

# **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

# **Colorectal Cancer Risk Factors**

- · Colorectal cancer risk factors you can change
- Colorectal cancer risk factors you cannot change
- Factors with unclear effects on colorectal cancer risk

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, 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.

# A personal history of inflammatory bowel disease

If you have inflammatory bowel disease (IBD), including either ulcerative colitis or

#### Having an inherited syndrome

About 5% of people who develop colorectal cancer have inherited <u>gene<sup>11</sup></u> changes (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* or *MSH6* gene, but changes in other genes can also cause Lynch syndrome. These genes normally help repair DNA that has been damaged.

The cancers linked to this syndrome tend to develop when people are relatively young. People with Lynch syndrome can have polyps, but they tend to only have 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.

person's colon and rectum, often starting at ages 10 to 12 years. Cancer usually

mutations in the CFTR gene.

Since many of these syndromes are linked to colorectal cancer at a young age and also linked to other types of cancer, identifying families with these inherited syndromes is important. It lets doctors recommend specific steps such as screening and other preventive measures when the person is younger. Information on risk assessment, and genetic 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.

## Your racial and ethnic background

American Indian and Alaska Native people have the highest rates of colorectal cancer in the US, 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.

## Having type 2 diabetes

People with type 2 (usually non-insulin dependent) diabetes have an increased risk of colorectal cancer. 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.

# Factors with unclear effects on colorectal cancer risk

#### Night shift work

Some studies suggest working a night shift regularly might raise the risk of rectal cancer. This might be due to changes in levels of melatonin, a hormone that responds to changes in light. More research is needed.

#### Previous treatment for certain cancers

Some studies have found that men who survive testicular cancer seem to have a higher rate of colorectal cancer and some other cancers. This might be because of the treatments they have received, such as radiation therapy.

Several studies have suggested that men who had radiation therapy to treat prostate cancer might have a higher risk of rectal cancer because the rectum receives some radiation during treatment. Most of these studies are based on men treated in the 1980s and 1990s, when radiation treatments were less precise than they are today. The effect of more modern radiation methods on rectal cancer risk is not clear, but research continues to be done in this area.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-</u> <u>cancer-risk.html</u>
- 2. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/take-control-your-weight.html</u>
- 3. www.cancer.org/cancer/risk-prevention/diet-physical-activity/get-active.html
- 4. www.cancer.org/cancer/risk-prevention/diet-physical-activity/eat-healthy.html
- 5. <u>www.cancer.org/cancer/risk-prevention/tobacco/health-risks-of-tobacco/health-risks-of-smoking-tobacco.html</u>
- 6. <u>www.cancer.org/cancer/risk-prevention/tobacco/guide-quitting-smoking.html</u>
- 7. www.cancer.org/cancer/risk-prevention/tobacco/guide-quitting-smoking.html
- 8. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/alcohol-use-and-cancer.html</u>
- 9. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/acs-guidelines-</u> <u>nutrition-physical-activity-cancer-prevention.html</u>
- 10. <u>www.cancer.org/cancer/types/colon-rectal-cancer/about/what-is-colorectal-cancer.html</u>
- 11. www.cancer.org/cancer/understanding-cancer/genes-and-cancer.html
- 12. www.cancer.org/cancer/risk-prevention/genetics/family-cancer-syndromes.html

## References

American Cancer Society.

Berger AH and Pandolfi PP. Ch 5 - Cancer Susceptibility Syndromes. In: DeVita VT, Hellman S, Rosenberg SA, eds.

Series. Chest. 2022;161(2):356-364.

McMaster M, Feuer EJ, Tucker MA. New Malignancies Following Cancer of the Male Genital Tract. In: Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker DG, Edwards BK, Tucker MA, Fraumeni JF Jr. (eds). New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000. National Cancer Institute. NIH Publ. No. 05-5302. Bethesda, MD, 2006. Accessed at

http://seer.cancer.gov/archive/publications/mpmono/MPMonograph\_complete.pdf on February 6, 2020.

National Cancer Institute. Physician Data Query (PDQ). Colorectal Cancer Prevention. 2019. Accessed at https://www.cancer.gov/types/colorectal/patient/colorectal-prevention-pdq on February 06, 2020.

National Center for Advancing Translational Sciences. Genetic and Rare Diseases Information Center. *Turcot syndrome*, 8/29/2012. Accessed at https://rarediseases.info.nih.gov/diseases/420/turcot-syndrome on February 5, 2020.

Nieder AM, Porter MP, Soloway MS. Radiation therapy for prostate cancer increases subsequent risk of bladder and rectal cancer: A population based cohort study. *J Urol.* 2008;180:2005-2009; discussion 2009-10.

Mazonak20 rg 6mE / / Fwa.ec 0 g ET LBT 1 0 0 ,-10.

