been established but should not be higher than those of MSH2.	

Endometrial Cancer Survival [1, 7-9]

Endometrial cancer usually develops at an earlier age in women with Lynch syndrome, but it is not necessarily more aggressive.

In a study of 210 women who did not undergo a hysterectomy, 69 developed endometrial cancer. Of these women, 76% were diagnosed as Stage I or II.

According to two studies, women with Lynch syndrome and endometrial cancer had an 88% 5-year survival rate and an 80% 10-year survival rate.

Symptoms of Endometrial Cancer

Pay attention.

Over 75% of endometrial cancer is caught early because of the symptoms. You know your body best. If something changes with your reproductive system, make an appointment with a gynecologist or gynecological oncologist who knows the cancer risks associated with Lynch syndrome.

It is important to be aware of the following symptoms which may be a sign of endometrial cancer:

- Abnormal vaginal bleeding between periods or after menopause
- Heavier periods than usual
- Unusual **vaginal discharge**
- Pain or pressure in the lower part of your **abdomen**
- Pelvic cramping
- Feeling unusually tired or weak (fatigued)
- Feeling sick or unhealthy (malaise)
- Difficulty or pain when urinating
- Pain during sexual intercourse

Consult your gynecologist if any of these symptoms seem to come and go, or if you experience them for more than 2 weeks at a time. The outcome is usually good if you investigate the symptoms early and treat them right away.

The National Cancer Institute provides more detailed information on endometrial cancer symptoms.

Screening for Endometrial Cancer

See your gynecologist yearly for a pelvic exam. The American College of Obstetricians and Gynocologists (ACOG) also recommends you have an endometrial biopsy every 1–2 yrs starting at age 30–35 years. This is especially true if you have **MLH1**- or **MSH2**-type Lynch syndrome. An ultrasound of the uterus and **ovaries** may also be recommended by your doctor. Close monitoring may help you to identify gynecological cancer at the earliest stage possible. Inform your doctor that you have, or may have, Lynch syndrome, because it will affect your care plan.

An endometrial biopsy may be painful and cause discomfort. To reduce the pain and discomfort ACOG recommends that ask your gynecologist and gastroenterologist to work together. Having an endometrial biopsy while unconscious, such as during a **colonoscopy** or **endoscopy**, has been reported to reduce the pain and discomfort associated with the the biopsy.[3]

Because it is still unclear how effective screening is, screening for endometrial cancer in women with Lynch syndrome is controversial. It is important to know that following this screening plan does not guarantee that endometrial cancer will be detected early.

Learning about the symptoms can be a powerful tool for early detection. Most endometrial cancers are caught early because the symptoms are recognizable.

Reducing Endometrial Cancer Risk

Chemoprevention

The **oral contraceptive** pill has been shown to reduce the risk of endometrial cancer by about a half (50%) when taken for several years. Progestin has also been to shown to CURE some cases of early (Stage I) endometrial cancer and HEAL **precancerous** endometrial tissue. The benefits and risks of taking the pill as a risk-reducing option should be carefully discussed with your doctors. If you are at high risk of breast cancer, be especially cautious when taking **oral contraceptives** with progesterone. [1, 2]

Surgery

A **total hysterectomy** is a surgery to remove the uterus (womb) and the cervix. A **total hysterectomy** is the only way to be certain that you will not develop endometrial cancer. It also means that you will not be able to get pregnant after the surgery.

A **total hysterectomy** may be performed in one of three ways:

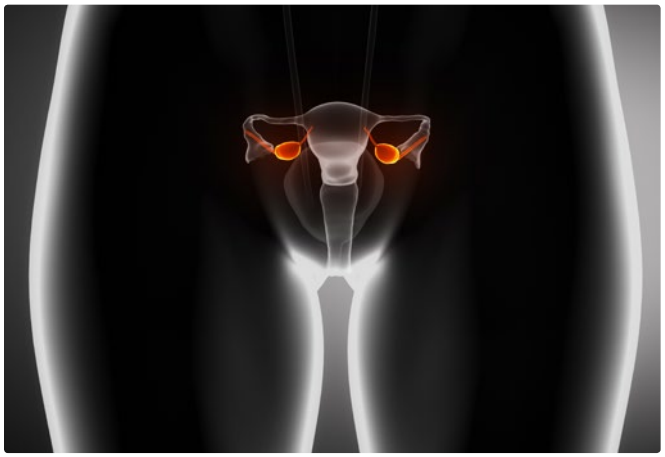
- **Abdominal hysterectomy**: when the cervix and uterus are removed through a large incision in the abdominal wall
- **Laparoscopic hysterectomy**: when the cervix and uterus are removed through small cuts in the abdominal wall
- **Vaginal hysterectomy**: when the cervix and the uterus are surgically removed by operating through the vagina.

A **bilateral salphingo-oophorectomy (BSO)** surgery is the removal of the **ovaries** and **Fallopian tubes**. A **total hysterectomy** and BSO will reduce your risk of both endometrial and ovarian cancer. It is common for doctors to recommend a **total hysterectomy** with BSO to women with Lynch syndrome who have completed childbearing. [1, 2]

A **hysterectomy** without BSO will reduce your risk of endometrial cancer without causing menopause. The **Fallopian tubes** should also be removed to reduce the risk of ovarian cancer associated with Lynch syndrome. [3]

Endometrial cancer caused by Lynch syndrome frequently occurs in the lower part of the uterus near the cervix. If you are considering a **hysterectomy**, both the uterus and the cervix should be removed. A **supracervical hysterectomy**, which only removes the uterus, should not be performed.

Ovaries



Ovarian Cancer Risk

The average woman has about a 1.6% chance of developing ovarian cancer in her lifetime. The risk of ovarian cancer increases if you have Lynch syndrome. Your risk depends on which **gene** is mutated, your age, and your family history.

