Lung Cancer (Non-Small Cell)

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues is what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called *metastasis*. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named (and treated) based on the place where it started. For example, breast cancer that has spread to the liver is still breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is still prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is non-small cell lung cancer?

Note: *This document is specifically for the non-small cell type of lung cancer. The treatment for the 2 main types of lung cancer (small cell and non-small cell) is very different, so much of the information for one type will not apply to the other type. If you are not sure which type of lung cancer you have, ask your doctor so you can be sure the information you receive is correct.*

Lung cancer is a cancer that starts in the lungs. To understand lung cancer, it helps to know about the normal structure and function of the lungs.

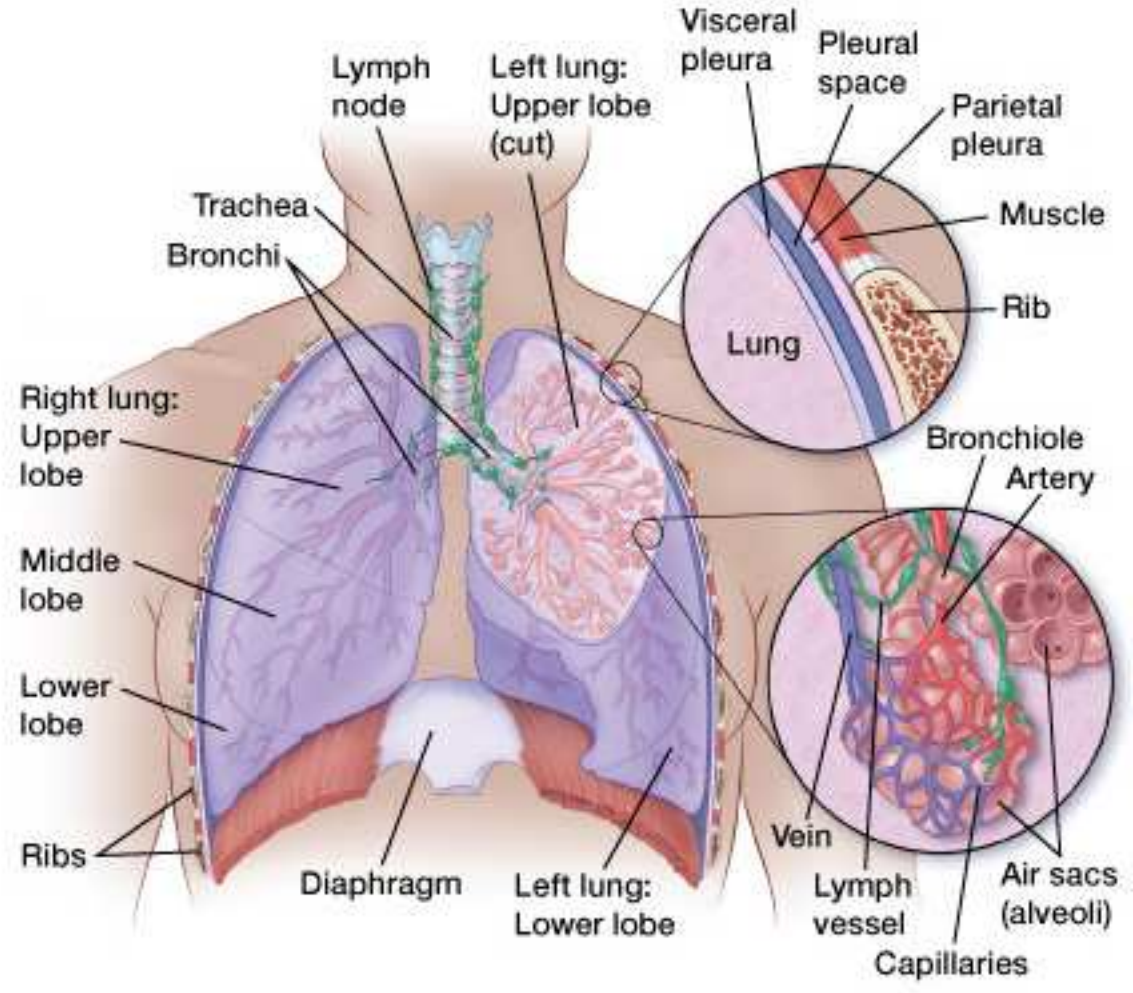
The lungs

Your lungs are 2 sponge-like organs found in your chest. Your right lung is divided into 3 sections, called *lobes*. Your left lung has 2 lobes. The left lung is smaller because the heart takes up more room on that side of the body.

When you breathe in, air enters through your mouth or nose and goes into your lungs through the *trachea* (windpipe). The trachea divides into tubes called the *bronchi* (singular, *bronchus*), which enter the lungs and divide into smaller bronchi. These divide to form smaller branches called *bronchioles*. At the end of the bronchioles are tiny air sacs known as *alveoli*.

Many tiny blood vessels run through the alveoli. They absorb oxygen from the inhaled air into your bloodstream and pass carbon dioxide from the body into the alveoli. This is

expelled from the body when you exhale. Taking in oxygen and getting rid of carbon dioxide are your lungs' main functions.



A thin lining layer called the *pleura* surrounds the lungs. The pleura protects your lungs and helps them slide back and forth against the chest wall as they expand and contract during breathing.

Below the lungs, a thin, dome-shaped muscle called the *diaphragm* separates the chest from the abdomen. When you breathe, the diaphragm moves up and down, forcing air in and out of the lungs.

Start and spread of lung cancer

Lung cancers can start in the cells lining the bronchi and parts of the lung such as the bronchioles or alveoli.

Lung cancers are thought to start as areas of pre-cancerous changes in the lung. The first changes in the genes (DNA) inside the lung cells may cause the cells to grow faster. These cells may look a bit abnormal if seen under a microscope, but at this point they do not form a mass or tumor. They cannot be seen on an x-ray and they do not cause symptoms.

Over time, the abnormal cells may acquire other gene changes, which cause them to progress to true cancer. As a cancer develops, the cancer cells may make chemicals that cause new blood vessels to form nearby. These blood vessels nourish the cancer cells, which can continue to grow and form a tumor large enough to be seen on imaging tests such as x-rays.

At some point, cells from the cancer may break away from the original tumor and spread (metastasize) to other parts of the body. Lung cancer is often a life-threatening disease because it tends to spread in this way even before it can be detected on an imaging test such as a chest x-ray.

The lymph (lymphatic) system

The lymph system is one of the ways in which lung cancers can spread. This system has several parts:

- *Lymph nodes* are small, bean-shaped collections of immune system cells (cells that fight infections) that are connected by lymphatic vessels.
- *Lymphatic vessels* are like small veins, except that they carry a clear fluid called lymph (instead of blood) away from the lungs.
- *Lymph* contains excess fluid and waste products from body tissues, as well as immune system cells.

Lung cancer cells can enter lymphatic vessels and begin to grow in lymph nodes around the bronchi and in the mediastinum (the area between the 2 lungs). Once lung cancer cells have reached the lymph nodes, they are more likely to have spread to other organs of the body as well. The stage (extent) of the cancer and decisions about treatment are based in part on whether or not the cancer has spread to the nearby lymph nodes in the mediastinum. These topics are discussed later in the section “How is non-small cell lung cancer staged?”

Types of lung cancer

There are 2 major types of lung cancer:

- Small cell lung cancer (SCLC)
- Non-small cell lung cancer (NSCLC)

(If a lung cancer has some cells with characteristics of SCLC and other cells with characteristics of NSCLC it is called a *combined small cell/non-small cell cancer*. This is uncommon.)

These 2 types of lung cancer are treated very differently. **This document focuses on non-small cell lung cancer.** Small cell lung cancer is discussed in a separate document, *Lung Cancer (Small Cell)*.

Non-small cell lung cancer

About 85% to 90% of lung cancers are non-small cell lung cancer (NSCLC). There are 3 main subtypes of NSCLC. The cells in these subtypes differ in size, shape, and chemical make-up when looked at under a microscope. But they are grouped together because the approach to treatment and prognosis (outlook) are often very similar.

Squamous cell (epidermoid) carcinoma: About 25% to 30% of all lung cancers are squamous cell carcinomas. These cancers start in early versions of squamous cells, which are flat cells that line the inside of the airways in the lungs. They are often linked to a history of smoking and tend to be found in the middle of the lungs, near a bronchus.

Adenocarcinoma: About 40% of lung cancers are adenocarcinomas. These cancers start in early versions of the cells that would normally secrete substances such as mucus. This type of lung cancer occurs mainly in current or former smokers, but it is also the most common type of lung cancer seen in non-smokers. It is more common in women than in men, and it is more likely to occur in younger people than other types of lung cancer.

Adenocarcinoma is usually found in outer parts of the lung. It tends to grow slower than other types of lung cancer, and is more likely to be found before it has spread outside of the lung.

People with a type of adenocarcinoma called *adenocarcinoma in situ* (previously called *bronchioloalveolar carcinoma*) tend to have a better outlook (prognosis) than those with other types of lung cancer.

Large cell (undifferentiated) carcinoma: This type of cancer accounts for about 10% to 15% of lung cancers. It can appear in any part of the lung. It tends to grow and spread quickly, which can make it harder to treat. A subtype of large cell carcinoma, known as *large cell neuroendocrine carcinoma*, is a fast-growing cancer that is very similar to small cell lung cancer (see below).

Other subtypes: There are also a few other subtypes of non-small cell lung cancer, such as adenosquamous carcinoma and sarcomatoid carcinoma. These are much less common.

Small cell lung cancer

About 10% to 15% of all lung cancers are small cell lung cancer (SCLC), named for the size of the cancer cells when seen under a microscope. Other names for SCLC are *oat cell cancer*, *oat cell carcinoma,* and *small cell undifferentiated carcinoma*. It is very rare for someone who has never smoked to have small cell lung cancer.

SCLC often starts in the bronchi near the center of the chest, and it tends to spread widely through the body fairly early in the course of the disease. This cancer is discussed in the document called *Lung Cancer (Small Cell).*

Other types of lung cancer

Along with the 2 main types of lung cancer, other tumors can occur in the lungs.

Lung carcinoid tumors: Carcinoid tumors of the lung account for fewer than 5% of lung tumors. Most are slow-growing tumors that are called *typical carcinoid tumors*. They are generally cured by surgery. Some typical carcinoid tumors can spread, but they usually have a better prognosis than small cell or non-small cell lung cancer. Less common are *atypical carcinoid tumors*. The outlook for these tumors is somewhere in between typical carcinoids and small cell lung cancer. For more information about typical and atypical carcinoid tumors, see the separate document *Lung Carcinoid Tumor*.

Other lung tumors: Other types of lung cancer such as adenoid cystic carcinomas, lymphomas, and sarcomas, as well as benign lung tumors such as hamartomas are rare. These are treated differently from the more common lung cancers and are not discussed in this document.

Cancers that spread to the lungs: Cancers that start in other organs (such as the breast, pancreas, kidney, or skin) can sometimes spread (metastasize) to the lungs, but these are not lung cancers. For example, cancer that starts in the breast and spreads to the lungs is still breast cancer, not lung cancer. Treatment for metastatic cancer to the lungs is based on where it started (the primary cancer site). For information on these primary cancers, see our separate documents on each.

What are the key statistics about lung cancer?

Most lung cancer statistics include both small cell and non-small cell lung cancers.

Lung cancer (both small cell and non-small cell) is the second most common cancer in both men and women (not counting skin cancer). In men, prostate cancer is more common, while in women breast cancer is more common. Lung cancer accounts for about 13% of all new cancers.

The American Cancer Society's estimates for lung cancer in the United States for 2015 are:

- About 221,200 new cases of lung cancer (115,610 in men and 105,590 in women)
- An estimated 158,040 deaths from lung cancer (86,380 in men and 71,660 among women).

Lung cancer accounts for about 27% of all cancer deaths and is by far the leading cause of cancer death among both men and women. Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined.

Lung cancer mainly occurs in older people. About 2 out of 3 people diagnosed with lung cancer are 65 or older; fewer than 2% of all cases are found in people younger than 45. The average age at the time of diagnosis is about 70.

Overall, the chance that a man will develop lung cancer in his lifetime is about 1 in 13; for a woman, the risk is about 1 in 16. These numbers include both smokers and non-smokers. For smokers the risk is much higher, while for non-smokers the risk is lower.

Black men are about 20% more likely to develop lung cancer than white men. The rate is about 10% lower in black women than in white women. Both black and white women have lower rates than men, but the gap is closing. The lung cancer rate has been dropping among men over the past 2 decades and has just recently begun to drop in women.

Statistics on survival in people with lung cancer vary depending on the stage (extent) of the cancer when it is diagnosed. Survival statistics based on the stage of the cancer are discussed in the section "Non-small cell lung cancer survival rates by stage."

Despite the very serious prognosis (outlook) of lung cancer, some people with earlier stage cancers are cured. More than 430,000 people alive today have been diagnosed with lung cancer at some point.

What are the risk factors for non-small cell lung cancer?

A risk factor is anything that affects a person's chance 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 risk factors don't tell us everything. 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 not have had any known risk factors. Even if a person with lung cancer has a risk factor, it is often very hard to know how much that risk factor may have contributed to the cancer.

Several risk factors can make you more likely to develop lung cancer.

Tobacco smoke

Smoking is by far the leading risk factor for lung cancer. In the early 20th century, lung cancer was much less common than some other types of cancer. But this changed once manufactured cigarettes became readily available and more people began smoking.

At least 80% of lung cancer deaths are thought to result from smoking. The risk for lung cancer among smokers is many times higher than among non-smokers. The longer you smoke and the more packs a day you smoke, the greater your risk.

Cigar smoking and pipe smoking are almost as likely to cause lung cancer as cigarette smoking. Smoking low-tar or "light" cigarettes increases lung cancer risk as much as regular cigarettes. There is concern that menthol cigarettes may increase the risk even more since the menthol allows smokers to inhale more deeply.

Secondhand smoke: If you don't smoke, breathing in the smoke of others (called secondhand smoke or environmental tobacco smoke) can increase your risk of developing lung cancer by almost 30%. Workers who have been exposed to tobacco smoke in the workplace are also more likely to get lung cancer. Secondhand smoke is thought to cause more than 7,000 deaths from lung cancer each year.

Some evidence suggests that certain people are more susceptible to the cancer-causing effect of tobacco smoke than others.

If you or someone you care about needs help in quitting, see our document called *Guide to Quitting Smoking* or call the American Cancer Society at 1-800-227-2345

Radon

Radon is a naturally occurring radioactive gas that results from the breakdown of uranium in soil and rocks. It cannot be seen, tasted, or smelled. According to the US Environmental Protection Agency (EPA), radon is the second leading cause of lung cancer in this country, and is the leading cause among non-smokers.

Outdoors, there is so little radon that it is not likely to be dangerous. But indoors, radon can be more concentrated. When it is breathed in, it enters the lungs, exposing them to small amounts of radiation. This may increase a person's risk of lung cancer.

The lung cancer risk from radon is much lower than that from tobacco smoke. However, the risk from radon is much higher in people who smoke than in those who don't.

Radon levels in the soil vary across the country, but they can be high almost anywhere. Homes in some parts of the United States built on soil with natural uranium deposits can have high indoor radon levels (especially in basements). Studies from these areas have

found that the risk of lung cancer is higher in those who have lived for many years in a radon-contaminated house.

If you are concerned about radon exposure, you can use a radon detection kit to test the levels in your home. State and local offices of the EPA can also give you the names of reliable companies that can test your home (or other buildings) for radon and help you fix the problem, if needed. For more information, see our document called *Radon.*

Asbestos

Workplace exposure to asbestos fibers is an important risk factor for lung cancer. Studies have found that people who work with asbestos (in some mines, mills, textile plants, places where insulation is used, shipyards, etc.) are several times more likely to die of lung cancer. In workers exposed to asbestos who also smoke, the lung cancer risk is much greater than even adding the risks from these exposures separately. It's not clear to what extent low-level or short-term exposure to asbestos might raise lung cancer risk.

Both smokers and non-smokers exposed to asbestos also have a greater risk of developing mesothelioma, a type of cancer that starts in the pleura (the lining surrounding the lungs). Because it is not usually considered a type of lung cancer, mesothelioma is discussed in our document called *Malignant Mesothelioma*.

In recent years, government regulations have greatly reduced the use of asbestos in commercial and industrial products. It is still present in many homes and other older buildings, but it is not usually considered harmful as long as it is not released into the air by deterioration, demolition, or renovation. For more information, see our document called *Asbestos*.

Other cancer-causing agents in the workplace

Other carcinogens (cancer-causing agents) found in some workplaces that can increase lung cancer risk include:

- Radioactive ores such as uranium
- Inhaled chemicals or minerals such as arsenic, beryllium, cadmium, silica, vinyl chloride, nickel compounds, chromium compounds, coal products, mustard gas, and chloromethyl ethers
- Diesel exhaust

The government and industry have taken steps in recent years to help protect workers from many of these exposures. But the dangers are still present, so if you work around these agents, you should be careful to limit your exposure whenever possible.

