CME

Lung cancer screening in primary care

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ABSTRACT

This article reviews the evidence supporting low-dose CT to screen for lung cancer, and the risks, costs, and challenges of implementing broad-based screening for eligible patients. Increased familiarity with lung cancer screening guidelines by primary care and specialty clinicians presents an opportunity to improve lung cancer screening rates and to save lives from the most common cause of cancer death in the United States.

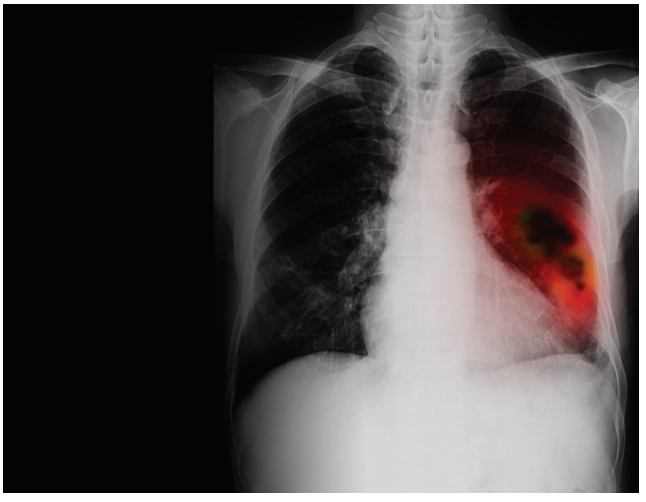
Keywords: lung cancer, screening, low-dose CT, mortality, shared decision-making, Lung-RADS

Learning objectives

- Discuss recommendations for lung cancer screening.
- Discuss essential information to include in a shared decision-making visit, including benefits and risks of lung cancer screening.
- Review the underuse of lung cancer screening in the United States.
- Describe the recommended follow-up and management of screening low-dose CT results.

Lung cancer is the leading cause of cancer death in adults in the United States.[1,2] Survival is strongly associated with the stage of disease at diagnosis.[1] The 5-year survival is much lower for patients with metastatic disease compared with localized disease.[1] Seventy-nine percent of patients who present with lung cancer receive a diagnosis of locally advanced metastatic disease.[1]

In 2013, the US Preventive Services Task Force (USPSTF), based on the results of the National Lung Screening Trial (NLST), recommended screening high-risk patients ages 55 to 80 years who were current smokers, had a 30 pack-year history of smoking, or had quit within the past 15 years.[1,3] Based on evidence that the initial guidelines may not optimally identify high-risk patients, especially in minority and underserved populations, the USPSTF guidelines were updated in March 2021.[1] The guidelines now include patients ages 50 to 80 years with a 20 pack-year smoking history.[1] Although other societies also provide lung cancer screening guidelines, this article focuses on the USPSTF guidelines, because the recent expansion may help to reduce racial disparities. Additionally, the USPSTF is a go-to evidence-based resource for primary care clinicians for preventive care recommendations.



Lung cancer screening rates remain critically low despite the proven benefit of screening to expand the diagnosis of early-stage, treatable lung cancer. Results from the lung cancer screening registry show that only 2% of 7.6 million patients eligible for low-dose CT under the USPSTF guidelines received screening.[3] Primary care providers need to develop the knowledge and skills to counsel patients about the benefits and harms of screening and encourage appropriate patients at high risk for lung cancer to engage in annual low-dose CT screening.

EVIDENCE FOR SCREENING

The NLST and the Dutch-Belgian Randomized Lung Cancer Screening Trial (NELSON) were the largest randomized clinical trials to evaluate lung cancer screening with low-dose CT. The NLST compared low-dose CT with chest radiograph; NELSON compared low-dose CT with no screening.

NLST The NLST was published in 2011 after screening 53,454 US patients ages 50 to 69 years who were at high risk for lung cancer.[4] Almost 91% of participants were White, 4.5% were Black, and fewer than 2% were Hispanic or Latino.[4] After three rounds of annual screening and mortality follow-up over 7 years, the study found a 20%

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Key points

- Lung cancer is the most common cause of cancer death in adults in the United States.
- Lung cancer screening rates are critically low; many clinicians are unaware of the eligibility criteria for screening.
- Screening can detect cancer in asymptomatic patients, providing an opportunity for earlier treatment and a greater chance of survival.

reduction in lung cancer mortality in patients screened with low-dose CT.[4] Based on these results, in 2013 the USPSTF implemented a recommendation for lung cancer screening with low-dose CT in high-risk patients.[5]

NELSON From 2003 to 2006, the NELSON trial enrolled and screened for lung cancer in 15,792 high-risk patients ages 50 to 74 years in the Netherlands and Belgium.[6] Most study participants were White.[6] Rather than screening annually, this trial completed four rounds of screening separated by increasing intervals.[6] Screenings occurred at 1, 3, and 5.5 years after the initial screening.[6] A 10-year follow-up found a 26% reduction in lung cancer mortality in men who were screened compared with those who were not screened; mortality results for women were not statistically significant.[7]

SCREENING RECOMMENDATIONS

The large randomized NLST and NELSON clinical trials led to multiple group recommendations for lung cancer screening with low-dose CT.[6] Recommendations came from the USPSTF, National Comprehensive Cancer Network (NCCN), American Cancer Society (ACS), American Association for Thoracic Surgeons (AATS), and the American College of Chest Physicians (CHEST) (**Table 1**).[5,8-11] Eligibility for each recommendation relates to smoking and older age, the two main risk factors for lung cancer.[1]