Average Ovarian Cancer Risk by Age 70: [3–5, 9, 10]

- 6% for women with **MLH1**
- 9% for women with **MSH2**
- Very low* for women with **EPCAM**, **MSH6**, and **PMS2**

*Women with MSH6 have an 11% risk of any one of following cancers: renal pelvic, stomach, small bowel, ureter, and brain. The risk of women with PMS2 to have any one of these cancers is about 6%. The risk has not been established for EPCAM, but is believed to be very low.

Women with Lynch syndrome have to consider if they want to have surgery to remove their **ovaries**. This is called a **bilateral salphingo-oophorectomy (BSO).**

If you are considering a BSO before menopause, below are the estimated risks of ovarian cancer by the age of 40 and 50: [5, 7]

Table 5: Average Ovarian Cancer Risk by Ages 40 and 50

	40 years	50 years
MLH1	0 (0–2)%	4 (0–11)%
MSH2	1 (0–3)%	4 (1–9)%
MSH6	0%	0 (0–1)%
PMS2	<1%	1 (0–8)%
EPCAM	The risk of ovarian cancer at these ages has not been established, but is believed to be very low.	

Cancer Survival

There are several types of ovarian cancer. The survival rate, and how aggressive the cancer behaves, depends on the type of cancer. Given that most types of ovarian cancer are possible with Lynch syndrome, the estimated survival rate is: [6]

5 years	10 years	20 years
82.7%	80.6%	78%

Your oncologist can tell you more about what to expect based on your diagnosis.

Symptoms of Ovarian Cancer

Ovarian cancer is sometimes called a "silent" disease, because its symptoms can be hard to notice. If you regularly experience any of the following symptoms, consult a gynecologist or gynecological oncologist with expertise in Lynch syndrome:

- Pelvic or abdominal pain that does not go away
- Swollen **abdomen** or bloating that does not go away (not bloating that comes and goes)
- Feeling full quickly, difficulty eating, or loss of appetite

Occasionally, women may also experience other symptoms. The following symptoms can occur on their own or at the same time as those listed above:

- Needing to urinate more frequently
- Persistent constipation
- Extreme fatigue or back pain
- Pain during sex
- Menstrual changes

The American Cancer Society provides more detailed information on ovarian cancer symptoms.

Screening

Women with Lynch syndrome have a greater risk of ovarian cancer than the general public. There is currently no test, or group of tests, that can reliably diagnose ovarian cancer at an early stage. As a result, no routine screening for ovarian cancer is currently available.

Transvaginal Ultrasounds (TVUS) and CA-125 Serum Blood Tests

It is unclear if these tests are reliable. They sometimes give 'false positive' results. This may lead to more tests to clarify the results. These extra tests can be invasive and/or expensive. This can be a stressful experience, even when you find out that everything is normal. These test can also give a 'false negative' result, which can mean you have cancer even though the test says you do not.[10] Experts in Lynch syndrome do not rely on either of these tests to screen for ovarian cancer.

Reducing Ovarian Cancer Risk

Pay Attention

Know the signs of ovarian cancer. Make an appointment as soon as you experience any of the symptoms listed above. You know your body best. If something changes with your reproductive system, make an appointment with a gynecologist or gynecological oncologist who knows the cancer risks associated with Lynch syndrome.

Which Gene? What age?

The risk of endometrial cancer depends on which type of Lynch syndrome you have. Your risk also changes with age. Any plan to reduce your ovarian cancer risk should be based on your **gene**, your age, and your family history.[1]

Chemoprevention

The **oral contraceptive** pill, containing progesterone, has been shown to reduce the risk of ovarian cancer by about a half (50%) when taken for several years. The benefits and risks of taking the pill as a risk-reducing option should be carefully discussed with your doctors. If you are at high risk of breast cancer, be especially cautious when taking **oral contraceptives** with progesterone.[1,2]

Surgery

Removing the Fallopian tube(s) is called a **salpingectomy**.

An **oophorectomy** is the removal of an ovary.

Bilateral salpingo-oophorectomy (BSO) is surgery to remove both **ovaries** and **Fallopian tubes**. BSO is an option for women with Lynch syndrome to reduce their risk of cancer. Women who undergo a BSO are no longer able to have children. This surgery is the only way to be certain that you will not develop ovarian cancer.[1, 2]

A **total hysterectomy** and **bilateral salpingo-oophorectomy (TH/BSO)** is surgery to remove the uterus, cervix, **ovaries** and **Fallopian tubes**.

If you are not in, or past, menopause, removing the **ovaries** will probably cause you to enter menopause immediately. If you choose to have this surgery, have a discussion with your gynecologist about hormone replacement therapy (HRT). Make a plan before your surgery, so that you may begin HRT immediately after surgery. This can prevent or reduce the sudden intense effects of surgical menopause.

Recent research suggests that some ovarian cancers start in the **Fallopian tubes**. It is unclear if ovarian cancers caused by Lynch syndrome also start in the **Fallopian tubes**. Discuss with your doctor the option to only remove the **Fallopian tubes** (**salpingectomy**) and keep your **ovaries** until you are closer to the natural age of menopause.

Effects of Gynecological Surgeries

We are passionate about making sure women learn as much as they can to make the right choices about their health care. This is why we highly recommend that you consult a genetic counselor, geneticist, or gynecologist with expertise in Lynch syndrome. These experts can assess your risk of these cancers based on your **mutation** and family history.

Gynecological surgery may eliminate your risk of cancer, but the long-term effects can greatly affect your quality of life and health. Surgery has not been proven to extend life. According to Dr. Karen Lu, MD, gynecologist and Lynch syndrome expert at MD Anderson:

> *"Because endometrial cancer often presents with symptoms such as vaginal bleeding, and because survival rates for endometrial cancer are high, it is not clear to what extent surgery would impact morbidity and mortality. While colonoscopies have been proven to reduce CRC morbidity and mortality in patients with LS, there is no such evidence regarding TH/BSO."* [2]

You will have to be your own advocate and educate yourself. Read credible books and websites. Talk to other women who have had these surgeries, or read their blogs. It is very important to feel that you have made the best decision possible for yourself.

