

## **Table of Contents**

Introduction: Risk Factors	3
Introduction: Symptoms	4
Screening	5
Lung Cancer Types & Staging	7
Diagnosis and Workup	8
Treatment	9
Resources	14

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## **Introduction: Risk Factors**

Smoking is the leading cause of lung cancer. Age, genetics, environmental exposures, and certain medical conditions can also play a role. The more risk factors you have, the higher your chance of developing lung cancer.

#### Risk factors are:

- Smoking and Secondhand Smoke: Smoking tobacco and carcinogens is the leading cause
  of cancer. Breathing in other people's smoke (secondhand smoke) can raise your risk,
  especially with long-term exposure.
- Age: Lung cancer risk increases with age. The majority of lung cancer cases are diagnosed in people over 50 years of age.
- Family History: Research shows that having a close relative (mother, father, brother, or sister) with lung cancer raises your risk of developing lung cancer, especially if you have smoked.
- Race: Asian females (even those who have not smoked) are at an increased risk of lung cancer due to higher incidence of a mutation in the epidermal growth factor receptor (EGFR) gene, which can lead to uncontrolled cell growth.
- **Gender:** Females are at a higher risk for developing lung cancer with an increase in the incidence of lung cancer. There is a high mortality with lung cancer being the leading cause of cancer-related death in women.
- **Prior Radiation Therapy:** While radiation is an important treatment for cancer, prior radiation to the chest may increase the risk of lung cancer.
- History of Cancer in another Part of the Body: People with other smoking-related cancers, including head and neck cancer, esophageal cancer, and bladder cancer, are at a higher risk of developing lung cancer. Patients with other cancers like breast, colon and prostate are also at an increased risk.
- **Radon:** Radon is a natural gas that can build up in homes and has been linked to causing lung cancer. Testing your home for radon is recommended.
- Asbestos and Other Industrial Chemicals: Asbestos, arsenic, beryllium, and uranium have been linked to lung cancer. Anyone who has been exposed to or worked with these chemicals may have an increased risk.
- Other Lung Diseases: Chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), and tuberculosis (TB) increase lung cancer risk.

Having more than one risk factor, in addition to smoking, makes your risk of developing lung cancer much higher. For example, a person who has asbestos exposure and smokes has about a 4x risk of developing lung cancer compared to a person who does not smoke.

## **Introduction: Symptoms**

Lung cancer usually does not cause symptoms in the early stages. Symptoms are more likely to appear later. Patients should not wait for symptoms to be screened.

Symptoms of lung cancer can be vague and similar to symptoms from infections and inflammation. While people occasionally may have an upper respiratory infection, cough, or shoulder pain, persistent symptoms, such as the ones listed below, should be discussed with your doctor.

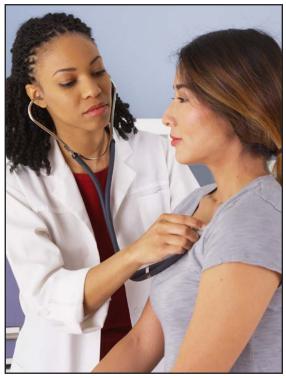
- Persistent cough that does not go away or get better.
- Coughing up blood
- Voice changes (especially hoarseness)
- Repeated lung infection or pneumonia
- Chest, shoulder, or back pain that does not go away or get better.
- Difficulty swallowing

Other more general symptoms can also be associated with advanced stage lung cancer, potentially when it has spread.

- Unexplained weakness
- Extreme fatique
- Unexplained weight loss
- Bone/joint pain
- Unexplained broken bones without any trauma
- Headaches
- · Blood clots
- New strokes/unsteady movement
- Memory loss
- Neck or face swelling

Persistent, unusual, or unexplained symptoms should be checked out by your doctor. Many symptoms are non-specific and can be a result of other medical conditions, such as heart problems and other lung problems like COPD. However, if you are worried or have persistent symptoms, you should see your doctor for evaluation. Like all cancers, lung cancer is easier to treat when caught early.







## **Screening for Lung Cancer**

#### What is screening?

Screening is a test done to detect cancer before symptoms develop.