Air pollution

In cities, air pollution (especially near heavily trafficked roads) appears to raise the risk of lung cancer slightly. This risk is far less than the risk caused by smoking, but some researchers estimate that worldwide about 5% of all deaths from lung cancer may be due to outdoor air pollution.

Radiation therapy to the lungs

People who have had radiation therapy to the chest for other cancers are at higher risk for lung cancer, particularly if they smoke; for example, people who have been treated for Hodgkin disease or women who get radiation after a mastectomy for breast cancer. Women who receive radiation therapy to the breast after a lumpectomy do not appear to have a higher than expected risk of lung cancer.

Arsenic in drinking water

Studies of people in parts of Southeast Asia and South America with high levels of arsenic in their drinking water have found a higher risk of lung cancer. In most of these studies, the levels of arsenic in the water were many times higher than those typically seen in the United States, even in areas where arsenic levels are above normal. For most Americans who are on public water systems, drinking water is not a major source of arsenic.

Personal or family history of lung cancer

If you have had lung cancer, you have a higher risk of developing another lung cancer.

Brothers, sisters, and children of those who have had lung cancer may have a slightly higher risk of lung cancer themselves, especially if the relative was diagnosed at a younger age. It is not clear how much of this risk might be due to genetics and how much might be from shared household exposures (such as tobacco smoke or radon).

Researchers have found that genetics does seem to play a role in some families with a strong history of lung cancer. For example, people who inherit certain DNA changes in a particular chromosome (chromosome 6) are more likely to develop lung cancer, even if they don’t smoke or only smoke a little. At this time these DNA changes cannot be routinely tested for. Research is ongoing in this area.

Certain dietary supplements

Studies looking at the possible role of vitamin supplements in reducing lung cancer risk have not been promising so far. In fact, 2 large studies found that smokers who took beta

carotene supplements actually had an increased risk of lung cancer. The results of these studies suggest that smokers should avoid taking beta carotene supplements.

Factors with uncertain or unproven effects on lung cancer risk

Marijuana smoking

There are some reasons to think that marijuana smoking might increase lung cancer risk. Marijuana smoke contains tar and many of same cancer-causing substances that are in tobacco smoke. (Tar is the sticky, solid material that remains after burning, and is thought to contain most of the harmful substances in smoke.) Marijuana cigarettes (joints) are typically smoked all the way to the end, where tar content is the highest. Marijuana is also inhaled very deeply and the smoke is held in the lungs for a long time, which gives any cancer causing substances more opportunity to deposit in the lungs. And because marijuana is often an illegal substance, it may not be possible to control what other substances it might contain.

But those who use marijuana tend to smoke fewer marijuana cigarettes in a day or week than the amount of tobacco consumed by cigarette smokers. For example, a light smoker may smoke half of a pack (10 cigarettes) a day, but 10 marijuana cigarettes in a day would be very heavy use of marijuana. In one study, most people who smoked marijuana did so 2 to 3 times per month. The lesser amount smoked would make it harder to see an impact on lung cancer risk.

It has been hard to study whether there is a link between marijuana and lung cancer because marijuana was illegal in many countries for so long, and it is not easy to gather information about the use of illegal drugs. Also, in the studies that looked at past marijuana use in people who had lung cancer, most of the marijuana smokers also smoked cigarettes. This can make it hard to know how much of the risk is from tobacco and how much might be from marijuana. More research is needed to know the cancer risks from smoking marijuana.

Talc and talcum powder

Talc is a mineral that in its natural form may contain asbestos. Some studies have suggested that talc miners and millers might have a higher risk of lung cancer and other respiratory diseases because of their exposure to industrial grade talc. But other studies have not found an increase in lung cancer rate.

Talcum powder is made from talc. By law since 1973, all home-use talcum products (baby, body, and facial powders) in the United States have been asbestos-free. The use of cosmetic talcum powder has not been found to increase the risk of lung cancer.

Do we know what causes non-small cell lung cancer?

We don’t know what causes each case of lung cancer. But we do know many of the risk factors for these cancers (see “What are the risk factors for non-small cell lung cancer?”) and how some of them cause cells to become cancerous.

Smoking

Tobacco smoking is by far the leading cause of lung cancer. At least 80% of lung cancer deaths are caused by smoking, and many others are caused by exposure to secondhand smoke.

Smoking is clearly the strongest risk factor for lung cancer, but it often interacts with other factors. Smokers exposed to other known risk factors such as radon and asbestos are at even higher risk. Not everyone who smokes gets lung cancer, so other factors like genetics likely play a role as well (see below).

Lung cancer in non-smokers

Not all people who get lung cancer are smokers. Many people with lung cancer are former smokers, but many others never smoked at all.

Lung cancer in non-smokers can be caused by exposure to radon, secondhand smoke, air pollution, or other factors. Workplace exposures to asbestos, diesel exhaust, or certain other chemicals can also cause lung cancers in some people who do not smoke.

A small portion of lung cancers occur in people with no known risk factors for the disease. Some of these might just be random events that don’t have an outside cause, but others might be due to factors that we don’t yet know about.

Lung cancers in non-smokers are often different in some ways from those that occur in smokers. They tend to occur at younger ages. Lung cancers in non-smokers often have certain gene changes that are different from those in tumors from smokers. In some cases, these changes can be used to guide treatment.

Gene changes that may lead to lung cancer

Scientists now know how some of the risk factors for lung cancer can cause certain changes in the DNA of lung cells. These changes can lead to abnormal cell growth and, sometimes, cancer. DNA is the chemical in each of our cells that makes up our genes – the instructions for how our cells function. We usually look like our parents because they

are the source of our DNA. But DNA affects more than how we look. It also can influence our risk for developing certain diseases, including some kinds of cancer.

Some genes contain instructions for controlling when cells grow, divide to make new cells, and die. Genes that help cells grow, divide, or stay alive are called *oncogenes*. Genes that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*. Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes.

Inherited gene changes

Some people inherit DNA mutations (changes) from their parents that greatly increase their risk for developing certain cancers. But inherited mutations alone are not thought to cause very many lung cancers.

Still, genes do seem to play a role in some families with a history of lung cancer. For example, some people seem to inherit a reduced ability to break down or get rid of certain types of cancer-causing chemicals in the body, such as those found in tobacco smoke. This could put them at higher risk for lung cancer.

Other people may inherit faulty DNA repair mechanisms that make it more likely they will end up with DNA changes. Every time a cell divides into 2 new cells, it must make a new copy of its DNA. This process is not perfect, and copying errors sometimes occur. Cells normally have repair enzymes that proofread the DNA to help prevent this. People with repair enzymes that don’t work as well might be especially vulnerable to cancer-causing chemicals and radiation.

Researchers are developing tests that may help identify such people, but these tests are not yet used routinely. For now, doctors recommend that all people avoid tobacco smoke and other exposures that might increase their cancer risk.

Acquired gene changes

Gene changes related to lung cancer are usually acquired during life rather than inherited. Acquired mutations in lung cells often result from exposure to factors in the environment, such as cancer-causing chemicals in tobacco smoke. But some gene changes may just be random events that sometimes happen inside a cell, without having an outside cause.

Acquired changes in certain genes, such as the *TP53* or *p16* tumor suppressor genes and the *K-RAS* or *ALK* oncogenes, are thought to be important in the development of non-small cell lung cancer. Changes in these and other genes may also make some lung cancers more likely to grow and spread than others. Not all lung cancers share the same gene changes, so there are undoubtedly changes in other genes that have not yet been found.

Can non-small cell lung cancer be prevented?

Not all lung cancers can be prevented, but there are some ways you can reduce your risk of getting lung cancer.

The best way to reduce your risk of lung cancer is not to smoke and to avoid breathing in other people's smoke.

If you stop smoking before a cancer develops, your damaged lung tissue gradually starts to repair itself. No matter what your age or how long you've smoked, quitting may lower your risk of lung cancer and help you live longer. People who stop smoking before age 50 cut their risk of dying in the next 15 years in half compared with those who continue to smoke. If you would like help quitting smoking, see our document *Guide to Quitting Smoking* or call the American Cancer Society at 1-800-227-2345.

Radon is an important cause of lung cancer. You can reduce your exposure to radon by having your home tested and treated, if needed. For more information, see the document *Radon*.

Avoiding exposure to known cancer-causing chemicals, in the workplace and elsewhere, may also be helpful (see "What are the risk factors for non-small cell lung cancer?"). When people work where these exposures are common, they should be kept to a minimum.

A healthy diet with lots of fruits and vegetables may also help reduce your risk of lung cancer. Some evidence suggests that a diet high in fruits and vegetables may help protect against lung cancer in both smokers and non-smokers. But any positive effect of fruits and vegetables on lung cancer risk would be much less than the increased risk from smoking.

Attempts to reduce the risk of lung cancer in current or former smokers by giving them high doses of vitamins or vitamin-like drugs have not been successful so far. In fact, some studies have found that beta-carotene, a nutrient related to vitamin A, appears to increase the rate of lung cancer in these people.

Some people who get lung cancer do not have any clear risk factors. Although we know how to prevent most lung cancers, at this time we don't know how to prevent all of them.

Can non-small cell lung cancer be found early?

Usually symptoms of lung cancer do not appear until the disease is already in an advanced, non-curable stage. Even when symptoms of lung cancer do appear, many

people may mistake them for other problems, such as an infection or long-term effects from smoking. This may delay the diagnosis.

Some lung cancers are diagnosed early because they are found by accident as a result of tests for other medical conditions. For example, lung cancer may be found by imaging tests (such as a chest x-ray or chest CT scan), bronchoscopy (viewing the inside of lung airways through a flexible lighted tube), or sputum exam (microscopic examination of cells in coughed up phlegm) done for other reasons in patients with heart disease, pneumonia, or other lung conditions. A small portion of these patients do very well and may be cured of lung cancer.

Screening is the use of tests or exams to detect a disease in people without symptoms of that disease. Doctors have looked for many years for a test to find lung cancer early and help people live longer, but only in recent years has a study shown that a lung cancer screening test can help lower the risk of dying from this disease.

The National Lung Screening Trial

The National Lung Screening Trial (NLST) was a large clinical trial that looked at using a type of CT scan known as low-dose CT (sometimes called low-dose spiral or helical CT) to screen for lung cancer. CT scans of the chest provide more detailed pictures than chest x-rays and are better at finding small abnormalities in the lungs (discussed in more detail in the next section). Low-dose CT (LDCT) of the chest uses lower amounts of radiation than a standard chest CT and does not require the use of intravenous (IV) contrast dye.

The NLST compared LDCT of the chest to chest x-rays in people at high risk of lung cancer to see if these scans could help lower the risk of dying from lung cancer. The study included more than 50,000 people aged 55 to 74 who were current or former smokers and were in fairly good health. To be on the study, they had to have at least a 30 pack-year history of smoking. A pack-year is the number of cigarette packs smoked each day multiplied by the number of years a person has smoked. Someone who smoked a pack of cigarettes per day for 30 years has a 30 pack-year smoking history, as does someone who smoked 2 packs a day for 10 years and then a pack a day for another 10 years. Former smokers could enter the study if they had quit within the past 15 years. The study did not include people if they had a prior history of lung cancer or lung cancer symptoms, if they had part of a lung removed, if they needed to be on oxygen at home to help them breathe, or if they had other serious medical problems.

People in the study got either 3 LDCT scans or 3 chest x-rays, each a year apart, to look for abnormal areas in the lungs that might be cancer. After several years, the study found that people who got LDCT had a 16% lower chance of dying from lung cancer than those who got chest x-rays. They were also 7% less likely to die overall (from any cause) than those who got chest x-rays.

Screening with LDCT was also shown to have some downsides that need to be considered. One drawback of this test is that it also finds a lot of abnormalities that have to be checked out with more tests, but turn out not to be cancer. (About 1 out of 4 people in the NLST had such a finding.) This may lead to additional tests such as other CT scans or more invasive tests such as needle biopsies or even surgery to remove a portion of lung in some people. These tests can sometimes lead to complications (like a collapsed lung) or rarely, death, even in people who do not have cancer (or who have very early stage cancer).

LDCTs also expose people to a small amount of radiation with each test. It is less than the dose from a standard CT, but it is more than the dose from a chest x-ray. Some people who are screened may end up needing further CT scans, which means more radiation exposure. When done in tens of thousands of people, this radiation may cause a few people to develop breast, lung, or thyroid cancers later on.

The NLST was a large study, but it left some questions that still need to be answered. For example, it's not clear if screening with LDCT scans would have the same effect on people different than those allowed in the study, such as those who smoke less (or not at all), or people younger than age 55 or older than 74. Also, in the NLST, patients got a total of 3 scans over 2 years. It's not yet clear what the effect would be if people were screened for longer than 2 years.

These factors, and others, need to be taken into account by people and their doctors who are considering whether or not screening with LDCT scans is right for them.

American Cancer Society's guidelines for lung cancer screening

The American Cancer Society has thoroughly reviewed the subject of lung cancer screening and issued guidelines that are aimed at doctors and other health care providers:

Patients should be asked about their smoking history. Patients who meet ALL of the following criteria may be candidates for lung cancer screening:

- 55 to 74 years old
- In fairly good health (discussed further down)
- Have at least a 30 pack-year smoking history (this was discussed above)
- Are either still smoking or have quit smoking within the last 15 years

These criteria were based on what was used in the NLST.

Doctors should talk to these patients about the benefits, limitations, and potential harms of lung cancer screening. Screening should only be done at facilities that have the right

type of CT scan and that have a great deal of experience in LDCT scans for lung cancer screening. The facility should also have a team of specialists that can provide the appropriate care and follow-up of patients with abnormal results on the scans.

For patients

If you fit all of the criteria for lung cancer screening listed above, you and your doctor (or other health care provider) should talk about starting screening. He or she will talk to you about what you can expect from screening, including possible benefits and harms, as well as the limitations of screening.

The main benefit is a lower chance of dying of lung cancer, which accounts for many deaths in current and former smokers. Still, it is important to be aware that, like with any type of screening, not everyone who gets screened will benefit. Screening with LDCT will not find all lung cancers, and not all of the cancers that are found will be found early. Even if a cancer is found by screening, you may still die from lung cancer. Also, LDCT often finds things that turn out not to be cancer, but have to be checked out with more tests to know what they are. This can mean more CT scans, or even invasive tests such as a lung biopsy, in which a piece of lung tissue is removed with a needle or in surgery. These tests have risks of their own (see above).

At this time, government and private insurance programs are not likely to provide coverage for a LDCT done for lung cancer screening.

Screening should only be done at facilities that have the right type of CT scanner and that have experience in LDCT scans for lung cancer screening. The facility should also have a team of specialists that can provide the appropriate care and follow-up of patients with abnormal results on the scans. You might not have the right kind of facility nearby, so you may need to travel some distance to be screened.

If you and your doctor decide that you should be screened, you should get a LDCT every year until you reach the age of 74, as long as you remain in good health.

If you are a current smoker, you should receive counseling about stopping. You should be told about your risk of lung cancer and referred to a smoking cessation program. Screening is not a good alternative to stopping smoking. For help quitting smoking, see our document *Guide to Quitting Smoking* or call the American Cancer Society at 1-800-227-2345.

What does “in fairly good health” mean?

Screening is meant to find cancer in people who do not have symptoms of the disease. People who already have symptoms that might be caused by lung cancer may need tests such as CT scans to find the underlying cause, which in some cases may be cancer. But this kind of testing is for diagnosis and is not the same as screening. Some of the possible

symptoms of lung cancer that kept people out of the NLST were coughing up blood and weight loss without trying.

To get the most potential benefit from screening, patients need to be in good health. For example, they need to be able to have surgery and other treatments to try to cure lung cancer if it is found. Patients who require home oxygen therapy most likely could not withstand having part of a lung removed, and so are not candidates for screening. Patients with other serious medical problems that would shorten their lives or keep them from having surgery may also not be able to benefit enough from screening for it to be worth the risks, and so should also not be screened.

Metal implants in the chest (like pacemakers) or back (like rods in the spine) can interfere with x-rays and lead to poor quality CT images of the lungs. People with these types of implants were also kept out of the NLST, and so should not be screened with CT scans for lung cancer according to the ACS guidelines.

People who have been treated for lung cancer often have follow-up tests, including CT scans to see if the cancer has come back or spread. This is called surveillance and is not the same as screening. (People with a prior history of lung cancer were not eligible for the NLST.)

