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Kidney Cancer Causes, Risk Factors, and Prevention

Learn about the risk factors for kidney 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 kidney cancer.

- Risk Factors for Kidney Cancer
- What Causes Kidney Cancer?

Prevention

At this time there is no way to prevent kidney cancer. But there are things you can do that might lower your risk for it. Learn more.

Can Kidney Cancer Be Prevented?

Risk Factors for Kidney Cancer

A risk factor is anything that increases your chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be

changed. Others, like your age or family history, can't be changed.

Having a risk factor, or even several risk factors, does not mean that you will get the disease. And some people who get the disease may have few or no known risk factors.

Several risk factors could make you more likely to develop kidney cancer. But, even if a person with kidney cancer has a risk factor, it is often very hard to know how much that risk factor contributed to the cancer.

- Smoking
- Excess body weight
- High blood pressure
- Family history of kidney cancer
- Workplace exposure to certain chemicals
- Being male
- Race and ethnicity
- Certain pain medicines
- Advanced kidney disease
- Genetic and hereditary risk factors

Smoking

<u>Smoking</u>¹ increases the risk of renal cell carcinoma (RCC), the most common type of kidney cancer. The increased risk seems to be related to how much you smoke. The risk drops slowly over time if you stop smoking.

Excess body weight

People who have excess body weight have a higher risk for RCC. Having excess body weight may cause changes in certain hormones that can lead to RCC.

High blood pressure

The risk of kidney cancer is higher in people with high blood pressure. This risk does not seem to be lowered even if someone is taking medicines to treat the high blood pressure.

Family history of kidney cancer

People with a strong family history of RCC (even without one of the known inherited conditions listed below) have a higher chance of developing cancer. This risk is highest for people who have a brother or sister with kidney cancer. This might be due to shared genes, something that both family members were exposed to in a shared environment, or both.

Workplace exposure to certain chemicals

Many studies have suggested that being exposed to certain substances at work, such as trichloroethylene or cadmium, increase the risk for RCC.

Being male

RCC is about twice as common in men as in women. This might be because men are more likely to smoke and historically have been more likely to be exposed to cancercausing chemicals at work.

Race and ethnicity

In the US, kidney cancer rates are highest among American Indian and Alaska Native people. They are slightly higher among African American people than among White people. The reasons for this are not clear.

Certain pain medicines

Some studies have suggested that long-term use of pain medicines such as acetaminophen (and possibly aspirin) may be linked to an increased risk of RCC.

Advanced kidney disease

People with advanced kidney disease, especially those needing dialysis, have a higher risk of RCC. (Dialysis is a treatment used to remove toxins from your body if your kidneys aren't working properly.)

Genetic and hereditary risk factors

Some people inherit gene changes from their parents that can increase their risk of RCC. Sometimes this might be the only effect of a gene change. But sometimes it might

lead to an inherited syndrome that increases a person's risk of other health issues (including other cancers), as well.

It's important that people who have hereditary conditions linked to RCC see their doctors often, especially if they have already been diagnosed with RCC. Some doctors might recommend regular imaging tests (such as CT scans) to look for new kidney tumors in these people.

Most of the conditions listed here result in a much higher risk for getting kidney cancer, although they account for only a small portion of kidney cancers overall.

To learn more about how some of the gene changes that cause these conditions might lead to kidney cancer, see What Causes Kidney Cancer?

von Hippel-Lindau disease

People with von Hippel-Lindau disease often develop several kinds of tumors and cysts (fluid-filled sacs) in different parts of the body. They have an increased risk for developing clear cell RCC, especially at a younger age. They may also have benign tumors in their eyes, brain, spinal cord, pancreas, and other organs; and a type of adrenal gland tumor called **pheochromocytoma**.

This condition is caused by mutations (changes) in the VHL gene.

Hereditary papillary renal carcinoma

People with hereditary papillary renal carcinoma tend to develop one or more papillary RCCs, but they do not have tumors in other parts of the body, as is the case with the other inherited conditions listed here. This disorder is usually linked to changes in the *MET* gene.