Rock CL, Thomson C, Gansler T, et al. American Cancer Society guideline for diet and physical activity for cancer prevention. CA: A Cancer Journal for Clinicians. 2020;70(4). doi:10.3322/caac.21591. Accessed at

https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21591 on June 9, 2020.

Travis LB, Fosså SD, Schonfeld SJ, et al. Second cancers among 40,576 testicular cancer patients: focus on long-term survivors. *J Natl Cancer Inst*. 2005;97(18):1354-1365.

Wallis CJ, Mahar AL, Choo R, et al. Second malignancies after radiotherapy for prostate cancer: systematic review and meta-analysis. *BMJ*. 2016;352:i851. Published 2016 Mar 2. doi:10.1136/bmj.i851.

Win AK. Lynch syndrome (hereditary nonpolyposis colorectal cancer): Clinical manifestations and diagnosis. Lamont JT and Grover S, eds. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com (Accessed on February 05, 2020.)

Zhu Z, Zhao S, Liu Y, et al. Risk of secondary rectal cancer and colon cancer after radiotherapy for prostate cancer: a meta-analysis. *Int J Colorectal Dis.* 2018;33(9):1149-1158. doi:10.1007/s00384-018-3114-7.

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# What Causes Colorectal Cancer?

- Inherited gene mutations
- Acquired gene mutations

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.

Cancer is caused by changes in the DNA inside our cells. DNA is the chemical 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 cause cells to die at the right time are called *tumor suppressor genes*.

Cancers can be caused by DNAmutations (changes) that turn on oncogenes or turn off

these conditions, you may want to ask your doctor about genetic counseling and genetic testing.

The American Cancer Society recommends discussing genetic testing with a qualified cancer genetics professional before any genetic testing is done. For more on this, see <u>Understanding Genetic Testing for Cancer Risk</u><sup>2</sup> and <u>What Happens during Genetic Testing for Cancer Risk</u><sup>3</sup>

# Acquired gene mutations

Most gene mutations that lead to cancer are *acquired* mutations. They happen during a person's lifetime and are not passed on to their children. These DNA changes affect only cells that come from the original mutated cell.

In most cases of colorectal cancer, the DNA mutations that lead to cancer are acquired during a person's life rather than having been inherited. Certain risk factors probably play a role in causing these acquired mutations, but so far it's not known what causes most of them.

There doesn't seem to be a single genetic pathway to colorectal cancer that's the same in all cases. In many cases, the first mutation occurs in the *APC* gene. This leads to an increased growth of colorectal cells because of the loss of this "brake" on cell growth. Further mutations may then occur in other genes, which can lead the cells to grow and spread uncontrollably. Other genes that aren't known yet are probably involved as well.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/understanding-cancer/genes-and-cancer.html</u>
- 2. <u>www.cancer.org/cancer/risk-prevention/genetics/genetic-testing-for-cancer-risk/understanding-genetic-testing-for-cancer.html</u>
- 3. <u>www.cancer.org/cancer/risk-prevention/genetics/genetic-testing-for-cancer-risk/what-happens-during-genetic-testing-for-cancer.html</u>

## References

Lawler M, Johnston B, Van Schaeybroeck S, Salto-Tellez M, Wilson R, Dunlop M, and Johnston PG. Chapter 74 – Colorectal Cancer. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa. Elsevier: 2020.

Libutti SK, Saltz LB, Willett CG, and Levine RA. Ch 62 - Cancer of the Colon. In: DeVita VT, Hellman S, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott-Williams &

# **Can Colorectal Cancer Be Prevented?**

Screening can also <u>find colorectal cancer early</u><sup>1</sup>, when it's small and easier 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.

If you have a strong family history of colorectal polyps or cancer, talk with your doctor about your risk. You might benefit from <u>genetic counseling</u><sup>2</sup> to review your family medical tree to see how likely it is that you have a <u>family cancer syndrome</u><sup>3</sup>.

# Body weight, physical activity, and diet

You might be able to lower your risk of colorectal cancer by managing your diet and physical activity.

**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. Limiting your sitting and lying down time may also lower your risk.<sup>4</sup> 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 probably lowers colorectal cancer risk. Research in this area is still under way. Recent studies looking specifically at whole grain intake, however, show that colorectal cancer risk appears to go down as you add more whole grains to your diet.

# 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><sup>5</sup>, 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 Prevention<sup>6</sup>.

# Not 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><sup>7</sup>, call the American Cancer Society at 1-800-227-2345.

## Vitamins, calcium, and magnesium

Some studies suggest that taking a daily multi-vitamin containing folic acid, or folate, 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. Avoiding a low vitamin D level may be helpful; 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. Other studies suggest that increasing calcium intake may lower colorectal cancer risk. 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 determine if this link exists.