Is there a screening test for lung cancer?
Lung cancer screening with low-dose
computed tomography (LDCT) is recommended
for those at higher risk of developing lung
cancer and is currently the only recommended
screening test. It has been shown to decrease
the risk of dying from lung cancer in people at
high risk.

#### How does lung cancer screening work?

- You lie on a table that moves through an open scanner (similar to a large ring).
- A low dose of radiation creates detailed pictures of your lungs.
- The scan takes only a few minutes, is painless, and does not require IVs or needles.
- · A radiologist reviews the results.

#### Possible results:

- Negative: no abnormal findings. You would be recommended to continue yearly screening.
- 2. Lung nodule(s): Lung cancer typically first appears as a nodule, or spot, in the lungs. Fortunately, most nodules that are seen on LDCT are not cancerous. Your doctor may recommend a follow up CT in 3 to 6 months. If a nodule looks concerning, another scan or biopsy (a medical procedure in which a small sample of the nodule is removed for examination under a microscope) may be recommended (See Diagnosis and Workup Section on different types of biopsy procedures).
- 3. Other health problems: Your lung cancer screening test may detect other lung and heart problems that are common in people who have smoked for a long time, such as emphysema (COPD) and coronary artery disease (hardening of the arteries in the heart). Discuss these findings with your doctor to determine whether additional tests are needed.

#### Who should get screened?

Annual LDCT screening is recommended if you:

- Are between 50 80 years old
- Have a greater than 20 pack-year smoking history (1 pack/day for 20 years, or 2 packs/ day for 10 years)
- Current smokers or have quit within the last 15 years

#### Is screening covered by insurance?

Yes, screening is covered for eligible patients by most insurance without co-pays or deductibles. However, additional testing that is recommended after a lung cancer screening may be subject to co-pays and deductibles.

#### What are the benefits of lung cancer screening?

- Screening can find lung cancer early, when it is more likely to be treatable.
- Most lung cancers do not cause symptoms until they are advanced stage or have spread.
- Catching cancer before symptoms occur lowers the chance of dying from lung cancer.

#### What are the risks of lung cancer screening?

Lung cancer screening is very safe, but there are some risks.

- False positive results. Lung cancer screening may suggest that a person has lung cancer who does not. This is called a false positive result and may lead to additional testing, as well as anxiety.
- 2. Radiation exposure. The amount of radiation you are exposed to during an LDCT is much less than that of a standard CT scan. It is equal to about half the radiation you're exposed to naturally from the environment in a year.
- 3. Finding cancer that is too advanced to cure. Some cancers may grow faster than normal, and these cancers may be found on screening at a more advanced stage.
- 4. Finding cancer that may never harm you. Some lung cancers grow slowly and may never cause symptoms or harm. It can be hard to know which cancers need treatment right away and which do not. If you're diagnosed with lung cancer, your doctor will likely recommend treatment. Rarely, some lung cancers or pre-cancers may remain small and confined (without spreading) for the rest of your life, and therefore may not need treatment.

More detailed information about lung cancer screening may be found <a href="here">here</a>.



# **Lung Cancer Types and Staging**

#### What are the different types of lung cancer?

There are two main categories of lung cancer: non-small cell and small cell.

The most common category is non-small cell lung cancer, which has two main types, adenocarcinoma and squamous cell carcinoma. Adenocarcinoma is more common.

Small cell lung cancer tends to be more aggressive and is often found in a more advanced stage. More detailed information on types of lung cancer may be found <a href="here">here</a>.

#### How is lung cancer staged?

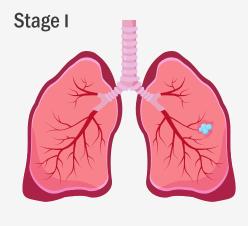
Your doctors will use various tests to determine the stage of your cancer. This is important as the stage will determine the treatment.