Signs and symptoms of non-small cell lung cancer

Most lung cancers do not cause any symptoms until they have spread too far to be cured, but symptoms do occur in some people with early lung cancer. If you go to your doctor when you first notice symptoms, your cancer might be diagnosed at an earlier stage, when treatment is more likely to be effective. The most common symptoms of lung cancer are:

- A cough that does not go away or gets worse
- Chest pain that is often worse with deep breathing, coughing, or laughing
- Hoarseness
- Weight loss and loss of appetite
- Coughing up blood or rust-colored sputum (spit or phlegm)
- Shortness of breath
- Feeling tired or weak
- Infections such as bronchitis and pneumonia that don’t go away or keep coming back

- New onset of wheezing

When lung cancer spreads to distant organs, it may cause:

- Bone pain (like pain in the back or hips)
- Neurologic changes (such as headache, weakness or numbness of an arm or leg, dizziness, balance problems, or seizures), from cancer spread to the brain or spinal cord
- Yellowing of the skin and eyes (jaundice), from cancer spread to the liver
- Lumps near the surface of the body, due to cancer spreading to the skin or to lymph nodes (collections of immune system cells), such as those in the neck or above the collarbone

Most of the symptoms listed above are more likely to be caused by conditions other than lung cancer. Still, if you have any of these problems, it's important to see your doctor right away so the cause can be found and treated, if needed.

Some lung cancers can cause a group of very specific symptoms. These are often described as *syndromes.*

Horner syndrome

Cancers of the top part of the lungs (sometimes called *Pancoast tumors*) may damage a nerve that passes from the upper chest into your neck. This can cause severe shoulder pain. Sometimes these tumors can affect certain nerves to the eye and part of the face, causing a group of symptoms called *Horner syndrome*:

- Drooping or weakness of one eyelid
- Having a smaller pupil (dark part in the center of the eye) in the same eye
- Reduced or absent sweating on the same side of the face

Conditions other than lung cancer can also cause Horner syndrome.

Superior vena cava syndrome

The superior vena cava (SVC) is a large vein that carries blood from the head and arms back to the heart. It passes next to the upper part of the right lung and the lymph nodes inside the chest. Tumors in this area may push on the SVC, which can cause the blood to back up in the veins. This can cause swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red skin color). It can also cause headaches, dizziness, and a change in consciousness if it affects the brain. While SVC syndrome can develop

gradually over time, in some cases it can become life-threatening, and needs to be treated right away.

Paraneoplastic syndromes

Some lung cancers can make hormone-like substances that enter the bloodstream and cause problems with distant tissues and organs, even though the cancer has not spread to those tissues or organs. These problems are called *paraneoplastic syndromes*. Sometimes these syndromes may be the first symptoms of lung cancer. Because the symptoms affect organs besides the lungs, patients and their doctors may suspect at first that a disease other than lung cancer is causing them.

Some of the more common paraneoplastic syndromes that can be caused by non-small cell lung cancer include:

- High blood calcium levels (*hypercalcemia*), which can cause frequent urination, thirst, constipation, nausea, vomiting, belly pain, weakness, fatigue, dizziness, confusion, and other nervous system problems
- Excess growth of certain bones, especially those in the finger tips, which is often painful
- Blood clots
- Excess breast growth in men (*gynecomastia*)

Again, many of the symptoms listed above are more likely to be caused by conditions other than lung cancer. Still, if you have any of these problems, it's important to see your doctor right away so the cause can be found and treated, if needed.

How is non-small cell lung cancer diagnosed?

Lung cancers can be found by screening, but most lung cancers are found because they are causing problems. If you are having signs or symptoms of lung cancer, you should see your doctor, who will examine you and order some tests. The actual diagnosis of lung cancer is made by looking at a sample of lung cells under a microscope.

Medical history and physical exam

If you have any signs or symptoms that suggest you might have lung cancer, your doctor will want to take a medical history to check for risk factors and learn more about your symptoms. Your doctor will also examine you to look for signs of lung cancer and other health problems.

If the results of the history and physical exam suggest you might have lung cancer, more involved tests will be done. These could include imaging tests and/or getting biopsies of lung tissue.

Imaging tests

Imaging tests use x-rays, magnetic fields, sound waves, or radioactive substances to create pictures of the inside of your body. Imaging tests may be done for a number of reasons both before and after a diagnosis of lung cancer, including:

- To help find a suspicious area that might be cancerous
- To learn how far cancer may have spread
- To help determine if treatment has been effective
- To look for possible signs of cancer coming back after treatment

Chest x-ray

This is often the first test your doctor will do to look for any masses or spots on the lungs. Plain x-rays of your chest can be done at imaging centers, hospitals, and even in some doctors' offices. If the x-ray is normal, you probably don't have lung cancer (although some lung cancers may not show up on an x-ray). If something suspicious is seen, your doctor may order more tests.

Computed tomography (CT) scan

A CT (or CAT) scan is more likely to show lung tumors than routine chest x-rays. A CT scan can also provide precise information about the size, shape, and position of any lung tumors and can help find enlarged lymph nodes that might contain cancer that has spread from the lung. This test can also be used to look for masses in the adrenal glands, liver, brain, and other internal organs that might be due to the spread of lung cancer.

The CT scan uses x-rays to produce detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you while you lie on a table. A computer then combines these pictures into images of slices of the part of your body being studied. Unlike a regular x-ray, a CT scan creates detailed images of the soft tissues in the body.

Before the CT scan, you may be asked to drink a contrast solution or you may get an injection of a contrast solution through an IV (intravenous) line. This helps better outline structures in your body. The contrast may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor

if you have any allergies or if you ever had a reaction to any contrast material used for x-rays.

A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. You will need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and you might feel a bit confined by the ring while the pictures are being taken.

CT-guided needle biopsy: If a suspected area of cancer lies deep within the body, a CT scan can be used to guide a biopsy needle precisely into the suspected area. For this procedure, you stay on the CT scanning table, while the doctor advances a biopsy needle through the skin and toward the mass. CT scans are repeated until the doctor can see that the needle is within the mass. A biopsy sample is then removed and looked at under a microscope.

Magnetic resonance imaging (MRI) scan

MRI scans are most often used to look for possible spread of lung cancer to the brain or spinal cord.

Like CT scans, MRI scans provide detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. A contrast material called gadolinium is often injected into a vein before the scan to better see details.

MRI scans take longer than CT scans (often up to an hour), and are a little more uncomfortable. You have to lie inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Special “open” MRI machines can sometimes help with this if needed, but the images may not be as sharp in some cases. MRI machines make buzzing and clicking noises, so some centers provide earplugs to help block this out.

Positron emission tomography (PET) scan

A PET scan can be a very important test if you appear to have early stage lung cancer. Your doctor can use this test to help see if the cancer has spread to nearby lymph nodes or other areas, which can help determine if surgery may be an option for you. This test can also be helpful in getting a better idea whether an abnormal area on a chest x-ray or CT scan might be cancer.

PET scans are also useful if your doctor thinks the cancer may have spread but doesn’t know where. PET can reveal spread of cancer to the liver, bones, adrenal glands, or some

other organs. It is not as useful for looking at the brain, since all brain cells use a lot of glucose.

For this test, a form of radioactive sugar (known as fluorodeoxyglucose or FDG) is injected into the blood. (The amount of radioactivity used is very low and will pass out of the body over the next day or so.) Because cancer cells in the body are growing rapidly, they absorb more of the radioactive sugar. After about an hour, you will be moved onto a table in the PET scanner. You lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information about your whole body.

Often a PET scan is combined with a CT scan using a special machine that can do both at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET with the more detailed appearance of that area on the CT. This is the type of PET scan most often used in patients with lung cancer.

Bone scan

A bone scan can help show if a cancer has spread to the bones.

For this test, a small amount of low-level radioactive material is injected into a vein (intravenously, or IV). The substance settles in areas of bone changes throughout the entire skeleton over the course of a couple of hours. You then lie on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of your skeleton.

Areas of active bone changes attract the radioactivity and show up as “hot spots.” These areas may suggest metastatic cancer, but arthritis or other bone diseases can also cause the same pattern. To distinguish among these conditions, your cancer care team may use other imaging tests such as plain x-rays or MRI scans to get a better look at the areas that light up, or they may even take biopsy samples of the bone.

Bone scans aren’t needed very often because PET scans, which are often done in patients with non-small cell lung cancer, can usually show if cancer has spread to the bones. Bone scans are done mainly when there is reason to think the cancer may have spread to the bones (because of symptoms such as bone pain) and other test results aren’t clear.

Tests to diagnose lung cancer

Symptoms and the results of certain tests may strongly suggest that a person has lung cancer, but the actual diagnosis of non-small cell lung cancer is made by looking at lung cells under a microscope.

The cells can be taken from lung secretions (sputum or phlegm), found in fluid removed from the area around the lung (thoracentesis), or removed from a suspicious area using a

needle or surgery (known as a *biopsy*). The choice of which test(s) to use depends on the situation.

Sputum cytology

A sample of sputum (mucus you cough up from the lungs) is looked at under a microscope to see if it contains cancer cells. The best way to do this is to get early morning samples from you 3 days in a row. This test is more likely to help find cancers that start in the major airways of the lung, such as most squamous cell lung cancers. It may not be as helpful for finding other types of non-small cell lung cancer.

Thoracentesis

If there is a buildup of fluid around the lungs (*pleural effusion*), doctors can perform thoracentesis to find out if it was caused by cancer spreading to the lining of the lungs (pleura). The buildup might also be caused by other conditions, such as heart failure or an infection.

For this procedure, the skin is numbed and a hollow needle is inserted between the ribs to drain the fluid. (In a similar test called *pericardiocentesis*, fluid is removed from within the sac around the heart.) The fluid is checked under a microscope for cancer cells. Chemical tests of the fluid are also sometimes useful in telling a malignant (cancerous) pleural effusion from a benign (non-cancerous) one.

If a malignant pleural effusion has been diagnosed, thoracentesis may be repeated to remove more fluid. Fluid buildup can keep the lungs from filling with air, so thoracentesis can help the patient breathe better.

Needle biopsy

Doctors can often use a hollow needle to get a small sample from a suspicious area (mass). In a *fine needle aspiration (FNA)* biopsy, the doctor uses a syringe with a very thin, hollow needle (thinner than the ones used for blood tests) to withdraw (aspirate) cells and small fragments of tissue. In a *core biopsy*, a larger needle is used to remove one or more small cylinders (cores) of tissue. Core biopsies provide a larger sample than FNA biopsies, so they are often preferred.

An advantage of needle biopsies is that they don’t require a surgical incision. The drawback is that they remove only a small amount of tissue. In some cases (particularly with FNA biopsies), the amount of tissue removed might not be enough to both make a diagnosis and to classify DNA changes in the cancer cells that can help doctors choose anticancer drugs.

If the suspected tumor is in the outer portion of the lungs, either kind of biopsy needle can be inserted through the skin on the chest wall. This is called a *transthoracic needle*

biopsy. The area where the needle is to be inserted may be numbed with local anesthesia first. The doctor then guides the needle into the area while looking at the lungs with either fluoroscopy (which is like an x-ray, but creates a moving image on a screen rather than a single picture on film) or CT scans. Unlike fluoroscopy, CT doesn't give a constant picture, so if CT is used, the needle is inserted toward the mass (tumor), a CT image is taken, and the direction of the needle is guided based on the image. This is repeated a few times until the needle is within the mass.

A possible complication of this procedure is that air may leak out of the lung at the biopsy site and into the space between the lung and the chest wall. This can cause part of the lung to collapse and may cause trouble breathing. This complication, called a *pneumothorax*, often gets better without any treatment. If not, it is treated by putting a small tube into the chest space and sucking out the air over a day or two, after which it usually heals on its own.

An FNA biopsy may also be done to check for cancer in the lymph nodes between the lungs:

- *Transtracheal FNA* or *transbronchial FNA* is done by passing the needle through the wall of the trachea (windpipe) or bronchi (the large airways leading into the lungs) during bronchoscopy or endobronchial ultrasound (described below).
- In some cases an FNA biopsy is done during endoscopic esophageal ultrasound (described below) by passing the needle through the wall of the esophagus.

Bronchoscopy

Bronchoscopy can help the doctor find some tumors or blockages in the larger airways of the lungs which can often be biopsied during the procedure.

For this exam, a lighted, flexible fiber-optic tube (called a *bronchoscope*) is passed through the mouth or nose and down into the windpipe and bronchi. The mouth and throat are sprayed first with a numbing medicine. You may also be given medicine through an intravenous (IV) line to make you feel relaxed.

Small instruments can be passed down the bronchoscope to take biopsies (samples of tissue). The doctor can also sample cells from the lining of the airways with a small brush (bronchial brushing) or by rinsing the airways with sterile saltwater (bronchial washing). These tissue and cell samples are then looked at under a microscope.

Tests to find lung cancer spread in the chest

Endobronchial ultrasound

Ultrasound is a type of imaging test that uses sound waves to create pictures of the inside of your body. For this test, a small, microphone-like instrument called a transducer gives off sound waves and picks up the echoes as they bounce off body tissues. The echoes are converted by a computer into a black and white image on a computer screen.

For endobronchial ultrasound, a bronchoscope is fitted with an ultrasound transducer at its tip and is passed down into the windpipe. This is done with numbing medicine (local anesthesia) and light sedation.

The transducer can be pointed in different directions to look at lymph nodes and other structures in the mediastinum (the area between the lungs). If suspicious areas such as enlarged lymph nodes are seen on the ultrasound, a hollow needle can be passed through the bronchoscope and guided into these areas to obtain a biopsy. The samples are then sent to a lab to be looked at under a microscope.

Endoscopic esophageal ultrasound

This test is like endobronchial ultrasound, except the doctor passes an endoscope (a lighted, flexible scope) down the throat and into the esophagus (the tube connecting the throat to the stomach). This is done with numbing medicine (local anesthesia) and light sedation.

The esophagus lies just behind the windpipe and is close to some lymph nodes inside the chest to which lung cancer may spread. As with endobronchial ultrasound, the transducer can be pointed in different directions to look at lymph nodes and other structures inside the chest that might contain lung cancer. If enlarged lymph nodes are seen on the ultrasound, a hollow needle can be passed through the endoscope to get biopsy samples of them. The samples are then sent to a lab to be looked at under a microscope.

Mediastinoscopy and mediastinotomy

These procedures may be done to look more directly at and get samples from the structures in the mediastinum (the area between the lungs). They are done in an operating room while you are under general anesthesia (in a deep sleep). The main difference between the two is in the location and size of the incision.

Mediastinoscopy: A small cut is made in the front of the neck and a thin, hollow, lighted tube is inserted behind the sternum (breast bone) and in front of the windpipe to look at the area. Instruments can be passed through this tube to take tissue samples from the lymph nodes along the windpipe and the major bronchial tube areas. Looking at the samples under a microscope can show whether cancer cells are present.

Mediastinotomy: The surgeon makes a slightly larger incision (usually about 2 inches long) between the left second and third ribs next to the breast bone. This lets the surgeon reach some lymph nodes that cannot be reached by mediastinoscopy.

Thoracoscopy

Thoracoscopy can be done to find out if cancer has spread to the spaces between the lungs and the chest wall, or to the linings of these spaces. It can also be used to sample tumors on the outer parts of the lungs as well as nearby lymph nodes and fluid, and to assess whether a tumor is growing into nearby tissues or organs. This procedure is not often done just to diagnose lung cancer, unless other tests such as needle biopsies are unable to get enough samples for the diagnosis.

Thoracoscopy is done in the operating room while you are under general anesthesia (in a deep sleep). A small cut (incision) is made in the side of the chest wall. (Sometimes more than one cut is made.) The doctor then inserts a thin, lighted tube with a small video camera on the end through the incision to view the space between the lungs and the chest wall. Using this, the doctor can see potential cancer deposits on the lining of the lung or chest wall and remove small pieces of tissue to be looked at under the microscope. (When certain areas can't be reached with thoracoscopy, the surgeon may need to make a larger incision in the chest wall, known as a *thoracotomy*.)

Thoracoscopy can also be used as part of the treatment to remove part of a lung in some early-stage lung cancers. This type of operation, known as *video-assisted thoracic surgery (VATS)*, is described in more detail in the "Surgery for non-small cell lung cancer" section.

Lab tests of biopsy and other samples

Samples that have been collected during biopsies or other tests are sent to a pathology lab. A pathologist, a doctor who uses lab tests to diagnose diseases such as cancer, will look at the samples under a microscope and may do other special tests to help better classify the cancer. (Cancers from other organs can spread to the lungs. It's very important to find out where the cancer started, because treatment is different depending on the type of cancer.)

The results of these tests are described in a pathology report, which is usually available within about a week. If you have any questions about your pathology results or any diagnostic tests, talk to your doctor. If needed, you can get a second opinion of your pathology report by having your tissue samples sent to a pathologist at another lab recommended by your doctor.

For more information on understanding your pathology report, see the "Lung Pathology" section of our website.

Immunohistochemistry

For this test, very thin slices of the sample are attached to glass microscope slides. The samples are then treated with special proteins (antibodies) designed to attach only to a specific substance found in certain cancer cells. If the patient's cancer cells contain that substance, the antibody will attach to the cells. Chemicals are then added so that antibodies attached to the cells change color. The doctor who looks at the sample under a microscope can see this color change.

Molecular tests

In some cases, doctors may look for specific gene changes in the cancer cells that could mean certain targeted drugs might help treat the cancer.

