**Small Cell Lung Cancer T115654**

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## **Overview and Recommendations**

Overview and RecommendationsOverview and Recommendations

### **Background**

* General information:
  + Small cell lung cancer is a malignant epithelial tumor consisting of small cells with scant cytoplasm, ill-defined cellular borders, finely granular nuclear chromatin, and absent or inconspicuous nucleoli.
  + It is characterized by rapid doubling time, high growth fraction, and widespread metastases early in disease; patients often present with hematogenous metastases.
  + World Health Organization (WHO) classifies small cell lung cancer as a neuroendocrine tumor; it can be further classified as pure small cell lung cancer or combined small cell lung cancer.
  + Small cell lung cancer is suspected in patients with a history of cigarette smoking, coughing, hemoptysis, wheezing, fever, dyspnea, and/or chest pain.
* Epidemiology:
  + An estimated 228,150 new cases of lung and bronchus cancer are expected worldwide in 2019. Small cell lung cancer accounts for about 13%-15% of lung cancer cases.
  + The annual incidence has decreased over the past 30 years in industrialized countries, likely due to decreased rate of smoking in these regions.
  + From 2009 to 2015 there were 33,824 total cases of small cell cancer of lung or bronchus in the United States; of these, about 75% of patients had metastatic disease at diagnosis.
  + The most common risk factor for small cell lung cancer is cigarette smoking.

### **Evaluation**

* The initial evaluation to establish diagnosis includes:
  + blood tests (Strong recommendation)
  + chest x-ray
  + IV contrast-enhanced computed tomography (CT) of chest, abdomen, and pelvis or of chest extending through liver and adrenal glands (Strong recommendation)
* Confirm the diagnosis in patients with radiographic/clinical evidence of small cell lung cancer with the least invasive biopsy/pathology method as dictated by the patient’s presentation (Strong recommendation). Options include sputum cytology, thoracentesis, bronchoscopy including transbronchial needle aspiration (TBNA), fine needle aspiration (FNA), and transthoracic needle aspiration (TTNA).
* Pretreatment testing aimed at staging typically includes:
  + brain magnetic resonance imaging (MRI) preferred or IV contrast-enhanced brain CT to detect brain metastases (Strong recommendation);
  + bone scan (Strong recommendation);
  + positron emission tomography (PET)/CT from skull base to mid-thigh if suspect limited stage or need clarification of stage (Conditional recommendation).
* Additional workup (if it is not done previously) for suspected limited stage disease includes:
  + pulmonary function tests in patients being evaluated for surgery or definitive radiation therapy (Conditional recommendation);
  + bone MRI or x-ray if PET/CT is inconclusive, followed by bone biopsy if MRI or bone scan is inconclusive (Conditional recommendation);
  + head MRI or CT in addition to PET, or abdominal CT plus bone scan in patients with clinical stage I disease considering definitive surgery (Strong recommendation);
  + thoracentesis with cytologic analysis if pleural effusion is present (Strong recommendation) and can be safely accessed;
  + bone marrow aspiration and biopsy in select patients with presentation suggestive of bone marrow invasion, including signs of blood-bone marrow barrier rupture (such as nucleated red blood cells on peripheral blood smear [peripheral blood erythroblasts]), or abnormal blood count (such as neutropenia and thrombocytopenia) (Conditional recommendation).
* Additional workup for never smokers with extensive stage disease includes molecular profiling to clarify diagnosis and evaluate possible targeted therapies (Conditional recommendation).

### **Management**

#### **Management of Limited Stage Disease**

* If limited stage disease and negative pathologic mediastinal staging, perform lobectomy and mediastinal lymph node dissection or sampling (Conditional recommendation), then follow with adjuvant treatment, based on findings from lymph node dissection or sampling.
  + If lymph nodes are negative, offer 4 cycles of systemic therapy (Conditional recommendation).
  + If lymph nodes are positive, offer sequential or concurrent systemic therapy with or without mediastinal radiation therapy (Conditional recommendation).
* If limited stage disease and positive pathologic mediastinal imaging or limited stage disease in excess of T1-T2, N0:
  + for performance status (PS) 0-2, offer initial treatment with concurrent systemic therapy plus thoracic radiation therapy (Strong recommendation);
  + for performance status 3-4 due to small cell lung cancer, offer systemic therapy with or without either concurrent or sequential radiation therapy (Conditional recommendation);
  + for performance status 3-4 not due to small cell lung cancer, offer an individualized treatment plan, including use of supportive care (Conditional recommendation).
* If limited stage disease and medically inoperable or decision not to pursue surgical resection, options include either stereotactic ablative radiation therapy (SABR) followed by adjuvant systemic therapy or concurrent chemoradiation (Strong recommendation).
* Offer adjuvant prophylactic cranial irradiation to patients with limited stage disease and a complete or partial response to initial therapy (Strong recommendation).

#### **Management of Extensive Stage Disease**

* For patients with extensive stage disease:
  + If no localized symptomatic sites or brain metastases, offer supportive care and base additional treatment on performance status.
    - For performance status 0-2 or 3-4 due to small cell lung cancer, offer combination systemic therapy (Strong recommendation).
    - For performance status 3-4 not due to small cell lung cancer, may offer an individualized treatment plan and consider best supportive care (Conditional recommendation).
  + If localized symptomatic sites with superior vena cava syndrome, lobar obstruction, or bone metastases, treatment options include:
    - systemic therapy with or without radiation therapy to symptomatic sites (Conditional recommendation);
    - orthopedic stabilization and palliative external beam radiation therapy, for patients with high risk of fracture due to osseous impairment (Conditional recommendation).
  + If spinal cord compression, consider radiation therapy to symptomatic sites before systemic therapy (unless immediate systemic therapy is indicated) (Conditional recommendation).
  + If brain metastases:
    - consider systemic therapy before brain radiation therapy if patient is asymptomatic (Conditional recommendation);
    - consider brain radiation therapy before systemic therapy (unless immediate systemic therapy is indicated) if patient is symptomatic (Conditional recommendation).
  + For patients with a complete or partial response to initial therapy, options include adjuvant prophylactic cranial irradiation (Conditional recommendation) or magnetic resonance imaging (MRI) surveillance of brain (Strong recommendation). May also offer sequential thoracic radiation therapy after systemic therapy, particularly in those with residual thoracic disease and low-bulk metastatic disease (Strong recommendation).

#### **Surveillance**

* Surveillance for patients with small cell lung cancer includes (Strong recommendation):
  + routine history and physical with assessment of symptoms
  + computed tomography (CT) of chest, abdomen, and pelvis
  + MRI or CT of brain
  + intervention for smoking cessation
  + survivorship care plan

#### **Management of Relapsed or Progressive Disease**

* Offer palliative management of symptoms to all patients with relapsing or progressive disease at any time during treatment regardless of PS, including localized radiation therapy to symptomatic sites (Strong recommendation).
* For patients with relapsing or progressive disease and PS 0-2, offer subsequent systemic therapy with response assessment by chest/abdomen/pelvic CT with contrast after every 2-3 cycles (Strong recommendation).
  + If response, continue therapy until disease progression or unacceptable toxicity (Strong recommendation).
  + If no response or unacceptable toxicity and PS remains 0-2, options include subsequent systemic therapy and palliative management of symptoms including localized radiation therapy to symptomatic sites (Strong recommendation).

## **Epidemiology**

Epidemiology

### **Who is Most Affected**

* almost all cases of small cell lung cancers are related to smoking[4](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__NCCN1.2022AUG)
* similar incidence in both men and women[4](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__NCCN1.2022AUG)

### **Incidence/Prevalance**

* small cell lung cancer accounts for about 13%-15% of all lung cancer cases[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168),[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF2497),[4](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__NCCN1.2022AUG)
* incidence of small cell lung cancer in United States based on Surveillance, Epidemiology, and End Results (SEER) data
  + age-adjusted incidence was 5.48 cases per 100,000 persons, with 6.05 cases per 100,000 men and 5.06 cases per 100,000 women in 2016
  + from 2009 to 2015
    - 33,824 total cases of small cell cancer of lung or bronchus, including 16,941 in men and 16,883 in women
    - about 75% of patients presented with metastatic disease at diagnosis, with only 4% presenting with localized disease and 19% with regional disease
  + Reference - [SEER](https://seer.cancer.gov/csr/1975_2016/browse_csr.php) accessed 2019 Dec 13
* annual incidence has decreased over past 30 years in industrialized countries, likely due to decreased rate of smoking in these regions[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168),[4](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__NCCN1.2022AUG)

### **Risk Factors**

#### **Cigarette Smoking**

* cigarette smoking greatly increases risk of lung cancer
  + **cigarette smoking associated with increased risk of all major histologic types of lung cancer compared to never smoking, with strongest risk increase for small cell lung cancer and squamous cell carcinoma**

Systematic Review[11165392Lung Cancer 2001 Feb-Mar;31(2-3):139](http://pubmed.ncbi.nlm.nih.gov/11165392?dopt=Abstract)

studySummary

* + - based on systematic reviewSystematic Review
    - systematic review of 1 cohort study and 27 case-control studies evaluating association between cigarette smoking and risk of different histologic types of lung cancer
    - comparing ever smokers to never smokers, ever smokers associated with increased risk of
      * small cell lung cancer (odds ratio [OR] 12.9, 95% CI 9.8-17.1) in analysis of 22 studies
      * squamous cell carcinoma (OR 11.3, 95% CI 9.4-13.5) in analysis of 27 studies
      * large cell carcinoma (OR 5.6, 95% CI 4.2-7.7) in analysis of 8 studies
      * adenocarcinoma (OR 3.2, 95% CI 2.6-4) in analysis of 27 studies
    - PubMed11165392Lung cancer (Amsterdam, Netherlands)20010201Lung Cancer312-3139139Reference - [11165392Lung Cancer 2001 Feb-Mar;31(2-3):139](http://pubmed.ncbi.nlm.nih.gov/11165392?dopt=Abstract)
  + **cigarette smoking > 2 packs/day associated with > 50-fold increase in lung cancer compared to never smoking**

Cohort Study[18556244Lancet Oncol 2008 Jul;9(7):649](http://pubmed.ncbi.nlm.nih.gov/18556244?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2601691/)

studySummary

* + - based on age-standardized incidence rates in a prospective cohort study with 463,837 men and women aged 50-71 years in United States Cohort Study
    - for current smokers who smoked > 2 packs/day
      * 1,259.2 per 100,000 person-years in men
      * 1,308.9 per 100,000 person-years in women
    - for never smokers
      * 20.3 per 100,000 person-years in men
      * 25.3 per 100,000 person-years in women
    - PubMed18556244The Lancet. Oncology20080701Lancet Oncol97649649Reference - [18556244Lancet Oncol 2008 Jul;9(7):649](http://pubmed.ncbi.nlm.nih.gov/18556244?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2601691/), editorial can be found in [18598927Lancet Oncol 2008 Jul;9(7):609](http://pubmed.ncbi.nlm.nih.gov/18598927?dopt=Abstract)
  + **pipe smoking associated with increased risk of lung cancer, but cigarette smoking and combination of pipe or cigar with cigarette smoking appears associated with greater risk**

Cohort Study[20162568Int J Cancer 2010 Nov 15;127(10):2402](http://pubmed.ncbi.nlm.nih.gov/20162568?dopt=Abstract)[Full Text](https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.25252)

studySummary

* + - based on cohort of 102,395 men evaluated for cancer incidence and smoking history (cigar, pipe, or cigarette smoking alone or in combination)Cohort Study
    - median follow-up 9 years
    - compared to persons who never smoked, increased risk of lung cancer associated with
      * exclusive pipe smoking (hazard ratio [HR] 9.8, 95% CI 5.2-18.5)
      * exclusive cigarette smoking (HR 15.3, 95% CI 10-23.4)
      * combined cigar and cigarette smoking (HR 15.2, 95% CI 9.1-25.5)
      * combined pipe and cigarette smoking (HR 14.1, 95% CI 8.8-22.4)
    - PubMed20162568International journal of cancer20101115Int J Cancer1271024022402Reference - [20162568Int J Cancer 2010 Nov 15;127(10):2402](http://pubmed.ncbi.nlm.nih.gov/20162568?dopt=Abstract)[full-text](https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.25252)
  + medium, low, and very low tar cigarettes associated with increased risk of lung cancer compared to not smoking in cohort study with 940,774 persons ([14715602BMJ 2004 Jan 10;328(7431):72](http://pubmed.ncbi.nlm.nih.gov/14715602?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC314045/))
  + mentholated cigarettes may be associated with increased risk of lung cancer compared to nonmentholated cigarettes in men in cohort study with 11,761 persons ([7695461Arch Intern Med 1995 Apr 10;155(7):727](http://pubmed.ncbi.nlm.nih.gov/7695461?dopt=Abstract))