Questions to Ask Your Doctor Before Surgery

There are potential complications with any surgery. If possible, choose a surgeon who has performed many successful surgeries to treat Lynch syndrome.

When considering a gynecological surgery, we recommend that you ask your doctor or genetic expert the following questions:

1. **How many Lynch syndrome patients do you care for?**
   An experienced doctor should know the most current research, screening, and treatment options.

2. **Have you considered my family's medical history?**
   If one or more family members have been diagnosed with a gynecological cancer, surgery is recommended five (5) years earlier than the youngest age of diagnosis.

3. **Are birth control pills or a progestin-containing IUD an option for reducing my personal risk?**
   Contraceptives containing progestin may decrease the risk of ovarian cancer by 50%.

4. **Which surgery(s) would best protect me against my personal risk?**
   See gynecological surgery options on page 23.

5. **Will this be an open surgery or laproscopic? If laproscopic, will a morcillator be used?**
   A morcillator should NEVER be used for a surgery in a patient with a high risk of cancer.

6. **Why do you recommend one surgery over the others?**

7. **How much will the recommended surgery decrease my chance of endometrial cancer? Of ovarian cancer?**

8. **Will I be able to have children after the surgery?**

9. What are the possible complications of the surgery?

10. How might my personal health affect the success of this surgery?
    Women with other illnesses, including those who are overweight, who smoke, or who have had a previous surgery, are at greater risk of complications.

11. How might my previous surgeries affect the success of this surgery?

12. What are the possible short and long-term side effects of this surgery? What can be done to prevent these side-effects?

13. If hormone replacement therapy is recommended, what are the possible side effects?

14. What is your experience with this surgery? How many times have you performed it? What complications have you encountered?

Menopause

Surgical Menopause

Menopause is the time in a woman's life when she stops having periods. Natural menopause normally gives a woman time to adjust to the changes that are happening to her body.

Women who have their **ovaries** removed usually experience menopause immediately after surgery. Rather than a gradual transition into menopause, a woman's body awakes from a BSO unable to produce important hormones, like estrogen, progesterone, and testosterone. These hormones play important roles in the day-to-day functioning of many organ systems, including the brain, heart, and bones.

The symptoms of surgical menopause can be very severe and may include: [9, 11]

- Hot flashes
- Night sweats
- Mood swings
- Depression, possibly severe
- Difficulty concentrating
- Insomnia (inability to sleep)
- Vaginal dryness/itching
- Pain during sexual intercourse
- Reduced sexuality and/or sensuality
- Reduced or zero sex drive
- Dry skin, brittle, and/or thinner hair
- Urinary incontinence, **urinary tract** infections
- Increased risks of heart disease, osteoporosis, and/or Parkinson's disease

Hormone Replacement Therapy

Hormone Replacement Therapy (HRT) replaces the hormones lost when a woman's **ovaries** are removed. The goal of hormone replacement therapy is to reduce the effects of the surgery.

Every woman is different, and every woman's body reacts uniquely to having her **ovaries** removed. It is unlikely that HRT will make you feel like you did before the surgery. Be sure to make a plan before your surgery, so that you may begin HRT immediately afterwards. This can help reduce or prevent the sudden, intense effects of surgical menopause.

HRT should be given to women up until the age of natural menopause—the average age is 55 years old. Women who have, or have had, breast cancer are not eligible for HRT. Your family history of breast cancer should also be discussed with your doctor before beginning HRT.

If you are considering HRT, find a doctor who you feel is taking your needs seriously. Consult a gynecologist or menopause specialist. Seek a second opinion if necessary.

If you experience serious symptoms of surgical menopause, or if you are concerned about the effects of HRT, request to meet with a menopause specialist.

Kidney, Bladder, and Ureter Surveillance

Cancer Risk

The **urinary tract** includes the kidneys, **bladder**, **ureter** (connects kidneys and **bladder**) and **urethra** (how urine exits the body). **Urinary tract** cancer is the third most common cancer caused by Lynch syndrome.

Symptoms of Cancer

- Blood in your Urine (Hematuria)

  Blood in your urine is the most common sign of cancer in the upper part of **urinary tract** (kidneys and **ureter**). A **urinalysis** can look for blood in your urine. Blood in your urine is painless.

  Cancer is not the only reason why you might have blood in your urine. Your doctor should check for all possible sources of any blood found in your urine.

- Pain and/or nausea

  A fast-growing **tumor** can cause pain by putting pressure on the kidneys. This could cause nausea and sharp pain in your lower back, side, or stomach. These symptoms can also be caused by kidney stones. If you experience these symptoms see a urologist right away.

Signs of advanced cancer include:

Weight loss, loss of appetite, pain in your bones and/or a growth in your side or **abdomen**.

The Urology Care Foundation provides more detailed information on urinary cancer symptoms.

Screening

A yearly urine test (**urinalysis**) to look for cancer should be considered starting by age 25 to 30. A **urinalysis** is a simple, inexpensive, and accurate test to screen for this cancer.

Some doctors recommend a cystoscopy to examine the lining of your **bladder** and the tube that carries urine out of your body (**urethra**). This exam is not included in the NCCN guidelines at this time.

Breast Surveillance

Breast Cancer

Recent research suggests Lynch syndrome increases the risk for breast cancer, although there is currently very little data to support this.

Symptoms of Breast Cancer

It is important to know the symptoms and signs of breast cancer. It will be easier to identify changes in your breast if you perform a breast exam on yourself every month.

