

Colorectal Cancer Causes, Risk Factors, and Prevention

Learn about the risk factors for colorectal cancer and what you might be able to do to help lower your risk.

Risk Factors

A risk factor is anything that increases your chance of getting a disease such as cancer. Learn more about the risk factors for colorectal cancer.

- Colorectal Cancer Risk Factors
- What Causes Colorectal Cancer?

Prevention

There's no way to completely prevent cancer. But there are things you can do that might help lower your risk. Learn more.

- Can Colorectal Cancer Be Prevented?
- Genetic Testing, Screening, and Prevention for People with a Strong Family History of Colorectal Cancer

Know Your Cancer Risk

Take the ACS CancerRisk360[™] assessment to learn more about what you can change to improve your health. By taking 5 minutes to answer a few questions, we will give you a personalized roadmap of actions with helpful resources you can use to lower your risk of cancer.

Colorectal Cancer Risk Factors

Researchers have found several risk factors that might increase a person's chance of developing colorectal polyps or colorectal cancer.

- What is a risk factor?
- Risk factors you can change
- · Colorectal cancer risk factors you cannot change

What is a risk factor?

A risk factor is anything that raises your chances of getting a disease such as cancer.

Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history of cancer, can't be changed.

But having a risk factor, or even many, does not mean that you will get the disease. And some people who get the disease may not have any known risk factors.

Risk factors you can change

Many lifestyle-related factors have been linked to colorectal cancer. In fact, more than half of all colorectal cancers are linked to risk factors that can be changed.

Being overweight or obese

If you are <u>overweight or obese</u>¹ (very overweight), your risk of developing and dying from colorectal cancer is higher. Being overweight raises the risk of colorectal cancer in people, but the link seems to be stronger in men. Getting to and staying at a <u>healthy</u> <u>weight</u>² may help lower your risk.

Diabetes mellitus, Type 2

People with type 2 diabetes mellitus are more likely than people who don't to develop colorectal cancer. Researchers suspect that this higher risk may be due to high levels of

insulin in people with diabetes mellitus. Both type 2 diabetes and colorectal cancer share some of the same risk factors (such as being overweight and physical inactivity). But even after taking these factors into account, people with type 2 diabetes still have an increased risk. They also tend to have a less favorable prognosis (outlook) after diagnosis.

Certain types of diets

A long-term diet that's high in red meats (such as beef, pork, lamb, or liver) and processed meats (like hot dogs and some lunch meats) raises your colorectal cancer risk.

Cooking meats at very high temperatures (frying, broiling, or grilling) creates chemicals that might raise your cancer risk.

Having a low blood level of vitamin D may also increase your risk.

Following a <u>healthy eating pattern³</u> that includes plenty of fruits, vegetables, and whole grains, and that limits or avoids red and processed meats and sugary drinks probably lowers risk.

Smoking

People who have smoked tobacco for a long time are more likely to develop and die from colorectal cancer than people who don't smoke. Smoking tobacco also increases the risk for people to develop colon polyps. Smoking is a well-known cause of lung cancer, but it's linked to a lot of <u>other cancers</u>⁴, too. If you smoke and want to know more about quitting, see <u>How to Quit Using Tobacco</u>⁵.

Alcohol use

Colorectal cancer has been linked to moderate to heavy <u>alcohol</u>⁶ use. Even light-tomoderate alcohol intake has been associated with some risk. It is best not to drink alcohol. If people do drink alcohol, they should have no more than 2 drinks a day for men and 1 drink a day for women. This could have many health benefits, including a lower risk of <u>many kinds of cancer</u>⁷.

Colorectal cancer risk factors you cannot change

Your age

Your risk of colorectal cancer goes up as you age. Younger adults can get it, but it's much more common after age 50. Colorectal cancer is rising among people who are younger than age 50, and the reason for this remains unclear.

Your racial and ethnic background

American Indian and Alaska Native people have the highest rates of colorectal cancer in the United States, followed by African American men and women.

Jews of Eastern European descent (Ashkenazi Jews) have one of the highest colorectal cancer risks of any ethnic group in the world.

