

Liver and intrahepatic bile duct cancer risk factor information

This document gives a general overview of risk factors. The document will cover:

- About cancer and risk factors
- About liver and intrahepatic bile duct (IBD) cancers
- Types of liver and IBD cancers
- Known risk factors
- Possible risk factors
- Other risk factors that have been investigated
- References / more information

About cancer and risk factors

Cancer is not just one disease.

Cancer is a group of over 100 different diseases. Cancer occurs when abnormal cells grow out of control and crowd out the normal cells. It can start anywhere in the body and can spread (“metastasize”) to other parts of the body. Cancer types are named for the original location in the body and the type of cell or tissue. Different types of cancer have different causes and risk factors.

Cancer can take a long time to develop.

The cause of cancer is usually related to events that happened many years ago. Most cancer types are thought to take anywhere from 10 to over 50 years to develop. A few types, such as leukemia or lymphoma, are thought to take less than 10 years.

A risk factor is anything that increases your chance of getting cancer.

Some risk factors can be controlled while others cannot. Risk factors can include:

- Hereditary conditions (such as genes passed down from parents)
- Medical conditions or treatments (such as a previous cancer diagnosis)
- Infections (such as human papilloma virus [HPV])
- Lifestyle factors (such as smoking cigarettes)
- Environmental exposures (such as certain air pollutants)

Most risk factors do not directly cause cancer.

A risk factor influences the development of cancer but usually does not directly cause cancer. Instead, a combination of risk factors likely drives cancer development. For example, genetic factors can make individuals more likely to get cancer when they are exposed to a cancer-causing chemical.

Environmental risk factors depend on how, how much, and how long you are exposed.

Your risk from exposure to certain chemicals or radiation depends on the type, extent, and duration of exposure. For example, breathing a certain chemical may increase your risk of getting cancer. However, touching the same chemical may not. In addition, some substances may increase your risk only if you are exposed to high amounts over a long time.

It is difficult to identify the exact causes of cancer.

- Many cancers can develop due to random chance.
- Multiple risk factors can act in combination.
- Risk factors can change over time.
- Cancer might not develop or get diagnosed for a long time after an initiating event (such as exposure or random cell mutation).

Knowing your risk factors can help you make more informed choices.

Discuss your risk factors with your health care provider to make more informed decisions on lifestyle and health care.

About liver and intrahepatic bile duct (IBD) cancer

Liver cancer starts in the liver and intrahepatic bile duct cancer starts in cells that line the small tubes inside the liver.

The liver is a large organ with two lobes (right and left) and is located just beneath the right lung. It provides many important functions that we cannot live without, including:

- Filtering and breaking down alcohol, drugs, and other harmful substances in the blood
- Making bile (a fluid that helps the body digest food, especially fats)
- Processing nutrients absorbed from the intestines and storing energy to be used later^{2,6}
- Making substances to help blood clot (stop bleeding from cuts or wounds)²

The intrahepatic bile ducts are small, branching tubes in the liver that collect bile and transport it to larger ducts that eventually lead to the gallbladder and small intestine.³ Bile duct cancer is classified as either intrahepatic (starting in the bile ducts within the liver) or extrahepatic (starting in the bile ducts outside the liver).^{3,6} The information in this summary is about liver and intrahepatic bile duct cancer (and not extrahepatic bile duct cancer), because they share many risk factors and often have similar treatments.⁶

Liver and IBD cancer is more common among men than women.

The American Cancer Society estimates 42,240 individuals (28,220 males and 14,020 females) will be diagnosed with liver and IBD cancer in the United States in 2025.^{1,2} During 2016-2020, the incidence rate (new diagnoses) among males in Massachusetts was 8.5% higher than the national rate (a difference that is statistically significant). During this 5-year period, a total of 2,903 males and 1,101 females were diagnosed with liver and IBD cancer in the Commonwealth.⁸

In the United States, liver and IBD cancer is more common among Hispanic, Black, Asian Americans and Pacific Islander, and American Indian and Alaska Native individuals.

In the United States, most recent data for 2018-2022 indicates that American Indian and Alaska Native individuals have the highest incidence rates of liver and IBD cancer, followed by those who are Hispanic, Asian or Pacific Islander, and Black. Non-Hispanic White individuals have the lowest incidence rate of liver and IBD cancer.⁷

The risk of liver and IBD cancer increases with age.