Talk to your doctor if you notice any changes or any of the following symptoms:

- A change in how your breast or nipple looks
- A change in how your breast or nipple feels
- A lump or thickening in or near the breast, including under your armpits
- Any fluid leaking from your nipples (discharge)
- Breast pain or nipple tenderness

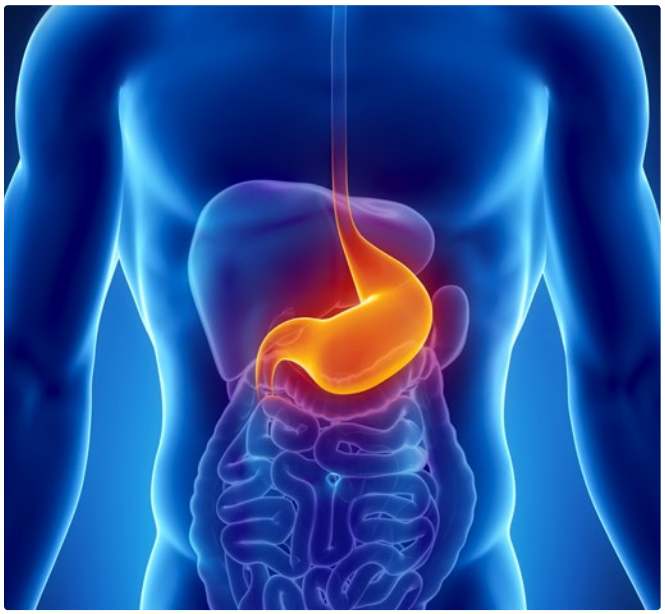
The presence of these symptoms does not mean that you have breast cancer. It is common for women to notice one or two of the symptoms even if they do not have cancer.

The National Breast Cancer Foundation provides more detailed information on breast cancer symptoms.

Screening

Women and men may consider yearly screening for breast cancer with **mammograms** beginning at 40 years old. If you have a family history of breast cancer, find out the youngest age of the diagnosis. Your **mammograms** should start 5 to 10 years BEFORE that age.

Stomach Surveillance



Stomach Cancer

If you have Lynch syndrome, the risk of developing stomach cancer is low for some populations and high for others. For example, the risk in the Netherlands is about 2-4%. In Korea, it can be as high as 30%. Most cases occur after age 40, and men seem to be at a higher risk than women.

Symptoms of Stomach Cancer

The symptoms of stomach cancer can be vague and confusing. This is especially true since many of the symptoms can be caused by another illness, such as a virus or ulcer.

Talk to your doctor if you notice any of the following symptoms that reoccur or don't go away:

- Poor appetite
- Weight loss (without trying)
- Abdominal (belly) pain
- Vague discomfort in the **abdomen**, usually above the navel
- A sense of fullness in the upper **abdomen** after eating a small meal
- Heartburn or indigestion
- Nausea
- Vomiting, with or without blood
- Swelling in the **abdomen**
- Low red blood **cell** count (anemia)

The American Cancer Society provides more detailed information on stomach cancer symptoms.

Screening

For most people with Lynch syndrome, the risk of stomach cancer is so low that regular screening is not recommended. However, your doctor may recommend an **upper endoscopy** (EGD) to look at your stomach.

If stomach cancer runs in your family, OR if you are of Asian descent with **MLH1** or **MSH2/EPCAM mutations**, an EGD may be recommended every 3 to 5 years starting at age 30 to 35. This usually happens at the same time as the small intestine screening.

H. Pylori

People with Lynch syndrome sometimes develop "**H. pylori**" (**Helicobacter pylori**) in their stomach. This infection can be detected in either your breath or stool. If **Helicobacter pylori** is present, antibiotics may be prescribed by your doctor.

Small Intestine Surveillance

The American Society of Clinical Oncology provides more detailed information on small intestinal cancer symptoms.

Screening

For most people with Lynch syndrome, the risk of small intestine cancer is so low that regular screening is not recommended. However, your doctor may recommend an **upper endoscopy** (EGD) to look at your small intestine.

If small intestine cancer runs in your family, or if you are of Asian descent with **MLH1** or **MSH2**/**EPCAM mutations**, an EGD may be recommended every 3 to 5 years starting at age 30 to 35. This usually happens at the same time as stomach screening.

Small Intestine Cancer

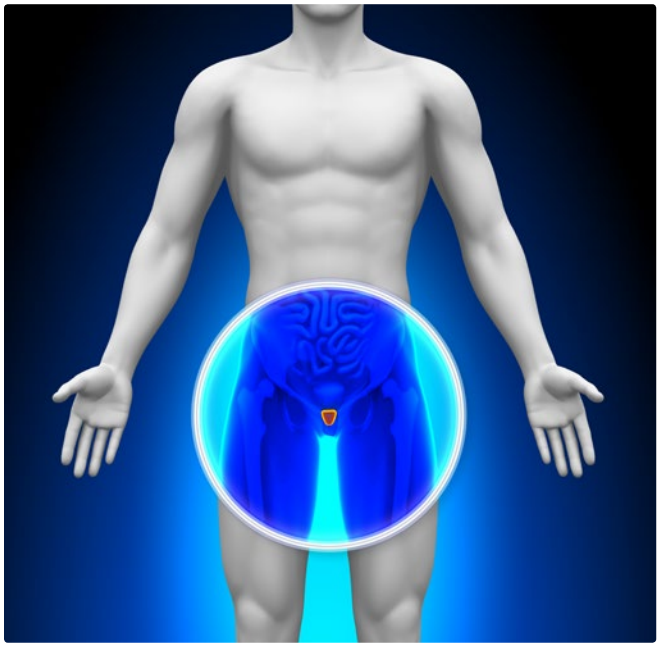
For most people with Lynch syndrome, the risk of cancer of the small intestine is so low that regular screening is not recommended.

Symptoms of Small Intestine Cancer

Talk to your doctor if you notice any of the following symptoms:

- Blood in your stool
- Dark or black stools
- Diarrhea
- A lump in your **abdomen** (belly)
- Pain or cramps in the **abdomen** (belly)
- Unexplained weight loss
- Abdominal (belly) pain with severe nausea or vomiting

Prostate Surveillance



Prostate Cancer Risk

Some studies have found that Lynch syndrome can increase a man's risk of prostate cancer.