#### **Environmental Tobacco Smoke**

* **environmental tobacco smoke increases risk of lung cancer**

Cohort Study[9365295BMJ 1997 Oct 18;315(7114):980](http://pubmed.ncbi.nlm.nih.gov/9365295?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2127653/)

studySummary

* + based on analysis of 37 epidemiologic studies of risk of lung cancer (4,626 cases) in nonsmokersCohort Study
  + 24% excess risk of lung cancer in nonsmokers who lived with a smoker compared to those who did not
  + dose-response relation found for environmental tobacco exposure
  + PubMed9365295BMJ (Clinical research ed.)19971018BMJ3157114980980Reference - [9365295BMJ 1997 Oct 18;315(7114):980](http://pubmed.ncbi.nlm.nih.gov/9365295?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2127653/), correction can be found in BMJ 1998 Oct 3;317(7163):951, commentary can be found in [9685291BMJ 1998 Aug 1;317(7154):346](http://pubmed.ncbi.nlm.nih.gov/9685291?dopt=Abstract)
  + estimated 3,000 deaths/year from lung cancer due to environmental tobacco smoke exposure ([Am Fam Physician 1998 Apr 1;57(7):1659](http://www.aafp.org/afp/1998/0401/p1659.html))
  + putting risk in individual perspective would mean that smoker quitting would lower spouse's risk of lung cancer from 0.25% to 0.17%, or 1,250 smokers would have to quit for 1 spouse to be saved from lung cancer (Evidence-Based Medicine 1998 Jul/Aug;3(4):126)
* **environmental tobacco smoke associated with increased risk of lung cancer and other respiratory diseases**

Cohort Study[BMJ 2005 Feb 5;330(7486):277](http://pubmed.ncbi.nlm.nih.gov/15681570)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC548173/)

studySummary

* + Cohort Study based on 7-year follow-up of prospective cohort of 123,479 persons who had never smoked or had stopped smoking for at least 10 years
  + frequent exposure to environmental tobacco smoke during childhood associated with lung cancer in adulthood
  + PubMed15681570BMJ (Clinical research ed.)BMJ200502053307486277277Reference - [BMJ 2005 Feb 5;330(7486):277](http://pubmed.ncbi.nlm.nih.gov/15681570)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC548173/), editorial can be found in [15695250BMJ 2005 Feb 5;330(7486):265](http://pubmed.ncbi.nlm.nih.gov/15695250?dopt=Abstract)
* **having a spouse who smokes may not increase risk of lung cancer**

Cohort Study[12750205BMJ 2003 May 17;326(7398):1057](http://pubmed.ncbi.nlm.nih.gov/12750205?dopt=Abstract)[Full Text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC155687/)

studySummary

* + based on cohort study with results limited by wide confidence intervalsCohort Study
  + 118,094 adults in California were followed for 39 years
  + 35,561 never-smokers married to ever-smokers were compared to never-smokers married to never-smokers
  + male and female persons analyzed separately
  + PubMed12750205BMJ (Clinical research ed.)20030517BMJ326739810571057Reference - [12750205BMJ 2003 May 17;326(7398):1057](http://pubmed.ncbi.nlm.nih.gov/12750205?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC155687/), editorial can be found in [12750182BMJ 2003 May 17;326(7398):1048](http://pubmed.ncbi.nlm.nih.gov/12750182?dopt=Abstract), commentary can be found in [BMJ 2003 Aug 30;327(7413):501](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC188396/?tool=pubmed)
  + Using the surrogate of marriage to spouse who smokes does not allow a valid conclusion about risk of environmental tobacco exposure.

#### **Environmental Exposure to Pollutants**

* environmental exposure to pollutants is a risk factor for lung cancer in general, but not specific to small cell lung cancer
* exposure to air pollutants
  + asbestos
    - asbestos exposure associated with mesothelioma and lung carcinoma ([21534086J Toxicol Environ Health B Crit Rev 2011;14(1-4):76](http://pubmed.ncbi.nlm.nih.gov/21534086?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3118517/))
    - asbestos exposure associated with increased risk of lung cancer, with higher risk when combined with cigarette smoking in systematic review of 17 observational studies with 75,147 persons ([26274395PLoS One 2015;10(8):e0135798](http://pubmed.ncbi.nlm.nih.gov/26274395?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4537132/))
  + long-term exposure to combustion-related fine particulate air pollution associated with increased risk for cardiopulmonary mortality and lung cancer mortality ([11879110JAMA 2002 Mar 6;287(9):1132](http://pubmed.ncbi.nlm.nih.gov/11879110?dopt=Abstract)), commentary can be found in [12186593JAMA 2002 Aug 21;288(7):830](http://pubmed.ncbi.nlm.nih.gov/12186593?dopt=Abstract)
  + **occupational silica dust exposure associated with increased risk of lung cancer and death from lung cancer**

Systematic Review[27814719BMC Public Health 2016 Nov 4;16(1):1137](http://pubmed.ncbi.nlm.nih.gov/27814719?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5095988/)

studySummary

* + - based on systematic review of observational studiesSystematic Review
    - systematic review of 96 observational studies (77 cohort studies, 17 case-control studies, and 2 proportional mortality studies) evaluating association between occupational silica exposure and risk of lung cancer in patients with or without silicosis
    - most studies included men only, but several studies included between 10% and 31% women
    - studies conducted world-wide (41 in Europe, 18 in United States, 21 in Asian countries, 9 in Canada, 3 in Australia, and 1 in South Africa)
    - occupations included mining, foundry, pottery and ceramic, refractory brick and diatomaceous earth processing, granite (both sand and quarry), cement production, and construction
    - comparing persons with occupational silica dust exposure (with or without diagnosis of silicosis) to general population, occupational silica dust exposure associated with
      * increased risk of lung cancer (standardized incidence ratio 1.68, 95% CI 1.45-1.96) in analysis of 19 cohort studies, results limited by significant heterogeneity
      * increased risk of mortality due to lung cancer (standardized mortality ratio [SMR] 1.55, 95% CI 1.38-1.75) in analysis of 63 cohort studies, results limited by significant heterogeneity
    - among industries evaluated, workers in mining industry had highest risk of death due to lung cancer comparing exposure to no exposure (SMR 1.48, 95% CI 1.18-1.86) in analysis of 18 studies, results limited by significant heterogeneity
    - PubMed27814719BMC public health20161104BMC Public Health16111371137Reference - [27814719BMC Public Health 2016 Nov 4;16(1):1137](http://pubmed.ncbi.nlm.nih.gov/27814719?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5095988/)
  + **occupational exposure to diesel exhaust, silica dust, and paint may increase lung cancer risk**

Case-Control Study[21102581Br J Cancer 2011 Jan 4;104(1):208](http://pubmed.ncbi.nlm.nih.gov/21102581?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3039806/)

studySummary

* + - based on case-control study of 132 nonsmoking Chinese men with newly diagnosed lung cancer and 536 matched controlsCase-Control Study
    - all had lifetime work history collected
    - increased lung cancer risk associated with occupational exposure to
      * silica dust (odds ratio [OR] 2.58, 95% CI 1.11-6.01)
      * diesel exhaust (OR 3.47, 95% CI 1.08-11.14)
      * spray painting (OR 2.81, 95% CI 1.14-6.93)
      * nonspray painting (OR 2.36, 95% CI 1.04-5.37)
    - silica dust exposure associated with increased risk of adenocarcinoma (OR 2.91, 95% CI 1.1-7.68)
    - PubMed21102581British journal of cancer20110104Br J Cancer1041208208Reference - [21102581Br J Cancer 2011 Jan 4;104(1):208](http://pubmed.ncbi.nlm.nih.gov/21102581?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3039806/)
  + **domestic use of smoky coal associated with increased risk of lung cancer-related mortality compared to smokeless coal**

Cohort Study[22936785BMJ 2012 Aug 29;345:e5414](http://pubmed.ncbi.nlm.nih.gov/22936785?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3431444/)

studySummary

* + - based on retrospective cohort studyCohort Study
    - 37,272 persons using coal for household cooking or heating in China were followed up to 20 years
    - 73% used smoky coal and 27% used smokeless coal during lifetime
    - 6.4% died from lung cancer
    - smoky coal associated with increased risk of lung cancer-related mortality in (vs. smokeless coal in adjusted analyses)
      * men (hazard ratio 36.2, 95% CI 20.3-64.7)
      * women (hazard ratio 98.8, 95% CI 36.8-265.6)
    - PubMed22936785BMJ (Clinical research ed.)20120829BMJ345e5414e5414Reference - [22936785BMJ 2012 Aug 29;345:e5414](http://pubmed.ncbi.nlm.nih.gov/22936785?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3431444/)
  + radon exposure
    - **radon concentrations in home associated with significantly increased risk of lung cancer**

Cohort Study[15613366BMJ 2005 Jan 29;330(7485):223](http://pubmed.ncbi.nlm.nih.gov/15613366?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC546066/)

studySummary

* + - * based on collaborative analysis of individual data from 13 case-control studies from 9 European countries with 7,148 cases of lung cancer and 14,208 controlsCohort Study
      * PubMed15613366BMJ (Clinical research ed.)20050129BMJ3307485223223Reference - [15613366BMJ 2005 Jan 29;330(7485):223](http://pubmed.ncbi.nlm.nih.gov/15613366?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC546066/), editorial can be found in [15613367BMJ 2005 Jan 29;330(7485):226](http://pubmed.ncbi.nlm.nih.gov/15613367?dopt=Abstract), commentary can be found in [15891242BMJ 2005 May 14;330(7500):1151](http://pubmed.ncbi.nlm.nih.gov/15891242?dopt=Abstract)
    - **residential radon exposure associated with increased risk for primary lung cancer**

Case-Control Study[10394313Am J Public Health 1999 Jul;89(7):1042](http://pubmed.ncbi.nlm.nih.gov/10394313?dopt=Abstract)

studySummary

* + - * based on population-based case-control study of women aged 30-84 years in Missouri, United StatesCase-Control Study
      * PubMed10394313American journal of public health19990701Am J Public Health89710421042Reference - [10394313Am J Public Health 1999 Jul;89(7):1042](http://pubmed.ncbi.nlm.nih.gov/10394313?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1508843/)

### **Factors Associated With Decreased Risk**

* **inconsistent evidence regarding association between cannabis inhalation and lung cancer in adolescent and adult cannabis users**

Systematic Review[rzh119227676pcxh119227676pRespir Care 2016 Nov;61(11):1543](http://pubmed.ncbi.nlm.nih.gov/27507173?dopt=Abstract)[PDF](http://rc.rcjournal.com/content/respcare/61/11/1543.full.pdf)

studySummary

* + based on systematic review of observational studies Systematic Review
  + systematic review of 48 studies evaluating adverse respiratory outcomes and history of cannabis inhalation in mostly adults and adolescents
    - outcomes not adjusted for frequency of marijuana inhalation or history of cigarette use in most studies
    - no pooled analyses performed
  + lung cancer evaluated in 12 studies (4 case-control, 1 experimental, 4 secondary data analyses of cohort studies, 1 secondary data analysis of pathology reports, 2 case reports)
    - increased risk of lung cancer from cannabis use, or cases indicating lung cancer occurrence in 8 studies, with risk range varying from 2.1 to 4.1
    - 4 studies found no significant association or lower risk for lung cancer compared to tobacco only smokers
  + PubMed27507173Respiratory care20161101Respir Care611115431543 Reference - [rzh119227676pcxh119227676pRespir Care 2016 Nov;61(11):1543](http://pubmed.ncbi.nlm.nih.gov/27507173?dopt=Abstract)[PDF](http://rc.rcjournal.com/content/respcare/61/11/1543.full.pdf)

## **Etiology and Pathogenesis**

Etiology and Pathogenesis

### **Causes**

* tobacco use[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)
  + > 90% of cases occur in elderly current or past heavy smokers
  + risk of small cell lung cancer increases with increasing duration and intensity of smoking

### **Pathogenesis**

* mutations causing establishment of autocrine growth loops, activation of proto-oncogenes, or loss or inactivation of tumor-suppressor appear to be involved[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)
  + mutations in tumor suppressor genes decrease apoptotic activity, leading to aggressive growth and survival advantage for tumor cells
  + genes commonly involved include
    - Fragile Histidine Triad (FHIT) gene - deletion observed in almost all cases
    - retinoblastoma 1 (RB1) gene - loss observed in almost all cases
    - MAD1L1 gene
    - tumor protein 53 (TP53) gene - more common in small cell lung cancer than non-small cell lung cancer
* tumor cells exhibit signs of neuroendocrine and neural differentiation, and tumor growth mediated by multiple neuropeptides and polypeptides
  + key peptides include gastrin-releasing peptide, stem cell factor, and insulin-like growth factor 1, which promote growth through creation of autocrine growth loops
  + insulin-like growth factor 1 also activates phosphoinositide 3-kinase (PI3K)-AKT1 pathway, leading to decreased apoptotic activity
  + PubMed18316005Mayo Clinic proceedingsMayo Clin Proc20080301833355-67355Reference - [Mayo Clin Proc 2008 Mar;83(3):355](http://pubmed.ncbi.nlm.nih.gov/18316005?dopt=Abstract)