Nearly 90% of people diagnosed with liver and IBD cancer are older than 55. It is most frequently diagnosed among people aged 65-74 with a median age at diagnosis of 67.⁷

The rate of new diagnoses of liver and IBD cancer have been increasing in the United States in recent decades.

The incidence rate of liver and IBD cancer in the United States has more than tripled since 1980.² More recently, it has continued to increase by about 2% each year in women from 2017 to 2022 but has stabilized in men.¹

Types of liver and IBD cancers

Both primary and secondary cancers can develop in the liver and IBD.

Primary liver and IBD cancers start in the liver or intrahepatic bile duct.^{2,6} Secondary liver cancers start elsewhere in the body, such as the pancreas, colon, or breast, and then spread (metastasize)

to the liver.² Risk factors and treatment are based on where the cancer started (primary site). For example, breast cancer that has spread to the liver is treated as breast cancer (not liver cancer). In the United States and Europe, metastatic (secondary) liver cancers are more common than cancers that start in the liver (primary cancers). The opposite is true for many parts of Asia and Africa. The information in this summary is about primary liver and IBD cancers and not metastatic liver tumors. Liver tumors can be either cancerous (malignant) or non-cancerous (benign).²

Hepatocellular carcinoma (HCC) is the most common type of liver cancer in adults.

Hepatocellular carcinoma (HCC), which has several subtypes, accounts for about 70% of all primary liver cancers in adults.^{1,2,6,9} Some begin as a single tumor that grows larger. Others start as many cancer nodules throughout the liver, which is the more common in the United States.²

Other types of liver and IBD cancer are less common.

- Intrahepatic cholangiocarcinoma (bile duct cancer) starts in the small bile ducts within the liver and accounts for about 10 to 20% of liver and IBD cancers.^{2,3}
- Angiosarcoma and hemangiosarcoma are rare forms of liver cancer that begin in cells that line the blood vessels in the liver.
- Fibrolamellar carcinoma (FLC) is rare and develops most often in women younger than age 35 (although it can also occur in older people).
- Hepatoblastoma is very rare and develops in children, usually under the age of four.²

Known risk factors

Hereditary conditions

Certain inherited metabolic diseases:

Certain inherited metabolic diseases can lead to cirrhosis (a disease in which liver cells become damaged and are replaced by scar tissue), which increases the risk of liver and IBD cancer.^{2,3,6} For example, people with untreated hereditary hemochromatosis absorb too much iron from their food, which can lead to cirrhosis.^{2,3,6} Others include tyrosinemia, acute intermittent porphyria, and glycogen storage diseases.^{2,6}

Other inherited gene mutations and conditions:

Other rare inherited diseases that increase the risk of liver and IBD cancer include α 1-antitrypsin deficiency, porphyria cutanea tarda, and Wilson disease.^{2,3,6} Lynch syndrome, BAP1 tumor predisposition syndrome, cystic fibrosis, and multiple biliary papillomatosis are inherited genetic disorders associated with an increased risk of bile duct cancer.³

Medical conditions

Cirrhosis:

Cirrhosis is a major risk factor for the development of liver and IBD cancers. It is a disease where liver cells become damaged and replaced by scar tissue.^{2,3,6} Most cirrhosis in the United States occurs in people with heavy alcohol use or long-term infection with the hepatitis B virus (HBV) or hepatitis C virus (HCV). Additional causes include non-alcoholic fatty liver disease (also called metabolic dysfunction-associated steatohepatitis), which occurs when fat builds up in the liver and is a common condition among people with excess body weight.^{2,3,9} Certain inherited metabolic diseases can also cause cirrhosis (as previously discussed) as well as some types of autoimmune diseases, such as primary biliary cirrhosis (PBC).^{2,6}

Diabetes:

Type 2 diabetes is associated with an increased risk of liver and IBD cancers, usually in those with additional risk factors, such as heavy alcohol consumption, excess body weight, and/or chronic viral hepatitis.^{2,3,9} Type 1 diabetes is also linked to bile duct cancer. It is unclear if this is due to high blood sugar levels or other diabetes-associated issues, such as excess body weight or high cholesterol.³

