

# Stomach Cancer Causes, Risk Factors, and Prevention

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

#### **Risk Factors**

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

- Stomach Cancer Risk Factors
- What Causes Stomach Cancer?

#### Prevention

There is no sure way to prevent stomach cancer. But there are things you can do that might lower your risk. Learn more.

Can Stomach Cancer Be Prevented?

# **Stomach Cancer Risk Factors**

- Sex
- Age

# Ethnicity

# Alcohol use

<u>Alcohol use</u><sup>1</sup> probably increases the risk of stomach cancer. The evidence for this link is strongest for people who have 3 or more drinks per day.

## Tobacco use

<u>Smoking</u><sup>2</sup> increases stomach cancer risk, particularly for cancers of the upper part of the stomach near the esophagus. The rate of stomach cancer is about doubled in people who smoke.

## Previous stomach surgery

Stomach cancers are more likely to develop in people who have had part of their stomach removed to treat non-cancerous diseases such as ulcers. This might be because the stomach makes less acid, which allows more harmful bacteria to be present. Reflux (backup) of bile from the small intestine into the stomach after surgery might also add to the increased risk. These cancers typically develop many years after the surgery.

# Some types of stomach polyps

Polyps are non-cancerous growths on the lining of the stomach. Most types of polyps (such as hyperplastic polyps or inflammatory polyps) do not seem to increase a person's risk of stomach cancer much, if at all. But adenomatous polyps – also called **adenomas** – can sometimes develop into cancer.

### **Pernicious anemia**

Certain cells in the stomach lining normally make a substance called **intrinsic factor**(IF)that the body needs to absorb vitamin B12 from foods. People without enough IF may end up with a vitamin B12 deficiency, which affects the body's ability to make new red blood cells and can cause other problems as well. This condition, called **pernicious anemia**, can be caused by certain autoimmune conditions, as well as by some types of stomach surgery. Along with anemia (having too few red blood cells), people with this disease have an increased risk of stomach cancer.

# Menetrier disease (hypertrophic gastropathy)

In this condition, excess growth of the stomach's inner lining causes large folds in the lining and leads to low levels of stomach acid. Because this disease is very rare, it is not known exactly how much this increases the risk of stomach cancer.

### Inherited cancer syndromes

Some people inherit gene mutations (changes) from their parents that lead to conditions that can raise their risk of stomach cancer. These inherited syndromes account for only a small percentage of stomach cancers worldwide.

#### Hereditary diffuse gastric cancer (HDGC)

This inherited syndrome greatly increases the risk of developing stomach cancer. This condition is rare, but the lifetime stomach cancer risk among affected people is up to 70%. Women with this syndrome also have an increased risk of invasive lobular <u>breast</u> <u>cancer</u><sup>3</sup>. This syndrome is most often caused by mutations in the *CDH1* gene.

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

Lynch syndrome (formerly known as HNPCC) is an inherited genetic disorder that increases the risk of<u>colorectal cancer</u><sup>4</sup>, stomach cancer, and some other cancers. This syndrome is caused by mutations in one of the mismatch repair (MMR) genes, such as *MLH1* or *MSH2*. These genes normally help repair DNA that has been damaged.

#### Familial adenomatous polyposis (FAP)

People with FAP get many polyps in the colon, and sometimes in the stomach and intestines, starting at an early age. People with this syndrome have a very high risk of getting <u>colorectal cancer</u><sup>5</sup> and a slightly increased risk of getting stomach cancer. FAP is caused by mutations in the *APC* gene.

#### Gastric adenoma and proximal polyposis of the stomach (GAPPS)

This rare condition is caused by a mutation in a specific part of the *APC* gene. People with GAPPS develop many polyps in the stomach and have an increased risk of stomach cancer.

#### Li-Fraumeni syndrome

People with this syndrome have an increased risk of several types of cancer, including

developing stomach cancer at a relatively young age. Li-Fraumeni syndrome is caused by a mutation in the *TP53* gene.

#### **Peutz-Jeghers syndrome (PJS)**

People with this condition develop polyps in the stomach and intestines, as well as in other areas including the nose, the airways of the lungs, and the bladder. The polyps in the stomach and intestines are called **hamartomas**. They can cause problems like bleeding or blockage of the intestines. PJS can also cause dark freckle-like spots on the lips, inner cheeks and other areas. People with PJS have an increased risk of several types of cancer, including cancers of the colon, <u>pancreas</u><sup>6</sup>, stomach, and breast. This syndrome is caused by mutations in the *STK11* gene.

## A family history of stomach cancer

People with first-degree relatives (parents, siblings, or children) who have had stomach cancer are more likely to develop this disease, even without one of the inherited cancer syndromes described above. Still, most people who get stomach cancer do not have a family history of it.