## **History and Physical**

History and Physical

### **Clinical Presentation**

* The following is an excerpt from clinical presentation in [Small Cell Lung Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/small-cell-lung-cancer-diagnosis-and-staging#LI_U3W_GSL_CMB); please see topic for details.
  + for initial evaluation of suspected or confirmed small cell lung cancer, perform complete history (especially history of cigarette smoking) and physical examination ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
  + most patients present with extrathoracic (hematogenous) metastases, and only about 33% of patients present with localized disease confined to chest
  + asymptomatic patients (about 25% of patients) usually have less advanced disease
  + timely identification of lung cancer and differentiation of intrathoracic spread or distant metastases through clinical history is critical for directing diagnostic testing and arranging efficient, well-coordinated delivery of care
  + signs and symptoms related to local primary tumor include
    - dyspnea, due to bronchial obstruction, pneumonia, or pleural effusion
    - persistent cough, due to endobronchial irritation or bronchial compression
    - wheezing, due to partial endobronchial obstruction
    - hemoptysis, particularly if central or cavitary lesion is present
    - fever, due to pneumonia
    - chest pain
    - PubMed17146245Annals of Saudi medicineAnn Saudi Med20020901225-6295-6295clubbing of digits
  + signs and symptoms related to invasive primary tumor or regional lymph node metastases include
    - hoarseness, due to left vocal cord paralysis resulting from tumor invasion or aortopulmonary lymphadenopathy
    - hemidiaphragm elevation, due to phrenic nerve compression
    - dysphagia, due to esophageal compression
    - chest pain (often dull and nonlocalized), particularly if pleura or chest wall are involved
    - [superior vena cava (SVC) syndrome](https://dpa-pde-oxford.shinyapps.io/condition/superior-vena-cava-syndrome), particularly if mediastinal invasion or right paratracheal lymphadenopathy
    - pericardial effusion and tamponade
    - cervical or supraclavicular lymphadenopathy
    - Pancoast syndrome (shoulder and arm pain)
    - [Horner syndrome](https://dpa-pde-oxford.shinyapps.io/evaluation/horner-syndrome-evaluation) (unilateral ptosis, meiosis, lack of facial sweating, weakness, pain, and paresthesias of arm and hand in distribution of eighth cervical and first and second thoracic nerve roots)
  + signs and symptoms related to extrathoracic (hematogenous) metastases
    - constitutional and nonspecific: anorexia/cachexia (weight loss) and fatigue
    - brain metastases: headache, focal weakness or numbness, confusion, slurred speech, gait instability, and lack of coordination
    - leptomeningeal carcinomatosis: headache, confusion, cranial nerve palsy, diplopia, slurred speech, radicular back pain, and spinal cord compression
    - adrenal metastases: mid-back or flank pain and costovertebral angle tenderness; tumor-related adrenal insufficiency is rare
    - liver metastases: right upper quadrant pain or tenderness, jaundice, fatigue, fever, and hepatomegaly
    - bone metastases
      * bone pain and tenderness
      * if spinal cord compression: back pain, muscle weakness, numbness, paresthesia, and loss of bowel and bladder control
  + small cell lung cancer often associated with [paraneoplastic syndromes](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-5B43DAF3-4677-4B89-9876-C5C00E6E3B1A__LI_CZN_DZN_BKB) (see [Complications](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-5B43DAF3-4677-4B89-9876-C5C00E6E3B1A) for details)
  + see clinical presentation in [Small Cell Lung Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/small-cell-lung-cancer-diagnosis-and-staging#LI_U3W_GSL_CMB) for details

### **History**

#### **History of Present Illness (HPI)**

* rapid onset of symptoms, with duration before presentation typically 8-12 weeks[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)
* [paraneoplastic syndromes](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-5B43DAF3-4677-4B89-9876-C5C00E6E3B1A__LI_CZN_DZN_BKB) frequently associated with small cell lung cancer and are often present at initial presentation[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168),[4](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__NCCN1.2022AUG)

#### **Past Medical History (PMH)**

* ask about recurrent pneumonia or relapsing acute exacerbations of chronic obstructive pulmonary disease (COPD)[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF2497)

#### **Social History (SH)**

* ask about tobacco use[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)

### **Physical**

#### **General Physical**

* check for localized or unilateral wheeze[2](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF2497)
* PubMed27178690Seminars in oncologySemin Oncol20160601433366-9366check for digital clubbing - may be indicative of hypertrophic pulmonary osteoarthropathy ([Semin Oncol 2016 Jun;43(3):366](http://pubmed.ncbi.nlm.nih.gov/27178690/))

## **Diagnosis and Staging**

Diagnosis

### **Making the Diagnosis**

* The following is an excerpt from Making the Diagnosis in [Small Cell Lung Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/small-cell-lung-cancer-diagnosis-and-staging#GUID-9EAEF1AD-129A-470C-81F5-C350009C4116); please see topic for details.
  + suspect small cell lung cancer in patients with
    - abnormal findings on chest x-ray
    - history of cigarette smoking
    - signs and symptoms suggestive of lung malignancy, including coughing, hemoptysis, wheezing, fever, dyspnea, and/or chest pain
  + diagnosis of small cell lung cancer is based on biopsy or cytology of primary and/or metastatic sites ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE)); confirm diagnosis in patients with radiographic/clinical evidence of small cell lung cancer with least invasive biopsy/pathology method (listed below) as dictated by patient’s presentation ([ACCP Grade 1C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
    - sputum cytology
    - thoracentesis
    - bronchoscopy including transbronchial needle aspiration (TBNA)
    - fine needle aspiration (FNA)
  + additional evaluation typically includes blood tests and imaging
  + see [Small Cell Lung Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/small-cell-lung-cancer-diagnosis-and-staging) for details

### **Differential Diagnosis**

#### **Other Cancers**

* The following is an excerpt from Differential Diagnosis in [Small Cell Lung Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/small-cell-lung-cancer-diagnosis-and-staging#OTHER_CANCERS); please see topic for details.
  + [non-small cell lung cancer](https://dpa-pde-oxford.shinyapps.io/condition/non-small-cell-lung-cancer)
  + [mesothelioma](https://dpa-pde-oxford.shinyapps.io/condition/malignant-pleural-mesothelioma)
  + other lung neuroendocrine tumors, especially typical and atypical carcinoids (see also [Neuroendocrine Neoplasms (Carcinoid Tumors)](https://dpa-pde-oxford.shinyapps.io/condition/neuroendocrine-neoplasms-carcinoid-tumors))
  + lung metastasis of other cancer (commonly from breast, colon, and prostate)
  + primary pulmonary lymphoma
  + malignant teratoma
  + pulmonary blastoma - rare malignant tumor (0.25%-0.5% of malignant lung neoplasms), most common x-ray pattern is large peripheral nodule, overall 5-year survival 16%

#### **Non-cancer Differential Diagnosis**

* The following is an excerpt from [Solitary Pulmonary Nodule - Approach to the Patient](https://dpa-pde-oxford.shinyapps.io/approach-to/solitary-pulmonary-nodule-approach-to-the-patient#BENIGN_NEOPLASMA); please see topic for details.
  + benign neoplasms
    - hamartoma
    - chondroma
    - hemangioma
    - arteriovenous malformation
    - fibroma
    - neural tumor (schwannoma, [neurofibroma](https://dpa-pde-oxford.shinyapps.io/condition/neurofibromatosis-type-1))
    - sclerosing hemangioma
  + infections
    - healed or nonspecific granulomas
    - granulomatous infections
      * [tuberculosis](https://dpa-pde-oxford.shinyapps.io/condition/pulmonary-tuberculosis-27)
      * [histoplasmosis](https://dpa-pde-oxford.shinyapps.io/condition/histoplasmosis)
      * [coccidioidomycosis](https://dpa-pde-oxford.shinyapps.io/condition/coccidioidomycosis)
      * blastomycosis
      * cryptococcosis
      * pulmonary aspergilloma
      * atypical mycobacteria
    - bacterial infection
      * [nocardiosis](https://dpa-pde-oxford.shinyapps.io/condition/nocardiosis)
      * [actinomycosis](https://dpa-pde-oxford.shinyapps.io/condition/actinomycosis)
      * round pneumonia
    - septic embolus
    - abscess
  + other causes
    - [amyloid](https://dpa-pde-oxford.shinyapps.io/condition/immunoglobulin-light-chain-al-amyloidosis)
    - infarct - pulmonary infarction can mimic lung cancer radiologically, 6 cases reported
    - lipoid pneumonia
    - pulmonary scar
    - [sarcoidosis](https://dpa-pde-oxford.shinyapps.io/condition/pulmonary-sarcoidosis)
    - subpleural lymph node
    - [rheumatoid arthritis](https://dpa-pde-oxford.shinyapps.io/condition/rheumatoid-arthritis-ra)
    - [granulomatosis with polyangiitis](https://dpa-pde-oxford.shinyapps.io/condition/granulomatosis-with-polyangiitis-gpa-and-microscopic-polyangiitis-mpa)
    - round atelectasis
    - focal hemorrhage
    - rib fracture
    - pleural thickening, mass, or fluid
    - skin nodule
  + see [Solitary Pulmonary Nodule - Approach to the Patient](https://dpa-pde-oxford.shinyapps.io/approach-to/solitary-pulmonary-nodule-approach-to-the-patient) for details

### **Testing Overview**

* The following is an excerpt from Testing Overview in [Small Cell Lung Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/small-cell-lung-cancer-diagnosis-and-staging#GUID-23CBB742-F2D9-4BB9-B94F-818369EFAD87); please see topic for details.
  + TESTING\_OVERVIEW\_\_LI\_OCS\_3XS\_1KB12/01/2021 05:46:15 AMguidelineSummaryUpdatelowOncologic\_Disease Pulmonary\_DisordersNational Comprehensive Cancer Network (NCCN) recommendations on diagnosis and staging of small cell lung cancer (NCCN 2021 Aug)initial evaluation to establish diagnosis of small cell lung cancer includes
    - history and physical examination, including history of smoking and evaluation of [signs and symptoms](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#TOPIC_OVQ_JJ3_5JB) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE)) related to primary tumor and/or metastases
    - blood tests, including complete blood count, electrolytes, liver function tests, calcium levels, blood urea nitrogen (BUN), and creatinine
    - chest x-ray
    - IV contrast-enhanced computed tomography (CT) of chest, abdomen, and pelvis ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade A, Level IV](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE)) for chest and abdomen or of chest extending through liver and adrenal glands
    - IV contrast-enhanced CT of chest, abdomen, and pelvis ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade A, Level IV](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
    - review pathological findings ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * confirm diagnosis in patients with radiographic/clinical evidence of small cell lung cancer with least invasive biopsy/pathology method as dictated by patient’s presentation; options include ([ACCP Grade 1C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
        + sputum cytology
        + thoracentesis
        + bronchoscopy including transbronchial needle aspiration (TBNA)
        + fine needle aspiration (FNA)
        + transthoracic needle aspiration (TTNA)
      * perform pathologic mediastinal staging in patients with clinical stage T1-T2, N0 disease if considering surgical resection as definitive therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade C, Level IV](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE) pathologic mediastinal staging is optional, however should be used to confirm positron emission tomography [PET]/CT findings that alter management)
  + pretreatment testing aimed at staging typically includes
    - brain magnetic resonance imaging (MRI) preferred or IV contrast-enhanced brain CT; MRI is more sensitive compared to CT for detection of brain metastases ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
    - bone scan ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
    - PET/CT, optional if there is evidence of extensive stage disease ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE) from skull base to mid-thigh if suspect limited stage or need clarification of stage; [ACCP Grade 2C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
      * alternatively, if PET/CT not available, bone scan may be used to detect metastases ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade B, Level V](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
      * if PET/CT alters stage, confirm findings on pathology ([ESMO Grade C, Level II](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
  + additional workup (if not done previously) for suspected limited-stage disease includes
    - pulmonary function tests in patients being evaluated for surgery or definitive radiation therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ESMO Grade A, Level V](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
    - bone MRI or x-ray if PET/CT inconclusive, and consider bone biopsy if results of MRI or x-ray are inconclusive ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - head MRI or CT in addition to PET, or abdominal CT plus bone scan in patients with clinical stage I disease considering definitive surgery ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
    - thoracentesis with cytologic analysis if pleural effusion present ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE)) and can be safely accessed
    - bone marrow aspiration and biopsy in select patients with presentation suggestive of bone marrow invasion, including signs of blood-bone marrow barrier rupture (such as nucleated red blood cells on peripheral blood smear [peripheral blood erythroblasts]), or abnormal blood count (such as neutropenia and thrombocytopenia) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ESMO Grade C, Level V](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
  + additional workup in for never smokers with extensive stage disease includes molecular profiling to clarify diagnosis and evaluate possible targeted therapies ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
  + see [Small Cell Lung Cancer Diagnosis and Staging](https://dpa-pde-oxford.shinyapps.io/evaluation/small-cell-lung-cancer-diagnosis-and-staging) for details