Hereditary leiomyomatosis and renal cell cancer

People with this syndrome often develop smooth muscle tumors called **leiomyomas** (fibroids) of the skin and uterus (in women) and have a higher risk for developing papillary RCCs.

This condition has been linked to changes in the *FH* gene.

Birt-Hogg-Dubé (BHD) syndrome

People with this syndrome tend to develop many small benign skin tumors and have an increased risk of different kinds of kidney tumors, including RCCs and oncocytomas. They may also have benign or malignant tumors of several other tissues.

This condition has been linked to changes in the *FLCN* gene.

Hereditary paraganglioma-pheochromocytoma syndromes

People with these syndromes often develop neuroendocrine tumors called **paragangliomas** including tumors in the adrenal gland called **pheochromocytomas**. They also have an increased risk of RCC.

These conditions are caused by defects in genes such as SDHA, *SDHB*, and *SDHC*, and *SDHD*.

Cowden syndrome

People with Cowden syndrome have a high risk of <u>breast</u>², <u>thyroid</u>, and kidney cancers.

This condition is linked to changes in the *PTEN* gene.

Tuberous sclerosis

People with tuberous sclerosis develop many, usually benign (non-cancerous) tumors in different parts of the body including the skin, brain, lungs, eyes, kidneys, and heart. Although the kidney tumors are most often benign, occasionally they can be clear cell RCC.

This condition is linked to defects in the genes *TSC1* and *TSC2*.

BAP1 tumor predisposition syndrome

People with this condition have an increased risk for some types of skin cancers, as well as melanomas of the eye, mesotheliomas, clear cell RCC, and possibly other cancers. This condition is caused by changes in the *BAP1* gene.

Sickle cell trait and disease

Some people inherit a change in a gene that codes for hemoglobin, the protein in red blood cells that helps them carry oxygen. People who inherit this gene change from one parent have sickle cell trait (SCT), but usually don't have obvious symptoms from it.

People who inherit gene changes from both parents have sickle cell disease (SCD).

People with either SCT or SCD have an increased risk of renal medullary carcinoma (RMC). This rare subtype of RCC most often occurs in younger people, tends to grow quickly, and can be hard to treat.

The increased risk of RMC is thought to be caused by changes in the SMARCB1 gene.

Hyperlinks

- 1. www.cancer.org/cancer/risk-prevention/tobacco.html
- 2. www.cancer.org/cancer/types/breast-cancer.html
- 3. www.cancer.org/cancer/types/thyroid-cancer.html

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Rock CL, Thomson C, Gansler T, et al. American Cancer Society guideline for diet and physical activity for cancer prevention. *CA Cancer J Clin.* 2020 Jul;70(4):245-271.

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What Causes Kidney Cancer?

Cancer is caused by changes in the DNA inside our cells. DNA carries our **genetic information (genes)**, which controls how our cells function. Our DNA, which comes from both our parents, affects more than just how we look.

- Changes (mutations) in genes
- Inherited gene mutations
- Acquired gene mutations

Changes (mutations) in genes

Some genes normally help control when our cells grow, divide to make new cells, or repair mistakes in DNA, or they cause cells to die when they're supposed to. If these genes aren't working properly, it can lead to cells growing out of control. For example:

• Changes in genes that normally help cells grow, divide, or stay alive can lead to

these genes being more active than they should be, causing them to become **oncogenes**. These genes can result in cells growing out of control.

- Genes that normally help keep cell division under control or cause cells to die at the right time are known as tumor suppressor genes. Changes that turn off these genes can result in cells growing out of control.
- Some genes normally help repair mistakes in a cell's DNA. Changes that turn off these DNA repair genes can result in the buildup of DNA changes within a cell, which might lead to them growing out of control.

Any of these types of DNA changes might lead to cells growing out of control and forming a tumor. To learn more, see <u>Oncogenes, Tumor Suppressor Genes, and DNA Repair Genes</u>¹.

Changes in several genes are usually needed to cause kidney cancer. These changes can either be **inherited** from a parent, or they can be **acquired** during a person's lifetime.

Inherited gene mutations

Certain inherited gene changes can run in some families and increase the risk of kidney cancer. The **inherited syndromes** these changes cause lead to a small portion of all kidney cancers, and are described in Risk Factors for Kidney Cancer.