Symptoms of Prostate Cancer

You should know the symptoms of prostate cancer. While early prostate cancer does not usually have symptoms, advanced prostate cancer can cause the symptoms listed below. Talk to your doctor if you notice any of the following:

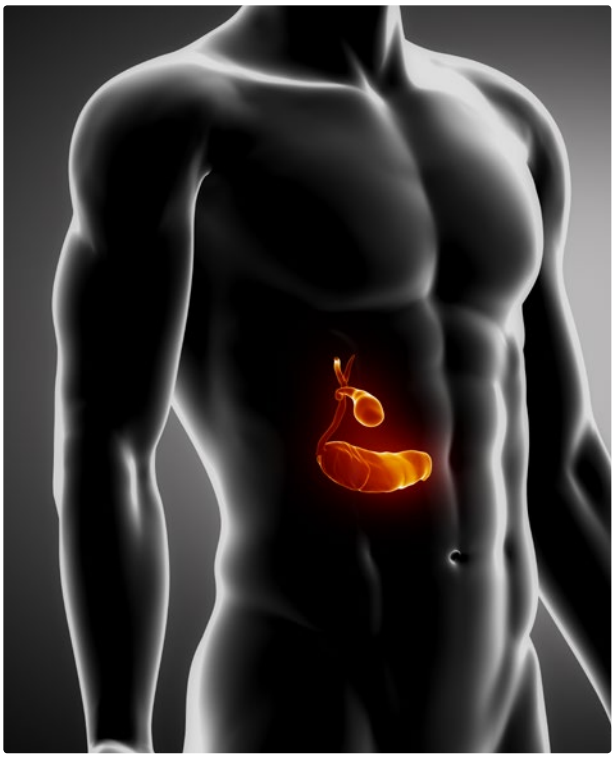
- Problems urinating, including a slow or weak stream
- The need to urinate more often, especially at night
- Blood in the urine or semen
- Painful ejaculation
- Trouble getting an erection (erectile dysfunction)
- Pain in the hips, spine, or ribs
- Weakness or numbness in the legs or feet
- Inability to control your urine or bowel movements (incontinence)

The Prostate Cancer Foundation provides more detailed information on prostate cancer symptoms.

Screening

The increased risk of prostate cancer is believed to be so low that regular screening is not recommended. Although it is not easily screened for, some doctors may recommend a cystoscopy to examine the lining of your **bladder** and your **urethra**. This exam is not included in the NCCN guidelines at this time.

Pancreas Surveillance



Pancreas Cancer Risk

Some studies have found that Lynch syndrome can increase the risk of pancreas cancer.

Symptoms of Pancreas Cancer

You should know the symptoms of pancreas cancer. Talk to your doctor if you notice any of the following symptoms:

- Jaundice is the most common symptom and is caused by the buildup of a dark yellow-brown substance made in the liver called bilirubin. Symptoms of jaundice include: yellowish eyes and skin, dark brown urine, light-colored or greasy stool (body waste), and itchy skin.
- One of the first clues of pancreatic cancer is a blood clot in a large vein, usually in the leg. Having this type of blood clot is called Deep Vein Thrombosis (DVT). Symptoms of DVT include: swelling, redness, pain, redness, and warmth in the affected leg.
- Belly or back pain
- Weight loss and poor appetite
- Nausea and vomiting
- Gallbladder or liver enlargement
- Uneven texture under the skin
- Diabetes (rare)

The American Cancer Society provides more detailed information on pancreatic cancer symptoms.

Screening

The increased risk of pancreatic cancer is believed to be so low that regular screening is not recommended. Although it is not easily screened for, some doctors may recommend a Magnetic Resonance Cholangiopancreatography (MRCP) to check the liver, gallbladder, bile ducts, pancreas and pancreatic duct. This exam is not included in the NCCN guidelines at this time.

Brain/Central Nervous System Surveillance

Brain Cancer Risk

Some studies have found that Lynch syndrome can increase the risk of brain cancer. The most common form of brain cancer associated with Lynch syndrome is a glioblastoma (GBM). GBM's are **tumors** that grow in the brain's "glue-like" tissue.

Symptoms of Brain Cancer

Talk to your doctor if you notice any of the following symptoms that reoccur or don't go away. GBMs can grow fast and press on the brain. This pressure can cause:

- headaches
- nausea
- vomiting
- drowsiness

The location of the **tumor** can cause other symptoms including:

- weakness on one side of the body
- memory problems
- difficulty speaking or understanding words
- blurred vision or blindness

The American Brain Tumor Association provides more detailed information on brain cancer symptoms.

Screening

The increased risk of brain cancer is believed to be so low that regular screening is not recommended for all types of Lynch syndrome. If you have **MLH1** or **MSH2**, a yearly physical exam is recommended starting at age 25 to 30 years. This exam may include assessing your nerves, senses, muscle strength, reflexes, balance and mental state.

Skin Surveillance

Skin Cancer Risk

For most people with Lynch syndrome, the risk of skin cancer of the small intestine is so low that regular screening is not recommended.

Symptoms of Skin Cancer

Unusual skin changes should be shown to a dermatologist. Most skin changes are not cancerous and treatment is often possible.

Talk to a dermatologist if you notice any of the following symptoms:

- A small, yellowish, hard bump, that is growing in the neck, face, or especially in the upper or lower eyelid
- A new spot on the skin or a spot that is changing in size, shape, or color
- A spot that looks different from all of the other spots on your skin

The American Society of Clinical Oncology provides more detailed information on skin cancer symptoms.

Screening

If you have a family history of skin cancer, yearly skin screening should begin in early adulthood. If you have a family history of skin cancer, find out the youngest age of the diagnosis. Your yearly screening should start 5 to 10 years BEFORE that age.

How Does Family History Affect My Care Plan?

It is impossible to know your exact risks of cancer due to Lynch syndrome because other factors influence these risks like your lifestyle, the foods you eat, and environmental toxins. The way Lynch syndrome behaves in you and/or your family can also be very different from others because of how your **MMR genes** interact with your other **genes**.

The cancer risks in Table 3 are based upon actual people in registries around the world who have had cancer. The screening recommendations we list above are based on these average risks, but do not consider your personal and/or family history.