## **Management**

Management

* The following is the overview from [Management of small cell lung cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-small-cell-lung-cancer); please see topic for details.
  + GUID-74DEEFE3-A83E-4342-8316-A032AF580C68\_\_LI\_P1W\_ZBT\_TRBGSU12012112/01/2021 05:50:11 AMguidelineSummaryUpdatelowOncologic\_Disease Pulmonary\_DisordersEuropean Society of Medical Oncology (ESMO) recommendations on management of small cell lung cancer (ESMO 2021 Apr)management of limited stage disease
    - for patients with limited stage disease and negative pathologic mediastinal staging, perform lobectomy and mediastinal lymph node dissection or sampling ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 2C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade B, Level III](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE)), then follow with adjuvant treatment, based on findings from lymph node dissection or sampling
      * if lymph nodes negative, offer 4 cycles of adjuvant systemic therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade A, Level IV](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
      * if lymph nodes positive, offer sequential or concurrent systemic therapy with or without mediastinal radiation therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ESMO Grade A, Level I](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
    - for patients with limited stage disease and positive mediastinal staging or limited stage disease in excess of T1-T2, N0
      * if performance status (PS) 0-2, offer concurrent systemic therapy plus thoracic radiation therapy ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade A, Level I](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
      * if PS 3-4 due to small cell lung cancer, offer systemic therapy with or without either concurrent or sequential radiation therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * if PS 3-4 but not due to small cell lung cancer, offer an individualized treatment plan, including use of supportive care ([NCCN Evidence 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - for patients with limited stage disease and medically inoperable or decide not to pursue surgical resection, treatment options include either stereotactic ablative radiation therapy (SABR) followed by adjuvant systemic therapy ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE)) or concurrent chemoradiation ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - for patients with limited disease and complete or partial response to initial therapy, offer adjuvant prophylactic cranial irradiation (PCI) ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade A, Level I](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
  + management of extensive stage disease
    - for patients with no localized symptomatic sites or brain metastases, offer supportive care and base additional treatment on performance status (PS)
      * for performance status 0-2 or 3-4 due to small cell lung cancer, offer combination systemic therapy
      * for performance status 3-4 not due to small cell lung cancer, may offer an individualized treatment plan and consider best supportive care ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - for patients with localized symptomatic sites with superior vena cava syndrome, lobar obstruction, or bone metastases, treatment options include
      * systemic therapy with or without radiation therapy to symptomatic sites ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * orthopedic stabilization and palliative external beam radiation therapy, for patients with high risk of fracture due to osseous impairment ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - for patients with spinal cord compression, consider radiation therapy to symptomatic sites before systemic therapy (unless immediate systemic therapy is indicated) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - for patients with brain metastases
      * consider systemic therapy before brain radiation therapy if patient is asymptomatic ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * consider brain radiation therapy before systemic therapy (unless immediate systemic therapy is indicated) if patient is symptomatic ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - for patients with extensive stage disease and complete or partial response to initial therapy, treatment options include
      * adjuvant PCI or magnetic resonance imaging (MRI) surveillance of brain ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE); [ESMO Grade B, Level II](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE)); brain MRI is recommended as part of surveillance regardless of PCI ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * sequential (consolidative) thoracic radiation therapy after systemic therapy, particularly in those with residual thoracic disease and low-bulk metastatic disease ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ESMO Grade C, Level II](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
  + surveillance includes ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - routine history and physical with assessment of symptoms ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - computed tomography (CT) of chest, abdomen, and pelvis ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ESMO Grade C, Level V](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
    - MRI or CT of brain ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ESMO Grade C, Level II](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
    - intervention for smoking cessation ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ESMO Grade B, Level IV](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ESMOGRADE))
    - survivorship care plan ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
  + management of relapsed or progressive disease
    - offer palliative management of symptoms to all patients with relapsing or progressive disease at any time during treatment regardless of PS, including localized radiation therapy to symptomatic sites ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - for patients with relapsing or progressive disease and PS 0-2, offer subsequent systemic therapy with response assessment by chest/abdomen/pelvic CT with contrast after every 2-3 cycles ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * if response, continue therapy until disease progression or unacceptable toxicity ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * if no response or unacceptable toxicity and PS remains 0-2, options include subsequent systemic therapy and palliative management of symptoms including localized radiation therapy to symptomatic sites ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
  + see [Management of Small Cell Lung Cancer](https://dpa-pde-oxford.shinyapps.io/management/management-of-small-cell-lung-cancer) for details

## **Prognosis**

* median survival without treatment reported to be 2-4 months[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)
* PubMed30207593CA: a cancer journal for cliniciansCA Cancer J Clin20181101686394-424394worldwide there were 1,761,007 deaths from lung cancer (including both small cell and non-small cell lung cancers) in 2018 ([CA Cancer J Clin 2018 Nov;68(6):394](http://pubmed.ncbi.nlm.nih.gov/30207593?dopt=Abstract)[full-text](https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21492))
* in the United States
  + PubMed30620402CA: a cancer journal for cliniciansCA Cancer J Clin201901016917-347lung cancer estimated to be leading cause of death in both men and women in 2019 ([CA Cancer J Clin 2019 Jan;69(1):7](http://pubmed.ncbi.nlm.nih.gov/30620402?dopt=Abstract)[full-text](https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21551))
  + small cell lung cancer survival
    - 5-year survival was 6.5% overall, however rates differed between men and women with 5-year survival only 4.9% among men and 8.1% among women in 2015
    - 5-year relative survival rates 2009-2015
      * 6.3% overall
      * 27.3% for localized disease
      * 15.6% for regional disease
      * 2.8% for distant disease
      * 9.5% for disease with unknown extent at diagnosis
    - Reference - [Surveillance, Epidemiology, and End Results (SEER)](https://seer.cancer.gov/csr/1975_2016/browse_csr.php) accessed 2019 Dec 13
* factors associated with improved prognosis include[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)
  + improved [performance status](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#PERFORMANCE_STATUS_SCALES) (Karnofsky performance status > 80 or Eastern Cooperative Oncology Group [ECOG] 0-1)
  + female sex
  + younger age (age < 70 years, < 65 years, and < 60 years each independently validated)
* brain metastases develop in up to 50% of patients with extensive stage disease[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)
* paraneoplastic syndromes are more common in patients with limited stage disease than extensive stage disease, but association with prognosis is unclear[1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-2706DF3F-DEBB-47CF-8403-7E84F39A5E06__GENREF8168)
* **small cell tumor diameter > 25 mm associated with increased risk of metastases**

Cohort Study[mdc16476872pArch Intern Med 2006 Feb 13;166(3):321](http://pubmed.ncbi.nlm.nih.gov/16476872?dopt=Abstract)

studySummary

* + based on prognostic cohort study Cohort Study
  + 28 patients with small cell carcinoma identified on lung cancer screening were evaluated
  + proportion of small cell carcinomas with no metastases were
    - 67% for tumors ≤ 25 mm
    - 23% for tumors > 25 mm
  + PubMed16476872Archives of internal medicine20060213Arch Intern Med1663321321 Reference - [mdc16476872pArch Intern Med 2006 Feb 13;166(3):321](http://pubmed.ncbi.nlm.nih.gov/16476872?dopt=Abstract)
* **increase in arterial blood carboxyhemoglobin on day 4 of chemotherapy associated with response to chemotherapy after 2-4 cycles of chemotherapy in patients with small cell lung cancer**

Cohort Study[16460400J Am Geriatr Soc 2006 Feb;54(2):373](http://pubmed.ncbi.nlm.nih.gov/16460400?dopt=Abstract)

studySummary

* + based on prognostic cohort study Cohort Study
  + 35 elderly patients with small cell lung cancer and 66 elderly patients with non-small cell lung cancer had arterial blood carboxyhemoglobin measured on days 4 and 21 of first round of chemotherapy
  + response to chemotherapy in patients with small cell lung cancer was 100% with high arterial blood carboxyhemoglobin increases (> 0.3% of the maximum increases) vs. 22% with low arterial blood carboxyhemoglobin increases
  + PubMed16460400Journal of the American Geriatrics Society20060201J Am Geriatr Soc542373373 Reference - [16460400J Am Geriatr Soc 2006 Feb;54(2):373](http://pubmed.ncbi.nlm.nih.gov/16460400?dopt=Abstract)

## **Prevention and Screening**

Prevention and Screening

### **Prevention**

#### **Smoking Cessation**

* The following is an excerpt from [Treatment for Tobacco Use](https://dpa-pde-oxford.shinyapps.io/management/treatment-for-tobacco-use-19#GUID-638F06B0-D1A7-4B7A-837B-29256BD42EC7); please see topic for details.
  + American Cancer Society (ACS) recommends avoiding tobacco use and environmental tobacco smoke and avoiding radon exposure to reduce risk for lung cancer ([mnh22237782pcxh70249524pmdc22237782pCA Cancer J Clin 2012 Jan-Feb;62(1):30](http://pubmed.ncbi.nlm.nih.gov/22237782?dopt=Abstract)[full-text](http://onlinelibrary.wiley.com/doi/10.3322/caac.20140/abstract?systemMessage=Wiley+Online+Library+will+be+disrupted+on+4+August+from+10%3A00-12%3A00+BST+%2805%3A00-07%3A00+EDT%29+for+essential+maintenance))
  + all physicians should strongly advise every patient who smokes to quit, because physician advice to quit smoking increases abstinence rates ([PHS Strength of Evidence A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__PHSGRADE))
    - in addition, treatment delivered by a variety of clinician types increases abstinence rates, so all clinicians should provide smoking cessation interventions ([PHS Strength of Evidence A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__PHSGRADE))
    - 5-A strategy for advising patients recommended by United States Preventive Services Task Force (USPSTF)
      * **A**sk about tobacco use
      * **A**dvise to quit through clear personalized messages
      * **A**ssess willingness to quit
      * **A**ssist to quit
      * **A**rrange follow-up and support
  + combination of counseling and medication is more effective than either alone and both should be offered ([PHS Strength of Evidence A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__PHSGRADE))
  + first-line medication options include nicotine replacement therapy, varenicline, or bupropion ([PHS Strength of Evidence A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__PHSGRADE))
  + other smoking cessation techniques may be useful include cognitive behavioral therapy, acupuncture, mind-body interventions, and hypnotherapy
  + for pregnant women, offer face-to-face psychosocial interventions to quit ([PHS Strength of Evidence A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__PHSGRADE)), at first prenatal visit and throughout pregnancy ([PHS Strength of Evidence B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__PHSGRADE))
  + see [Treatment for Tobacco Use](https://dpa-pde-oxford.shinyapps.io/management/treatment-for-tobacco-use-19) for details

#### **Chemoprevention (Including Supplementation)**

* American College of Chest Physicians (ACCP) recommendations for primary, secondary, and tertiary chemoprevention of lung cancer
  + beta-carotene supplementation not recommended for persons with smoking history > 20 pack years or history of lung cancer ([ACCP Grade 1A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
  + in persons at risk of lung cancer or with history of lung cancer
    - the following agents are not recommended ([ACCP Grade 1A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
      * vitamin E
      * retinoids
      * N-acetylcysteine
      * isotretinoin
    - the following agents are not recommended outside of a well-designed clinical trial
      * selenium for tertiary prevention ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
      * aspirin ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
      * inhaled steroids ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
      * prostacyclin analogs, cyclo-oxygenase (COX)-2 inhibitors, or anethole dithiolethione ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
      * pioglitazone or myoinositol ([ACCP Grade 1B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
      * tea extract or metformin ([ACCP Grade 2C](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCPGRADE))
  + Reference - ACCP evidence-based clinical practice guideline on lung cancer chemoprevention ([23649449Chest 2013 May;143(5 Suppl):e40S](http://pubmed.ncbi.nlm.nih.gov/23649449?dopt=Abstract))
* CHEMOPREVENTION\_\_LI\_KZQ\_J1S\_L4BEU01272101/27/2021 02:41:20 PMevidenceUpdatelowplusFamily\_Medicine Internal\_Medicine Primary\_Carevitamin A may increase risk of lung cancer in persons who smoked and had previous asbestos exposure, but not in low-risk persons (Cochrane Database Syst Rev 2020 Mar 4)

**vitamin A may increase risk of lung cancer in persons who smoked and had previous asbestos exposure, but not in low-risk persons (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cochrane Review[Cochrane Database Syst Rev 2020 Mar 4;3:CD002141](http://pubmed.ncbi.nlm.nih.gov/32130738-drugs-for-preventing-lung-cancer-in-healthy-people/?dopt=Abstract)

studySummary

* + Cochrane Review based on Cochrane review with no significant difference in high-quality trials for persons with high risk, and with wide confidence interval for persons with low risk of developing lung cancer
  + systematic review of 12 randomized trials comparing vitamins, minerals, or other dietary supplements vs. placebo in healthy adults
  + 6 trials compared vitamin A to placebo
    - 3 trials included persons at high risk of developing lung cancer (smokers and previous exposure to asbestos)
    - 3 trials included persons at low risk of developing lung cancer
  + comparing vitamin A to placebo
    - in persons at high risk of developing lung cancer, vitamin A associated with
      * increased risk of lung cancer in analysis of 3 trials with 43,995 persons
        + risk ratio (RR) 1.1 (95% CI 1.01-1.2)
        + NNH 128-2,564 with lung cancer in 3.9% of placebo group
        + analysis included 3 high-quality trials, with nonsignificant increase in risk of lung cancer in 2 trials, and no significant difference in risk in 1 trial
      * increased lung cancer mortality in analysis of 2 trials with 29,426 persons
        + RR 1.18 (95% CI 1.01-1.38)
        + NNH 131-5,000 with lung cancer mortality 2% in placebo group
      * increased all-cause mortality in analysis of 2 trials with 32,883 persons
        + RR 1.09 (95% CI 1.05-1.13)
        + NNH 33-87 with all-cause mortality 23% in placebo group
    - in persons at low risk of developing lung cancer, no significant differences in
      * risk of lung cancer (RR 0.99, 95% CI 0.69-1.42) in analysis of 3 trials with 168,319 persons
      * lung cancer mortality (RR 0.71, 95% CI 0.35-1.44) in analysis of 2 trials with 160,692 persons
      * both results not significant, but CI includes possibility of benefit or harm
    - in 1 trial with 22,071 persons (mixed population)
      * yellowing of skin in 15.8% vs. 13.9% (p < 0.0001, NNH 52)
      * minor gastrointestinal symptoms in 2.4% vs. 1.1% (p < 0.0001, NNH 76)
  + PubMed32130738The Cochrane database of systematic reviewsCochrane Database Syst Rev202003043CD002141CD002141Reference - [Cochrane Database Syst Rev 2020 Mar 4;3:CD002141](http://pubmed.ncbi.nlm.nih.gov/32130738-drugs-for-preventing-lung-cancer-in-healthy-people/?dopt=Abstract)
* CHEMOPREVENTION\_\_LI\_TPX\_Y1S\_L4BEU01272101/27/2021 02:46:04 PMevidenceUpdatelowplusFamily\_Medicine Internal\_Medicine Primary\_Carevitamin C increases risk of lung cancer in women but may not increase risk of lung cancer in men (Cochrane Database Syst Rev 2020 Mar 4)