# Non-steroidal anti-inflammatory drugs (NSAIDs)

Many studies have found that people who regularly take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (Motrin, Advil) and naproxen (Aleve), have a lower risk of colorectal cancer and polyps.

But aspirin and other NSAIDs can cause serious or even life-threatening side effects, such as bleeding from stomach irritation or stomach ulcers, which may outweigh the benefits of these medicines for the general public. For this reason, the American Cancer Society does not recommend taking NSAIDs just to lower colorectal cancer risk if you are someone at average risk.

Still, for some people in their 50s who have a high risk of heart disease, where low-dose aspirin is found to be beneficial, the aspirin may also have the added benefit of reducing the risk of colorectal cancer.

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.

Because taking estrogen and progesterone after menopause can also increase a woman's risk of heart disease, blood clots, and cancers of the breast and lung, it's not commonly recommended just to lower colorectal cancer risk.

If you're considering using menopausal hormone therapy, be sure to discuss the risks and benefits with your doctor. Wilkins; 2019.

National Cancer Institute. Physician Data Query (PDQ). Colorectal Cancer Prevention. 2019. Accessed at https://www.cancer.gov/types/colorectal/patient/colorectal-prevention-pdq on February 23, 2020.

Rock CL, Thomson C, Gansler T, et al. American Cancer Society guideline for diet and physical activity for cancer prevention. CA: A Cancer Journal for Clinicians. 2020;70(4). doi:10.3322/caac.21591. Accessed at https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21591 on June 9, 2020.

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# Genetic Testing, Screening, and Prevention for People with a Strong Family History of Colorectal Cancer

- Testing for Lynch syndrome (hereditary non-polyposis colorectal cancer, or HNPCC)
- Testing for familial adenomatous polyposis (FAP)
- Testing for other inherited cancer syndromes

If you have a family history of colorectal polyps or cancer, you have a higher risk of getting colorectal cancer yourself. This risk can be even higher in people with a strong 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 one relative with it. It's also more concerning if your relatives were diagnosed with cancer at a younger age than usual.

**If you have a family history of colorectal cancer, talk with your doctor.** You might benefit from speaking with a genetic counselor or other health professional who is trained in genetic counseling. They can review your family history to see how likely it is that you have a family cancer syndrome. The counselor can also help you decide if genetic testing is right for you. If you have testing and are found to have an abnormal

gene, there might be steps you can take to help lower your risk of colorectal cancer, such as starting routine screening at an earlier age or even having surgery.

But before getting genetic testing, it's important to know ahead of time what the results might or might not tell you about your risk. Genetic testing is not perfect. The tests might not provide clear answers for some people. This is why meeting with a genetic counselor or cancer genetics professional is important before deciding to be tested. To learn more about this, see <u>Understanding Genetic Testing for Cancer</u><sup>1</sup> and <u>What</u> <u>Happens During Genetic Testing for Cancer</u><sup>2</sup>

Genetic tests can help show if members of certain families have inherited a high risk of colorectal cancer due to inherited cancer syndromes such as Lynch syndrome (also known as hereditary non-polyposis colorectal cancer, or HNPCC) or familial adenomatous polyposis (FAPv8c 0 0 759k ncerc-polypetf

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 **microsatelliteinstability or MSI.**) These criteria include at least one of the following:

- The person is younger than 50 years when diagnosed with colorectal cancer.
- The person has or had a second colorectal cancer or another cancer (<u>endometrial</u><sup>3</sup>, <u>stomach</u><sup>4</sup>, <u>pancreas</u><sup>5</sup>, <u>small intestine</u><sup>6</sup>, <u>ovary</u><sup>7</sup>, <u>kidney</u><sup>8</sup>, <u>brain</u><sup>9</sup>, ureters, or <u>bile duct</u><sup>10</sup>) linked to Lynch syndrome.
- The person is younger than 60 years, 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 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.

Lawler M, Johnston B, Van Schaeybroeck S, Salto-Tellez M, Wilson R, Dunlop M, and Johnston PG. Chapter 74 – Colorectal Cancer. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa. Elsevier: 2020.

Libutti SK, Saltz LB, Willett CG, and Levine RA. Ch 62 - Cancer of the Colon. In: DeVita VT, Hellman S, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott-Williams & Wilkins; 2019.

Libutti SK, Willett CG, Saltz LB, and Levine RA. Ch 63 - Cancer of the Rectum. In: DeVita VT, Hellman S, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott-Williams & Wilkins; 2019.

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Colorectal. V.3.2019. Accessed at https://www.nccn.org/professionals/physician\_gls/pdf/genetics\_colon.pdf on Feb 23, 2020.

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