For example, the *VHL* gene is a **tumor suppressor gene**. It normally helps keep cells from growing out of control. Mutations (changes) in this gene can be inherited from parents, leading to von Hippel-Lindau (VHL) disease. When the *VHL* gene is mutated, it is no longer able to control the abnormal growth, and kidney cancer is more likely to develop.

Inherited changes in the following tumor suppressor genes also lead to an increased risk of kidney cancer:

- The *FH* genes (linked to hereditary leiomyomas which can cause fibroids in the skin and uterus)
- The FLCN gene (as seen in Birt-Hogg-Dube syndrome)
- The SDHA, SDHB, SDHC, and SDHD genes (as seen in the paragangliomapheochromocytoma syndromes)

People with hereditary papillary renal carcinoma have inherited changes in

the *MET* **oncogene** that cause it to be turned on all the time. This can lead to uncontrolled cell growth and make a person more likely to develop papillary RCC.

Special **genetic tests** can detect some of the gene mutations linked with these inherited syndromes. If you have a family history of kidney cancer or other cancers linked to these syndromes, you may want to ask your doctor about genetic counseling and genetic testing.

Genetic testing can be complex. Before having it done, it's important to speak with a qualified cancer genetics professional. They can explain how testing might help you, how it is done, its limitations, and what the results might mean. For more on this, see Gene Changes and Cancer.²

Acquired gene mutations

Some gene mutations happen during a person's lifetime and are not passed on. They affect only cells that come from the original mutated cell. These changes are called **acquired** mutations. In most people with kidney cancer, the gene mutations that lead to cancer are acquired rather than having been inherited.

Certain risk factors, such as exposure to cancer-causing chemicals, might play a role in causing some of these acquired mutations. For example, when people smoke, the lungs absorb many of the cancer-causing chemicals in tobacco smoke into the bloodstream. Because the kidneys filter this blood, many of these chemicals become concentrated in the kidneys. Several of these chemicals are known to damage kidney cells in ways that can cause the cells to become cancer.

Excess body weight³, another risk factor for kidney cancer, alters the balance of some of the body's hormones. Researchers are now learning how certain hormones help control the growth (both normal and abnormal) of many different tissues in the body, including the kidneys.

However, many of the acquired gene changes that can lead to kidney cancer can be just random events that sometimes happen inside a cell, without having an outside cause.

Most people with non-inherited clear cell RCC have changes in the *VHL* tumor suppressor gene in their cancer cells that have caused the gene to stop working properly. These gene changes are acquired during a person's life.

Other gene changes may also cause renal cell carcinomas. Researchers continue to

look for these changes. For more about how genes changes can lead to cancer, see Gene Changes and Cancer ⁴.

Hyperlinks

- 1. <u>www.cancer.org/cancer/understanding-cancer/genes-and-cancer/oncogenes-tumor-suppressor-genes.html</u>
- 2. <u>www.cancer.org/cancer/understanding-cancer/genes-and-cancer/gene-changes.html</u>
- 3. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-cancer-risk.html</u>
- 4. <u>www.cancer.org/cancer/understanding-cancer/genes-and-cancer/gene-changes.html</u>

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Can Kidney Cancer Be Prevented?

There is no sure way to prevent kidney cancer. Some kidney cancer risk factors such as your race/ethnicity and family history can't be controlled. But there are some things you can do that might lower your risk of kidney cancer.

<u>Cigarette smoking</u>¹ is responsible for a large percentage of kidney cancers, so if you smoke, stopping may help lower your risk.

Excess body weight² is also a risk factor for renal cell cancer. Doing your best to stay at a healthy weight by being active and eating a healthy diet may help lower your chances of getting kidney cancer.

Avoiding exposure to harmful substances such as trichloroethylene at work may also reduce your risk for renal cell cancer.

Hyperlinks

- 1. www.cancer.org/cancer/risk-prevention/tobacco.html
- 2. <u>www.cancer.org/cancer/risk-prevention/diet-physical-activity/body-weight-and-cancer-risk.html</u>

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