**vitamin C increases risk of lung cancer in women (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**) but may not increase risk of lung cancer in men (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cochrane Review[Cochrane Database Syst Rev 2020 Mar 4;3:CD002141](http://pubmed.ncbi.nlm.nih.gov/32130738-drugs-for-preventing-lung-cancer-in-healthy-people/?dopt=Abstract)

studySummary

* + Cochrane Review based on Cochrane review with wide confidence interval for lung cancer in men
  + systematic review of 12 randomized trials comparing vitamins, minerals, and other dietary supplements vs. placebo in healthy adults
  + 3 trials compared vitamin C (ascorbic acid) to placebo
  + mean follow-up ranged from 8 to 9 years
  + comparing vitamin C to placebo
    - incidence of lung cancer
      * 1.2% vs. 0.6% (p = 0.01, NNH 166) in 1 trial with 7,627 women
      * 1.3% vs. 1.4% (risk ratio 0.94, 95% CI 0.64-1.38) in 1 trial with 7,326 men, not significant, but CI includes possibility of benefit or harm
    - no significant difference in lung cancer mortality or all-cause mortality in 1 trial with 7,326 men
  + PubMed32130738The Cochrane database of systematic reviewsCochrane Database Syst Rev202003043CD002141CD002141Reference - [Cochrane Database Syst Rev 2020 Mar 4;3:CD002141](http://pubmed.ncbi.nlm.nih.gov/32130738-drugs-for-preventing-lung-cancer-in-healthy-people/?dopt=Abstract)
* CHEMOPREVENTION\_\_LI\_GVV\_2BS\_L4BEU01272101/27/2021 02:47:32 PMevidenceUpdatestandardFamily\_Medicine Internal\_Medicine Primary\_Carevitamin E does not reduce risk of lung cancer, and vitamin D plus calcium and selenium each may not reduce risk of lung cancer in healthy adults (Cochrane Database Syst Rev 2020 Mar 4)

**vitamin E does not reduce risk of lung cancer (**[**level 1 [likely reliable] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**), and vitamin D plus calcium and selenium each may not reduce risk of lung cancer (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**) in healthy adults**

Cochrane Review[Cochrane Database Syst Rev 2020 Mar 4;3:CD002141](http://pubmed.ncbi.nlm.nih.gov/32130738)

studySummary

* + Cochrane Review based on Cochrane review with wide confidence intervals for vitamin D plus calcium and selenium
  + systematic review of 12 randomized trials comparing vitamins, minerals, and other dietary supplements vs. placebo in healthy adults
  + 5 trials compared vitamin E (alpha-tocopherol) to placebo in healthy adults
  + comparing vitamin E to placebo
    - no significant differences in
      * lung cancer incidence (risk ratio [RR] 1.01, 95% CI 0.9-1.14) in analysis of 3 trials with 36,841 adults
      * lung cancer mortality (RR 0.96, 95% CI 0.77-1.18) in analysis of 2 trials with 29,214 adults
    - vitamin E associated with increased risk of hemorrhagic stroke (hazard ratio 1.74, 95% CI 1.04-2.91) in 1 trial with 14,641 adults
  + 3 trials compared vitamin D plus calcium to placebo in healthy postmenopausal women
    - dose ranged from vitamin D3 400 to 2000 units/day plus 1000 to 1500 mg/day calcium carbonate
    - mean follow-up ranged from 4 to 7 years
  + comparing vitamin D plus calcium to placebo, no significant differences in
    - risk of lung cancer in analysis of 3 trials with 37,601 women
      * RR 0.9 (95% CI 0.39-2.08)
      * not significant, but CI includes possibility of benefit or harm
    - risk of renal calculi in analysis of 2 trials with 2,931 women
  + 1 trial compared selenium to placebo in healthy adults
  + mean follow-up was 7 years
  + comparing selenium to placebo in 1 trial with 17,448 men
    - no significant differences in
      * risk of lung cancer (RR 1.11, 95% CI 0.8-1.54), not significant, but CI includes possibility of benefit or harm
      * lung cancer mortality (RR 1.09, 95% CI 0.72-1.66)
    - selenium associated with increased risk of dermatitis and alopecia
  + PubMed32130738The Cochrane database of systematic reviewsCochrane Database Syst Rev202003043CD002141CD002141Reference - [Cochrane Database Syst Rev 2020 Mar 4;3:CD002141](http://pubmed.ncbi.nlm.nih.gov/32130738)
* **no vitamin supplements appear effective for lung cancer prevention while vitamin E use and long-term beta-carotene, lutein, or retinol use each appear to increase risk (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Cohort Study[19208726Am J Epidemiol 2009 Apr 1;169(7):815](http://pubmed.ncbi.nlm.nih.gov/19208726?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2842198/)Cohort Study[Am J Respir Crit Care Med 2008 Mar 1;177(5):524](http://pubmed.ncbi.nlm.nih.gov/17989343/)

studySummary

* + Cohort StudyCohort Study based on 2 analyses of data from VITAL cohort of > 77,000 adults aged 50-76 years
  + 77,126 adults aged 50-76 years completed baseline survey about supplement use during previous 10 years and were then followed for mean of 4 years
    - 47% were never smokers
    - beta-carotene use > 4 years associated with increased risk for small cell lung cancer compared to no beta-carotene use (adjusted hazard ratio [HR] 3.22, 95% CI 1.29-8.07)
    - lutein use > 10 years as individual supplement associated with increased risk compared to no lutein use
      * for all lung cancer (adjusted HR 2.02, 95% CI 1.28-3.17)
      * for non-small cell lung cancer (adjusted HR 2.48, 95% CI 1.53-4.02)
    - retinol use > 4 years associated with increased risk compared to no retinol use
      * for all lung cancer (adjusted HR 1.53, 95% CI 1.12-2.08)
      * for non-small cell lung cancer (adjusted HR 1.8, 95% CI 1.29-2.52)
    - PubMed19605516American journal of epidemiologyAm J Epidemiol200908011703401-2401 Reference - [19208726Am J Epidemiol 2009 Apr 1;169(7):815](http://pubmed.ncbi.nlm.nih.gov/19208726?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2842198/), commentary can be found in [Am J Epidemiol 2009 Aug 1;170(3):401](http://pubmed.ncbi.nlm.nih.gov/19605516/)
  + 77,721 men and women aged 50-76 years were evaluated for supplement use (including multivitamin supplements, vitamin C, vitamin E, and folate) and incidence of lung cancer
    - lung cancer identified in 0.67%
    - adjusting for smoking, age, and sex, there was no association between lung cancer and any supplement
    - vitamin E associated with increased risk of lung cancer (hazard ratio [HR] 1.05 for every 100-mg/day increase in dose, 95% CI 1-1.09), especially for
      * current smokers (HR 1.11 for every 100-mg/day increase, 95% CI 1.03-1.19)
      * non-small cell lung cancer (HR 1.07 for every 100-mg/day increase, 95% CI 1.02-1.12)
    - PubMed17989343American journal of respiratory and critical care medicineAm J Respir Crit Care Med200803011775524-30524 Reference - [Am J Respir Crit Care Med 2008 Mar 1;177(5):524](http://pubmed.ncbi.nlm.nih.gov/17989343/)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2258445/), editorial can be found in [18296467Am J Respir Crit Care Med 2008 Mar 1;177(5):470](http://pubmed.ncbi.nlm.nih.gov/18296467?dopt=Abstract)
* **regular aspirin use does not appear to reduce risk of lung cancer in women or men (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Randomized Trial[ACP J Club 2006 Jan;144(1):8](http://pubmed.ncbi.nlm.nih.gov/16388558/)Cohort Study[Br J Cancer 2003 Nov 3;89(9):1705](http://pubmed.ncbi.nlm.nih.gov/14583773/)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2394407/)

studySummary

* + Randomized TrialCohort Study based on 1 randomized trial with low adherence rate and 1 cohort study
  + 39,876 healthy women > 45 years old who completed 3-month placebo run-in period were randomized to aspirin 100 mg vs. placebo orally every other day (and also randomized to vitamin E 600 units vs. placebo orally every other day) for mean 10 years (range 8-11 years)
    - 13% of women were current smokers and 36% were past smokers
    - 76% of women reported taking at least two-thirds of assigned aspirin or placebo tablets at 5 years (67% at 10 years)
    - 79% of women reported taking at least two-thirds of assigned vitamin E dosage or placebo at 5 years (72% at 10 years)
    - comparing aspirin vs. placebo, incidence of lung cancer 0.45% vs. 0.58% (p = 0.08)
    - PubMed16388558ACP journal clubACP J Club2006010114418-98 Reference - Women's Health Study ([ACP J Club 2006 Jan;144(1):8](http://pubmed.ncbi.nlm.nih.gov/16388558/)), editorial can be found in [mdc15998897pJAMA 2005 Jul 6;294(1):105](http://pubmed.ncbi.nlm.nih.gov/15998897?dopt=Abstract), commentary can be found in [Am Fam Physician 2005 Nov 15;72(10):2087](http://www.aafp.org/afp/2005/1115/p2087.html)
  + prospective cohort study of 49,383 male physicians aged 40-75 years in United States
    - 328 developed lung cancer during 601,453 person-years of follow-up
    - regular use of aspirin (twice or more weekly, dose information not available) not associated with reduced risk of lung cancer (adjusted risk ratio 1.13, 95% CI 0.89-1.43) compared to nonusers
    - PubMed14583773British journal of cancerBr J Cancer200311038991705-81705 Reference - [Br J Cancer 2003 Nov 3;89(9):1705](http://pubmed.ncbi.nlm.nih.gov/14583773/)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2394407/)

#### **Dietary Measures**

* **increased cruciferous vegetable consumption associated with decreased risk of lung cancer in women (**[**level 2 [mid-level] evidence**](https://www.dynamed.com/home/editorial/editorial-process)**)**

Systematic Review[23553059Ann Oncol 2013 Jul;24(7):1918](http://pubmed.ncbi.nlm.nih.gov/23553059?dopt=Abstract)[Full Text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3690909/)

studySummary2

* + based on systematic review of observational studies Systematic Review
  + systematic review of 10 observational studies evaluating association between cruciferous vegetable consumption with risk of lung cancer in women
  + compared to lowest quartile, highest quartile of cruciferous vegetable consumption associated with reduced risk of lung cancer (relative risk 0.75, 95% CI 0.63-0.89), results limited by significant heterogeneity
  + PubMed23553059Annals of oncology : official journal of the European Society for Medical Oncology20130701Ann Oncol24719181918 Reference - [23553059Ann Oncol 2013 Jul;24(7):1918](http://pubmed.ncbi.nlm.nih.gov/23553059?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3690909/)

### **Screening**

* The following is the overview from [Lung Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/lung-cancer-screening); please see topic for details.
  + goal of screening is to benefit individuals by increasing life expectancy and quality of life, but with low false-positive results to prevent additional, unnecessary testing
  + low-dose computed tomography (LDCT) screening detects lung cancer in about 1%-2% of patients who smoke or have other risk factors for lung cancer
  + risk stratification
    - low risk if < 50 years old and/or < 20 pack-year history of smoking ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - moderate risk if ≥ 50 years old and ≥ 20 pack-year history of smoking or second-hand smoke exposure and no additional risk factors ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
    - high risk if either of the following
      * age 55-74 years and ≥ 30 pack-year history of smoking and smoking cessation < 15 years ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
      * age ≥ 50 years and ≥ 20 pack-year history of smoking and presence of additional risk factors that increase risk of lung cancer to ≥ 1.3% (not including second-hand smoke exposure), including personal history of cancer or lung disease, family history of lung cancer, radon exposure, or relevant occupational exposure ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE))
  + recommendations
    - screening of lung cancer using LDCT recommended or suggested in patients with
      * age 55-74 years, ≥ 30 pack-year history of smoking, and smoking cessation < 15 years ([NCCN Category 1](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Weak recommendation, Moderate-quality evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCP2018GRADE) also includes patients aged 75-77 years; [USPSTF Grade B](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__USPSTFGRADE), also includes patients aged 75-80 years)
      * age ≥ 50 years, ≥ 20 pack-year history of smoking, and presence of additional risk factors that increase risk of lung cancer to ≥ 1.3% (not including second-hand smoke exposure) ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE)); risk factors include personal history of cancer or lung disease, family history of lung cancer, radon exposure, or relevant occupational exposure
    - routine lung cancer screening with LDCT not recommended or suggested in patients who
      * are asymptomatic, do not meet above criteria, and are at high risk based on clinical prediction calculators ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Weak recommendation, Low-quality evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCP2018GRADE))
      * do not meet above criteria, and are not at high risk based on clinical prediction calculators ([NCCN Category 2A](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__NCCNGRADE); [ACCP Strong recommendation, Moderate-quality evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCP2018GRADE))
      * have severe comorbidities which would preclude evaluation of findings or potentially definitive treatment, or limit life expectancy ([ACCP Strong recommendation, Low-quality evidence](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-3E28B394-A066-44F6-BB6F-EC6648BC6C22__ACCP2018GRADE))
  + diagnostic accuracy of LDCT
    - LDCT screening has high sensitivity and moderate specificity for lung cancer, but may be associated with high rate of false-positives, leading to unnecessary, invasive follow-up procedures
    - LDCT reported to be as accurate as standard-dose CT for detection of solid nodules, but reported to be less sensitive for detection of very low-density nonsolid nodules or ground-glass opacity nodules
  + follow-up testing based on LDCT findings
  + see [Lung Cancer Screening](https://dpa-pde-oxford.shinyapps.io/prevention/lung-cancer-screening) for details