For example, the epidermal growth factor receptor (EGFR) is a protein that sometimes appears in high amounts on the surface of cancer cells and helps them grow. Some newer anti-cancer drugs that target EGFR seem to work best against lung cancers with certain changes in the *EGFR* gene, which are more common in certain groups, such as non-smokers, women, and Asians. But these drugs don't seem to be as helpful in patients whose cancer cells have changes in the *KRAS* gene. Many doctors now test for changes in genes such as *EGFR* and *KRAS* to determine if these newer treatments are likely to be helpful.

About 5% of NSCLCs have been found to have a rearrangement in a gene called *ALK*. This change is most often seen in non-smokers (or light smokers) who have the adenocarcinoma subtype of NSCLC. Doctors may test cancers for changes in the *ALK* gene to see if drugs (such as crizotinib) that target this change may help them.

About 1% to 2% of NSCLCs have a rearrangement in the *ROS1* gene, which might make the tumor respond to the targeted drug crizotinib. A similar percentage have a rearrangement in the *RET* gene. Certain drugs that target cells with *RET* gene changes might be options for treating these tumors.

Newer lab tests for certain other genes or proteins may also help guide the choice of treatment. Some of these are described in the section "What's new in non-small cell lung cancer research and treatment?"

Blood tests

Blood tests are not used to diagnose lung cancer. But they can help to get a sense of a person's overall health; for example, to see if a person is healthy enough to have surgery.

A complete blood count (CBC) determines whether your blood has normal numbers of various cell types. For example, it can show if you are anemic (have a low number of red blood cells), if you could have trouble with bleeding (due to a low number of blood

platelets), or if you are at increased risk for infections (because of a low number of white blood cells). This test will be repeated regularly if you are treated with chemotherapy, because these drugs can affect blood-forming cells of the bone marrow.

Blood chemistry tests can help spot abnormalities in some of your organs, such as the liver or kidneys. For example, if cancer has spread to the liver and bones, it may cause abnormal levels of certain chemicals in the blood, such as a higher than normal level of lactate dehydrogenase (LDH).

Pulmonary function tests

Pulmonary function tests (PFTs) are often done after lung cancer is diagnosed to see how well your lungs are working (for example, how much emphysema or chronic bronchitis is present). This is especially important if surgery might be an option in treating the cancer. Surgery to remove lung cancer may mean removing part or all of a lung, so it's important to know how well the lungs are working beforehand. Some people with poor lung function (like those with lung damage from smoking) don't have enough lung reserve to withstand removing even part of a lung. These tests can give the surgeon an idea of whether surgery is a good option, and if so, how much lung can safely be removed.

There are different types of PFTs, but they all basically have you breathe in and out through a tube that is connected to a machine that measures airflow.

Sometimes PFTs are coupled with a test called an *arterial blood gas*. In this test, blood is removed from an artery (most blood tests use blood removed from a vein) to measure the amount of oxygen and carbon dioxide that it contains.

How is non-small cell lung cancer staged?

The stage of a cancer describes how far it has spread. Your treatment and prognosis (outlook) depend, to a large extent, on the cancer's stage.

There are actually 2 types of staging descriptions for non-small cell lung cancer (NSCLC).

- The *clinical stage* is based on the results of the physical exam, biopsies, and imaging tests (CT scan, chest x-ray, PET scan, etc.), which are described in the section "How is non-small cell lung cancer diagnosed?"

- If you have surgery, your doctor can also determine the *pathologic stage*, which is based on the same factors as the clinical stage, plus what is found as a result of the surgery.

The clinical and pathologic stages may be different in some cases. For example, during surgery the doctor may find cancer in an area that did not show up on imaging tests, which might give the cancer a more advanced pathologic stage.

Because many patients with NSCLC do not have surgery, the clinical stage is often used when describing the extent of this cancer. But when it is available, the pathologic stage is likely to be more accurate than the clinical stage, as it uses the additional information obtained at surgery.

The TNM staging system

The system used to describe the growth and spread of NSCLC is the American Joint Committee on Cancer (AJCC) **TNM** staging system. The TNM system is based on 3 key pieces of information:

- **T** indicates the size of the main (primary) **tumor** and whether it has grown into nearby areas.
- **N** describes the spread of cancer to nearby (regional) lymph **nodes**. Lymph nodes are small bean-shaped collections of immune system cells to which cancers often spread before going to other parts of the body.
- **M** indicates whether the cancer has spread (**metastasized**) to other organs of the body. (The most common sites are the brain, bones, adrenal glands, liver, kidneys, and the other lung.)

Numbers or letters appear after T, N, and M to provide more details about each of these factors. The numbers 0 through 4 indicate increasing severity.

The TNM staging system is complex and can be hard for patients (and even some doctors) to understand. If you have any questions about the stage of your cancer, ask your doctor to explain it to you.

T categories for lung cancer

TX: The main (primary) tumor can’t be assessed, or cancer cells were seen on sputum cytology or bronchial washing but no tumor can be found.

T0: There is no evidence of a primary tumor.

Tis: The cancer is found only in the top layers of cells lining the air passages. It has not invaded into deeper lung tissues. This is also known as *carcinoma in situ*.

T1: The tumor is no larger than 3 centimeters (cm)—slightly less than 1¼ inches—across, has not reached the membranes that surround the lungs (visceral pleura), and does not affect the main branches of the bronchi.

If the tumor is 2 cm (about 4/5 of an inch) or less across, it is called **T1a**. If the tumor is larger than 2 cm but not larger than 3 cm across, it is called **T1b**.

T2: The tumor has 1 or more of the following features:

- It is larger than 3 cm across but not larger than 7 cm.
- It involves a main bronchus, but is not closer than 2 cm (about ¾ inch) to the carina (the point where the windpipe splits into the left and right main bronchi).
- It has grown into the membranes that surround the lungs (visceral pleura).
- The tumor partially clogs the airways, but this has not caused the entire lung to collapse or develop pneumonia.

If the tumor is 5 cm or less across, it is called **T2a**. If the tumor is larger than 5 cm across (but not larger than 7 cm), it is called **T2b**.

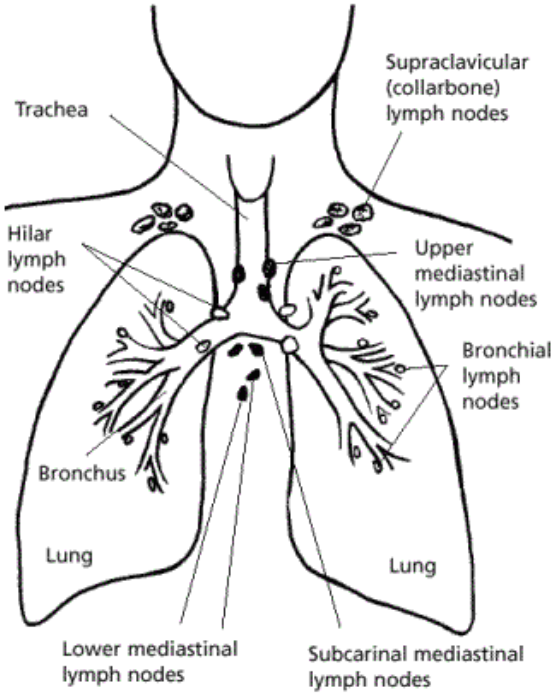
T3: The tumor has 1 or more of the following features:

- It is larger than 7 cm across.
- It has grown into the chest wall, the breathing muscle that separates the chest from the abdomen (diaphragm), the membranes surrounding the space between the two lungs (mediastinal pleura), or membranes of the sac surrounding the heart (parietal pericardium).
- It invades a main bronchus and is closer than 2 cm (about ¾ inch) to the carina, but it does not involve the carina itself.
- It has grown into the airways enough to cause an entire lung to collapse or to cause pneumonia in the entire lung.
- Two or more separate tumor nodules are present in the same lobe of a lung.

T4: The cancer has 1 or more of the following features:

- A tumor of any size has grown into the space between the lungs (mediastinum), the heart, the large blood vessels near the heart (such as the aorta), the windpipe (trachea), the tube connecting the throat to the stomach (esophagus), the backbone, or the carina.
- Two or more separate tumor nodules are present in different lobes of the same lung.

N categories for lung cancer



NX: Nearby lymph nodes cannot be assessed.

N0: There is no spread to nearby lymph nodes.

N1: The cancer has spread to lymph nodes within the lung and/or around the area where the bronchus enters the lung (hilar lymph nodes). Affected lymph nodes are on the same side as the primary tumor.

N2: The cancer has spread to lymph nodes around the carina (the point where the windpipe splits into the left and right bronchi) or in the space between the lungs (mediastinum). Affected lymph nodes are on the same side as the primary tumor.

N3: The cancer has spread to lymph nodes near the collarbone on either side, and/or spread to hilar or mediastinal lymph nodes on the side opposite the primary tumor.

M categories for lung cancer

M0: No spread to distant organs or areas. This includes the other lung, lymph nodes further away than those mentioned in the N stages above, and other organs or tissues such as the liver, bones, or brain.

M1a: Any of the following:

- The cancer has spread to the other lung.
- Cancer cells are found in the fluid around the lung (called a *malignant pleural effusion*).
- Cancer cells are found in the fluid around the heart (called a *malignant pericardial effusion*).

M1b: The cancer has spread to distant lymph nodes or to other organs such as the liver, bones, or brain.

Stage grouping for lung cancer

Once the T, N, and M categories have been assigned, this information is combined to assign an overall stage of 0, I, II, III, or IV. This process is called *stage grouping*. Some stages are subdivided into A and B. The stages identify cancers that have a similar outlook (prognosis) and thus are treated in a similar way. Patients with lower stage numbers tend to have a better outlook.

Occult (hidden) cancer

TX, N0, M0: Cancer cells are seen in a sample of sputum or other lung fluids, but the cancer isn't found with other tests, so its location can't be determined.

Stage 0

Tis, N0, M0: The cancer is found only in the top layers of cells lining the air passages. It has not invaded deeper into other lung tissues and has not spread to lymph nodes or distant sites.

Stage IA

T1a/T1b, N0, M0: The cancer is no larger than 3 cm across, has not reached the membranes that surround the lungs, and does not affect the main branches of the bronchi. It has not spread to lymph nodes or distant sites.

Stage IB

T2a, N0, M0: The cancer has 1 or more of the following features:

- The main tumor is larger than 3 cm across but not larger than 5 cm.
- The tumor has grown into a main bronchus, but is not within 2 cm of the carina (and it is not larger than 5 cm).
- The tumor has grown into the visceral pleura (the membranes surrounding the lungs) and is not larger than 5 cm.
- The tumor is partially clogging the airways (and is not larger than 5 cm).

The cancer has not spread to lymph nodes or distant sites.

Stage IIA

Three main combinations of categories make up this stage.

T1a/T1b, N1, M0: The cancer is no larger than 3 cm across, has not grown into the membranes that surround the lungs, and does not affect the main branches of the bronchi. It has spread to lymph nodes within the lung and/or around the area where the bronchus enters the lung (hilar lymph nodes). These lymph nodes are on the same side as the cancer. It has not spread to distant sites.

OR

T2a, N1, M0: The cancer has 1 or more of the following features:

- The main tumor is larger than 3 cm across but not larger than 5 cm.
- The tumor has grown into a main bronchus, but is not within 2 cm of the carina (and it is not larger than 5 cm).
- The tumor has grown into the visceral pleura (the membranes surrounding the lungs) and is not larger than 5 cm.
- The tumor is partially clogging the airways (and is not larger than 5 cm).

The cancer has also spread to lymph nodes within the lung and/or around the area where the bronchus enters the lung (hilar lymph nodes). These lymph nodes are on the same side as the cancer. It has not spread to distant sites.

OR

T2b, N0, M0: The cancer has 1 or more of the following features:

- The main tumor is larger than 5 cm across but not larger than 7 cm.
- The tumor has grown into a main bronchus, but is not within 2 cm of the carina (and it is between 5 and 7 cm across).
- The tumor has grown into the visceral pleura (the membranes surrounding the lungs) and is between 5 and 7 cm across.
- The tumor is partially clogging the airways (and is between 5 and 7 cm across).

The cancer has not spread to lymph nodes or distant sites.

Stage IIB

Two combinations of categories make up this stage.

T2b, N1, M0: The cancer has 1 or more of the following features:

- The main tumor is larger than 5 cm across but not larger than 7 cm.
- The tumor has grown into a main bronchus, but is not within 2 cm of the carina (and it is between 5 and 7 cm across).
- The tumor has grown into the visceral pleura (the membranes surrounding the lungs) and is between 5 and 7 cm across.
- The cancer is partially clogging the airways (and is between 5 and 7 cm across).

It has also spread to lymph nodes within the lung and/or around the area where the bronchus enters the lung (hilar lymph nodes). These lymph nodes are on the same side as the cancer. It has not spread to distant sites.

OR

T3, N0, M0: The main tumor has 1 or more of the following features:

- It is larger than 7 cm across.
- It has grown into the chest wall, the breathing muscle that separates the chest from the abdomen (diaphragm), the membranes surrounding the space between the lungs (mediastinal pleura), or membranes of the sac surrounding the heart (parietal pericardium).
- It invades a main bronchus and is closer than 2 cm (about ¾ inch) to the carina, but it does not involve the carina itself.
- It has grown into the airways enough to cause an entire lung to collapse or to cause pneumonia in the entire lung.
- Two or more separate tumor nodules are present in the same lobe of a lung.

The cancer has not spread to lymph nodes or distant sites.

Stage IIIA

Three main combinations of categories make up this stage.

T1 to T3, N2, M0: The main tumor can be any size. It has **not** grown into the space between the lungs (mediastinum), the heart, the large blood vessels near the heart (such as the aorta), the windpipe (trachea), the tube connecting the throat to the stomach (esophagus), the backbone, or the carina. It has not spread to different lobes of the same lung.

The cancer has spread to lymph nodes around the carina (the point where the windpipe splits into the left and right bronchi) or in the space between the lungs (mediastinum).

These lymph nodes are on the same side as the main lung tumor. The cancer has not spread to distant sites.

OR

T3, N1, M0: The cancer has 1 or more of the following features:

- It is larger than 7 cm across.
- It has grown into the chest wall, the breathing muscle that separates the chest from the abdomen (diaphragm), the membranes surrounding the space between the lungs (mediastinal pleura), or membranes of the sac surrounding the heart (parietal pericardium).
- It invades a main bronchus and is closer than 2 cm to the carina, but it does not involve the carina itself.
- Two or more separate tumor nodules are present in the same lobe of a lung.
- It has grown into the airways enough to cause an entire lung to collapse or to cause pneumonia in the entire lung.

It has also spread to lymph nodes within the lung and/or around the area where the bronchus enters the lung (hilar lymph nodes). These lymph nodes are on the same side as the cancer. It has not spread to distant sites.

OR

T4, N0 or N1, M0: The cancer has 1 or more of the following features:

- A tumor of any size has grown into the space between the lungs (mediastinum), the heart, the large blood vessels near the heart (such as the aorta), the windpipe (trachea), the tube connecting the throat to the stomach (esophagus), the backbone, or the carina.
- Two or more separate tumor nodules are present in different lobes of the same lung.

It may or may not have spread to lymph nodes within the lung and/or around the area where the bronchus enters the lung (hilar lymph nodes). Any affected lymph nodes are on the same side as the cancer. It has not spread to distant sites.

Stage IIIB

Two combinations of categories make up this stage.

Any T, N3, M0: The cancer can be of any size. It may or may not have grown into nearby structures or caused pneumonia or lung collapse. It has spread to lymph nodes near the collarbone on either side, and/or has spread to hilar or mediastinal lymph nodes on the side opposite the primary tumor. The cancer has not spread to distant sites.

OR

T4, N2, M0: The cancer has 1 or more of the following features:

- A tumor of any size has grown into the space between the lungs (mediastinum), the heart, the large blood vessels near the heart (such as the aorta), the windpipe (trachea), the tube connecting the throat to the stomach (esophagus), the backbone, or the carina.
- Two or more separate tumor nodules are present in different lobes of the same lung.

The cancer has also spread to lymph nodes around the carina (the point where the windpipe splits into the left and right bronchi) or in the space between the lungs (mediastinum). Affected lymph nodes are on the same side as the main lung tumor. It has not spread to distant sites.

Stage IV

Two combinations of categories make up this stage.

Any T, any N, M1a: The cancer can be any size and may or may not have grown into nearby structures or reached nearby lymph nodes. In addition, any of the following is true:

- The cancer has spread to the other lung.
- Cancer cells are found in the fluid around the lung (called a *malignant pleural effusion*).
- Cancer cells are found in the fluid around the heart (called a *malignant pericardial effusion*).

OR

Any T, any N, M1b: The cancer can be any size and may or may not have grown into nearby structures or reached nearby lymph nodes. It has spread to distant lymph nodes or to other organs such as the liver, bones, or brain.

Non-small cell lung cancer survival rates by stage

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may even not want to know them. If you do not want to read about survival rates for non-small cell lung cancer, stop reading here and skip to the next section.