Your sex at birth

Men who have colorectal cancer are more likely to die from it than women. The reasons are not fully clear. Women who have colorectal cancer are more likely to have right-sided colon cancer, particularly if they are no longer menstruating (postmenopausal).

Cholecystectomy

People who have had their gallbladder removed (cholecystectomy) have been found to have a mildly higher risk for right-sided colon cancer. It's not fully understood why this is. Research is ongoing.

A personal history of colorectal polyps oropausal).

have had IBD for many years, especially if untreated, often develop **dysplasia**. Dysplasia is a term used to describe cells in the lining of the colon or rectum that look abnormal, but are not cancer cells. They can change into cancer over time.

If you have IBD, you may need to start getting screened for colorectal cancer when you are younger and be screened more often.

risk of colon cancer. (Adenomatous polyps are the kind of polyps that can become cancer.)

If you have a family history of adenomatous polyps or colorectal cancer, talk with your doctor about the possible need to start screening at a younger age. If you've had adenomatous polyps or colorectal cancer, it's important to tell your close relatives so that they can pass along that information to their doctors and start screening at the right age.

Having an inherited syndrome

About 5% of people who develop colorectal cancer have inherited <u>gene</u> <u>changes</u>⁹ (mutations) that cause family cancer syndromes and can lead to them getting the disease.

The most common inherited syndromes linked with colorectal cancers are Lynch syndrome (hereditary non-polyposis colorectal cancer, or HNPCC) and familial adenomatous polyposis (FAP), but other rarer syndromes can increase colorectal cancer risk, too.

Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC)

Lynch syndrome is the most common hereditary colorectal cancer syndrome. It accounts for about 2% to 4% of all colorectal cancers. In most cases, this disorder is caused by an inherited defect in either the *MLH1*, *MSH2,MSH6*, *PMS2*, or *EPCAM* gene, but changes in other genes can also cause Lynch syndrome. These genes, called DNA mismatch repair (MMR) genes, normally help repair DNA that has been damaged.

The cancers linked to this syndrome tend to develop when people are relatively young and tend to develop right-sided colon cancer. People with Lynch syndrome can have polyps, but they tend to have only a few. The lifetime risk of colorectal cancer in people with this condition may be as high as 50%, but this depends on which gene is affected.

Women with this condition also have a very high risk of developing cancer of the endometrium (lining of the uterus). Other cancers linked with Lynch syndrome include cancer of the ovary, stomach, small intestine, pancreas, kidney, prostate, breast, ureters (tubes that carry urine from the kidneys to the bladder), and bile duct. People with Turcot syndrome (a rare inherited condition) who have a defect in one of the Lynch syndrome genes are at a higher risk of colorectal cancer as well as a specific type of brain cancer called glioblastoma.

For more on Lynch syndrome, see What Causes Colorectal Cancer?, Can Colorectal Cancer Be Prevented?, and <u>Family Cancer Syndromes¹⁰</u>.

Familial adenomatous polyposis (FAP)

FAP is caused by changes (mutations) in the *APC* gene that a person inherits from their parents. About 1% of all colorectal cancers are caused by FAP.

In the most common type of FAP, hundreds or thousands of polyps develop in a

fixing any mistakes) and often leads to cancer at a younger age.

• **Cystic fibrosis (CF):** CF is an inherited condition in which the cells in some body organs make mucus that is thicker and stickier than normal. This can lead to health problems, especially in the lungs and pancreas. As better medical care has helped people with CF live longer, it's become clear that people with CF are also at increased risk for colorectal cancer, which usually occurs at a much earlier age than in people without the condition. The risk for colorectal cancer is even higher in people who have had an organ transplant, such as a lung transplant. CF is caused by mutations in the *CFTR* gene.

Since many of these syndromes are linked to colorectal cancer at a young age and other types of cancer, identifying families with these inherited syndromes is important. It lets doctors recommend specific steps such as screening and other preventive **1.43:479.** And the 72:496:03: Trope 0 Difor **R44:r05846**: as **2.5ticbeR:1846** ger **16** 0 0.2 0.6274 counseling and testing for many of these syndromes can be found in Genetic Testing, Screening, and Prevention for People with a Strong Family History of Colorectal Cancer.