# Common variable immune deficiency (CVID)

In people with CVID, the immune system can't make enough antibodies to help protect against germs. This can lead to frequent infections as well as other problems, including atrophic gastritis and pernicious anemia. People with CVID are more likely to get gastric lymphoma and stomach cancer.

# Epstein-Barr virus (EBV) infection

Epstein-Barr virus causes infectious mononucleosis (also called mono). Most people are infected with this virus at some time in their lives, usually as children or teens.

EBV has been linked to <u>nasopharyngeal cancer</u><sup>7</sup> and to some forms of <u>lymphoma</u><sup>8</sup>. It is also found in the cancer cells of about 5% to 10% of people with stomach cancer, although it isn't yet clear if the virus actually causes stomach cancer. Stomach cancers linked to EBV tend to be slower growing and have less of a tendency to spread.

### **Certain occupations**

Workers in the coal, metal, and rubber industries seem to have a higher risk of getting stomach cancer.

# Having type A blood

Blood type groups refer to certain substances that are normally present on the surface of red blood cells and some other types of cells. These groups are important in matching blood for transfusions. For unknown reasons, people with type A blood have a higher risk of getting stomach cancer.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/alcohol-use-and-</u> <u>cancer.html</u>
- 2. <u>www.cancer.org/cancer/risk-prevention/tobacco/health-risks-of-tobacco/smokeless-tobacco.html</u>
- 3. www.cancer.org/cancer/types/breast-cancer.html
- 4. www.cancer.org/cancer/types/colon-rectal-cancer.html
- 5. www.cancer.org/cancer/types/colon-rectal-cancer.html
- 6. www.cancer.org/cancer/types/pancreatic-cancer.html
- 7. www.cancer.org/cancer/types/nasopharyngeal-cancer.html
- 8. www.cancer.org/cancer/types/lymphoma.html

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# What Causes Stomach Cancer?

• Pre-cancerous changes in the stomach

#### · Changes in genes (DNA) in stomach cancer cells

There are many known risk factors for stomach cancer (also called gastric cancer), but often it's not clear exactly how these factors might affect how cells in the stomach become cancer cells. This is the subject of ongoing research.

# Pre-cancerous changes in the stomach

Several changes thought to be pre-cancerous can occur in the inner lining of the stomach.

In **atrophic gastritis**, the normal gland cells of the stomach are either fewer or absent. There is also some degree of inflammation (in which the stomach cells are damaged by cells of the immune system). Atrophic gastritis is often caused by infection with *H pylori* bacteria (see below). It can also be caused by an autoimmune reaction, in which a person's immune system attacks the cells lining the stomach. Some people with this condition go on to develop pernicious anemia or other stomach problems, including cancer.

Another possible pre-cancerous change is **intestinal metaplasia**. In this condition, the cells that normally line the stomach are replaced by cells that look like the cells that usually line the intestine. People with this condition often have chronic atrophic gastritis as well. This might also be related to *H pylori* infection.

Both atrophic gastritis and intestinal metaplasia can lead to having too few gland cells, which would normally secrete substances that help protect the cells in the stomach's inner lining. Damage to the DNA inside these cells can sometimes lead to **dysplasia**, in which the cells become larger and very abnormal looking (more like cancer cells). In some cases, dysplasia can then progress to stomach cancer.

# Changes in genes (DNA) in stomach cancer cells

Recent research has provided clues on how some stomach cancers form. For instance, *H pylori* bacteria, particularly certain subtypes, can convert substances in some foods into chemicals that cause mutations (changes) in the DNA of the cells in the stomach lining. This may help explain why certain foods such as preserved meats increase a person's risk for stomach cancer. On the other hand, some of the foods that might lower stomach cancer risk, such as fruits and vegetables, contain antioxidants (like vitamins A and C) that can block substances that damage a cell's DNA.

Stomach cancers, like other cancers, are caused by changes in the DNA inside cells. DNA is the chemical that carries our **genes**, which control how our cells function. We look like our parents because they are the source of our DNA. But DNA affects more than how we look.

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

- Genes that normally help cells grow, divide, and stay alive can sometimes change to become **oncogenes**.
- Genes that help keep cell division under control, repair mistakes in DNA, or cause cells to die at the right time are called **tumor suppressor genes**.

Cancers can be caused by DNA changes that keep oncogenes turned on, or that turn off tumor suppressor genes.

#### Inherited versus acquired gene mutations

**Inherited mutations** in some genes (as explained in Stomach Cancer Risk Factors) can increase a person's stomach cancer risk. But these are thought to cause only a small percentage of stomach cancers.