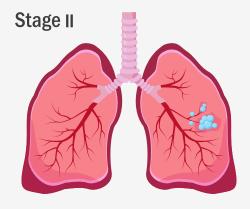
#### The stages are:

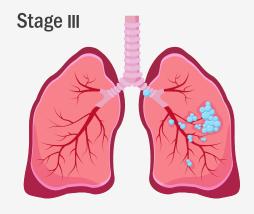
- Stage I: A small tumor (4 cm or less) that has not spread to any lymph nodes. This is divided into two substages, Stage IA (3 cm or less) and Stage IB (3-4 cm or tumor invading into the pleural lining of the lung).
- Stage II: A large tumor (over 4 cm up to 7 cm), a tumor that has spread to lymph nodes inside of the lung (hilar lymph nodes), or a tumor that involves nearby structures, such as the ribs. This stage also has two substages, Stage IIA and Stage IIB, depending on the size and involvement of lymph nodes.
- Stage III: A tumor larger than 7 cm that has spread to lymph nodes outside of the lung (in the mediastinum), or has grown into nearby structures or organs, but has not spread outside of the chest. This stage has three substages: IIIA, IIIB, and IIIC.
- Stage IV: A tumor that has spread to the other lung or other parts of the body, such as bone, the brain, or liver.

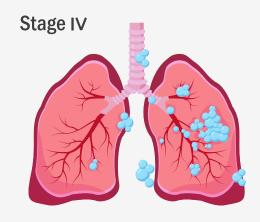
  The term metastatic is used in Stage IV cancer, meaning the cancer has spread beyond the original site to more distant parts of the body.

More detailed information on lung cancer staging may be found <u>here</u>.









## **Diagnosis and Workup**

If a suspicious spot is found, your healthcare team will work quickly to find out what it is and what stage the cancer may be. This information helps guide the best treatment plan.

Diagnosis usually requires imaging tests and a biopsy. The type of biopsy depends on where the tumor is located.

How suspicious areas are found:

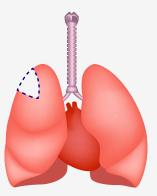
- Screening CT scans
- Other imaging (Chest x-rays or CT scans) done for unrelated reasons

#### Other imaging tests:

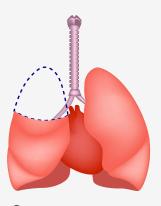
- Chest X-ray This is a basic form of imaging that can sometimes show an abnormality. If something is seen on a CXR, a CT scan is often performed.
- **CT Chest** Shows more detailed pictures of your anatomy and the location of a tumor.
- **PET CT** This type of scan is ordered after a suspicious CT scan or after a cancer has been diagnosed. It allows your treatment team to stage your cancer. It can also help show areas to focus on for a biopsy.
- MRI / CT Brain Depending on the stage and size of your cancer, a scan may be performed to complete the workup and finalize the cancer stage.

Many advancements have been made that allow for sampling of a tumor, using minimally invasive techniques that are often done in an outpatient setting, such as:

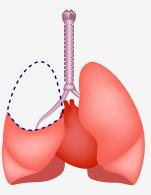
- **Image-guided biopsy** A CT scan where the radiologist can use a small needle to biopsy your tumor to obtain tissue for diagnosis.
- **Surgical biopsy** If your tumor is of a location and stage that qualifies you for surgery, your surgeon may recommend a minimally invasive approach (videoassisted thoracoscopic (VATS) or robotic surgery) to diagnose and treat your tumor at the same time.
- **Bronchoscopy** This test involves using a flexible camera that goes down your airway to biopsy areas of concern. This technology has evolved and now allows for diagnosing smaller tumors in most locations.
  - Navigational / Robotic Bronchoscopy allows for biopsy of an area using GPS technology, where your surgeon or pulmonologist can follow a road map and use a small needle to biopsy the tumor.
  - Endobronchial Ultrasound is a specialized type of scope that is often done at the same time as the above test and allows for sampling a tumor or lymph nodes. This allows for diagnosis and staging of your tumor.



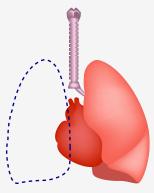
Wedge resection



Segmentectomy



Lobectomy



**Pneumonectomy** 

## **Lung Cancer Treatment**

Lung cancer treatment depends on the type of cancer, stage at time of diagnosis, molecular targets (special markers found on some cancer cells), and your overall health. Treatment may include surgery, radiation, chemotherapy, targeted therapy, immunotherapy, or a combination of these approaches.