Injection of thorium dioxide (Thorotrast) in the past:

Exposure to thorium dioxide (Thorotrast), a radioactive substance used as an x-ray contrast agent until the mid-1950s, raises the risk of angiosarcoma (and bile duct cancer and HCC to a lesser extent).^{2,3,9}

Conditions that cause inflammation in the bile ducts:

Certain conditions that cause inflammation in the bile ducts can increase the risk of bile duct cancer. For example:

- Bile duct stones, also called hepatolithiasis, are like gallstones but much smaller. Inflammation due to bile duct stones can increase the risk of bile duct cancer.³
- Some people are born with a rare condition called choledochal cyst disease, which causes bile-filled sacs along the bile ducts.^{3,6} If untreated, the bile in the sacs cause inflammation of the duct walls, which can set off changes to the cells and eventually become bile duct cancer.³
- People with inflammatory bowel diseases, such as ulcerative colitis and Crohn's disease, have an increased risk of bile duct cancer.^{3,6}
- Primary sclerosing cholangitis (PSC) is a condition of inflammation in the bile duct that leads to scar tissue formation.^{3,6,9} PSC is usually strongly associated with ulcerative

colitis, an inflammatory bowel disease.^{3,9} The cause of the inflammation is not usually known, but people with PSC are at increased risk of bile duct cancer.^{3,6,9}

Abnormal bile duct anatomy:

Some people are born with an abnormality where the bile duct and pancreas meet that allows digestive juices from the pancreas to flow back into the bile ducts and prevents bile from moving through the ducts. People with these abnormalities have a higher risk of bile duct cancer.^{3,9}

Infections

Chronic (long-term) infection with hepatitis B virus (HBV) or hepatitis C virus (HCV):

Worldwide, the most common risk factor for developing liver cancer is long-term infection with HBV or HCV, both of which can also lead to cirrhosis.^{2,9} HCV infection is the leading cause of liver cancer in North America, Europe, and Japan, whereas HBV infection is more commonly the cause in Asia and Africa.⁶ HBV and HCV can both be spread by sharing needles used to inject drugs. HBV can also be passed from one person to another through unprotected sexual intercourse and to a baby during childbirth. In the past, HCV was spread through blood transfusions or organ transplants but this is very rare now in the United States because all blood donations are screened.^{2,6} While only a very small percentage of adults with HBV become chronic carriers, infants and young children who are infected are much more likely – though routine vaccination against HBV during infancy is reducing the incidence.^{2,6} Most people with HCV infection are likely to become chronic carriers and, therefore, are at a higher risk for liver cancer.²

Liver fluke infection:

Infection of the bile duct with a parasite called a liver fluke from eating raw or undercooked fish can cause liver cancer.^{3,6} Liver fluke infection is rare in the U.S. but does occur in some Southeast Asian countries and can affect people who travel to Asia.^{3,6,9}

Environmental exposures

Aflatoxins:

Aflatoxins are made by a fungus that grows in warm, moist environments and can contaminate peanuts, wheat, soybeans, ground nuts, corn, and rice.² Long-term exposure to aflatoxins is a risk factor for liver cancer.^{2,6,9} The risk is increased when individuals exposed to aflatoxins are also infected with HBV or HCV.² Aflatoxins can occur anywhere in the world but are more common in tropical countries.^{2,6} Developed countries such as the U.S. and those in Europe regulate and test the levels of aflatoxins in foods.²

Vinyl chloride:

The chemical vinyl chloride is used in making some kinds of plastics, such as polyvinyl chloride (PVC) resin.^{2,9} Exposure to vinyl chloride raises the risk of angiosarcoma of the liver (and bile duct cancer and HCC to a lesser extent).^{2,9} Workplace exposure to vinyl chloride is now strictly regulated.²

Lifestyle factors**Drinking alcohol:**

Long-term alcohol use is linked to a higher risk of liver and IBD cancers.^{2,3,6} In the United States, heavy alcohol use is a leading cause of cirrhosis, which increases the risk of liver and IBD cancer (as previously discussed).^{2,3,6} Although liver cancer can occur in heavy alcohol users who do not have cirrhosis, those with cirrhosis are ten times more likely to develop it.⁶ While it is best not to drink alcohol, the American Cancer Society recommends that if people do drink alcohol that men should have no more than 2 drinks a day and women should have no more than 1 drink a day.⁵

Tobacco use:

Smoking tobacco increases the risk of liver cancer.^{2,6} Former smokers have a lower risk than current smokers, but both have a higher risk than those who never smoked.^{2,9} For information about quitting tobacco use, contact the [DPH Tobacco Cessation and Prevention Program](#) at 1-800-QUIT-NOW or 1-800-784-8669.