## **Guidelines and Resources**

### **Guidelines**

#### **International Guidelines**

* American Society of Clinical Oncology/Cancer Care Ontario (ASCO/CCO) guideline on systemic therapy for small cell lung cancer can be found at [ASCO 2023 Oct](https://old-prod.asco.org/practice-patients/guidelines/thoracic-cancer#/189544)
* College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology (CAP/IASLC/AMP) updated guideline on molecular testing for selection of lung cancer patients for treatment with targeted tyrosine kinase inhibitors can be found in [29355391Arch Pathol Lab Med 2018 Mar;142(3):321](http://pubmed.ncbi.nlm.nih.gov/29355391?dopt=Abstract)[full-text](http://www.archivesofpathology.org/doi/10.5858/arpa.2017-0388-CP)
* American Thoracic Society/European Respiratory Society (ATS/ERS) statement on role of pulmonologist in diagnosis and management of lung cancer can be found in [23947517Am J Respir Crit Care Med 2013 Aug 15;188(4):503](http://pubmed.ncbi.nlm.nih.gov/23947517?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5448508/)
* International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society (IASLC/ATS/ERS) international multidisciplinary classification of lung adenocarcinoma can be found in [21252716J Thorac Oncol 2011 Feb;6(2):244](http://pubmed.ncbi.nlm.nih.gov/21252716?dopt=Abstract), executive summary can be found in [21926387Proc Am Thorac Soc 2011 Sep;8(5):381](http://pubmed.ncbi.nlm.nih.gov/21926387?dopt=Abstract), editorial can be found in [21252714J Thorac Oncol 2011 Feb;6(2):239](http://pubmed.ncbi.nlm.nih.gov/21252714?dopt=Abstract), commentary can be found in [21847046J Thorac Oncol 2011 Jul;6(7):1298](http://pubmed.ncbi.nlm.nih.gov/21847046?dopt=Abstract)

#### **United States Guidelines**

* American College of Chest Physicians (ACCP)
  + executive summary of ACCP evidence-based clinical practice guidelines on diagnosis and management of lung cancer can be found in [23649434Chest 2013 May;143(5 Suppl):7S](http://pubmed.ncbi.nlm.nih.gov/23649434?dopt=Abstract)
  + evidence-based clinical practice guidelines on
    - treatment of small cell lung cancer can be found in [23649448Chest 2013 May;143(5 Suppl):e400S](http://pubmed.ncbi.nlm.nih.gov/23649448?dopt=Abstract), American Society of Clinical Oncology (ASCO) endorsement of guideline can be found in [cxh111081074pmdc26351333pJ Clin Oncol 2015 Dec 1;33(34):4106](http://pubmed.ncbi.nlm.nih.gov/26351333?dopt=Abstract)
    - chemoprevention of lung cancer can be found in [23649449Chest 2013 May;143(5 Suppl):e40S](http://pubmed.ncbi.nlm.nih.gov/23649449?dopt=Abstract)
    - treatment of tobacco use in lung cancer can be found at [23649454Chest 2013 May;143(5 Suppl):e61S](http://pubmed.ncbi.nlm.nih.gov/23649454?dopt=Abstract)
    - screening for lung cancer can be found in [23649455Chest 2013 May;143(5 Suppl):e78S](http://pubmed.ncbi.nlm.nih.gov/23649455?dopt=Abstract)
    - evaluation of individuals with pulmonary nodules can be found in [23649456Chest 2013 May;143(5 Suppl):e93S](http://pubmed.ncbi.nlm.nih.gov/23649456?dopt=Abstract)
    - clinical and organizational factors in initial evaluation of patients with lung cancer can be found in [23649435Chest 2013 May;143(5 Suppl):e121S](http://pubmed.ncbi.nlm.nih.gov/23649435?dopt=Abstract)
    - establishing diagnosis of lung cancer can be found in [23649436Chest 2013 May;143(5 Suppl):e142S](http://pubmed.ncbi.nlm.nih.gov/23649436?dopt=Abstract)
    - physiologic evaluation of patient with lung cancer being considered for resectional surgery can be found in [23649437Chest 2013 May;143(5 Suppl):e166S](http://pubmed.ncbi.nlm.nih.gov/23649437?dopt=Abstract)
    - diagnostic surgical pathology in lung cancer can be found in [23649441Chest 2013 May;143(5 Suppl):e251S](http://pubmed.ncbi.nlm.nih.gov/23649441?dopt=Abstract)
    - diagnosis and treatment of bronchial intraepithelial neoplasia and early lung cancer of central airways can be found in [23649442Chest 2013 May;143(5 Suppl):e263S](http://pubmed.ncbi.nlm.nih.gov/23649442?dopt=Abstract)
    - complementary therapies and integrative medicine in lung cancer can be found in [23649450Chest 2013 May;143(5 Suppl):e420S](http://pubmed.ncbi.nlm.nih.gov/23649450?dopt=Abstract)
    - follow-up and surveillance of patient with lung cancer after curative-intent therapy can be found in [23649451Chest 2013 May;143(5 Suppl):e437S](http://pubmed.ncbi.nlm.nih.gov/23649451?dopt=Abstract)
    - symptom management in patients with lung cancer can be found at [23649452Chest 2013 May;143(5 Suppl):e455S](http://pubmed.ncbi.nlm.nih.gov/23649452?dopt=Abstract)
    - palliative and end-of-life care in lung cancer can be found in [23649453Chest 2013 May;143(5 Suppl):e498S](http://pubmed.ncbi.nlm.nih.gov/23649453?dopt=Abstract)
    - symptomatic treatment of cough among adult patients with lung cancer can be found in [Chest 2017 Apr;151(4):861](http://pubmed.ncbi.nlm.nih.gov/28108179?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6026217/)
* UNITED\_STATES\_GUIDELINES\_\_LI\_YLR\_F45\_CWBGNU01092301/09/2023 11:13:44 AMguidelineNotationUpdatelowOncologic\_DiseaseAmerican Thoracic Society guideline on stakeholder research priorities to promote implementation of shared decision-making for lung cancer screening (Am J Respir Crit Care Med 2022 Mar 15)American Thoracic Society (ATS) guideline on stakeholder research priorities to promote implementation of shared decision-making for lung cancer screening can be found in [Am J Respir Crit Care Med 2022 Mar 15;205(6):619](https://pubmed.ncbi.nlm.nih.gov/35289730)
* American College of Radiology (ACR) Appropriateness Criteria for hemoptysis can be found at [ACR 2019 PDF](https://acsearch.acr.org/docs/69449/Narrative/)
* UNITED\_STATES\_GUIDELINES\_\_LI\_K4C\_PDD\_5XBGNU06132306/13/2023 10:23:57 AMguidelineNotationUpdatelowOncologic\_DiseaseNational Comprehensive Cancer Network (NCCN) statement on mitigating the impacts of anticancer drug shortages (NCCN 2023 Jun 7)National Comprehensive Cancer Network (NCCN) statement on mitigating the impacts of anticancer drug shortages can be found at [NCCN 2023 Jun 7 PDF](https://www.nccn.org/docs/default-source/oncology-policy-program/NCCN-Statement-on-Anti-Cancer-Drug-Shortages.pdf)
* National Comprehensive Cancer Network (NCCN) clinical practice guidelines on
  + small cell lung cancer can be found at [NCCN website](https://www.nccn.org/professionals/physician_gls/default.aspx) (free registration required)
  + lung cancer screening can be found at [NCCN website](https://www.nccn.org/professionals/physician_gls/default.aspx) (free registration required)
  + smoking cessation for patients with cancer can be found at [NCCN website](http://www.nccn.org/professionals/physician_gls/f_guidelines.asp) (free registration required)
* UNITED\_STATES\_GUIDELINES\_\_LI\_D1K\_12D\_5XBGNU06132306/13/2023 10:27:54 AMguidelineNotationUpdatelowOncologic\_DiseaseASCO position on prioritization of antineoplastic agents in limited supply for first intervention (ASCO 2023 Jun 13)American Society of Clinical Oncology (ASCO) position on prioritization of antineoplastic agents in limited supply for first intervention can be found at [ASCO](https://old-prod.asco.org/practice-patients/practice-support/drug-shortages/clinical-guidance), accessed 2023 Jun 13
* American Cancer Society (ACS)
  + guideline on nutrition and physical activity for cancer prevention can be found in [CA Cancer J Clin 2020 Jul;70(4):245](http://pubmed.ncbi.nlm.nih.gov/32515498)[full-text](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21591)
  + guideline on nutrition and physical activity for cancer survivors can be found in [22539238CA Cancer J Clin 2012 Jul;62(4):242](http://pubmed.ncbi.nlm.nih.gov/22539238?dopt=Abstract)[full-text](http://onlinelibrary.wiley.com/doi/10.3322/caac.21142/full), correction can be found in CA Cancer J Clin 2013 May;63(3):215
  + review of guidelines and issues in cancer screening can be found in [mnh25581023pcxh100399216t pmdc25581023pCA Cancer J Clin 2015 Jan-Feb;65(1):30](http://pubmed.ncbi.nlm.nih.gov/25581023?dopt=Abstract)[full-text](http://onlinelibrary.wiley.com/doi/10.3322/caac.21261/full)
* UNITED\_STATES\_GUIDELINES\_\_LI\_E3K\_RBM\_3BCGNU05082405/08/2024 02:23:14 PMguidelineNotationUpdatelowOncologic\_DiseaseCollege of American Pathologists (CAP) guideline on PD-L1 and TMB testing of patients with lung cancer for immunooncology therapies (CAP 2024 Apr 16)College of American Pathologists (CAP) guideline on PD-L1 and TMB testing of patients with lung cancer for immunooncology therapies can be found at [CAP 2024 Apr 16](https://www.cap.org/protocols-and-guidelines/current-cap-guidelines/pd-l1-testing-of-patients-with-lung-cancer-for-immunooncology-therapies).

#### **United Kingdom Guidelines**

* National Institute for Health and Care Excellence (NICE) guidelines on
  + AI-derived computer-aided detection (CAD) software for detecting and measuring lung nodules in CT scan images can be found at [NICE 2023 Jul 5:DG55](https://www.nice.org.uk/guidance/dg55)[PDF](https://www.nice.org.uk/guidance/dg55/resources/aiderived-computeraided-detection-cad-software-for-detecting-and-measuring-lung-nodules-in-ct-scan-images-pdf-1053873334213)
  + atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer can be found at [NICE 2020 Jul 1:TA638](https://www.nice.org.uk/guidance/ta638)[PDF](https://www.nice.org.uk/guidance/ta638/resources/atezolizumab-with-carboplatin-and-etoposide-for-untreated-extensivestage-smallcell-lung-cancer-pdf-82609084441285)
  + UNITED\_KINGDOM\_GUIDELINES\_\_LI\_BPW\_5ML\_51CGNU03192403/19/2024 11:09:35 AMguidelineNotationUpdatelowOncologic\_DiseaseNational Institute for Health and Care Excellence (NICE) guideline on diagnosis and management of lung cancer can be found at (NICE 2019 Mar 28:NG122, last updated 2024 Mar 8)diagnosis and management of lung cancer can be found at [NICE 2019 Mar 28:NG122, last updated 2024 Mar 8](https://www.nice.org.uk/guidance/ng122)[PDF](https://www.nice.org.uk/guidance/ng122/resources/lung-cancer-diagnosis-and-management-pdf-66141655525573)
  + Oncologic\_DiseaseNICE guideline on recognition and referral of suspected cancer (NICE 2015 Jun)11/04/2015 01:07:00 PMrecognition and referral of suspected cancer can be found at [NICE 2015 Jun 23:NG12, last updated 2021 Dec 15](http://www.nice.org.uk/guidance/ng12)[PDF](http://www.nice.org.uk/guidance/ng12/resources/suspected-cancer-recognition-and-referral-1837268071621)
* Scottish Intercollegiate Guidelines Network (SIGN) national clinical guideline on management of lung cancer can be found at [SIGN 2014 Feb PDF](https://www.sign.ac.uk/media/1075/sign137.pdf)