Screening recommendations for cancer change when you or someone in your family has had cancer. For instance, if you have Lynch syndrome AND your father had **colon** cancer at the age of 32, your colonoscopies should start 10 years earlier, at the age of 22. Similarly, if your mother had ovarian cancer at age 38, your screening or treatment should begin several years earlier.

If you have Lynch syndrome, it is important that you learn about your family's history of cancer AND discuss it with your medical team. Your family history is an important tool in deciding when to start screening and, hopefully, preventing cancer.

Communicating My Diagnosis With Family

Finding out that you have Lynch syndrome can be life-saving information for you and for your family. It is very important that you tell your adult relatives. They need to know that it is passed down through families. Perhaps one of your most difficult decisions will be whether to tell your children and how to approach the conversation.

Deciding how and when to have these talks can be difficult. A genetic counselor can help you come up with a plan. Here are three more resources that might help you:

- **www.kintalk.org**: A service of the University of California San Francisco
- **www.nsgc.org**: The website of the National Society of Genetic Counselors
- **www.HCCTakesGuts.org**: Under "Family Communication" you will find excellent tips, created by Dana Farber Cancer Institute, for explaining **hereditary** cancer to children

Family Planning

If you have Lynch syndrome and would like to have children in the future, you may have questions about their cancer risk and how you can minimize this risk.

Families with Lynch syndrome have several family planning options. Each has pros and cons. It is a personal decision for you and your partner. There is no "right" or "wrong" decision—you have to make the choice that is best for your circumstances, feelings, and beliefs.

Here are some choices that others have made:

- Some couples have children naturally.
- Some couples decide not to have children.
- Some couples adopt a child.
- Some couples use an egg or sperm donor to have a child.
- Some couples choose Pre-implantation Genetic Diagnosis (PGD). PGD allows doctors to remove embryos, select those that do not have Lynch syndrome, and implant them back into the mother.

Hospital Patient Registries

Hospitals and universities that specialize in **hereditary** cancer syndromes sometimes create a patient registry. They gather and store information on patients and families who have been diagnosed with, or are at risk for, a **hereditary colorectal cancer** syndrome. Some registries are used for research. Others focus on patient care. Some are a combination of both.

Joining a registry can help you by:

- offering education
- providing excellent medical care
- being a source of support and counseling
- providing opportunities to participate in research studies

To find a hospital registry that may offer all of the above benefits, visit the web site of The Collaborative Group of the Americas on Inherited Colorectal Cancer (CGA) at www.CGAICC.com.

Online Patient Registries

The HEROIC Registry was created by Alive and Kickn to support research on Lynch syndrome. It enables patients to take an active role in furthering Lynch syndrome research. The HEROIC Registry allows patients to contribute their medical information and experiences living with Lynch syndrome in order to help researchers:

- develop new treatments,
- understand the various Lynch genetic **mutations**,
- write medical papers and
- conduct further studies and clinical trials.

When you join, you control what information you would like to share, who views it, and which research studies you are willing to participate in.

For more information and to participate in the HEROIC Registry go to AliveandKickn.org/heroic-registry.

Additional Resources

The following sources offer tools and information for families affected by Lynch syndrome.

Alive And Kickn's mission is to improve the lives of individuals and families affected by Lynch syndrome and associated cancers through research, education, and screening. AliveandKickn.org

Cancer Family: The Search for the Cause of Hereditary Colorectal Cancer, an autobiographical book by C. Richard Boland MD. The author recognized that there was a hereditary cancer syndrome in his family and resolved to solve the problem as a medical researcher. He went on to co-discover Lynch syndrome.

The mission of **The Colon Cancer Alliance for Research & Education for Lynch Syndrome (CCARE Lynch)** is to educate the public and healthcare professionals about Lynch syndrome and to help fund research for a cure for this disease. FightLynch.org

The mission of the **Colon Cancer Alliance** is to knock colon cancer out of the top three cancer killers by championing prevention, funding cutting-edge research and providing the highest quality patient support services. www.CCAlliance.org

The mission of **Facing Our Risk of Cancer Empowered (FORCE)** is to improve the lives of individuals and families affected by hereditary breast, ovarian, and related cancers. www.FacingOurRisk.org

Fight Colorectal Cancer (Fight CRC) envisions victory over colon and rectal cancers. They raise their voice to empower and activate a community of patients, fighters and champions to push for better policies and to support research, education and awareness for all those touched by this disease. FightColorectalCancer.org

The Hereditary Colon Cancer Foundation's vision is to be a beacon of light—extending life expectancy, enhancing life quality, and instilling hope in those born with hereditary colon cancer syndromes. Their web site offers many patient and provider resources including a list of doctors and genetic counselors who specialize in caring for families affected by Lynch syndrome. HCCTakesGuts.org

The Hysterectomy Educational Resources and Services Foundation (HERS) is an international women's health education organization. HERS provides information about alternatives to hysterectomy and the after effects of the surgery. HersFoundation.com

The mission of **I Have Lynch Syndrome, Inc.**, is to save lives through education and raising awareness about Lynch among the global medical community and the general public. IHaveLynchSyndrome.com

Informed DNA's genetic counselors use state-of-the-art telephone and web-based technology to provide counseling anywhere in the world, any time of the day, and any day of the week. www.informeddna.com

The **Kintalk** site was developed by genetic counselors at the University of California San Francisco. It helps people easily and securely share important genetic health information with at risk family members and learn about hereditary cancer syndromes. KinTalk.org

The 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 professional,s and providing support for Lynch syndrome research endeavors. LynchCancers.com

Michael's Mission is focused on improving the quality of life and treatment options for those suffering from colorectal cancer through education, research and patient support. michaelsmission.org

The National Society of Genetic Counselors' Find a Genetic Counselor directory can assist in locating genetic counseling services near you. nsgc.org

Sources Used to Create This Guide

All screening and treatment recommendations, with the exception of those for the gynecological effects of Lynch syndrome, presented in this guide were based on the following National Comprehensive Cancer Network (NCCN) guidelines and retrieved from www.NCCN.org:

- Genetic/Familial High Risk Assessment: Colorectal (Ver. 1.2015)
- Ovarian Cancer including Fallopian Tube Caner and Primary Peritoneal Cancer (Ver 2.2015)
- Uterine Neoplasms (Ver. 2. 2016)

The screening and treatment recommendations in the Endometrial and Ovarian sections are based upon those presented by the American College of Obstetrics and Gynecology and the following peer-reviewed journal articles:

1. Chen L, Cohn DE, Fishman DA, et al. Practice Bulletin - Clinical management guidelines for obstetrician-gynecologists: Lynch syndrome; Obstetrics and Gynecology. Number 147; November 2014.