Most of the gene changes that lead to stomach cancer occur after birth. Some of these **acquired mutations** might be caused by risk factors such as *H pylori* infection or tobacco use. But other gene changes may just be random events that sometimes happen inside cells, without having an outside cause.

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# **Can Stomach Cancer Be Prevented?**

- Diet, nutrition, body weight, physical activity, and alcohol use
- Not smoking
- Treating H pylori infection
- Aspirin use
- For people at greatly increased risk

There is no sure way to prevent stomach cancer (also known as gastric cancer), but there are things you can do that could lower your risk.

# Diet, nutrition, body weight, physical activity, and alcohol use

Being overweight or obese increases the risk of some types of stomach cancer, so **getting to and staying at a healthy weight** might lower your risk.

Getting regular physical activity might also help lower your risk of stomach cancer.

Aside from possible effects on stomach cancer risk, staying at a healthy weight and being active may also lower your risk of several other cancers and health problems.

A diet that includes plenty of fresh fruits and vegetables probably also lowers stomach cancer risk. Citrus fruits (such as oranges, lemons, and grapefruit) may be especially helpful, but be aware that grapefruit and grapefruit juice can change the blood levels of certain drugs you take. Talk to your health care team about this before adding grapefruit to your diet.

The American Cancer Society recommends that people **follow a healthy eating pattern**, which includes a variety of colorful fruits and vegetables and whole grains, and avoids or limits red and processed meats, sugar-sweetened beverages, and highly processed foods.

Alcohol use probably increases the risk of stomach cancer, so **avoiding or limiting alcohol** might lower your risk.

For more on diet, body weight, physical activity, and alcohol use, see the <u>American</u> <u>Cancer Society Guideline for Diet and Physical Activity for Cancer Prevention</u><sup>1</sup>.

Studies that have looked at other dietary factors, such as taking **dietary supplements** or **drinking tea** (particularly **green tea**) have not led to firm conclusions when it comes

recommend taking NSAIDs specifically to prevent stomach cancer. Studies have not yet determined for which people the benefits of lowering cancer risk would outweigh the risks of bleeding complications.

# For people at greatly increased risk

**Hereditary diffuse gastric cancer (HDGC)** is a rare inherited condition in which people have a greatly increased risk of stomach cancer, which often develops at a fairly early age. This rare syndrome is most often caused by an inherited mutation in the *CDH1* gene.

It's very important to recognize people and families with this inherited syndrome, because most people who have it will develop stomach cancer. Families with HDGC typically have two or more close relatives who develop stomach cancer (usually the <u>diffuse type</u><sup>5</sup>), and/or at least one person who is diagnosed before age 50. Some family members might also develop invasive lobular breast cancer.

Doctors often refer people who might have HDGC to a genetics professional, so they can discuss possibly getting <u>genetic testing</u><sup>6</sup>. If testing is done and shows a person has a mutation (abnormal change) in the *CDH1* gene, doctors often recommend they consider having their stomach removed (typically between the ages of 20 and 30) before cancer develops. However, this operation (called a total gastrectomy) can lead to long-term changes in the way a person eats.

Some other hereditary cancer syndromes are also linked with an increased risk for stomach cancer, including Lynch syndrome, familial adenomatous polyposis (FAP), Li-Fraumeni syndrome, and Peutz-Jeghers syndrome. The risk of stomach cancer with these syndromes is not nearly as high as it is with HDGC, so removal of the stomach is not typically recommended for people who have these syndromes. However, doctors might recommend getting regular tests to try to find stomach cancer early<sup>7</sup> in some of these people.

# **Hyperlinks**

- 1. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/acs-guidelines-</u> <u>nutrition-physical-activity-cancer-prevention.html</u>
- 2. www.cancer.org/cancer/risk-prevention/tobacco/guide-quitting-smoking.html
- 3. www.cancer.org/cancer/types/stomach-cancer/detection-diagnosis-staging/how-

diagnosed.html

- 4. <u>www.cancer.org/cancer/types/colon-rectal-cancer.html</u>
- 5. www.cancer.org/cancer/types/stomach-cancer/about/what-is-stomach-cancer.html
- 6. <u>www.cancer.org/cancer/risk-prevention/genetics/genetic-testing-for-cancer-</u> risk/understanding-genetic-testing-for-cancer.html
- 7. <u>www.cancer.org/cancer/types/stomach-cancer/detection-diagnosis-</u> staging/detection.html

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#### Written by

The American Cancer Society medical and editorial content team (<u>https://www.cancer.org/cancer/acs-medical-content-and-news-staff.html</u>)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

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