### Surgery

Surgery is used to remove the tumor (cancer) in the lung. Lymph nodes within and around the lung are also removed to check for cancer spread. Surgery is usually performed through small incisions between the ribs using video-assisted thoracic surgery (VATS or thoracoscopy) or robotic-assisted thoracic surgery (RATS). In some cases, surgery may require making a larger incision and spreading the ribs (thoracotomy).

### Types of Surgery

- Wedge resection Removes a small piece of a lobe that includes the tumor and a margin of normal tissue.
- **Segmentectomy** Removes one or more segments of a lobe. Each lobe of the lung is divided into 2-5 segments based on the airway anatomy.
- Lobectomy Removes an entire lobe of the lung. The right lung has 3 lobes (upper, middle, and lower) and the left lung has 2 lobes (upper and lower).
- **Pneumonectomy** Removes one entire lung. This is performed if the tumor involves a large part of the lung or is centrally located near the heart.

The recommended type of surgery depends on the size and location of the tumor, as well as your overall health and lung function. Surgery may not be recommended if the tumor is very large, has spread to other parts of the body, or if your lung function is not normal.

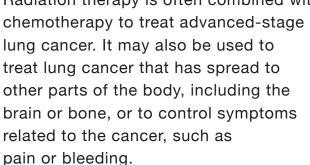
### Radiation therapy

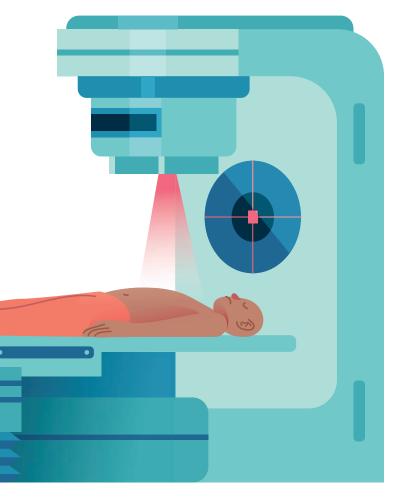
Radiation therapy uses X-rays or particles (protons or electrons) to kill cancer cells. Treatments are carefully planned to target the tumor while protecting nearby healthy tissue. A special scan, called a "simulation," is performed to create a personalized plan prior to starting treatment. Each radiation plan undergoes rigorous safety checks before treatment begins.

During treatment, you will lie on a table while a machine directs radiation to precise points on your body. It is painless and only takes seconds or minutes.

The number of treatments depends on the amount of radiation (fractions) given during each treatment. Treatments are usually scheduled 5 days a week for several weeks. Common side effects include fatigue, skin irritation, cough, and inflammation in the lungs.

Stereotactic body radiotherapy (SBRT) is a specialized type of radiation therapy that is used for small tumors. It delivers higher doses in fewer treatments. It may be used to treat lung tumors if you cannot safely undergo surgery. Radiation therapy is often combined with





### Chemotherapy

Chemotherapy uses strong medicines to destroy cancer cells by preventing them from growing and dividing. However, because chemotherapy drugs target all rapidly dividing cells, they can also harm healthy cells, leading to side effects. Side effects are specific to the medications used, but commonly include fatigue, loss of appetite, nausea, diarrhea, low blood counts, risk of infection, and nerve damage.

Chemotherapy is mostly given by IV, and sometimes as pills. A combination of medicines is given in a series of treatments (cycles) over weeks or months, with breaks between cycles to allow the body to recover.



Chemotherapy may be given before surgery (neoadjuvant) to shrink a tumor or after surgery (adjuvant) to kill any cancer cells that remain in the body. Chemotherapy can be used in combination with radiation therapy, immunotherapy, or targeted therapy to treat advanced-stage lung cancer. Chemotherapy with or without immunotherapy is the primary treatment for lung cancer that has spread to other organs in the body.

### Targeted therapy

Targeted therapies work differently from chemotherapy by recognizing and blocking specific molecular targets (or biomarkers) on some cancer cells. If a cancer cell expresses one of these molecular targets, the drug specific to that molecule can block the cell from growing and dividing and can cause cell death.