The 5-year survival rate refers to the percentage of patients who live *at least* 5 years after their cancer is diagnosed. Of course, many of these people live much longer than 5 years.

To get 5-year survival rates, doctors look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a more favorable outlook for people now being diagnosed with non-small cell lung cancer.

The rates below are based on the stage of the cancer *at the time of diagnosis*. When looking at survival rates, it's important to understand that the stage of a cancer does not change over time, even if the cancer progresses. A cancer that spreads or comes back is still referred to by the stage it was given when it was first found, but more information is added to explain the current extent of the cancer. (And of course, the treatment plan is adjusted based on the change in cancer status.)

The numbers below are survival rates published in 2007. They are calculated from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database, based on people who were diagnosed with non-small cell lung cancer between 1998 and 2000. Although they are based on patients diagnosed several years ago, they are the most recent published for survival by the current AJCC staging system.

These survival rates are for observed survival. Patients with cancer can die of other things, and these don't take that into account.

Stage	**5-year Observed Survival Rate**
IA	49%
IB	45%
IIA	30%
IIB	31%
IIIA	14%
IIIB	5%
IV	1%

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen to any person. Knowing the type and the stage of a person's cancer helps estimate their outlook. But many other factors can also affect outlook, such as the genetic changes in the cancer cells, the treatment received, how well the cancer responds to treatment, and a person's overall health. Even when taking these other factors into account, survival rates are at best rough estimates. Your doctor can tell you how the numbers above may apply to you.

How is non-small cell lung cancer treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Making treatment decisions for non-small cell lung cancer

After the cancer is found and staged, your cancer care team will discuss your treatment options with you. Depending on the stage of the disease and other factors, the main treatment options for people with non-small cell lung cancer (NSCLC) can include:

- Surgery
- Radiofrequency ablation (RFA)
- Radiation therapy
- Chemotherapy
- Targeted therapies
- Immunotherapy

Palliative procedures can also be used to help with symptoms.

In many cases, more than one of type of treatment is used.

You may have different types of doctors on your treatment team, depending on the stage of your cancer and your treatment options. These doctors may include:

- A thoracic surgeon: a doctor who treats diseases of the lungs and chest with surgery.

- A radiation oncologist: a doctor who treats cancer with radiation therapy.
- A medical oncologist: a doctor who treats cancer with medicines such as chemotherapy.
- A pulmonologist: a doctor who specializes in medical treatment of diseases of the lungs.

Many other specialists may be involved in your care as well, including physician assistants, nurse practitioners, nurses, respiratory therapists, social workers, and other health professionals.

It is important to discuss all of your treatment options as well as their possible side effects with your doctors to help make the decision that best fits your needs. (See the section "What should you ask your doctor about non-small cell lung cancer?") One of the most important factors in choosing a treatment plan is the stage of the cancer, so be sure your doctor has ordered all the tests needed to determine the cancer's stage.

Other factors to consider include your overall health, the likely side effects of the treatment, and the probability of curing the disease, extending life, or relieving symptoms. Age alone is not a barrier to treatment. Older people can benefit from treatment as much as younger people, as long as they are in good health overall. Be sure that you understand the risks and side effects of the various treatments before making a decision.

If time permits, it is often a good idea to get a second opinion. This can provide you with more information and help you feel more confident about the treatment plan that you choose. Your doctor should be willing to help you find another cancer doctor who can give you a second opinion. If you have already had tests done, the results can be sent to the second doctor so that you will not have to have them done again.

The next few sections describe the various types of treatments used for non-small cell lung cancer. This is followed by a description of the most common approaches used for these cancers based on the stage of the cancer.

Surgery for non-small cell lung cancer

Surgery to remove the cancer (often along with other treatments) may be an option for early stage non-small cell lung cancer (NSCLC). If surgery can be done, it provides the best chance to cure NSCLC. Lung cancer surgery is a complex operation that can have serious consequences, so it should be done by a surgeon who has a lot of experience operating on lung cancers.

If your doctor thinks the lung cancer can be treated with surgery, pulmonary function tests will be done beforehand to see if you would still have enough healthy lung tissue

left after surgery. Other tests will check the function of your heart and other organs to be sure you're healthy enough for surgery.

Because more advanced stage lung cancers are not helped by surgery, your doctor will also want to know if the cancer has already spread to the lymph nodes between the lungs. This can be done before surgery with mediastinoscopy or with some of the other techniques described in the section "How is non-small cell lung cancer diagnosed?"

Types of lung surgery

Different operations can be used to treat (and possibly cure) non-small cell lung cancer. These operations require general anesthesia (where you are in a deep sleep) and are usually done through a surgical incision between the ribs in the side of the chest (called a *thoracotomy*).

- **Pneumonectomy:** an entire lung is removed in this surgery.
- **Lobectomy:** an entire section (lobe) of a lung is removed in this surgery.
- **Segmentectomy or wedge resection:** part of a lobe is removed in this surgery.

Another type of operation, known as a **sleeve resection**, may be used to treat some cancers in large airways in the lungs. If you think of the large airway with a tumor as similar to the sleeve of a shirt with a stain an inch or 2 above the wrist, the sleeve resection would be like cutting across the sleeve above and below the stain and sewing the cuff back onto the shortened sleeve. A surgeon may be able to do this operation instead of a pneumonectomy to preserve more lung function.

With any of these operations, nearby lymph nodes are also removed to look for possible spread of the cancer.

The type of operation your doctor recommends depends on the size and location of the tumor and on how well your lungs are functioning. People whose lungs are healthier can withstand having more lung tissue removed. Doctors often prefer to do a more extensive operation (for example, a lobectomy instead of a segmentectomy) if a person's lungs are healthy enough, as it may provide a better chance to cure the cancer.

When you wake up from surgery, you will have a tube (or tubes) coming out of your chest and attached to a special canister to allow excess fluid and air to drain out. The tube(s) will be removed once the fluid drainage and air leak subside. Generally, you will need to spend 5 to 7 days in the hospital after the surgery.

Video-assisted thoracic surgery: Some doctors now treat some early stage lung cancers near the outside of the lung with a procedure called *video-assisted thoracic surgery* (VATS), which requires smaller incisions than a thoracotomy.

During this operation, a thin, rigid tube with a tiny video camera on the end is placed through a small cut in the side of the chest to help the surgeon see inside the chest on a TV monitor. One or two other small cuts are created in the skin, and long instruments are passed through these cuts to do the same operation that would be done using an open approach (thoracotomy). One of the incisions is enlarged if a lobectomy or pneumonectomy is done to allow the specimen to be removed. Because usually only small incisions are needed, there is less pain after the surgery and a shorter hospital stay – usually 4 to 5 days.

Most experts recommend that only early stage tumors near the outside of the lung be treated this way. The cure rate after this surgery seems to be the same as with surgery done with a larger incision. But it is important that the surgeon doing this procedure is experienced, because it requires a great deal of technical skill.

Possible risks and side effects of lung surgery

Possible complications during and soon after surgery depend on the extent of the surgery and the person's health beforehand. Serious complications can include excess bleeding, wound infections, and pneumonia. While it is rare, in some cases people may not survive the surgery, which is why surgery isn't a good idea for everyone.

Surgery for lung cancer is a major operation, and recovering from the operation typically takes weeks to months. If the surgery is done through a thoracotomy, the surgeon must spread ribs to get to the lung, so the area near the incision will hurt for some time after surgery. Your activity will be limited for at least a month or two. People who have VATS instead of thoracotomy have less pain after surgery and tend to recover more quickly.

If your lungs are in good condition (other than the presence of the cancer) you can usually return to normal activities after some time if a lobe or even an entire lung has been removed. If you also have a non-cancerous lung disease such as emphysema or chronic bronchitis (which are common among heavy smokers), you may become short of breath with certain level of activity after surgery.

Surgery for lung cancers with limited spread to other organs

If the lung cancer has spread to the brain or adrenal gland and there is only one tumor, you may benefit from having the metastasis removed. This surgery should be considered only if the tumor in the lung can also be completely removed. Even then, not all lung cancer experts agree with this approach, especially if the tumor is in the adrenal gland.

For tumors in the brain, this is done by surgery through a hole in the skull (called a *craniotomy*). It should only be done if the tumor can be removed without damaging vital areas of the brain that control movement, sensation, and speech.

For more general information about surgery, please see our separate document *A Guide to Cancer Surgery*.

Radiofrequency ablation (RFA) for non-small cell lung cancer

This technique might be an option for some small lung tumors that are near the outer edge of the lungs, especially in people who can't tolerate surgery. It uses high-energy radio waves to heat the tumor. A thin, needle-like probe is placed through the skin and moved along until the end is in the tumor. Placement of the probe is guided by CT scans. Once it is in place, an electric current is passed through the probe, which heats the tumor and destroys the cancer cells.

RFA is usually done as an outpatient procedure, using local anesthesia (numbing medicine) where the probe is inserted. You may be given medicine to help you relax as well.

Major complications are uncommon, but they can include the partial collapse of a lung (which often resolves on its own) or bleeding into the lung.

Radiation therapy for non-small cell lung cancer

Radiation therapy uses high-energy rays (such as x-rays) or particles to kill cancer cells. There are 2 main types of radiation therapy – external beam radiation therapy and brachytherapy (internal radiation therapy).

External beam radiation therapy

External beam radiation therapy (EBRT) focuses radiation from outside the body on the cancer. This is the type of radiation therapy most often used to treat a primary lung cancer or its spread to other organs.

Before your treatments start, the radiation team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. Treatment is much like getting an x-ray, but the radiation dose is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer. Most often, radiation treatments to the lungs are given 5 days a week for 5 to 7 weeks, but this can vary based on the type of EBRT and the reason it's being given.

Standard (conventional) EBRT is used much less often than in the past. Newer techniques help doctors treat lung cancers more accurately while lowering the radiation exposure to nearby healthy tissues. These techniques may offer better success rates and fewer side

effects. Most doctors now recommend using these newer techniques when they are available.

Three-dimensional conformal radiation therapy (3D-CRT): 3D-CRT uses special computers to precisely map the location of the tumor(s). Radiation beams are shaped and aimed at the tumor(s) from several directions, which makes it less likely to damage normal tissues.

Intensity modulated radiation therapy (IMRT): IMRT is an advanced form of 3D therapy. It uses a computer-driven machine that moves around you as it delivers radiation. Along with shaping the beams and aiming them at the tumor from several angles, the intensity (strength) of the beams can be adjusted to limit the dose reaching the most sensitive normal tissues. This technique is used most often if tumors are near important structures such as the spinal cord. Many major hospitals and cancer centers now use IMRT.

Stereotactic body radiation therapy (SBRT): SBRT, also known as stereotactic ablative radiotherapy (SABR), is sometimes used to treat very early stage lung cancers when surgery isn't an option due to issues with a patient's health or in people who do not want surgery.

Instead of giving small doses of radiation each day for several weeks, SBRT uses very focused beams of high-dose radiation given in fewer (usually 1 to 5) treatments. Several beams are aimed at the tumor from different angles. To target the radiation precisely, you are put in a specially designed body frame for each treatment. This reduces the movement of the lung tumor during breathing. Like other forms of external radiation, the treatment itself is painless.

Early results with SBRT for smaller lung tumors have been very promising, and it seems to have a low risk of complications. It is also being studied for tumors that have spread to other parts of the body, such as the bones or liver.

Stereotactic radiosurgery (SRS): SRS is a type of stereotactic radiation therapy that is given in only one session. It can sometimes be used instead of or along with surgery for single tumors that have spread to the brain. In one version of this treatment, a machine called a Gamma Knife® focuses about 200 beams of radiation on the tumor from different angles over a few minutes to hours. Your head is kept in the same position by placing it in a rigid frame. In another version, a linear accelerator (a machine that creates radiation) that is controlled by a computer moves around your head to deliver radiation to the tumor from many different angles. These treatments can be repeated if needed.

Brachytherapy (internal radiation therapy)

In people with lung cancer, brachytherapy is sometimes used to shrink tumors in the airway to relieve symptoms. But it is used less often for lung cancer than for other cancers such as head and neck cancers.

For this type of treatment, the doctor places a small source of radioactive material (often in the form of small pellets) directly into the cancer or into the airway next to the cancer. This is usually done through a bronchoscope, but it may also be done during surgery. The radiation travels only a short distance from the source, limiting the effects on surrounding healthy tissues. The radiation source is usually removed after a short time. Less often, small radioactive "seeds" are left in place permanently, and the radiation gets weaker over several weeks.

When is radiation therapy used?

Radiation therapy might be given at different times, depending on the purpose:

- As the main treatment of lung cancer (sometimes along with chemotherapy), especially if the lung tumor cannot be removed by surgery because of its size or location, if a person's health is too poor for surgery, or if a person does not want surgery.
- After surgery (alone or along with chemotherapy) to try to kill any small deposits of cancer that surgery may have missed.
- Before surgery (usually along with chemotherapy) to try to shrink a lung tumor to make it easier to operate on.
- To relieve (palliate) symptoms of advanced lung cancer such as pain, bleeding, trouble swallowing, cough, or problems caused by spread to other organs such as the brain. For example, brachytherapy is most often used to help relieve blockage of large airways by cancer.

Possible side effects of radiation therapy

Common side effects depend on where the radiation is aimed and can include:

- Fatigue
- Nausea and vomiting
- Loss of appetite and weight loss
- Skin changes in the area being treated, which can range from mild redness to blistering and peeling
- Hair loss where the radiation enters the body

Often these go away after treatment. When radiation is given with chemotherapy, the side effects are often worse.

Radiation therapy to the chest may damage your lungs and cause a cough, problems breathing, and shortness of breath. These usually improve after treatment is over, although sometimes they may not go away completely.

Your esophagus, which is in the middle of your chest, may be exposed to radiation, which could cause a sore throat and trouble swallowing during treatment. This might make it hard to eat anything other than soft foods or liquids for a while.

Radiation therapy to large areas of the brain can sometimes cause memory loss, headaches, trouble thinking, or reduced sexual desire. Usually these symptoms are minor compared with those caused by a brain tumor, but they can reduce your quality of life. Side effects of radiation therapy to the brain usually become most serious 1 or 2 years after treatment.

For more information, please see the "Radiation Therapy" section of our website or our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Chemotherapy for non-small cell lung cancer

Chemotherapy (chemo) is treatment with anti-cancer drugs injected into a vein or taken by mouth. These drugs enter the bloodstream and go throughout the body, making this treatment useful for cancer anywhere in the body. Depending on the stage of non-small cell lung cancer (NSCLC), chemo may be used in different situations:

- Before surgery (sometimes along with radiation therapy) to try to shrink a tumor. This is known as *neoadjuvant therapy*.
- After surgery (sometimes along with radiation therapy) to try to kill any cancer cells that may have been left behind. This is known as *adjuvant therapy*.
- As the main treatment (sometimes along with radiation therapy) for more advanced cancers or for some people who aren't healthy enough for surgery.

Doctors give chemo in cycles, with a period of treatment (usually 1 to 3 days) followed by a rest period to allow the body time to recover. Some chemo drugs, though, are given every day. Chemo cycles generally last about 3 to 4 weeks. Chemo is often not recommended for patients in poor health, but advanced age by itself is not a barrier to getting chemo.

The chemo drugs most often used for NSCLC are:

- Cisplatin
- Carboplatin
- Paclitaxel (Taxol®)

- Albumin-bound paclitaxel (nab-paclitaxel, Abraxane®)
- Docetaxel (Taxotere®)
- Gemcitabine (Gemzar®)
- Vinorelbine (Navelbine®)
- Irinotecan (Camptosar®)
- Etoposide (VP-16®)
- Vinblastine
- Pemetrexed (Alimta®)

Most often, treatment for NSCLC uses a combination of 2 chemo drugs. Studies have shown that adding a third chemo drug doesn't add much benefit and is likely to cause more side effects. Single-drug chemo is sometimes used for people who might not tolerate combination chemotherapy well, such as those in poor overall health or who are elderly.

If a combination is used, it often includes cisplatin or carboplatin plus one other drug. Sometimes combinations that do not include these drugs, such as gemcitabine with vinorelbine or paclitaxel, may be used.

For people with advanced lung cancers who meet certain criteria, a targeted therapy drug such as bevacizumab (Avastin®) or cetuximab (Erbitux®) may be added to treatment as well (see "Targeted therapies for non-small cell lung cancer").

For advanced cancers, the initial chemo combination is often given for 4 to 6 cycles. Some doctors now recommend giving treatment beyond this with a single chemo or targeted drug, even in people who have had a good response to their initial chemotherapy. Some studies have found that this continuing treatment, known as *maintenance therapy*, might help keep the cancer in check and help some people live longer. For more information, see "What's new in non-small cell lung cancer research and treatment?"

If the initial chemo treatment for advanced lung cancer is no longer working, the doctor may recommend second-line treatment with a single drug such as docetaxel or pemetrexed. Again, advanced age is no barrier to receiving these drugs as long as the person is in good general health.