Know Your Cancer Risk ¹¹

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What Causes Colorectal Cancer?

Researchers have found several factors that can increase a person's risk of colorectal cancer, but it's not yet clear exactly how all of these factors might cause this cancer.

- · Gene changes that may lead to colorectal cancer
- Inherited (germline) gene mutations

Acquired (somatic) gene mutations

Gene changes that may lead to colorectal cancer

Cancer is caused by changes in the DNA inside our cells. DNA is the substance in our cells that makes up our genes, which control how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects more than just how we look.

Some genes help control when our cells grow, divide into new cells, and die:

- Certain genes that help cells grow, divide, and stay alive are called **oncogenes**.
- Genes that help keep cell division under control or instruct cells to die at the right time are called **tumor suppressor genes**.

Cancers can be caused by DNA mutations (changes) that turn on oncogenes or turn off tumor suppressor genes. This leads to cells growing out of control. Changes in many different genes are usually needed to cause colorectal cancer.

For more about how genes changes can lead to cancer, see <u>Genes and Cancer¹</u>.

Inherited (germline) gene mutations

Some DNA mutations can be passed on in families and are found in all of a person's cells. These are called **inherited mutations.** A very small portion of colorectal cancers are caused by inherited gene mutations. Many of these DNA changes and their effects on the growth of cells are now known. For example:

- Familial adenomatous polyposis (FAP), attenuated FAP (AFAP), and Gardner syndrome are caused by inherited changes in the *APC* gene. The *APC* gene is a tumor suppressor gene; it normally helps keep cell growth in check. In people with inherited changes in the *APC* gene, this "brake" on cell growth is turned off, causing hundreds of polyps to form in the colon. Over time, cancer will nearly always develop in one or more of these polyps.
- Lynch syndrome (hereditary non-polyposis colon cancer, or HNPCC) is caused by changes in genes that normally help a cell repair damaged DNA. A mutation in one of the DNA repair genes like *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM* can allow DNA errors to go unfixed. These errors will sometimes affect growth-regulating genes, which may lead to the development of cancer.

Peutz-Jeghers syndrome is caused by inherited changes in the STK11 (LKB1)

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Can Colorectal Cancer Be Prevented?

There's no sure way to prevent colorectal cancer, but screening can find abnormal cells before they become cancer. You might also be able to lower your risk for colorectal cancer by changing the risk factors that you can control.

- Colorectal cancer screening
- · Body weight, physical activity, and diet
- Quitting smoking
- Vitamins, calcium, and magnesium
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Hormone replacement therapy for women

Colorectal cancer screening

Screening is the process of looking for cancer or precancer in people who have no symptoms of the disease. Regular colorectal cancer screening is one of the most powerful tools for preventing colorectal cancer.

From the time the first abnormal cells start to grow into polyps, it usually takes about 10 to 15 years for them to develop into colorectal cancer. With regular screening, most polyps can be found and removed before they have the chance to turn into cancer. Screening can also <u>find colorectal cancer early</u>¹, when it's small, hasn't spread, and might beeasier to treat.

If you're age 45 or older, you should start getting screened for colorectal cancer. Several types of tests can be used. Talk to your health care provider about which ones might be good options for you. No matter which test you choose, the most important thing is to get tested.

Weight: Being overweight or obese increases the risk of colorectal cancer in both men and women, but the link seems to be stronger in men. Staying at a healthy weight may help lower your risk.

Physical activity: Being more active lowers your risk of colorectal cancer and polyps. Regular moderate to vigorous activity can lower the risk. **Increasing the amount and intensity of your physical activity may help reduce your risk.**

Diet: Overall, diets that are high in vegetables, fruits, and whole grains, and low in red and processed meats, probably lower colorectal cancer risk, although it's not exactly clear which factors are important. Many studies have found a link between red meats (beef, pork, and lamb) or processed meats (such as hot dogs, sausage, and lunch meats) and increased colorectal cancer risk.

