Family Cancer Syndromes

When a gene change that greatly increases cancer risk runs in a family, it is often referred to as a family cancer syndrome. Other terms that you might hear include inherited cancer syndrome or genetic cancer syndrome.

- Is cancer inherited?
- How do you recognize an inherited or family cancer syndrome?
- Examples of family cancer syndromes
- Genetic counseling and testing

Is cancer inherited?

It’s important to understand that not every cancer that seems to run in a family is caused by a family cancer syndrome. About 1 in 3 people in the United States will develop cancer during their lifetime, so it’s not uncommon to have many cancers in a family. Sometimes, cancer might be more common in certain families because family members share certain behaviors or exposures that increase cancer risk, such as smoking, or because of other factors that can run in some families, like obesity.

But cancer can sometimes be caused by an abnormal gene that is passed from generation to generation. Although these cancers are often referred to as inherited cancers, what is actually inherited is the abnormal gene that can lead to cancer, not the cancer itself. Only about 5% to 10% of all cancers are known to be strongly linked to gene defects (called mutations) inherited from a parent.

To learn about the role of genes and how mutations can lead to cancer, see Genes and Cancer¹.

How do you recognize an inherited or family cancer syndrome?
Certain things make it more likely that cancers in a family are caused by a family cancer syndrome, such as:

- Many cases of the same type of cancer (especially if it is an uncommon or rare type of cancer)
- Cancers occurring at younger ages than usual (like colon cancer in a 20-year-old)
- More than one type of cancer in a single person (like a woman with both breast and ovarian cancer)
- Cancers occurring in both of a pair of organs (like both eyes, both kidneys, or both breasts)
- More than one childhood cancer in siblings (like sarcoma in both a brother and a sister)
- Cancer occurring in the sex not usually affected (like breast cancer in a man)
- Cancer occurring in many generations (like in a grandfather, father, and son)

When trying to determine if cancer might run in your family, first collect some information. For each case of cancer, look at:

- Who has the cancer? How are you related? Which side of the family are they on (mother’s or father’s)?
- What type of cancer is it? Is it rare?
- How old was this relative when they were diagnosed?
- Did this person get more than one type of cancer?
- Did they have any known risk factors for their type of cancer (such as smoking for lung cancer)?
- Has anyone in the family with or without cancer had genetic testing, and did that testing show any abnormal genes?

Cancer in a close relative, like a parent or sibling (brother or sister), is more likely to be a cause for concern for you than cancer in a more distant relative. Even if the cancer in a distant relative was from a gene mutation, the chance of the abnormal gene being passed on to you is less likely than with a closer relative.

It’s also important to look at each side of the family separately. **Having 2 relatives with cancer is more concerning if they are on the same side of the family.** For example, it’s more concerning if both relatives are your mother’s brothers (because they share some of the same genes) than if one was your father’s brother and the other was your mother’s brother.
The type of cancer matters, too. **It is more concerning if many relatives have the same type of cancer than if they have several different kinds of cancer.** Still, in some family cancer syndromes, there’s an increased risk of different types of cancer. For example, the risk of breast cancer and ovarian cancer is increased (as well as some other cancers) in families with inherited breast and ovarian cancer syndrome. Colon and endometrial cancer risk are increased in Lynch syndrome (also known as hereditary non-polyposis colorectal cancer, or HNPCC).

Likewise, **more than one case of the same rare cancer is more worrisome than cases of a more common cancer.** For some rare cancers, the risk of a family cancer syndrome is relatively high with even one case.

**The age of the person when the cancer was diagnosed is also important.** For example, colon cancer is rare in people younger than 30. Having close relatives under 30 with colon cancer could be a sign of a family cancer syndrome. On the other hand, prostate cancer is very common in elderly men, so if both your father and his brother were found to have prostate cancer when they were in their 80s, it is less likely to be due to an inherited cancer syndrome.

**Certain kinds of benign (not cancer) tumors and medical conditions are sometimes also part of a family cancer syndrome.** For example, people with the multiple endocrine neoplasia, type II syndrome (MEN II) have a high risk of a certain type of thyroid cancer. They also may develop benign tumors of the parathyroid glands and can also get tumors in the adrenal glands called pheochromocytomas, which are usually benign.

**When many relatives have the same type of cancer, it’s important to note if the cancer could be related to a risk factor like smoking.** For example, lung cancer is commonly caused by smoking, so having several cases of lung cancer in a family of people who all smoke is more likely to be due to smoking than to an inherited or family cancer syndrome.