Possible side effects

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also

divide quickly. These cells are also likely to be affected by chemo, which can lead to certain side effects.

The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. Some common side effects include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

These side effects are usually short-term and go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting.

Some drugs can have specific side effects. For example, drugs such as cisplatin, vinorelbine, docetaxel, or paclitaxel can cause nerve damage (*peripheral neuropathy*). This can sometimes lead to symptoms (mainly in the hands and feet) such as pain, burning or tingling sensations, sensitivity to cold or heat, or weakness. In most people this goes away or gets better once treatment is stopped, but it may be long lasting in some people. For more information, see our document *Peripheral Neuropathy Caused by Chemotherapy*.

You should report any side effects you notice while getting chemotherapy to your medical team so that they can be treated promptly. In some cases, the doses of the chemo drugs may need to be reduced or treatment may need to be delayed or stopped to prevent the effects from getting worse.

For more information, please see the “Chemotherapy” section of our website, or our document *A Guide to Chemotherapy*.

Targeted therapies for non-small cell lung cancer

As researchers have learned more about the changes in lung cancer cells that help them grow, they have developed newer drugs that specifically target these changes. These targeted drugs work differently from standard chemotherapy (chemo) drugs. They sometimes work when chemo drugs don’t, and they often have different (and less severe)

side effects. At this time, they are most often used for advanced lung cancers, either along with chemo or by themselves.

Drugs that target tumor blood vessel growth (angiogenesis)

For tumors to grow, they must form new blood vessels to keep them nourished. This process is called *angiogenesis*. Some targeted drugs, called *angiogenesis inhibitors*, block this new blood vessel growth.

Bevacizumab (Avastin®) is an angiogenesis inhibitor used to treat advanced non-small cell lung cancer. It is a *monoclonal antibody* (a man-made version of a specific immune system protein) that targets vascular endothelial growth factor (VEGF), a protein that helps new blood vessels to form.

This drug is often used with chemo for a time. Then if the cancer responds, the chemo may be stopped and the bevacizumab is given by itself until the cancer starts growing again.

Ramucirumab (Cyramza®) is another angiogenesis inhibitor that can be used to treat advanced non-small cell lung cancer. VEGF has to bind to proteins called receptors to act. This drug is a monoclonal antibody that targets a certain type of receptor for VEGF. This helps stop the formation of new blood vessels.

This drug is most often given after another treatment stops working. It is often combined with chemo.

These drugs can have side effects that are different from (and may add to) those of chemotherapy. Some of these can be serious, and can include problems with bleeding as well as blood clots. Rarely, these drugs can cause a hole to form in the intestine or stomach (called a *perforation*). These drugs can also cause problems with wound healing and so need to be stopped prior to surgery.

Because of the risks of bleeding, these drugs aren't used in patients who are coughing up blood or who are on drugs considered blood thinners. The risk of serious bleeding in the lungs is higher in patients with the squamous cell type of lung cancer, which is why most current guidelines do not recommend using bevacizumab in patients with this type of lung cancer.

Drugs that target EGFR

Epidermal growth factor receptor (EGFR) is a protein found on the surface of cells. It normally helps the cells to grow and divide. Some NSCLC cells have too much EGFR, which causes them to grow faster. Drugs that target EGFR used to treat non-small cell lung cancer (NSCLC) include:

- Erlotinib (Tarceva®)

- Afatinib (Gilotrif®)
- Gefitinib (Iressa®)

These drugs block the signal from EGFR that tells cells to grow. They can be used alone (without chemo) as the first treatment for advanced NSCLCs that have certain mutations in the *EGFR* gene. These are more common in women and people who haven't smoked. Erlotinib is also used for advanced NSCLC without those mutations if chemo isn't working. All of these medicines are taken as pills.

Common side effects of these drugs include:

- Skin problems
- Diarrhea
- Mouth sores
- Loss of appetite

Skin problems can include an acne-like rash on the face and chest, which in some cases can lead to skin infections.

For more detailed information on the skin problems that can result from anti-EGFR drugs, see our document *Targeted Therapy*.

Drugs that target the ALK gene

About 5% of NSCLCs have been found to have a rearrangement in a gene called *ALK*. This change is most often seen in non-smokers (or light smokers) who have the adenocarcinoma subtype of NSCLC. The *ALK* gene rearrangement produces an abnormal ALK protein that causes the cells to grow and spread. Drugs that target ALK include:

- **Crizotinib** (Xalkori®)
- **Ceritinib** (Zykadia™)

These drugs block the abnormal ALK protein and can shrink tumors in patients whose lung cancers have the *ALK* gene change. Although they can help after chemo has stopped working, they are often used instead of chemo in people whose cancers have the *ALK* gene rearrangement.

Both of these drugs are pills. Common side effects include:

- Nausea and vomiting
- Diarrhea
- Constipation

- Fatigue
- Changes in vision

Some side effects can be severe, such as low white blood cell counts, lung inflammation, liver damage, and heart rhythm problems.

Immunotherapy for non-small cell lung cancer

Immunotherapy is the use of medicines to stimulate a patient's own immune system to recognize and destroy cancer cells more effectively. Immunotherapy can be used to treat some forms of non-small cell lung cancer (NSCLC).

Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking normal cells in the body. To do this, it uses "checkpoints" – molecules on immune cells that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. But newer drugs that target these checkpoints hold a lot of promise as cancer treatments.

Nivolumab (Opdivo) and **pembrolizumab (Keytruda)** are drugs that target PD-1, a protein on immune system cells called *T cells* that normally helps keep these cells from attacking other cells in the body. By blocking PD-1, these drugs boost the immune response against cancer cells. This can shrink some tumors or slow their growth.

These drugs can be used in people with certain types of NSCLC whose cancer starts growing again after chemotherapy or other drug treatments.

These drugs are given as an intravenous (IV) infusion every 2 or 3 weeks.

Possible side effects

Side effects of these drugs can include fatigue, cough, nausea, itching, skin rash, decreased appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often. These drugs work by basically removing the brakes on the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your health care team promptly. If serious side effects do occur, treatment may need to be stopped and you may get high doses of corticosteroids to suppress your immune system.

Palliative procedures for non-small cell lung cancer

Palliative, or supportive care, is aimed at relieving suffering and improving quality of life.

People with lung cancer often benefit from procedures aimed at helping with problems caused by the cancer. For example, people with advanced lung cancer can have problems with shortness of breath. This can be caused by a number of things, including fluid around the lung or an airway blockage. Although treating the cancer with chemotherapy may help with this over time, other treatments may be needed as well.

Treating fluid buildup in the area around the lungs

Sometimes fluid can build up in the chest outside of the lungs (called a pleural effusion). It can press on the lungs and cause trouble breathing.

Thoracentesis

This is done to drain the fluid. A doctor will numb an area in the chest, and then place a needle into the space between the lungs and the ribs and drain the fluid. This is often done using ultrasound to guide the needle into the area of fluid buildup.

Pleurodesis

A *pleurodesis* might be done to remove the fluid and keep it from coming back.

One way to do this is to make a small cut in the skin of the chest wall, and place a hollow tube (called a chest tube) into the chest to remove the fluid. Then a substance is instilled into the chest cavity through the tube that causes the linings of the lung (visceral pleura) and chest wall (parietal pleura) to become irritated. This causes the linings to stick together, sealing the space and limiting further fluid buildup. The tube is often left in for a couple of days to drain any new fluid that might collect. A number of things can be placed through the tube to irritate the linings, such as talc, the antibiotic doxycycline, or a chemotherapy drug like bleomycin.

Another way to do this is to blow talc into the space around the lungs (the pleural space) during an operation. This is done through a small incision using thoracoscopy.

Catheter placement

This is another way to control the buildup of fluid. One end of the catheter (a thin, flexible tube) is placed in the chest through a small cut in the skin, and the other end is left outside the body. This is done in a doctor’s office or hospital. Once in place, the catheter can be attached to a special bottle or other device to allow the fluid to drain out on a regular basis.

Treating fluid buildup around the heart

Lung cancer can sometimes spread to the area around the heart. This can lead to fluid buildup (a pericardial effusion) that presses on the heart so that it doesn't work well.

Pericardiocentesis

In this procedure, the fluid is drained with a needle placed into the space around the heart. This is usually done using an echocardiogram (like an ultrasound of the heart), to guide the needle.

Pericardial window

This is done to keep the fluid from building up again. In an operation, a piece of the tissue around the heart (the pericardium) is removed to allow the fluid to drain into the chest or belly.

Treating airway blockage

If the cancer is growing into an airway in the lung, it can block the airway and cause problems like pneumonia or shortness of breath. Treatments can be used to relieve the blockage in the airway.

Photodynamic therapy (PDT)

Photodynamic therapy is sometimes used to treat very early stage lung cancers that are still confined to the outer layers of the lung airways when other treatments aren't appropriate. It can also be used to help open up airways blocked by tumors to help people breathe better.

For this technique, a light-activated drug called porfimer sodium (Photofrin®) is injected into a vein. This drug is more likely to collect in cancer cells than in normal cells. After a couple of days (to give the drug time to build up in the cancer cells), a bronchoscope is passed down the throat and into the lung. This may be done with either local anesthesia (where the throat is numbed) and sedation or with general anesthesia (where you are in a deep sleep). A special laser light on the end of the bronchoscope is aimed at the tumor, which activates the drug and causes the cells to die. The dead cells are then removed a few days later during a bronchoscopy. This process can be repeated if needed.

PDT may cause swelling in the airway for a few days, which may lead to some shortness of breath, as well as coughing up blood or thick mucus. Some of this drug also collects in normal cells in the body, such as skin and eye cells. This can make you very sensitive to sunlight or strong indoor lights. Too much exposure can cause serious skin reactions (like a severe sunburn), so doctors recommend staying out of any strong light for 4 to 6 weeks after the injection.

For more information, see our document *Photodynamic Therapy*.

Laser therapy

Lasers can sometimes be used to treat very small tumors in the linings of airways. They can also be used to help open up airways blocked by larger tumors to help people breathe better.

You are usually asleep (under general anesthesia) for this type of treatment. The laser is on the end of a bronchoscope, which is passed down the throat and next to the tumor. The doctor then aims the laser beam at the tumor to burn it away. This treatment can usually be repeated, if needed.

Stent placement

Lung tumors that have grown into an airway can sometimes cause trouble breathing or other problems. To help keep the airway open (often after other treatments such as PDT or laser therapy), a hard silicone or metal tube called a *stent* may be placed in the airway using a bronchoscope.

Clinical trials for non-small cell lung cancer

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. Sometimes they might be the only way to get access to some newer treatments. They are also the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document *Clinical Trials: What You Need to Know*.

Complementary and alternative therapies for non-small cell lung cancer

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and websites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.

- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods. You can also find information in the “Complementary and Alternative Medicine” section of our website.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment choices by stage for non-small cell lung cancer

The treatment options for non-small cell lung cancer (NSCLC) are based mainly on the stage (extent) of the cancer, but other factors, such as a person’s overall health and lung function, as well as certain traits of the cancer itself, are also important.

If you smoke, one of the most important things you can do to be ready for treatment is to try to quit. Studies have shown that patients who stop smoking after a diagnosis of lung cancer tend to have better outcomes than those who don’t.

Occult cancer

For these cancers, malignant cells are seen on sputum cytology but no obvious tumor can be found with bronchoscopy or imaging tests. They are usually early stage cancers. Bronchoscopy and possibly other tests are usually repeated every few months to look for a tumor. If a tumor is found, treatment will depend on the stage.

Stage 0

Because stage 0 non-small cell lung cancer is limited to the lining layer of airways and has not invaded deeper into the lung tissue or other areas, it is usually curable by surgery alone. No chemotherapy or radiation therapy is needed.

If you are healthy enough for surgery, you can usually be treated by segmentectomy or wedge resection (removal of defined segments or small wedges of the lung). Cancers in some locations, such as where the windpipe divides into the left and right main bronchi, may be treated with a sleeve resection, but in some cases they may be hard to remove completely without removing a lobe (lobectomy) or even an entire lung (pneumonectomy).

In some cases, treatments such as photodynamic therapy (PDT), laser therapy, or brachytherapy may be alternatives to surgery for stage 0 cancers. If your cancer is truly stage 0, these treatments should cure you.

Stage I

If you have stage I non-small cell lung cancer (NSCLC), surgery may be the only treatment you need. The tumor may be removed either by taking out one lung lobe (lobectomy) or by taking out a smaller piece of a lung (sleeve resection, segmentectomy, or wedge resection). At least some lymph nodes within the lung and outside the lung in the mediastinum will be removed to check them for cancer cells.

Segmentectomy or wedge resection is recommended only for treating the smallest stage I cancers (those less than 2 cm across) and for patients with other medical conditions that make removing the entire lobe dangerous. It is not yet clear that this type of surgery is as good as removing the whole lung, even for these small tumors. This is now being studied. Until the results are known, most surgeons believe it is better to do a lobectomy if the patient can tolerate it, as it offers the best chance for cure.

For people with stage I NSCLC that has a higher risk of coming back (based on size, location, or other factors), adjuvant chemotherapy after surgery may lower the risk that cancer will return. But doctors aren't always sure how to determine which people are likely to be helped by chemo. New lab tests that look at the patterns of certain genes in the cancer cells may help with this. Studies are now under way to see if these tests are accurate. Recent studies suggest that patients whose tumors are greater than 4 cm in size might benefit from adjuvant chemotherapy.

After surgery, the tissue that is removed is checked to see if there are cancer cells at the edges of the surgery specimen. This, called *positive margins*, means that some cancer may have been left behind, and so a second surgery might be done to try to ensure that all the cancer has been removed. (This might be followed by chemotherapy as well.) Another option might be to use radiation therapy after surgery.

If you have serious medical problems that would prevent you from having surgery, you may receive stereotactic body radiation therapy (SBRT) or conventional radiation therapy as your main treatment. Radiofrequency ablation (RFA) may be another option if the tumor is small and in the outer part of the lung.

Stage II

People who have stage II non-small cell lung cancer (NSCLC) and are healthy enough for surgery usually have the cancer removed by lobectomy or sleeve resection. Sometimes removing the whole lung (pneumonectomy) is needed.

Any lymph nodes likely to have cancer in them are also removed. The extent of lymph node involvement and whether or not cancer cells are found at the edges of the removed tissues are important factors when planning the next step of treatment.

In some cases, chemotherapy (often along with radiation) may be recommend before surgery to try to shrink the tumor to make the operation easier.

After surgery, the tissue that is removed is checked to see if there are cancer cells at the edges of the surgery specimen. This, called *positive margins*, means that some cancer may have been left behind. This is often treated with additional surgery to remove any cancer that may have been left behind. This may be combined with chemotherapy (chemo). Another option is to treat with radiation, sometimes along with chemo.

Even if positive margins are not found, chemo is usually recommended to try to destroy any cancer cells that might have been left behind but are too small to see. As with stage I cancers, newer lab tests now being studied may help doctors find out which patients need this adjuvant treatment and which are less likely to benefit from it.

If you have serious medical problems that would prevent you from having surgery, you may receive only radiation therapy as your main treatment.

Stage IIIA

Treatment for stage IIIA non-small cell lung cancer (NSCLC) may include radiation therapy, chemotherapy (chemo), surgery, or some combination of these. For this reason, planning treatment for stage IIIA NSCLC will often require input from a medical oncologist, radiation oncologist, and a thoracic surgeon. Treatment options will depend on the size of the tumor, where it is located in your lung, which lymph nodes it has spread to, your overall health, and how well you are tolerating treatment.

For patients who can tolerate it, treatment usually starts with chemo, sometimes combined with radiation therapy. Surgery may be an option after this if the doctor thinks any remaining cancer can be removed and the patient is healthy enough. (In some cases, surgery may be an option as the first treatment.) This is often followed by chemo, and possibly radiation therapy if it hasn’t been given before.

For people who can’t tolerate surgery, radiation therapy, which may be combined with chemo, is often used.

Stage IIIB

Stage IIIB non-small cell lung cancer (NSCLC) has spread to lymph nodes that are near the other lung or in the neck, and may also have grown into important structures in the chest. These cancers cannot be completely removed by surgery. As with other stages of lung cancer, treatment depends on the patient’s overall health and how well they are expected to tolerate treatments. If you are in fairly good health you may be helped by

chemotherapy (chemo) combined with radiation therapy. Some people can even be cured with this treatment. Patients who cannot tolerate this combination are often treated with radiation therapy alone, or, less often, chemo alone.

These cancers can be hard to treat, so taking part in a clinical trial of newer treatments may be a good option for some people.

Stage IV

Stage IV non-small cell lung cancer (NSCLC) is widespread when it is diagnosed. Because these cancers have spread to distant sites, they are very hard to cure. Treatment options depend on where the cancer has spread, the number of tumors, and your overall health. If you are in otherwise good health, treatments such as surgery, chemotherapy (chemo), targeted therapy, and radiation therapy may help you live longer and make you feel better by relieving symptoms, even though they aren't likely to cure you. Other treatments, such as photodynamic therapy (PDT) or laser therapy, may also be used to help relieve symptoms. In any case, if you are going to be treated for advanced NSCLC, be sure you understand the goals of treatment before you start.