In recent years, some large studies have shown conflicting evidence that fiber in the diet lowers colorectal cancer risk. Research in this area is still under way.

Limiting red and processed meats and eating more vegetables, fruits, and whole grains may help lower your risk.

Alcohol: Several studies have found a higher risk of colorectal cancer with increased <u>alcohol intake</u>⁴, especially among men. It is best not to drink alcohol. For people who do drink, they should have no more than 1 drink per day for women or two drinks per day for men. **Not drinking alcohol may help reduce your risk.**

For more about diet and physical activity, see the <u>American Cancer Society Guidelines</u> for Diet and Physical Activity for Cancer Prevention⁵.

Quitting smoking

Long-term smoking is linked to an increased risk of colorectal cancer, as well as many other cancers and health problems. **Quitting smoking may help lower you risk of colorectal cancer and many other types of cancer, too.** If you smoke <u>and would like help quitting</u>⁶, call the American Cancer Society at 1-800-227-2345.

Vitamins, calcium, and magnesium

Some studies suggest that taking a daily multivitamin containing folic acid may lower colorectal cancer risk, but not all studies have found this. In fact, some studies have hinted that folic acid might help existing tumors grow. More research is needed in this area.

Some studies have suggested that vitamin D, which you can get from sun exposure, in certain foods, or in a vitamin pill, might lower colorectal cancer risk. Studies have shown that low vitamin D levels are associated with an increased risk of colorectal cancer, as well as other cancers. Because of concerns that excess sun exposure can cause skin cancer, most experts do not recommend this as a way to lower colorectal cancer risk at this time. More studies are needed to determine if increasing vitamin D intake from a supplement can help prevent colorectal cancer. It is best to talk with your doctor about whether your vitamin D level should be tested.

Low levels of dietary calcium have been linked with an increased risk of colorectal cancer in some studies. Others suggest that increasing calcium intake may lower the risk for the recurrence of colorectal adenomas. Calcium is important for a number of health reasons aside from possible effects on cancer risk. But because of the possible increased risk of prostate cancer in men with high calcium/dairy product intake, and the possible lower risk of other cancers like colorectal cancer and breast cancer, the American Cancer Society does not have any specific recommendations regarding dairy food consumption for cancer prevention.

Calcium and vitamin D might work together to reduce colorectal cancer risk, as vitamin D aids in the body's absorption of calcium. Still, not all studies have found that supplements of these nutrients reduce risk.

A few studies have found a possible link between a diet that's high in magnesium and reduced colorectal cancer risk, especially among women. More research is needed to **Deteids in the biad A B Austg**./GS683 gs (oer in men with 6 0 1 76 trisk 0 imin)Tj0q()Tj t6m 0ht 0 0 0 rg /(

Nonsteroidal anti-inflammatory drugs (NSAIDs)

Many studies have found that people who regularly take aspirin or other nonsteroidal to

Because aspirin or other NSAIDs can have serious side effects, check with your doctor before starting any of them on a regular basis.

Hormone replacement therapy for women

Some studies have shown that taking estrogen and progesterone after menopause (sometimes called **menopausal hormone therapy** or **combined hormone replacement therapy**) may reduce a woman's risk of developing colorectal cancer, but other studies have not.

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Genetic Testing, Screening, and Prevention for People with a Strong

Family History of Colorectal Cancer

If you have a family history of colorectal polyps or cancer, you have a higher risk of getting colorectal cancer yourself. The risk can be even higher in people with a strong family history of colorectal cancer.

- Is genetic testing right for you?
- Testing for Lynch syndrome (hereditary non-polyposis colorectal cancer, or HNPCC)
- Testing for familial adenomatous polyposis (FAP)
- Testing for other inherited cancer syndromes

Is genetic testing right for you?

Whether genetic testing is right for you will depend on your family history of colorectal cancer. Cancer in close (first-degree) relatives such as parents, brothers, and sisters is most concerning, but cancer in more distant relatives can also be important. Having 2 or more relatives with colorectal cancer is more concerning than having only 1 relative with it. It's also more concerning if your relatives were diagnosed with cancer at a younger age than usual.