Unlike chemotherapy, these drugs have fewer side effects as they have less impact on normal cells in the body. However, targeted therapies only work if the tumor expresses certain molecular targets such as Epidermal Growth Factor Receptor (EGFR), anaplastic lymphoma kinase (ALK), or a mutation in the ROS1 gene.

Common targeted therapies include:

- **EGFR inhibitors:** osimertinib, afatinib, erlotinib, gefitinib, lazertinib
- ALK inhibitors: alectinib, brigatinib, lorlatinib, crizotinib, ceritinib
- ROS1 inhibitors: entrectinib, repotrectinib, taletrectinib, crizotinib

To know if you are a candidate for this type of therapy, your tumor may be sent for molecular testing. Testing may be performed on a tumor biopsy, a surgically removed tumor or on a blood sample in advanced-stage disease. Your physicians will often wait for the test results before making critical treatment decisions.

### *Immunotherapy*

Immunotherapy uses the body's immune system (lymphocytes) to recognize and kill cancer cells. These medications stop lung cancers from escaping the immune system through a process called checkpoint inhibition. Immunotherapy medications do not require molecular targets, so more patients are eligible for treatment.

Immune checkpoint inhibitors help your immune system recognize and attack cancer cells. They work by blocking the interaction between two proteins—PD-L1, (found on some tumor cells) and PD-1 (found on immune cells).

Before starting treatment, doctors will check your tumor's PD-L1 level. Tumors with high levels of PD-L1 (half or more of the cancer cells have this protein) are more likely to respond well to these medicines. If you have certain pre-existing autoimmune disorders, you should discuss with your oncologist whether it is safe to use immunotherapy in your treatment.

Common immune checkpoint inhibitors used for lung cancer include nivolumab, pembrolizumab, cemiplimab, atezolizumab, and durvalumab. Fatigue and rashes are the most common side effects of immunotherapy. More severe immune-related reactions may occur, including inflammation of the endocrine system (commonly thyroid), and rarely, inflammation of the lungs, colon, heart, central nervous system, and joints (arthritis).

Based on cancer stage, immunotherapy (with or without chemotherapy) may be used before or after surgery. It may also be used with chemotherapy and radiation therapy to treat advanced-stage lung cancers.

#### Managing side effects of drug therapies

It is important to maintain open communication with your care team throughout treatment for several reasons: it allows for early and effective management of side effects, improves quality of life during and after treatment, and leads to better outcomes.

#### Palliative care

Palliative care can help people with advanced-stage lung cancer improve their quality of life by relieving symptoms (like pain or shortness of breath). It can also help provide comfort and strength to a patient's loved ones. Palliative care can be combined with active cancer treatment.



#### Who treats lung cancer?

Depending on your treatment, you may be cared for by a team of specialists, including:

- A pulmonologist: A doctor who specializes in the medical treatment of lung disease.
   This doctor may assist with the diagnosis and staging of your cancer or may help manage any underlying lung disease, such as emphysema.
- A thoracic surgeon: A doctor who performs surgery to remove cancers of the lung and chest.
- A radiation oncologist: A doctor who treats cancer with radiation therapy.
- A medical oncologist: A doctor who treats cancer with chemotherapy, targeted therapy, and immunotherapy.

Because lung cancer treatment is complex, most institutions will have a multidisciplinary care team of physician specialists, nurse practitioners, physician assistants, social workers, rehabilitation therapists, and other health professionals to provide comprehensive care to meet a patient's physical, emotional, social and psychological needs. More complex lung cancer cases are commonly presented at a "tumor board" which includes thoracic surgeons, pulmonologists, radiologists, pathologists, radiation oncologists, and medical oncologists where all provide input to recommend an optimal treatment plan.

Facing a lung cancer diagnosis can feel overwhelming, but you are not alone. Many treatment options are available, and your care team will work closely with you to choose the approach that is best for you. Ongoing advances in surgery, radiation therapy, chemotherapy, targeted therapy and immunotherapy continue to improve outcomes and offer new hope.

#### Resources

Additional resources regarding lung cancer diagnosis and treatment:

https://go2.org/what-is-lung-cancer/

https://www.thoracic.org/professionals/clinical-resources/disease-related-resources/ cancer.php

https://go2.org/risk-early-detection/about-screening/

https://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/stagingnsclc.html