Cancer that is limited in the lungs and has only spread to one other site (such as the brain) is not common, but it can sometimes be treated (and even potentially cured) with surgery and/or radiation therapy to treat the area of cancer spread, followed by treatment of the cancer in the lung. For example, a single tumor in the brain may be treated with surgery or stereotactic radiation, followed by radiation to the whole brain. Treatment for the lung tumor is then based on its T and N stages, and may include surgery, chemo, radiation, or some of these in combination.

Cancer that has spread widely throughout the body is usually treated with chemo, as long as the person is healthy enough for it. For people who are not at high risk for bleeding (that is, they do not have squamous cell NSCLC and have not coughed up blood), the targeted drug bevacizumab (Avastin) might be given with chemo. Some people with squamous cell cancer might still be given bevacizumab, as long as the tumor is not near large blood vessels in the center of the chest. If bevacizumab is used, it is often continued even after chemo is finished.

Other targeted drugs may also be useful in some situations. For tumors that have the *ALK* gene change, crizotinib (Xalkori) is often the first treatment. Ceritinib (Zykadia) can be used if crizotinib stops working or is not tolerated well.

For people whose cancers have certain changes in the *EGFR* gene, the anti-EGFR drugs erlotinib (Tarceva), gefitinib (Iressa), or afatinib (Gilotrif) may be used without chemotherapy as the first treatment.

If the cancer has caused fluid buildup in the space around the lungs (a malignant pleural effusion), the fluid may be drained. If it keeps coming back, options include pleurodesis

or placement of a catheter into the chest through the skin to let the fluid drain out (details of these were discussed in “Surgery to relieve symptoms” in the section about surgery).

As with other stages, treatment for stage IV lung cancer depends on a person’s overall health. For example, some people not in good health might get only 1 chemo drug instead of 2. For people who can’t have chemo, radiation therapy is usually the treatment of choice. Local treatments such as laser therapy, PDT, or stent placement may also be used to help relieve symptoms caused by lung tumors.

Because treatment is unlikely to cure these cancers, taking part in a clinical trial of newer treatments may be a good option.

You can also find more information about living with stage IV cancer in our document *Advanced Cancer*.

Cancer that progresses or recurs after treatment

If cancer continues to grow during treatment (progresses) or comes back (recurs), further treatment will depend on the location and extent of the cancer, what treatments have been used, and on the person’s health and desire for further treatment. It is important to understand the goal of any further treatment – if it is to try to cure the cancer, to slow its growth, or to help relieve symptoms – as well as the likelihood of benefits and risks.

If cancer continues to grow during initial treatment such as radiation therapy, chemotherapy (chemo) may be tried. If a cancer continues to grow during chemo as the first treatment, second line treatment most often consists of a single chemo drug such as docetaxel or pemetrexed, the targeted therapy erlotinib (Tarceva), or chemo plus a targeted drug like ramucirumab (Cyramza). If a targeted drug was the first treatment and is no longer working, another targeted drug or combination chemo might be tried. For some people with certain types of NSCLC, treatment with an immunotherapy drug such as nivolumab (Opdivo) or pembrolizumab (Keytruda) might be an option.

Smaller cancers that recur locally in the lungs can sometimes be retreated with surgery or radiation therapy (if it hasn’t been used before). Cancers that recur in the lymph nodes between the lungs are usually treated with chemo, possibly along with radiation if it hasn’t been used before. For cancers that return at distant sites, chemo and/or targeted therapies are often the treatments of choice.

Should your cancer come back, our document *When Your Cancer Comes Back: Cancer Recurrence* can give you information on how to manage and cope with this phase of your treatment.

In some people, the cancer may never go away completely. These people may get regular treatments with chemo, radiation therapy, or other therapies to try to help keep the cancer in check. Learning to live with cancer that does not go away can be difficult and very

stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away*, talks more about this.

If treatment is no longer working

At some point, it may become clear that standard treatments are no longer controlling the cancer. If you want to continue anti-cancer treatment, you might think about taking part in a clinical trial of newer lung cancer treatments. While these are not always the best option for every person, they may benefit you as well as future patients.

Even if your cancer can't be cured, you can be as free of symptoms as possible. If curative treatment is not an option, treatment aimed at specific areas of cancer can often relieve symptoms and may even slow the spread of the disease. Symptoms such as shortness of breath or coughing up blood caused by cancer in the lung airways can often be treated effectively with radiation therapy, brachytherapy, laser therapy, PDT, stent placement, or even surgery if needed. Radiation therapy can be used to help control cancer spread in the brain or relieve pain in a specific area if cancer has spread.

Many people with lung cancer are concerned about pain. If the cancer grows near certain nerves it can sometimes cause pain, but this can almost always be treated effectively with pain medicines. Sometimes radiation therapy or other treatments will help as well. It is important that you talk to your doctor and take advantage of these treatments.

Deciding on the right time to stop treatment aimed at curing the cancer and focus on care that relieves symptoms is never easy. Good communication with doctors, nurses, family, friends, and clergy can often help people facing this situation.

For more information, please see "What happens if non-small cell lung cancer treatment is no longer working?"

More treatment information about non-small cell lung cancer

For more details on treatment options – including some that may not be addressed in this document – the National Cancer Institute (NCI) and the National Comprehensive Cancer Network (NCCN) are good sources of information.

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its website (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. These are available on the NCCN website (www.nccn.org). The NCCN also has a patient version of the treatment guidelines for non-small cell lung cancer, available at www.nccn.com.

What should you ask your doctor about non-small cell lung cancer?

It is important for you to have honest, open discussions with your cancer care team. You should feel free to ask any question, no matter how small it might seem. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions. Here are some questions you might want to ask:

- What kind of lung cancer do I have?
- Where exactly is the cancer? Has it spread beyond where it started?
- What is the stage of my cancer, and what does that mean in my case?
- Are there other tests that need to be done before we can decide on treatment? Have the cancer cells been checked for gene changes that could affect my treatment options?
- Are there other doctors I need to see?
- How much experience do you have treating this type of cancer?
- What treatment choices do I have?
- What do you recommend and why?
- What is the goal of the treatment?
- What are the chances my cancer can be cured with these options?
- What risks or side effects are there to the treatments you suggest? How long are they likely to last?
- How quickly do we need to decide on treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect my daily activities?
- What would we do if the treatment doesn’t work or if the cancer comes back?
- What type of follow-up will I need after treatment?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so you can plan your work or activity schedule. Or you may want to ask about getting a second opinion or

about clinical trials for which you may qualify. You can find more information about communicating with your health care team in our document *Talking With Your Doctor*.

What happens after treatment for non-small cell lung cancer?

For some people with lung cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer growing or coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are living full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this.

For some other people, the lung cancer may never go away completely. These people may get regular treatments with chemotherapy, radiation therapy, or other therapies to help keep the cancer in check. Learning to live with cancer as a more of a chronic disease can be difficult and very stressful. It has its own type of uncertainty. Our document called *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

If you have completed treatment, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask about any problems you may have and may do exams and lab tests or imaging tests (such as x-rays or CT scans).

In people with no signs of cancer remaining, many doctors recommend follow-up visits and CT scans about every 6 to 12 months for the first 2 years after treatment, and yearly visits and CT scans after this, although doctor visits might be more frequent at first.

Follow-up is needed to look for signs of cancer recurrence or spread, as well as possible side effects of certain treatments. This is a good time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

Almost any cancer treatment can have side effects. Some may last for a few weeks to several months, but others can last the rest of your life. Be sure to tell your cancer care team about any symptoms or side effects that bother you so they can help you manage them.

It is important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

If cancer does recur, treatment will depend on where the cancer is and what treatments you've had before. Surgery, radiation therapy, chemotherapy, targeted therapy, or some combination of these might be options. Other types of treatment might also be used to help relieve any symptoms from the cancer. For more on how recurrent cancer is treated, see the section "Treatment choices by stage for non-small cell lung cancer." For more general information on dealing with a recurrence, you may also want to see our document *When Your Cancer Comes Back: Cancer Recurrence*.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you stayed in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had radiation therapy, a copy of the treatment summary
- If you had chemotherapy or targeted therapies, a list of the drugs, drug doses, and when you took them
- Copies of your x-rays, CT scans, and other imaging tests (these can often be stored digitally on a DVD, etc.)

Can I get another cancer after having non-small cell lung cancer?

Cancer survivors can be affected by a number of health problems, but often their greatest concern is facing cancer again. If a cancer comes back after treatment it is called a "recurrence." But some cancer survivors may develop a new, unrelated cancer later. This is called a "second cancer." No matter what type of cancer you have had, it is still possible to get another (new) cancer, even after surviving the first.

Unfortunately, being treated for cancer doesn't mean you can't get another cancer. People who have had cancer can still get the same types of cancers that other people get. In fact,

certain types of cancer and cancer treatments can be linked to a higher risk of certain second cancers.

Survivors of non-small cell lung cancer can get any type of second cancer, but they have an increased risk of:

- A second lung cancer (this is different than the first cancer coming back)
- Cancer of the larynx (voice box)
- Cancer of the mouth and throat
- Esophagus cancer
- Stomach cancer
- Small intestine cancer
- Colon cancer
- Rectal cancer
- Pancreas cancer
- Bladder cancer
- Cancer of the kidney and renal pelvis
- Thyroid cancer
- Acute myeloid leukemia (AML)

Lung cancer is the most common second cancer in someone with a previous lung cancer. Smoking is a risk factor for many of these cancers, and the risks of a second cancer are especially high among lung cancer survivors who continue to smoke cigarettes. The risk of cancer of the esophagus is higher among patients treated with radiation therapy to the chest.

Follow-up after treatment

After completing treatment for lung cancer, you should still see your doctor regularly. You may have tests to look for signs the cancer has come back or spread. These tests can also help find second lung cancers. Let your doctor know about any new symptoms or problems, because they could be caused by the cancer coming back or by a new disease or second cancer. Experts do not recommend any additional testing to look for second cancers in patients without symptoms.

Survivors of lung cancer should follow the American Cancer Society guidelines for the early detection of cancer and stay away from tobacco products. Smoking increases the

risk of dying from lung cancer, as well as the risk of many of the second cancers seen after lung cancer.

To help maintain good health, survivors should also:

- Achieve and maintain a healthy weight
- Adopt a physically active lifestyle
- Consume a healthy diet, with an emphasis on plant foods
- Limit consumption of alcohol to no more than 1 drink per day for women or 2 per day for men

These steps may also lower the risk of some cancers.

See *Second Cancers in Adults* for more information about causes of second cancers.

Lifestyle changes after non-small cell lung cancer

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Make healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you smoke, one of the most important things you can do to improve your chances for treatment success is to quit. Studies have shown that patients who stop smoking after a diagnosis of lung cancer have better outcomes than those who don't. If you are thinking about quitting smoking and need help, call the American Cancer Society at 1-800-227-2345.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may

not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for some other cancers, as well as having many other health benefits. Get more information in our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a bone-weary exhaustion that often doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on fatigue and other side effects, please see the "Physical Side Effects" section of our website or "Additional resources for non-small cell lung cancer" to get a list of available information.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

Can I lower my risk of the cancer progressing or coming back?

Most people want to know if there are specific lifestyle changes they can make to reduce their risk of cancer progressing or coming back. Unfortunately, for most cancers there is little solid evidence to guide people. This doesn't mean that nothing will help – it's just that for the most part this is an area that hasn't been well studied. Most studies have looked at lifestyle changes as ways of preventing cancer in the first place, not slowing it down or preventing it from coming back.

However, there are some things people can do that might help them live longer or reduce the risk of lung cancer returning.

Quitting smoking: If you smoke, quitting is important. Quitting has been shown to help people with lung cancer live longer, even when the cancer has spread. It also lowers the chance of getting another lung cancer, which is especially important for people with early stage lung cancer.

Of course, quitting smoking may have other health benefits as well, including lowering the risk of some other cancers. If you need help quitting, talk to your doctor or call the American Cancer Society at 1-800-227-2345.

Diet and nutrition: The possible link between diet and lung cancer growing or coming back is much less clear. Some studies have suggested that diets high in fruits and vegetables might help prevent lung cancer from developing in the first place, but this has not been studied in people who already have lung cancer.

Some early studies have suggested that people with early stage lung cancer who have higher vitamin D levels might have better outcomes, but so far no study has shown that taking extra vitamin D (as a supplement) helps. On the other hand, studies have found that beta carotene supplements may actually increase the risk of lung cancer in smokers.

Because of the lack of data in this area, it's important to talk with your health care team before making any major changes to your diet (including taking any supplements) to try to improve your outlook.

How might having non-small cell lung cancer affect your emotional health?

During and after treatment, you may find yourself overcome with many different emotions. This happens to a lot of people.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationships with those around you. Unexpected issues may also cause concern. For instance, you might see your health care team less often after treatment and have more time on your hands. These changes can make some people anxious.

Almost everyone who is going through or has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People with Cancer* or see the "Emotional Side Effects" section of our website for more information.

What happens if non-small cell lung cancer treatment is no longer working?

If cancer keeps growing or comes back after one kind of treatment, it is often possible to try another treatment plan that might still help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides, including treatment side effects. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer – when you have been through many treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more treatment might have about a 1 in 100 chance of working. Some people are still tempted to try this. But it is important to have realistic expectations if you do choose this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose – the main goal of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using medicines to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer. You can learn more about the physical and emotional changes, as well as plans and preparations for yourself and your family, in our document *Nearing the End of Life*.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends – times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

What’s new in non-small cell lung cancer research and treatment?

Research into the prevention, early detection, and treatment of lung cancer is being done in many medical centers throughout the world.

Prevention

Tobacco

Prevention offers the greatest opportunity to fight lung cancer. Although decades have passed since the link between smoking and lung cancers became clear, smoking is still responsible for at least 80% of lung cancer deaths. Research is continuing on:

- Ways to help people quit smoking and stay quit through counseling, nicotine replacement, and other medicines
- Ways to convince young people to never start smoking
- Inherited differences in genes that may make some people much more likely to get lung cancer if they smoke or are exposed to someone else’s smoke

Environmental causes

Researchers also continue to look into some of the other causes of lung cancer, such as exposure to radon and diesel exhaust. Finding new ways to limit these exposures could potentially save many more lives.

Diet, nutrition, and medicines

Researchers are looking for ways to use vitamins or medicines to prevent lung cancer in people at high risk, but so far none have been shown to conclusively reduce risk.

Some studies have suggested that a diet high in fruits and vegetables may offer some protection, but more research is needed to confirm this. While any protective effect of fruits and vegetables on lung cancer risk is likely to be much less than the increased risk from smoking, following the American Cancer Society dietary recommendations (such as maintaining a healthy weight and eating a diet high in fruits and vegetables, and whole grains) may still be helpful.

Early detection

As mentioned in the section “Can non-small cell lung cancer be found early?”, a large clinical trial called the National Lung Screening Trial (NLST) recently found that spiral CT scans in people at high risk of lung cancer (due to smoking history) lowers the risk of death from lung cancer, when compared to chest x-rays. This finding has led to the development of screening guidelines for lung cancer.

Another approach now being studied uses newer, more sensitive tests to look for cancer cells in sputum samples. Researchers have found several changes often seen in the DNA of lung cancer cells. Current studies are looking at new tests that can spot these DNA changes to see if this approach is useful in finding lung cancers at an earlier stage.

Diagnosis

Fluorescence bronchoscopy

Also known as *autofluorescence bronchoscopy*, this technique may help doctors find some lung cancers earlier, when they may be easier to treat. For this test, the doctor inserts a bronchoscope through the mouth or nose and into the lungs. The end of the bronchoscope has a special fluorescent light on it, instead of a normal (white) light.

The fluorescent light causes abnormal areas in the airways to show up in a different color than healthy parts of the airway. Some of these areas might not be visible under white light, so the color difference may help doctors find these areas sooner. Some cancer centers now use this technique to look for early lung cancers, especially if there are no obvious tumors seen with normal bronchoscopy.

Virtual bronchoscopy

This imaging test uses CT scans to create detailed 3-dimensional pictures of the airways in the lungs. The images can be viewed as if the doctor were actually using a bronchoscope.

Virtual bronchoscopy has some possible advantages over standard bronchoscopy. First, it is non-invasive and doesn’t require anesthesia. It also helps doctors view some airways that might not be seen with standard bronchoscopy, such as those being blocked by a tumor. But it has some drawbacks as well. For example, it doesn’t show color changes in the airways that might indicate a problem. It also doesn’t let a doctor take samples of suspicious areas like bronchoscopy does. Still, it can be a useful tool in some situations, such as in people who might be too sick to get a standard bronchoscopy.

This test will likely become more available as the technology improves.

Electromagnetic navigation bronchoscopy

Lung tumors near the center of the chest can be biopsied during bronchoscopy, but bronchoscopes have trouble reaching the outer parts of the lungs, so tumors in that part of the lung often need to have a needle biopsy. This test can be a way to use a bronchoscope to biopsy a tumor in the outer part of the lung.