In families known to have one of these inherited syndromes, family members who decide not to get tested are still usually advised to start routine screening for colorectal cancer at an early age, and to get screened more often.

Testing for Lynch syndrome (hereditary non-polyposis colorectal cancer, or HNPCC)

Lynch syndrome can greatly increase a person's risk for colorectal cancer. The lifetime risk of colorectal cancer in people with this condition can range from about 10% to about 80%, depending on which gene mutation is causing the syndrome.

People with Lynch syndrome are also at increased risk for some other cancers, such as cancers of the uterus (endometrium), ovaries, stomach, small bowel, pancreas, kidneys, brain, ureters (tubes that carry urine from the kidneys to the bladder), and bile duct.

Who should be tested for Lynch syndrome?

There are two sets of guidelines that doctors often use to determine who might be likely to benefit from genetic counseling or testing: the Amsterdam criteria (based on family history) and the revised Bethesda guidelines (for people diagnosed with colorectal cancer).

Amsterdam criteria

Doctors have found that many families with Lynch syndrome tend to have certain characteristics, which are known as the **Amsterdam criteria**:

At least 3 relatives have a cancer linked with Lynch syndrome and:

- One is a first-degree relative (parent, brother or sister, or child) of the other 2 relatives.
- At least 2 successive generations are affected.
- At least 1 relative had their cancer when they were younger than age 50.

If all of these apply to your family, then you might want to seek genetic counseling. But even if your family history satisfies the Amsterdam criteria, it doesn't always mean you have Lynch syndrome. And many families with Lynch syndrome do not meet the Amsterdam criteria.

Revised Bethesda guidelines

A second set of criteria, called the **revised Bethesda guidelines**, can be used to help decide whether a person with colorectal cancer should be tested for genetic changes that are seen with Lynch syndrome. (These changes are called **microsatellite instability or MSI**.) These criteria include at least one of the following:

- The person is younger than age 50 when diagnosed with colorectal or uterine cancer.
- The person has or had a second colorectal cancer or another cancer (<u>endometrial</u>⁴, <u>stomach</u>⁵, <u>pancreas</u>⁶, <u>small intestine</u>⁷, <u>ovary</u>⁸, <u>kidney</u>⁹, <u>brain</u>¹⁰, ureters, or <u>bile</u> <u>duct</u>¹¹) linked to Lynch syndrome.
- The person is younger than age 60, and the cancer has certain characteristics seen with Lynch syndrome when it's viewed under a microscope.
- The person has a first-degree relative (parent, sibling, or child) younger than age 50 who was diagnosed with colorectal cancer or another cancer linked to Lynch syndrome.
- The person has 2 or more first- or second-degree relatives (aunts, uncles, nieces, nephews, or grandparents) who had colorectal cancer or another Lynch syndrome-related cancer at any age.

If a person with colorectal cancer has any of the Bethesda criteria, testing for MSI may be advised. If MSI is found, the doctor typically will recommend that the patient be tested for Lynch syndrome-associated gene mutations.

It's important to know that most people who meet the Bethesda criteria do not have Lynch syndrome, and that you can have Lynch syndrome and not meet any of the criteria listed. Not all doctors use the Bethesda guidelines to decide who should have MSI testing. In fact, it is now recommended that all colorectal cancers be tested for <u>MMR deficiency or MSI¹²</u>. For anyone whose cancer has a high MSI level or is missing (deficient in) one of the MMR proteins, doctors will most likely recommend genetic testing for Lynch syndrome.

Even if you don't have cancer, your doctor may suspect that Lynch syndrome runs in your family based on cases of colorectal cancer and other cancers associated with this syndrome in your relatives. In that case, your doctor might recommend genetic counseling to evaluate your risk.

If your family carries Lynch syndrome

In families known to carry a Lynch syndrome gene mutation, doctors recommend that family members who have tested positive for the mutation and those who have not been

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