#### **Canadian Guidelines**

* PubMed37504325Current oncology (Toronto, Ont.)Curr Oncol202306303076289-63156289expert Canadian consensus recommendations on the management of extensive-stage small cell lung cancer can be found in [Curr Oncol 2023 Jun 30;30(7):6289](https://pubmed.ncbi.nlm.nih.gov/37504325)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10378571/)
* Cancer Care Ontario (CCO)
  + CCO Program in Evidence-Based Care guidelines on
    - prophylactic cranial irradiation and consolidative radiation for patients with small cell lung cancer can be found at [CCO 2019 Nov](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/2396)
    - initial management of small cell lung cancer and the role of thoracic radiotherapy and first-line chemotherapy can be found at [CCO 2017 Oct](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/49411)
    - focal tumor ablation for early-stage primary lung cancer and lung metastases can be found at [CCO 2016 Aug](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/4106)
    - role of intensity-modulated radiation therapy (IMRT) in lung cancer can be found at [CCO 2010 Nov](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/2186)
    - follow-up and surveillance of curatively treated lung cancer patients can be found at [CCO 2014 Aug](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/261)
  + CCO best practices on oncologic pathology secondary review: lung cancer can be found at [CCO 2014 Jun](https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/406)
* Alberta Health Services (AHS)
  + clinical practice guideline on small cell lung cancer: extensive stage can be found at [AHS 2012 Jul PDF](http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-lu007-lcsc-extens-stage.pdf)
  + clinical practice guideline on small cell lung cancer: limited stage can be found at [AHS 2012 Jul PDF](http://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-lu006-lcsc-ltd-stage.pdf)

#### **European Guidelines**

* European Society of Medical Oncology (ESMO)
  + PubMed33864941Annals of oncology : official journal of the European Society for Medical OncologyAnn Oncol20210701327839-853839 clinical practice guideline on diagnosis, treatment, and follow-up of small cell lung cancer can be found in [Ann Oncol 2021 Jul;32(7):839](http://pubmed.ncbi.nlm.nih.gov/33864941)
  + consensus statement on small cell lung cancer can be found in [21727198Ann Oncol 2011 Sep;22(9):1973](http://pubmed.ncbi.nlm.nih.gov/21727198?dopt=Abstract)
  + clinical practice guideline on diagnosis, treatment, and follow-up of neuroendocrine bronchial and thymic tumors can be found in [22997444Ann Oncol 2012 Oct;23 Suppl 7:vii120](http://pubmed.ncbi.nlm.nih.gov/22997444?dopt=Abstract)
  + bone health in cancer patients can be found in [24782453Ann Oncol 2014 Sep;25 Suppl 3:iii 124](http://pubmed.ncbi.nlm.nih.gov/24782453?dopt=Abstract)
* Cardiovascular and Interventional Radiological Society of Europe (CIRSE) guideline on thermal ablation of primary and secondary lung tumors can be found in [32095842Cardiovasc Intervent Radiol 2020 May;43(5):667](http://pubmed.ncbi.nlm.nih.gov/32095842?dopt=Abstract)
* National Board of Health and Welfare (NBHW [Socialstyrelsen]) guideline on lung cancer can be found at [NBHW 2011 Mar PDF](https://www.socialstyrelsen.se/globalassets/sharepoint-dokument/artikelkatalog/nationella-riktlinjer/2011-3-2.pdf) [Swedish]
* EUROPEAN\_GUIDELINES\_\_LI\_WBB\_4Z3\_Y1CGNU04022404/02/2024 10:06:32 AMguidelineNotationUpdatelowOccupational\_and\_Environmental\_MedicineDeutsche Gesellschaft für Pneumologie und Beatmungsmedizin e.V./Deutsche Krebsgesellschaft e.V. (German Society for Pulmonology and Respiratory Medicine/German Cancer Society eV) (DGP/DKG) guideline on prävention, diagnostik, therapie und nachsorge des lungenkarzinoms (prevention, diagnosis, therapy and aftercare of lung cancer) (AWMF 2024 Mar 20)Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e.V./Deutsche Krebsgesellschaft e.V. (German Society for Pulmonology and Respiratory Medicine/German Cancer Society eV) (DGP/DKG) guideline on prävention, diagnostik, therapie und nachsorge des lungenkarzinoms (prevention, diagnosis, therapy and aftercare of lung cancer) can be found at Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften [(AWMF) 2024 Mar 20 PDF](https://register.awmf.org/assets/guidelines/020-007OLl_S3_Praevention-Diagnostik-Therapie-Nachsorge-Lungenkarzinom_2024-03.pdf) [German].
* Nemzeti Erőforrás Minisztérium (Department of Human Resources [NEFMI]) basic principles on prevention, diagnosis, and therapy of lung cancer can be found in [22724157Magy Onkol 2012 May;56(2):114](http://pubmed.ncbi.nlm.nih.gov/22724157?dopt=Abstract)[PDF](http://huon.hu/2012/56/2/0114/0114a.pdf) [Hungarian]
* European Lung Cancer Working Party (ELCWP) guidelines on
  + treatment of limited small cell lung cancer can be found in [25102582Rev Med Brux 2014 May-Jun;35(3):160](http://pubmed.ncbi.nlm.nih.gov/25102582?dopt=Abstract) [French]
  + management of extensive disease small cell lung cancer can be found in [25102583Rev Med Brux 2014 May-Jun;35(3):164](http://pubmed.ncbi.nlm.nih.gov/25102583?dopt=Abstract) [French]
* Italian Association of Medical Oncologists (Associazione Italiana Oncologi Medici) (AIOM) guideline on lung cancers can be found at Sistema Nazionale Linee Guida dell’Istituto Superiore di Sanità [(SNLG-ISS) Mar 2020, updated 2021 Oct PDF](https://snlg.iss.it/wp-content/uploads/2021/11/LG-149_Polmone_agg2021.pdf) [Italian]
* Spanish Society of Medical Oncology (SEOM) clinical guideline on treatment of small cell lung cancer can be found in [20080468Clin Transl Oncol 2010 Jan;12(1):27](http://pubmed.ncbi.nlm.nih.gov/20080468?dopt=Abstract)
* Sociedad Española Neumología y Cirugía Torácica (Spanish Society of Pulmonology and Thoracic Surgery [SEPAR]) guideline on lung cancer staging can be found in [21824707Arch Bronconeumol 2011 Sep;47(9):454](http://pubmed.ncbi.nlm.nih.gov/21824707?dopt=Abstract) [English, Spanish], commentary can be found in [22100701Arch Bronconeumol 2012 Jan;48(1):32](http://pubmed.ncbi.nlm.nih.gov/22100701?dopt=Abstract) [English, Spanish]
* Gruppo Italiano Patologi Apparato Digerente (Italian Group of Gastrointestinal Pathologists [GIPAD]) report on gastroenteropancreatic (neuro)endocrine neoplasms can be found in [21459341Dig Liver Dis 2011 Mar;43 Suppl 4:S356](http://pubmed.ncbi.nlm.nih.gov/21459341?dopt=Abstract).
* PubMed33999752Acta oncologica (Stockholm, Sweden)Acta Oncol20210701607931-941931 Nordic expert guideline on diagnosis and treatment of gastroenteropancreatic neuroendocrine neoplasms can be found in [Acta Oncol 2021 Jul;60(7):931](https://pubmed.ncbi.nlm.nih.gov/33999752).
* European Federation of Neurological Societies (EFNS) report on screening for tumors in paraneoplastic syndromes can be found in [20880069Eur J Neurol 2011 Jan;18(1):19](http://pubmed.ncbi.nlm.nih.gov/20880069?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086523/?tool=pubmed)
* Norwegian Directorate of Health (DOH) national guideline on treatment and follow-up of lung cancer, mesothelioma and thymoma can be found at [DOH 2018 Jul PDF](https://helsedirektoratet.no/Lists/Publikasjoner/Attachments/1400/IS-2745%20-%20Lungekrefthandlingsprogram%20170718.pdf) [Norwegian]
* Polskie Towarzystwo Chorób Płuc (Polish Respiratory Society) (PTCHP) recommendations on palliative care in chronic lung diseases can be found in [22187179Pneumonol Alergol Pol 2012;80(1):41](http://pubmed.ncbi.nlm.nih.gov/22187179?dopt=Abstract) [Polish], commentary can be found in [22187173Pneumonol Alergol Pol 2012;80(1):1](http://pubmed.ncbi.nlm.nih.gov/22187173?dopt=Abstract).
* Dutch Society for Neuro-Oncology/Comprehensive Cancer Centre the Netherlands (LWNO/IKNL) guideline on brain metastases can be found in [22217243Ned Tijdschr Geneeskd 2011;155(52):A4141](http://pubmed.ncbi.nlm.nih.gov/22217243?dopt=Abstract) [Dutch], commentary can be found in [22166181Ned Tijdschr Geneeskd 2011;155(49):A4294](http://pubmed.ncbi.nlm.nih.gov/22166181?dopt=Abstract)

#### **Mexican Guidelines**

* Grupos de Desarrollo de las Instituciones Públicas del Sistema Nacional de Salud de México (Secretaría de Salud, IMSS, ISSSTE, SEDENA, SEMAR, DIF, PEMEX) guías de práctica clínica en prevención y detección temprana del cáncer de pulmón en el primer nivel de atención se pueden encontrar en [Secretaría de Salud-México 2013 PDF](http://www.cenetec.salud.gob.mx/descargas/gpc/CatalogoMaestro/022_GPC_Ca_Pulmonar1erNivel/SSA_022_08_EyR.pdf" \t "_blank) [Spanish]

#### **Middle Eastern Guidelines**

* Saudi Thoracic Society guideline on lung cancer management can be found at [STS 2019 Feb 25](https://saudithoracicsociety.org/wp-content/uploads/2019/11/Saudi-Lung-Cancer-Guidelines-2019-Feb-25-2019-revised.pdf)
* expert guideline on multimodality radiological staging of lung cancer can be found in [23244181J Infect Public Health 2012 Dec;5 Suppl 1:S14](http://pubmed.ncbi.nlm.nih.gov/23244181?dopt=Abstract)
* expert guideline on role of fluorodeoxyglucose positron emission tomography/computed tomography in lung cancer management can be found in [23244185J Infect Public Health 2012 Dec;5 Suppl 1:S35](http://pubmed.ncbi.nlm.nih.gov/23244185?dopt=Abstract)

### **Review Articles**

* PubMed31378235Mayo Clinic proceedingsMayo Clin Proc201908019481599-16221599review of small cell lung cancer can be found in [Mayo Clin Proc 2019 Aug;94(8):1599](http://pubmed.ncbi.nlm.nih.gov/31378235/)
* PubMed35559635American family physicianAm Fam Physician202205011055487-494487review of diagnosis, treatment principles, and screening of lung cancer can be found in [Am Fam Physician 2022 May 1;105(5):487](https://pubmed.ncbi.nlm.nih.gov/35559635)
* PubMed34742731The Annals of thoracic surgeryAnn Thorac Surg2022110111451965-19731965review of lung cancer in women can be found in [Ann Thorac Surg 2022 Nov;114(5):1965](https://pubmed.ncbi.nlm.nih.gov/34742731)
* PubMed35040882JAMAJAMA202201183273264-273264review of evaluating the patient with a pulmonary nodule can be found in [JAMA 2022 Jan 18;327(3):264](https://pubmed.ncbi.nlm.nih.gov/35040882)
* review of cutaneous manifestations of lung cancer can be found in [Semin Oncol 2016 Jun;43(3):366](http://pubmed.ncbi.nlm.nih.gov/27178690/)
* Oncologic\_Disease Pulmonary\_Disordersreview of lung cancer: current therapies and new targeted treatments (Lancet 2017 Jan 21)10/27/2017 01:58:00 PM27574741review of lung cancer: current therapies and new targeted treatments can be found in [27574741Lancet 2017 Jan 21;389(10066):299](http://pubmed.ncbi.nlm.nih.gov/27574741?dopt=Abstract)
* review of therapies and targets for small cell lung cancer can be found in [24565587Semin Oncol 2014 Feb;41(1):133](http://pubmed.ncbi.nlm.nih.gov/24565587?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4176613/)
* review of staging and imaging can be found in [mnh22245990pcxh72454628pmdc22245990pCancer Imaging 2012 Jan 12;11:253](http://pubmed.ncbi.nlm.nih.gov/22245990?dopt=Abstract)[full-text](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3266593/)
* review of treatment of limited stage disease can be found in [24327434Cancer 2014 Mar 15;120(6):790](http://pubmed.ncbi.nlm.nih.gov/24327434?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3947683/)
* review of radiation therapy can be found in [cxh89151247pmdc23625345pCurr Oncol Rep 2013 Aug;15(4):405](http://pubmed.ncbi.nlm.nih.gov/23625345?dopt=Abstract)
* review of targeted therapies can be found in [23288650Adv Exp Med Biol 2013;779:385](http://pubmed.ncbi.nlm.nih.gov/23288650?dopt=Abstract)
* review of thoracic radiotherapy for limited stage small cell lung carcinoma can be found in [22495055Curr Probl Cancer 2012 May-Jun;36(3):88](http://pubmed.ncbi.nlm.nih.gov/22495055?dopt=Abstract)
* review of stereotactic body radiation therapy for treatment of primary and metastatic pulmonary malignancies can be found in [23622074Surg Oncol Clin N Am 2013 Jul;22(3):463](http://pubmed.ncbi.nlm.nih.gov/23622074?dopt=Abstract)
* review of clinical implications of genomic discoveries in lung cancer can be found in [27168435N Engl J Med 2016 May 12;374(19):1864](http://pubmed.ncbi.nlm.nih.gov/27168435?dopt=Abstract)
* Oncologic\_Disease Pulmonary\_Disordersreview of new horizons in systemic anticancer therapy in older people (Age Ageing 2018 May 1)05/01/2018 12:00:00 AM29617715review of new horizons in systemic anti-cancer therapy in older people can be found in [29617715Age Ageing 2018 May 1;47(3):340](http://pubmed.ncbi.nlm.nih.gov/29617715?dopt=Abstract)
* reviews of lung cancer screening
  + review of lung cancer screening with low-dose computed tomography can be found in [25372089N Engl J Med 2014 Nov 6;371(19):1813](http://pubmed.ncbi.nlm.nih.gov/25372089?dopt=Abstract)
  + review of screening for cancer: concepts and controversies can be found in [mnh25368922pcxh99014606pmdc25368922pAm Fam Physician 2014 Nov 1;90(9):625](http://pubmed.ncbi.nlm.nih.gov/25368922?dopt=Abstract)[full-text](http://www.aafp.org/afp/2014/1101/p625.html)
  + review of population-based screening for lung cancer can be found in [23972816Lancet 2013 Aug 24;382(9893):732](http://pubmed.ncbi.nlm.nih.gov/23972816?dopt=Abstract)
  + review of screening for lung cancer can be found in [mdc23512063pJAMA 2013 Mar 20;309(11):1163](http://pubmed.ncbi.nlm.nih.gov/23512063?dopt=Abstract)
  + review of screening and early detection of lung cancer can be found in [22987984Ann Oncol 2012 Sep;23 Suppl 10:x320](http://pubmed.ncbi.nlm.nih.gov/22987984?dopt=Abstract)
  + review of computed tomography screening for lung cancer can be found in [22974776Radiol Clin North Am 2012 Sep;50(5):877](http://pubmed.ncbi.nlm.nih.gov/22974776?dopt=Abstract)
* review on differences in Asian countries compared to Western countries on lung cancer risk due to smoking can be found in [28092929Epidemiol Health 2016 Dec 20;38:e2016060](http://pubmed.ncbi.nlm.nih.gov/28092929?dopt=Abstract)
* PubMed31216176Annals of the American Thoracic SocietyAnn Am Thorac Soc201909011691099-11061099review of contemporary approach to the diagnosis of malignant pleural effusion can be found in [Ann Am Thorac Soc 2019 Sep;16(9):1099](http://pubmed.ncbi.nlm.nih.gov/31216176/)