**Examples of family cancer syndromes**

There are many family cancer syndromes. Some of these are discussed briefly here as examples, but this is not a full list. See our [information on specific cancer types](#) to learn more about their possible causes.

**Hereditary Breast and Ovarian Cancer (HBOC) syndrome**

Families with hereditary breast and ovarian cancer syndrome (HBOC) have family
members who have developed breast cancer and/or ovarian cancer. Often these cancers are found in women who are younger than the usual age these cancers are found, and some women might have more than one cancer (such as breast cancer in both breasts, or both breast and ovarian cancer).

Most often, HBOC is caused by an inherited mutation in either the BRCA1 or BRCA2 gene. Some families have HBOC based on cancer history, but don’t have mutations in either of these genes. Scientists believe that there might also be other genes that can cause HBOC that are not yet known.

The risk of breast and ovarian cancer is very high in women with mutations in either BRCA1 or BRCA2. This syndrome can also lead to fallopian tube cancer, primary peritoneal cancer, male breast cancer\(^4\), pancreatic cancer\(^5\), and prostate cancer\(^6\), as well as some others. Some people might have more than one cancer. For example, a woman might have breast cancer in both breasts, or both breast and ovarian cancer, or a man might have both pancreatic and prostate cancer. Male breast cancer, pancreatic cancer, and prostate cancer can be seen with mutations in either gene, but are more common in people with BRCA2 mutations. In the US, mutations in the BRCA genes are more common in people of Ashkenazi Jewish descent than in the general population.

Women with a strong family history of breast cancer and/or ovarian cancer may choose to get genetic counseling to help estimate their risk for having a mutation in one of the BRCA genes. The genetics professional can estimate the risk based on a person’s history of cancer, the history of cancer in their family, and other factors. If they have a high risk, they might choose to be tested for BRCA mutations (see Understanding Genetic Testing for Cancer\(^7\)). If a BRCA mutation is present, the woman has a high risk of developing breast cancer and ovarian cancer (as well as some other cancers). She can then consider taking steps to find cancer early with screening tests and to lower her risk of getting cancer.

Because breast cancer is rare in men, men with this cancer are often offered genetic counseling and testing for BRCA mutations. Having a BRCA mutation can also affect a man’s risk of some other cancers, such as prostate and pancreatic cancer. It can also be helpful for a man’s close relatives to know that he has a mutation and that they might be at risk.

If someone has a BRCA mutation, it means that their close relatives (parents, siblings, and children) have a 50% chance of having the mutation, too. These relatives may wish to be tested for the mutation, or even without testing may want to start screening for certain cancers early or take other precautions to lower their risk of cancer.

HBOC is not the only family cancer syndrome that can cause breast or ovarian cancer.
For information about other genes and syndromes that raise the risk of these cancers, see Breast Cancer⁸ and Ovarian Cancer⁹.

**Lynch syndrome (hereditary non-polyposis colorectal cancer)**

The most common inherited cancer syndrome that increases a person’s risk for colon cancer is Lynch syndrome, also called hereditary non-polyposis colorectal cancer (HNPCC). People with this syndrome are at high risk of developing colorectal cancer. These cancers are more likely to develop at earlier ages, often before the age of 50.

Lynch syndrome also leads to a high risk of endometrial cancer¹⁰ (cancer in the lining of the uterus), as well as cancers of the ovary¹¹, stomach¹², small intestine¹³, pancreas¹⁴, kidney¹⁵, brain¹⁶, skin¹⁷, breast¹⁸, prostate¹⁹, ureters²⁰ (tubes that carry urine from the kidneys to the bladder), and bile duct²¹.

Lynch syndrome is caused by a mutation in any of several mismatch repair (MMR) genes, including MLH1, MSH2, MSH6, PMS2, and EPCAM. These genes are normally involved in repairing damaged DNA. When one of these genes isn’t working, cells can develop mistakes in their DNA, which might lead to other gene mutations and eventually cancer.

Doctors and genetics professionals can check if you are likely to have Lynch syndrome, based on your personal and family cancer history using certain criteria known as the Amsterdam criteria and the revised Bethesda guidelines. These are discussed in detail in Genetic Testing, Screening, and Prevention for People with a Strong Family History of Colorectal Cancer.²² Mutations in the genes that cause Lynch syndrome can then be tested for with genetic testing.

For people who have colorectal, endometrial, or other cancers that are linked with Lynch syndrome, the cancer cells can be tested for microsatellite instability (MSI). Having MSI means that one of the MMR genes probably isn’t working properly. Having normal findings (no MSI or MMR gene changes) suggests that a person probably does not have Lynch syndrome. But if the MSI tests shows that some of the MMR genes are not working, the person may have Lynch syndrome, and should be referred for genetic counseling and possible testing. For more information about genetic testing, see What Should I Know Before Getting Genetic Testing?.