Excess body weight:

Having excess body weight increases the risk of liver and IBD cancers. This is likely because obesity can contribute to non-alcoholic fatty liver disease and cirrhosis, as well as an increased risk of bile duct stones.^{2,3,9}

Possible risk factors

Medical conditions

Long-term infection with hepatitis B virus (HBV) or hepatitis C virus (HCV):

HBV and HCV infection also appear to increase the risk for bile duct cancer.^{3,9}

Long-term use of anabolic steroids:

Anabolic steroids are male hormones sometimes used to increase strength and muscle mass by athletes and medically for certain types of anemia and osteoporosis. Long-term use of anabolic steroids can slightly increase the risk of HCC, though evidence is limited.^{2,9}

Infections

Schistosomiasis:

Although rare in the United States, schistosomiasis is a disease caused by infection with a specific parasite (trematode blood flukes of the genus *Schistoma*) found in tropical areas of Africa, South America, Asia, and the Caribbean. Infection may increase the risk of HCC, though recent studies identified infection with this parasite as a co-factor with HBV and HCV infection (and not necessarily a primary cause of HCC).⁹

Environmental exposures

Arsenic in drinking water:

Arsenic occurs naturally in soil and bedrock. Exposure to arsenic in drinking water has been found to increase the risk of angiosarcoma in some studies.^{2,4,9} The chance of arsenic exposure from drinking water depends on where you live and the source of your drinking water. Groundwater is more likely to have high levels of arsenic than surface water (such as lakes or reservoirs). Drinking water is not a major source of arsenic exposure for most people living in the United States.⁴ In Massachusetts, it naturally occurs in some groundwater, usually in bedrock aquifers in the central part of the state and in the Merrimack River Valley. For more information on arsenic in private well water and how to test your well water, visit this [FAQ](#).

Workplace exposures:

Some evidence suggests that exposure to polychlorinated biphenyls (PCBs) may increase the risk of liver cancer.¹⁰ Some research also suggests that workplace exposure to dioxin, nitrosamines, or PCBs may increase the risk of bile duct cancer. People who work in rubber plants and automotive industries may be exposed more often to these chemicals.³

Lifestyle factors

Tobacco use:

While smoking tobacco does increase the risk of liver cancer (as previously discussed), the risk is not as clear for IBD cancer. Smoking is a possible risk factor for bile duct cancer.^{3,6}

Other risk factors that have been investigated

Infections

Other hepatitis viruses:

Although the hepatitis A virus and the hepatitis E virus can cause hepatitis (liver inflammation), people infected with these viruses do not develop chronic hepatitis or cirrhosis and do not have an increased risk of liver cancer.²

Human immunodeficiency virus (HIV):

Several studies have examined whether infection with HIV (the virus that causes AIDS) increases the risk of liver cancer. Although liver cancer tends to occur more frequently in people with HIV, this could be due to other risk factors. Overall, the relationship between HIV and HCC is still unclear.⁹

Lifestyle factors

Birth control pills:

Oral contraceptives (birth control pills) have been linked to benign liver tumors called hepatic adenomas. However, it is unclear if they increase the risk of HCC.⁹

Cortisone-like steroids:

Long-term use of cortisone-like steroids (such as hydrocortisone, prednisone, and dexamethasone) does not increase the risk of liver cancer.²

References / more information

This information sheet should not be considered exhaustive. For more information on other possible risk factors and health effects being researched, please see the resources below. Much of the information contained in this summary has been taken directly from these sources. This material is provided for informational purposes only and should not be considered as medical advice. Consult your physician if you have questions regarding a specific medical problem or condition.

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