2. Lu KH, Daniels M. Endometrial and ovarian cancer in women with Lynch syndrome: Update in screening and prevention. Familial Cancer. 2013; 12(2).

3. Senter L, Clendenning M, Sotamaa K, et al. The clinical phenotype of Lynch syndrome due to germline PMS2 mutations. Gastroenterology. 2008; 135(2); 419-428.

4. Bonadona V, Bonaiti B, Olschwang S, et al. Cancer risks associated with germline Mutations in MLH1, MSH2, and MSH6 Genes in Lynch syndrome. Journal of the American Medical Association. 2011; 305(22); 2004-2010.

5. Crispins MA. Endometrial and ovarian cancer in Lynch syndrome. Clinical Colon and Rectal Surgery. 2012; 25; 97-102.

6. Vasen HFA, Blanco I, Aktan-Collan K, et al. Revised guidelines for the clinical management of Lynch syndrome (HNPCC): Recommendations by a group of European experts. Gut. 2013; 0; 1-13.

7. Schmeler KM, Lynch HT, Chen L, et al. Prophylactic surgery to reduce the rcableisk of gynecological cancers in Lynch syndrome. New England Journal of Medicine. 2006; 354(3); 261-9.

8. Watson P, Buetzow R, Lynch HT, et al. The clinical features of ovarian cancer in hereditary nonpolyposis colorectal cancer. Gynecologic Oncology. 2001; 82; 223-228.

9. Baglietto L, Lindor NM, Dowty, JG. et al. Risks of Lynch syndrome cancers for MSH6 mutation carriers. Journal of the National Cancer Institute. 2010; 102; 193-201.

10. Lynch HT, Riegert-Johnson DL, Snyder C, et al. Lynch syndrome-associated extracolonic tumors are rare in two extended families with the same EPCAM deletion. The American Journal of Gastroenterology. 2011; 106; 1829-36.

11. Shuster, LT, Gosout, BS, Grossardt, BR, and Rocca, WA. Prophylactic oophorectomy in pre-menopausal women and long term health - a review. Menopause International. 2008; 14(3); 111-116.

The following patient guides were as inspiration during the development of the guide:

"Lynch Syndrome - A guide for people with Lynch syndrome and their family and friends" by Cancer Institute NSW, Australia - https://www.cancerinstitute.org.au/media/390323/lynch-syndrome-guide.pdf

"A Beginner's Guide to BRCA1 and BRCA2 - Patient Information" by The Royal Mardsen NHS Foundation Trust - https://www.royalmarsden.nhs.uk/sites/default/files/files_trust/brca_0.pdf

The peer-reviewed journal articles "Lynch Syndrome" in Gene Reviews by Wendy Kohlmann, MS, CGC and Stephen Gruber, MD, PHD, MPH was instrumental in forming a general understanding of Lynch syndrome.

In addition, the following is a list of resources used throughout the guide:

Do I Have Lynch Syndrome?
2004 Bethesda Guidelines (Modified to Include Endometrial Cancer).

Colon & Rectum - Chemoprevention
Burn, J, Gerdes, AM, Macrae, F, et al. Long term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomized controlled trial. Lancet. 2011; 378(9809); 2081-2087.

Uterus (Endometrium)
The National Cancer Institute provides more detailed information on endometrial cancer symptoms. This information was retrieved from: Endometrial Cancer Treatment (PDQ) - Patient Version; www.cancer.gov; (2015).

Ovarian
The American Cancer Society provides more detailed information on ovarian cancer symptoms. This information was retrieved from: Retrieved from: Signs and Symptoms of Ovarian Cancer; www.cancer.org; (2016).

Breast Surveillance
The National Breast Cancer Foundation provides more detailed information on breast cancer symptoms. This information was retrieved from: Signs and Symptoms (of Breast Cancer); www.nationalbreastcancer.org; (2015).

Kidney, Bladder, and Ureter Surveillance
The Urology Care Foundation provides more detailed information on urinary cancer symptoms. This information was retrieved from: What are the Symptoms of Upper Urinary Tract Cancer; www.urologyhealth.org; (2016).

Stomach Surveillance
The American Cancer Society provides more detailed information on stomach cancer symptoms. This information was retrieved from: Signs and Symptoms of Stomach Cancer; www.cancer.org; (2016).

Small Intestine
The American Society of Clinical Oncology provides more detailed information on small intestinal cancer symptoms. This information was retrieved from: Small Bowel Cancer - Signs and Symptoms; www.cancer.net; (2015).

Prostate
The Prostate Cancer Foundation provides more detailed information on prostate cancer symptoms. This information was retrieved from: Prostate Cancer Symptoms; www.pcf.org.

Pancreas
The American Cancer Society provides more detailed information on pancreatic cancer symptoms. This information was retrieved from: Signs and Symptoms of Pancreatic Cancer; www.cancer.org; (2016).

Brain/Central Nervous System
The American Brain Tumor Association provides more detailed information on brain cancer symptoms. This information was retrieved from: Glioblastoma; www.abta.org.

Skin
The American Society of Clinical Oncology provides more detailed information on skin cancer symptoms. This information was retrieved from: Skin Cancer (Non-Melanoma) - Signs and Symptoms; www.cancer.net.