Someone who is known to carry a gene mutation linked to Lynch syndrome may be advised to start screening for colorectal cancer when they are younger (such as during their early 20s), or take other steps to try to lower their risk of colorectal cancer (discussed in more detail in Colorectal Cancer²³). Women with Lynch syndrome may be advised to start screening for endometrial cancer or take other steps to try to lower their
risk of this cancer. These are discussed in more detail in Endometrial Cancer\textsuperscript{24}.

If someone has Lynch syndrome, it means that their close relatives (parents, siblings, and children) have a 50\% chance of having the mutation that causes it, too. They may wish to be tested, or even without testing they may want to start screening early for certain cancers or take other precautions to help lower their risk of cancer.

\textbf{Li-Fraumeni syndrome}

Li-Fraumeni syndrome (also called the sarcoma, breast, leukemia, and adrenal gland \textit{[SBLA] cancer syndrome}) is a rare inherited syndrome that can lead to an increased risk of a number of cancers, including sarcoma (such as osteosarcoma\textsuperscript{25} and soft-tissue sarcomas\textsuperscript{26}), leukemia\textsuperscript{27}, brain (central nervous system) cancers\textsuperscript{28}, cancer of the adrenal cortex,\textsuperscript{29} and breast cancer\textsuperscript{30}. These cancers often develop in relatively young adults or even children.

People with Li-Fraumeni syndrome can develop more than one cancer in their lifetime. They also seem to have a higher risk of getting cancer from radiation exposure, so doctors treating these patients might try to avoid giving them radiation therapy when possible.

This syndrome is most often caused by inherited mutations in the $TP53$ gene, which is a tumor suppressor gene. A normal $TP53$ gene makes a protein that helps stop abnormal cells from growing.

If someone has Li-Fraumeni syndrome, their close relatives (especially their children) have an increased chance of having the mutation, too. Close relatives may wish to be tested, or even without testing they may want to start screening for certain cancers early or take other precautions to help lower their risk of cancer.

\textbf{Other family cancer syndromes}

You can learn more about the family cancer syndromes listed above, along with other inherited syndromes and gene mutations that might affect a person's risk for cancer, by reading:

- \textit{Genetic Counseling and Testing for Breast Cancer Risk}\textsuperscript{31}: Hereditary Breast and Ovarian Cancer Syndrome (HBOC), $BRCA1$ and $BRCA2$ mutations, and other specific gene mutations
- \textit{Genetic Testing, Screening, and Prevention for People with a Strong Family History of Colorectal Cancer}\textsuperscript{32}: Lynch syndrome, familial adenomatous polyposis (FAP),
and other specific gene mutations

**Genetic Counseling and Testing for People at High Risk of Melanoma**\(^{33}\): Specific gene mutations

**Ovarian Cancer Risk Factors**\(^{34}\): Hereditary Breast and Ovarian Cancer Syndrome (HBOC), Lynch syndrome, Peutz-Jeghers syndrome, MUTYH-associated polyposis, \textit{BRCA1} and \textit{BRCA2} mutations, and other specific gene mutations

**Risk Factors for Retinoblastoma**\(^{35}\): Hereditary Retinoblastoma

**Risk Factors for Kidney Cancer**\(^{36}\): von Hippel-Lindau disease, Cowden syndrome, Birt-Hogg-Dube (BHD) syndrome

**Risk Factors for Soft Tissue Sarcomas**\(^{37}\): Neurofibromatosis, Tuberous sclerosis, Gorlin syndrome

### Genetic counseling and testing

People with a strong family history of cancer may want to learn more about their genes. This may help the person or other family members plan their health care for the future. Since inherited mutations affect all cells of a person’s body, they can often be found by genetic testing done on blood or saliva (spit) samples. Still, genetic testing is not helpful for everyone, so it’s important to speak with a genetic counselor first to find out if testing might be right for you. For more information, see **Understanding Genetic Testing for Cancer**\(^{38}\).

### Hyperlinks

37. www.cancer.org/cancer/types/soft-tissue-sarcoma/causes-risks-prevention/risk-
Additional resources

Along with the American Cancer Society, other sources of information and support include:

National Society of Genetic Counselors (NSGC) Telephone: 1-312-321-6834
Website: www.nsgc.org

*Inclusion on this list does not imply endorsement by the American Cancer Society.

References


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Written by
The American Cancer Society medical and editorial content team

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