### **MEDLINE Search**

* to search MEDLINE for (Small cell carcinoma of lung) with targeted search (Clinical Queries), click [therapy](http://www.ncbi.nlm.nih.gov/sites/entrez?termClinical=Small%20cell%20carcinoma%20of%20lung&precision=specificity&strategy=therapy&filters=&orig_db=PubMed&db=pubmed&cmd=Search&term=%28Small%20cell%20carcinoma%20of%20lung%29%20AND%20%28randomized%20controlled%20trial%5BPublication%20Type%5D%20OR%20%28randomized%5BTitle%2FAbstract%5D%20AND%20controlled%5BTitle%2FAbstract%5D%20AND%20trial%5BTitle%2FAbstract%5D%29%29), [diagnosis](http://www.ncbi.nlm.nih.gov/sites/entrez?termClinical=Small%20cell%20carcinoma%20of%20lung&precision=specificity&strategy=diagnosis&filters=&orig_db=PubMed&db=pubmed&cmd=Search&term=%28Small%20cell%20carcinoma%20of%20lung%29%20AND%20%28specificity%5BTitle%2FAbstract%5D%29), or [prognosis](http://www.ncbi.nlm.nih.gov/sites/entrez?termClinical=Small%20cell%20carcinoma%20of%20lung&precision=specificity&strategy=prognosis&filters=&orig_db=PubMed&db=pubmed&cmd=Search&term=%28Small%20cell%20carcinoma%20of%20lung%29%20AND%20%28prognos%2A%5BTitle%2FAbstract%5D%20OR%20%28first%5BTitle%2FAbstract%5D%20AND%20episode%5BTitle%2FAbstract%5D%29%20OR%20cohort%5BTitle%2FAbstract%5D%29)

## **References**

### **General References Used**

The references listed below are used in this DynaMed topic primarily to support background information and for guidance where evidence summaries are not felt to be necessary. Most references are incorporated within the text along with the evidence summaries.

1. van Meerbeeck JP, Fennell DA, De Ruysscher DK. Small-cell lung cancer. [Lancet. 2011 Nov 12;378(9804):1741-55](http://pubmed.ncbi.nlm.nih.gov/21565397?dopt=Abstract).
2. Ost DE, Yeung SC, Tanoue LT, Gould MK. Clinical and organizational factors in the initial evaluation of patients with lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. [Chest. 2013 May;143(5 Suppl):e121S-41S](http://pubmed.ncbi.nlm.nih.gov/23649435?dopt=Abstract)[full-text](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4694609/).
3. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. [Chest. 2013 May;143(5 Suppl):e142S-65S](http://pubmed.ncbi.nlm.nih.gov/23649436?dopt=Abstract).
4. Ganti AK, Loo BW, Bassetti M, et al. Small cell lung cancer. Version 1.2022. In: National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines). NCCN 2021 Aug from [NCCN website](https://www.nccn.org/professionals/physician_gls/default.aspx) (free registration required) .

### **Recommendation Grading Systems Used**

* American College of Chest Physicians (ACCP) grading system for recommendations
  + Grade 1 - strong recommendation based on clear risk/benefit balance
  + Grade 2 - weak recommendation based on unclear or close risk/benefit balance
  + Grade A - high-quality evidence based on consistent evidence from randomized trials without important limitations or exceptionally strong evidence from observational studies
  + Grade B - moderate-quality evidence based on randomized trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise results) or very strong evidence from observational studies
  + Grade C - low- or very low-quality evidence based on observational studies, case series, or randomized trials with serious flaws or indirect evidence
  + Reference - ACCP evidence-based clinical practice guidelines methodology for development of guidelines for lung cancer ([23649432Chest 2013 May;143(5 Suppl):41S](http://pubmed.ncbi.nlm.nih.gov/23649432?dopt=Abstract))
* European Society for Medical Oncology (ESMO) grades of recommendation
  + grades of recommendation
    - Grade A - strong evidence for efficacy with substantial clinical benefit, strongly recommended
    - Grade B - strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
    - Grade C - insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages, optional
    - Grade D - moderate evidence against efficacy or for adverse outcomes, generally not recommended
    - Grade E - strong evidence against efficacy or for adverse outcomes, never recommended
  + levels of evidence
    - Level I - evidence from ≥ 1 large, randomized, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
    - Level II - small randomized trials or large randomized trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity
    - Level III - prospective cohort studies
    - Level IV - retrospective cohort studies or case-control studies
    - Level V - studies without control group, case reports, expert opinions
  + Reference - ESMO clinical practice guideline on diagnosis, treatment and follow-up of small-cell lung cancer ([20555060Ann Oncol 2010 May;21 Suppl 5:v120](http://pubmed.ncbi.nlm.nih.gov/20555060?dopt=Abstract))
* National Comprehensive Cancer Network (NCCN) categories of evidence and consensus
  + Category 1 - based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate
  + Category 2A - based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate
  + Category 2B - based on lower-level evidence, there is NCCN consensus that the intervention is appropriate
  + Category 3 - based on any level of evidence, there is major NCCN disagreement that the intervention is appropriate
  + Reference - [NCCN Categories of Evidence and Consensus](https://www.nccn.org/professionals/physician_gls/default.aspx)
* United States Department of Health and Human Services, Public Health Service (PHS) guideline panel grading system
  + strength of evidence ratings
    - Strength of Evidence A - multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings
    - Strength of Evidence B - some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optimal
    - Strength of Evidence C - reserved for important clinical situations in which Panel achieved consensus on recommendation in the absence of relevant randomized controlled trials
  + Reference - PHS clinical practice guideline on treating tobacco use and dependence ([USPHS 2008 May](https://www.ncbi.nlm.nih.gov/books/NBK63952/)[PDF](https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/update/treating_tobacco_use08.pdf) or in [Spanish](https://www.ncbi.nlm.nih.gov/books/NBK47499/" \t "_blank)[PDF](https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/update/treating_tobacco_use08_sp.pdf)), endorsed by American Academy of Pediatrics [Pediatrics 2008 Aug;122(2):471])
* United States Preventive Services Task Force (USPSTF) grades of recommendation (after July 2012)
  + Grade A - USPSTF recommends the service with high certainty of substantial net benefit
  + Grade B - USPSTF recommends the service with high certainty of moderate net benefit or moderate certainty of moderate-to-substantial net benefit
  + Grade C - USPSTF recommends selectively offering or providing the service (based on professional judgment and patient preference) with at least moderate certainty of small net benefit
  + Grade D - USPSTF recommends against providing the service with moderate-to-high certainty of no net benefit or harms outweighing benefits
  + Grade I - insufficient evidence to assess balance of benefits and harms
  + Reference - [USPSTF Grade Definitions](https://www.uspreventiveservicestaskforce.org/Page/Name/grade-definitions)
* American College of Chest Physicians (ACCP) uses Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to recommendations
  + grades of recommendation
    - Strong - benefits outweigh risk and burdens, or vice versa
    - Weak (Conditional) - benefits closely balanced with risks and burden or uncertainty in estimates of benefits, risks, and burden
    - Ungraded Consensus-Based Statement- uncertainty due to lack of evidence but expert opinion that benefits outweigh risk and burdens, or vice versa; insufficient evidence for a graded recommendation
  + quality of evidence
    - High - panel very confident that true effect lies close to estimate of effect
    - Moderate - moderate confidence in effect estimate; true effect likely to be close to estimate of effect, but possibility it is substantially different
    - Low - confidence in effect estimate is limited; true effect may be substantially different from estimate of effect
    - Very low - very little confidence in the effect estimate; true effect likely to be substantially different from estimate of effect
  + Reference - ACCP CHEST guideline and expert panel report on screening for lung cancer ([Chest 2018 Apr;153(4):954](http://pubmed.ncbi.nlm.nih.gov/29374513?dopt=Abstract))

### **Synthesized Recommendation Grading System for DynaMed Content**

* The DynaMed Team systematically monitors clinical evidence to continuously provide a synthesis of the most valid relevant evidence to support clinical decision-making (see [7-Step Evidence-Based Methodology](https://www.ebsco.com/clinical-decisions/dynamed-solutions/about/evidence-based-process/methodology)).
* Guideline recommendations summarized in the body of a DynaMed topic are provided with the recommendation grading system used in the original guideline(s) and allow users to quickly see where guidelines agree and where guidelines differ from each other and from the current evidence.
* In DynaMed content, we synthesize the current evidence, current guidelines from leading authorities, and clinical expertise to provide recommendations to support clinical decision-making in the [Overview & Recommendations section](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-F55F4D14-4E2F-4114-8DD5-5486B20306D0).
* We use the [Grading of Recommendations Assessment, Development and Evaluation (GRADE)](http://www.gradeworkinggroup.org/) approach to classify synthesized recommendations as Strong or Conditional.
  + **Strong recommendations** may be used when, based on the available evidence, clinicians (without conflicts of interest) consistently have a high degree of confidence that the desirable consequences (health benefits, decreased costs and burdens) outweigh the undesirable consequences (harms, costs, burdens).
  + **Conditional recommendations** may be used when, based on the available evidence, clinicians believe that desirable and undesirable consequences are finely balanced, or appreciable uncertainty exists about the magnitude of expected consequences (benefits and harms).
  + **Conditional recommendations** may be used when clinicians disagree in judgments of the relative benefit and harm or have limited confidence in their judgments.
  + **Conditional recommendations** may also be used when the range of patient values and preferences suggests that informed patients are likely to make different choices.
* DynaMed synthesized recommendations (in the [Overview & Recommendations section](https://dpa-pde-oxford.shinyapps.io/Phenotyping_ESBCO_Shiny/_w_1d5cbdd8/#GUID-F55F4D14-4E2F-4114-8DD5-5486B20306D0)) are determined with a systematic methodology.
  + Recommendations are explicitly labeled as **Strong recommendations** or **Conditional recommendations** when a qualified organization has explicitly deliberated on making such a recommendation.
  + Recommendations are phrased to match the strength of recommendation.
    - **Strong recommendations** use "should do" phrasing, or phrasing implying an expectation to perform the recommended action for most patients.
    - **Conditional recommendations** use "consider" or "suggested" phrasing.
  + Recommendations are verified by ≥ 1 editor with methodological expertise, not involved in recommendation drafting or development, with explicit confirmation that Strong recommendations are adequately supported.
  + Recommendations are published only after consensus is established with agreement in phrasing and strength of recommendation by all editors.
  + If recommendations are questioned during peer review or post publication by a qualified individual, or reevaluation is warranted based on new information detected through systematic literature surveillance, the recommendation is subject to additional internal review.

### **DynaMed Editorial Process**

* DynaMed topics are created and maintained by the [DynaMed Editorial Team](https://www.ebsco.com/clinical-decisions/dynamed-solutions/about/meet-our-experts" \t "_blank) and adhere to [evidence-based methodology](https://www.ebsco.com/clinical-decisions/dynamed-solutions/about/evidence-based-process/methodology) and [inclusive language standards](https://www.ebsco.com/clinical-decisions/dynamed-solutions/about/health-equity-inclusive-language).
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