Glossary

Abdomen
The area below your chest and above your belly button.

Abdominal Hysterectomy
Surgery to remove the uterus through a cut in the abdominal wall.

Bilateral Salpingo-Oophorectomy (BSO)
This surgery removes a woman's ovaries and fallopian tubes to prevent ovarian cancer.
bilateral - "both sides"
salpingo - "fallopian tube"
oophor - "ovaries"
ectomy - "removal of..."

Bladder
An organ that stores urine and is located just above and behind the pubic bone.

Blood Vessels
Tubes that carry blood throughout the body. Blood vessels include veins, arteries and capillaries.

Cell
The smallest building block of the body that can live on its own. Cells makes up all living organisms and tissues of the body.

Colectomy
Removal of all, or part of, the large intestine.

Colon
The large intestine, not including the rectum.

Colonoscopy
Exam of the inside of the colon, with a camera on a flexible tube, inserted through the rectum.

Colorectal Cancer
Cancer of the colon and/or rectum.

de Novo
Refers to a person who is the first person in their family to have Lynch syndrome. It means 'from the beginning' because the gene mutation happened at the time of conception and was not inherited.

DNA
The genetic material, or blueprint, that provides the information necessary for a body to grow.

Endometrium
The inside surface of the uterus or womb.

Endoscopy
Using a flexible tube to look inside parts of the body, such as the stomach, small intestine, and/or large intestine.

EPCAM Gene
This gene provides the information to make the EPCAM protein. It can sometime cause Lynch syndrome by turning off the MSH2 gene.

Fallopian Tubes
Two tubes in a woman's body that carry eggs from the ovaries to the womb.

False-negative

An incorrect test result that says a person DOES NOT have a condition when he/she actually DOES have the condition.

False-positive

An incorrect test result that says a person DOES have a condition when he/she actually DOES NOT have the condition.

Gene

Genes carry the information that determines a person's features or characteristics. Genes are inherited from parents. Genes are made up of DNA and provide instructions for making proteins.

Helicobacter pylori (H. pylori)

A type of bacteria that can live in your digestive tract and cause sores in the lining of the stomach or small intestine. H. Pylori does not cause problems in most people. H. pylori can be treated with medicines to kill the bacteria and help heal the sores.

Hereditary

Conditions or characteristics passed from parents to children through their genes.

Hysterectomy

Surgery to remove the cervix and uterus, including the lining of the uterus.

Immunohistochemistry (IHC)

A laboratory test that looks for certain proteins in a piece of tissue. IHC can help diagnose diseases like Lynch syndrome.

Inherit

To receive genes from your parents.

Intestines

A long (nearly 20 feet long!) tube running from the stomach to the anus. The intestines absorb most of our nutrients and water. The intestines consist of the small intestine, large intestine, and rectum.

Intestinal Obstruction

This is when food is stuck inside the intestines and prevents other food from passing through. An obstruction can be caused by scars from a surgery on the intestines. Medical help is sometimes needed to remove the obstruction. Obstructions are sometimes called 'blockages.'

Laparoscopic Hysterectomy

Surgery to remove the uterus in small pieces by making small cuts in the abdomen.

Lynch-Related Cancers

Colorectal, endometrial, ovarian, renal pelvis, small intestine, and/or **ureter** cancers.

MLH1

MutL Homolog 1 is a gene associated with Lynch syndrome.

MSH2

MutS Homolog 2 is a gene associated with Lynch syndrome.

MSH6

MutS Homolog 6 is a gene associated with Lynch syndrome.

Mammogram

An X-ray of the breast. A mammogram is the most common way to screen for breast cancer in women who do not have symptoms of breast cancer.

Microsatellites

short sections of DNA that repeat over and over. Microsatellite instability (MSI) is when this type of change occurs much more frequently because the MMR system is not working.

Mismatch Repair Genes (MMR)

Genes that make sure that DNA is copied correctly when a cell divides.

Mutation

When a gene is changed from its natural form.

Non-Polyposis

Used to describe conditions which do not cause hundreds, or thousands, of polyps to grow in the colon and rectum.

Oophorectomy

Surgery to remove one or both ovaries.

Oral contraceptive

Also known as birth control, these pills are taken to prevent pregnancy.

Ovaries

Two female organs that hold the eggs needed for reproduction.

PMS2

PMS1 Homolog 2 is a gene associated with Lynch syndrome.

Polyp

A type of growth in the intestines that can become a cancerous tumor.

Polyposis

The growth of a large numbers of polyps, often hundreds or thousands of polyps.

Precancerous

Refers to cells or tissue likely to develop into cancer if left untreated.

Protein

The building blocks for everything in the body. Proteins are necessary for our bodies to grow, work properly, and stay healthy.

Renal Pelvis

The part of the kidney that collects the urine and passes it to the ureter.

Resection

A surgery to remove all or part of an organ or other body structure.

Salpingectomy

Surgery to remove of one or both Fallopian tubes.

Total Hysterectomy (Total Abdominal Hysterectomy or Radical Hysterectomy)

Surgery to remove the uterus, cervix, ovaries and Fallopian tubes.

Supracervical (Subtotal or Partial) Hysterectomy

Surgery to remove the upper part of the uterus, but not the cervix.

Tumor

Abnormal body cells grouped together in a mass or lump. Tumors are classified as benign (will not spread to other organs) or malignant (may spread to other organs).

Upper Endoscopy

An exam of the esophagus, the stomach and the upper part of the small intestine using a camera on a flexible tube inserted through the mouth.

Urethra

The body part that carries urine out of the body when you urinate (pee).

Urinalysis

A chemical test that can look for cancer cells in urine (pee).

Urinary Tract

This includes the kidneys, ureter, bladder, and urethra.

Ureter

One of two tubes that carry urine from the kidneys to the bladder.

Vaginal Discharge

When fluid or mucus comes out of the vagina.

Vaginal Hysterectomy

Surgery to remove the cervix and the uterus by operating through the vagina.