First, CT scans are used to create a virtual bronchoscopy. The abnormal area is identified, and a computer helps guide a bronchoscope to the area so that it can be biopsied. The bronchoscope used has some special attachments that allow it to reach further than a regular bronchoscope.

This takes extra equipment and training for the doctor, and is not widely available.

Treatment

Surgery

Doctors now use video-assisted thoracic surgery (VATS) to treat some small lung tumors. It lets doctors remove parts of the lung through smaller incisions, which can result in shorter hospital stays and less pain for patients. Doctors are now studying whether it can be used for larger lung tumors.

In a newer approach to this type of operation, the doctor sits at a specially designed control panel inside the operating room to maneuver long surgical instruments using robotic arms. This approach, known as *robotic-assisted surgery*, is now being tested in some larger cancer centers.

Real-time tumor imaging

Researchers are looking to use new imaging techniques, such as four-dimensional computed tomography (4DCT), to help improve treatment. In this technique, the CT machine scans the chest continuously for about 30 seconds. It shows where the tumor is in relation to other structures as a person breathes, as opposed to just giving a ‘snapshot’ of a point in time, like a standard CT does.

4DCT can be used to determine exactly where the tumor is during each part of the breathing cycle, which can help doctors deliver radiation to a tumor more precisely. This technique might also be used to help show if a tumor is attached to or invading important structures in the chest, which could help doctors determine if a patient might be eligible for surgery.

Chemotherapy

New combinations: Many clinical trials are looking at newer combinations of chemotherapy drugs to determine which are the safest and most effective. This is especially important in patients who are older and have other health problems. Doctors are also studying better ways to combine chemotherapy with radiation therapy and other treatments.

Lab tests to help predict if chemo will be helpful: Doctors know that adjuvant chemotherapy after surgery may be more helpful for some people with early (stage I or II) cancers than for others, but figuring out which patients to give it to is not easy. In early studies, newer lab tests that look at patterns of certain genes in the cancer cells have shown promise in telling which people might benefit most. Larger studies of these tests are now trying to confirm their usefulness.

Other lab tests may help predict whether a lung cancer will respond to particular chemo drugs. For example, studies have found that tumors with high levels of the ERCC1 protein are less likely to respond to chemo that includes cisplatin or carboplatin, while tumors with high levels of the RRM1 protein seem less likely to respond to chemo with gemcitabine. Doctors are now looking to see if tests for these markers can help guide the choice of treatment, so these are not a part of standard treatment.

Maintenance chemotherapy: For people with advanced lung cancers who can tolerate chemotherapy, combinations of 2 chemo drugs (sometimes along with a targeted drug) are typically given for about 4 to 6 cycles. Some recent studies have found that with cancers that have not progressed, continuing treatment beyond the 4 to 6 cycles with a single chemo drug such as pemetrexed or a targeted drug such as erlotinib may help some people live longer. This is known as *maintenance therapy*. A possible downside to this continued treatment is that people may not get a break from having side effects from chemotherapy. Some doctors now recommend maintenance therapy, while others await further research on this topic.

Targeted therapies

Researchers are learning more about the inner workings of lung cancer cells that control their growth and spread. This is being used to develop new targeted therapies. Some of these treatments, such as bevacizumab (Avastin), erlotinib (Tarceva), cetuximab (Erbitux), and crizotinib (Xalkori) are already being used to treat non-small cell lung cancer. Others are now being tested in clinical trials to see if they can help people with advanced lung cancer live longer or relieve their symptoms.

Other targeted drugs being studied include ganetespib, custirsen, and dacomitinib. Some targeted drugs already approved for use against other types of cancer, such as sorafenib (Nexavar) and sunitinib (Sutent), are also being tested for use against NSCLC.

Researchers are also working on lab tests to help predict which patients might be helped by which drugs. Studies have found that some patients do not benefit from certain targeted therapies, whereas others are more likely to have their tumors shrink. For example, a test can find changes in the *EGFR* gene that make it much more likely that a person's lung cancer will respond to treatment with erlotinib (Tarceva), an EGFR inhibitor. Similar gene tests for other treatments are now being studied. Predicting who might benefit could save some people from trying treatments that are unlikely to work for them and would probably cause unneeded side effects.

Immune treatments

Researchers are hoping to develop drugs that can help the body's immune system fight the cancer.

Drugs that block PD-1 and PD-L1: Cancer cells may use natural pathways in the body to help avoid detection and destruction by the immune system. For example, they often have a protein called PD-L1 on their surface that helps them evade the immune system. New drugs that block the PD-L1 protein, or the corresponding PD-1 protein on immune cells called T cells, can help the immune system recognize the cancer cells and attack them.

Nivolumab (Opdivo) and pembrolizumab (Keytruda) are anti-PD-1 drugs that have been shown to shrink or slow the growth of some tumors. They are now approved for use in advanced NSCLC, and are typically used after certain other treatments have been tried.

Other, similar drugs such as atezolizumab (MPDL3280A) and MEDI4736 might also shrink some lung cancer tumors. Larger studies of these new drugs are now being done.

Vaccines: Several types of vaccines for boosting the body's immune response against lung cancer cells are being tested in clinical trials. Unlike vaccines against infections like measles or mumps, these vaccines are designed to help treat, not prevent, lung cancer. These types of treatments seem to have very limited side effects, so they might be useful in people who can't tolerate other treatments.

Some vaccines are made up of lung cancer cells that have been grown in the lab, or even of cell components, such as parts of proteins commonly found on cancer cells. For example, the MUC1 protein is found on some lung cancer cells. A vaccine called TG4010 causes the immune system to react against that protein. A recent study compared combining the vaccine with chemotherapy to treatment with the same chemotherapy alone in patients with advanced lung cancer. The cancers in the group that got the vaccine were more likely to shrink or stop growing than the cancers in the group that just got chemo. More studies are planned to see if the vaccine will actually help patients live longer.

L-BLP25 (tecemotide) is another vaccine that targets the MUC1 protein. It is made up of the protein (MUC1) encased in a fat droplet (liposome) to try to make it more effective.

A small study of patients with advanced NSCLC suggested it might improve survival time, although recent results from a larger study did not find it helped people live longer. This vaccine is now being studied for patients with stage III disease after treatment with chemotherapy and radiation, in efforts to improve the cure rate.

At this time, vaccines are only available in clinical trials.

Additional resources for non-small cell lung cancer

More information from your American Cancer Society

The following related information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

Living with cancer

After Diagnosis: A Guide for Patients and Families (also in Spanish)

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also in Spanish)

Guide to Controlling Cancer Pain (also in Spanish)

Distress in People With Cancer

Living With Uncertainty: The Fear of Cancer Recurrence

When Your Cancer Comes Back: Cancer Recurrence

Advanced Cancer

Understanding cancer treatments

A Guide to Cancer Surgery (also in Spanish)

A Guide to Chemotherapy (also in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Families (also in Spanish)

Lasers in Cancer Treatment

Photodynamic Therapy

Cancer treatment side effects

Nausea and Vomiting

Anemia in People With Cancer

Fatigue in People With Cancer

Peripheral Neuropathy Caused by Chemotherapy

Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

What It Takes to Be a Caregiver

Helping Children When a Family Member Has Cancer: Dealing With Diagnosis (also in Spanish)

Work, insurance, and finances

Health Insurance and Financial Assistance for the Cancer Patient

Returning to Work After Cancer Treatment

Working During Cancer Treatment

Carcinogens and lung cancer

Asbestos

Diesel Exhaust

Radon

Questions About Smoking, Tobacco, and Health (also in Spanish)

Guide to Quitting Smoking (also in Spanish)

When treatment isn’t working

Nearing the End of Life

Hospice Care

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and websites*

In addition to the American Cancer Society, other sources of patient information and support include:

American Lung Association
Toll-free number: 1-800-586-4872 (1-800-LUNGUSA)
Website: www.lungusa.org

> Offers information on lung cancer and coping with breathing problems, side effects, and physical activity

Lungcancer.org
Toll-free number: 1-800-813-4673 (1-800-813-HOPE)
Website: www.lungcancer.org

> Provides information, support, and other assistance to people with lung cancer. Also offers phone counseling and phone support groups for people with lung cancer, with online support for caregivers

Lung Cancer Alliance
Toll-free number: 1-800-298-2436
Website: www.lungcanceralliance.org

> Offers lung cancer treatment information, including a lung cancer information line, as well as a phone buddy program, referrals to support groups, and more

National Cancer Institute
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
Website: www.cancer.gov

> Provides information on all types of cancer, living with cancer, support information for families of people with cancer, research, and more

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

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

References: Non-small cell lung cancer detailed guide

Alberg AJ, Brock MV, Stuart JM. Epidemiology of lung cancer: Looking to the future. *J Clin Oncol*. 2005;23:3175–3185.

American Cancer Society. *Cancer Facts & Figures 2015*. Atlanta, Ga: American Cancer Society; 2015.

American Cancer Society. *Cancer Treatment & Survivorship Facts & Figures 2014/2015*. Atlanta, Ga: American Cancer Society; 2015.

American Cancer Society. *Cancer Facts & Figures for African Americans 2013-2014*. Atlanta, Ga: American Cancer Society; 2013.

American Joint Committee on Cancer. Lung. *AJCC Cancer Staging Manual*. 7th ed. New York: Springer. 2010:253–266.

Amos CI, Pinney SM, Li Y, et al. A susceptibility locus on chromosome 6q greatly increases lung cancer risk among light and never smokers. *Cancer Res*. 2010;70:2359–2367.

Berthiller J, Straif K, Boniol M, Voirin N, Benhaïm-Luzon V, Ayoub WB, Dari I, Laouamri S, Hamdi-Cherif M, Bartal M, Ayed FB, Sasco AJ. Cannabis smoking and risk of lung cancer in men: a pooled analysis of three studies in Maghreb. *J Thorac Oncol*. 2008 Dec;3(12):1398-403.

Brahmer JR, Tykodi SS, Chow LQ, et al. Safety and activity of anti-PD-L1 antibody in patients with advanced cancer. *N Engl J Med*. 2012;366:2455–2465.

Butts C, Maksymiuk A, Goss G, et al. Updated survival analysis in patients with stage IIIB or IV non-small-cell lung cancer receiving BLP25 liposome vaccine (L-BLP25): phase IIB randomized, multicenter, open-label trial. *J Cancer Res Clin Oncol*. 2011;137:1337–1342.

Caporaso N, Dodd KW, Tucker MA. New Malignancies Following Cancer of the Respiratory 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 on 4/18/2014 at http://seer.cancer.gov/archive/publications/mpmono/MPMonograph_complete.pdf.

Ciuleanu T, Brodowicz T, Zielinski C, et al. Maintenance pemetrexed plus best supportive care versus placebo plus best supportive care for non-small-cell lung cancer: A randomised, double-blind, phase 3 study. *Lancet*. 2009;374:1432−1440.

Cohen AJ, Ross Anderson H, Ostro B, et al. The global burden of disease due to outdoor air pollution. *J Toxicol Environ Health A*. 2005;68:1301–1307.

Groome PA, Bolejack V, Crowley JJ, et al. The IASLC Lung Cancer Staging Project: Validation of the proposals for revision of the T, N, and M descriptors and consequent stage groupings in the forthcoming (seventh) edition of the TNM classification of malignant tumours. *J Thorac Oncol*. 2007;2:694–705.

Hashibe M, Morgenstern H, Cui Y, Tashkin DP, Zhang ZF, Cozen W, Mack TM, Greenland S. Marijuana use and the risk of lung and upper aerodigestive tract cancers:

results of a population-based case-control study. *Cancer Epidemiol Biomarkers Prev*. 2006 Oct;15(10):1829-34.

Horn L, Eisenberg R, Gius D, et al. Cancer of the lung: non-small cell lung cancer and small cell lung cancer. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa: Elsevier; 2014:1143–1192.

Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/, based on November 2013 SEER data submission, posted to the SEER web site, April 2014.

Kaufman EL, Jacobson JS, Hershman DL, et al. Effect of breast cancer radiotherapy and cigarette smoking on risk of second primary lung cancer. *J Clin Oncol*. 2008;26:392–398.

Kwak EL, Bang Y, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non-small cell lung cancer. *New Engl J Med*. 2010;363:1693–1703.

Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV, Gapstur S, Patel AV, Andrews K, Gansler T; American Cancer Society 2010 Nutrition and Physical Activity Guidelines Advisory Committee. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 2012 Jan-Feb;62(1):30-67.

Leong S, Ju H, Marshall H, Bowman R, Yang I, Ree AM, Saxon C, Fong KM. Electromagnetic navigation bronchoscopy: A descriptive analysis. *J Thorac Dis*. 2012 Apr 1;4(2):173-85.

Moir D, Rickert WS, Levasseur G, Larose Y, Maertens R, White P, Desjardins S. A Comparison of Mainstream and Sidestream Marijuana and Tobacco Cigarette Smoke Produced under Two Machine Smoking Conditions. *Chem Res Toxicol*. 2008; 21 : 494-502.

National Cancer Institute. Physician Data Query (PDQ). Non-Small Cell Lung Cancer Treatment. 2/21/2014. Accessed at www.cancer.gov/cancertopics/pdq/treatment/non-small-cell-lung/healthprofessional on July 9, 2014.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. V.4.2014. Accessed at www.nccn.org/professionals/physician_gls/PDF/nscl.pdf on July 9, 2014.

National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011;365:395–409.

Obedian E, Fischer DB, Haffty BG. Second malignancies after treatment of early-stage breast cancer: Lumpectomy and radiation therapy versus mastectomy. *J Clin Oncol*. 2000;18:2406–2412.

Omenn GS, Goodman GE, Thornquist et al. Risk factors for lung cancer and for intervention effects in CARET, the Beta-Carotene and Retinol Efficacy Trial. *J Natl Cancer Inst*. 1996 Nov 6;88(21):1550-9.

Parsons A, Daley A, Begh R, Aveyard P. Influence of smoking cessation after diagnosis of early stage lung cancer on prognosis: Systematic review of observational studies with meta-analysis. *BMJ*. 2010;340:b5569.

Pinsky PF, Church TR, Izmirlian G, Kramer BS. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. *Cancer*. 2013 Nov 15;119(22):3976-83. Epub 2013 Aug 26.

Posther KE, Harpole DH. The surgical management of lung cancer. *Cancer Investigation*. 2006;24:56–67.

Pletcher MJ, Vittinghoff E, Kalhan R, et al. Association between marijuana exposure and pulmonary function over 20 years. *JAMA*. 2012;307:173–181.

Quoix E, Ramlau R, Westeel V, et al. Therapeutic vaccination with TG4010 and first-line chemotherapy in advanced non-small-cell lung cancer: A controlled phase 2B trial. *Lancet Oncol*. 2011;12:1125–1133.

Schottenfeld D. The etiology and epidemiology of lung cancer. In: Pass HI, Carbone DP, Johnson DH, Minna JD, Scagliotti GV, Turrisi AT, eds. *Principles and Practice of Lung Cancer*. 4th ed. Philadelphia, Pa: Lippincott Williams & Wilkins. 2010:3–22.

Schrump DS, Carter D, Kelsey CR, Marks LB, Giaccone G. Non-small cell lung cancer. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 9th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2011:799–847.

Sequist LV, Yang JC, Yamamoto N, et al. Phase III Study of Afatinib or Cisplatin Plus Pemetrexed in Patients With Metastatic Lung Adenocarcinoma With EGFR Mutations. *J Clin Oncol*. 2013 Sep 20;31(27):3327-34. Epub 2013 Jul 1.

The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. *N Engl J Med*. 1994 Apr 14;330(15):1029-35.Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. *N Engl J Med*. 2012;366:2443–2454.

Travis WD, Brambilla E, Noguchi M, et al. International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society international

multidisciplinary classification of lung adenocarcinoma. *J Thorac Oncol*. 2011;6:244–285.

US Department of Health and Human Services. The Health Consequences of Smoking – 50 Years of Progress. A Report of the Surgeon General. 2014. Accessed at http://www.surgeongeneral.gov/library/reports/50-years-of-progress/full-report.pdf on July 9, 2014.

Wender R, Fontham E, Barrera E, et al. American Cancer Society lung cancer screening guidelines. *CA Cancer J Clin*. 2013;63:106–117.

Wozniak AJ, Gadgeel SM. Clinical presentation of non-small cell carcinoma of the lung. In: Pass HI, Carbone DP, Johnson DH, Minna JD, Scagliotti GV, Turrisi AT, eds. *Principles and Practice of Lung Cancer*. 4th ed. Philadelphia, Pa: Lippincott Williams & Wilkins. 2010:327–340.

Zhou W, Heist RS, Liu G, et al. Circulating 25-hydroxyvitamin D levels predict survival in early-stage non-small-cell lung cancer patients. *J Clin Oncol*. 2007;25:479–485.

Last Medical Review: 8/15/2014
Last Revised: 10/2/2015