In 2013, the USPSTF recommended annual lung cancer screening with low-dose CT for patients ages 55 to 80 years with a 30 pack-year smoking history and who are current smokers or have quit in the past 15 years.[1] In March 2021, this was expanded to include patients ages 50 to 80 years with a 20 pack-year smoking history who are current smokers or have quit in the past 15 years.[1] The expanded eligibility should improve racial disparities by identifying more high-risk minority and underserved patients; for example, Black patients have a higher risk of lung cancer at lower pack-years than White patients.[1] The USPSTF has determined a moderate net benefit of annual screening of high-risk patients with low-dose CT.[1]

The NLST and NELSON trials screened at different intervals. The USPSTF recommends annual rather than biennial screening. Modeling studies suggest a greater benefit with annual screening.[1] Reasons for discontinuing or not initiating screening include reaching 15 years smoke-free, or developing a health condition that limits life expectancy or one that limits the patient's ability or willingness to have curative surgery.[1]

BENEFITS OF SCREENING

Early detection and diagnosis of lung cancer in asymptomatic patients provides the opportunity for treatment much sooner than a diagnosis when patients are symptomatic with advanced disease. Patients with stage 1A lung cancer have a greater than 75% chance of 5-year survival compared with 4.7% for patients with metastatic lung cancer.[7,12] Between 1% and 3% of patients who participate in annual lung cancer screening with low-dose CT are diagnosed

TABLE 1. Lung cancer screening recommendations[5,7-11]

	USPSTF	NCCN	ACS	AATS	CHEST
Age (years)	50-80	55-77	50-80	55-79	55-77
Smoking history (pack-years)	At least 20	At least 30	At least 20	At least 30	At least 30
Smoking status	Current or quit in past 15 years	Current or quit in past 14 years	Current or quit in past 15 years	Not specified	Current or quit in past 15 years
Shared decision-making visit	Required	Required	Required	Not required	Suggested
Other notes		May start at 50 years**	Must receive tobacco cessation counseling	May start at 50 years***	Must be asymptomatic
Method	Low-dose CT	Low-dose CT	Low-dose CT	Low-dose CT	Low-dose CT
Interval	Annual*	Annual	Annual	Annual	Annual****
Last updated	2021	2020	2021	2012	2018

*Stop screening if patient develops a comorbidity that substantially limits life expectancy.
**Start screening at age 50 years and 20 pack-years if the patient also has at least one other risk factor other than secondhand smoke (contact with radon, asbestos, or other cancer-causing agents; history of cancer; family history of lung cancer; history of COPD or pulmonary fibrosis).
***Start screening at age 50 years and 20 pack-years if the patient also has an additional cumulative risk of developing lung cancer of at least 5% over the next 5 years.
****Do not screen if the patient has comorbidities that adversely influence the ability to tolerate screening or treatment of detected lung cancer, or that substantially limit life expectancy.

with lung cancer; 50% to 70% of them are stage 1.[7] The NLST found a 20% relative reduction in mortality from lung cancer with annual low-dose CT compared with chest radiography.[4] Annual screening also reduces all-cause mortality; the NLST found a significant reduction of 6.7% compared with screening using chest radiography.[4,6]

POTENTIAL HARMS OF SCREENING

Potential harms of lung cancer screening with low-dose CT include false positives, incidental findings, overdiagnosis, and radiation exposure.

False positives Positive results often require additional evaluation to determine if they are true or false, which increases the risk of harm from additional imaging, biopsy, or surgical procedures, as well as distress or anxiety to the patient.[1] The rates of false positives in the NLST were 26.3% at baseline, 27.2% at year 1, and 15.9% at year 2; in the NELSON trial, false positives were 19.8% at baseline, 7.1% at year 1, 9% at year 3 (males), and 3.9% at year 5.5 (males).[1]

Since these trials, the Lung CT Screening Reporting and Data System (Lung-RADS) was developed. This is a standardized approach to reporting the recommendations for the management of findings on low-dose CT and may reduce false-positive results.[1,13] A retrospective study reviewed images from the NLST using Lung-RADS and found reduced false-positive rates (12.8%) in the baseline screenings.[1] Additionally, the use of Lung-RADS would have prevented about 23% of invasive procedures for false-positive results.[6] The ACR updated Lung-RADS in 2019 to further reduce false-positive results.[13] Lung-RADS values are easy to interpret and similar to BI-RADS for mammograms (**Table 2**).[14]

Incidental findings A low-dose CT of a large area, from the lower neck to the upper abdomen, may reveal incidental findings (**Table 3**).[15] In a retrospective review of 320 low-dose CTs, the most common incidental findings were in the pulmonary, cardiovascular, and gastrointestinal systems; 15% of the scans with an incidental finding required further evaluation.[16] Incidental findings may prove to be clinically significant; for example, 0.39% of NSLT participants were diagnosed with kidney, thyroid, or liver cancer during low-dose CT screening.[1] Incidental findings, such as the early diagnosis of severe coronary artery calcifications and subsequent intervention, may benefit some patients.[15] The discovery of incidental findings may result in further evaluation, including consultations, imaging, and invasive procedures, each of which may have costs, burdens, and potential complications from procedures.[1]

Overdiagnosis Screening low-dose CT carries a risk of overdiagnosis (that is, detecting cancers that would have never become symptomatic or affected the patient).[4] Overdiagnosis may lead to psychological and physical harm, including depression, anxiety, chemotherapy, radiation, and surgery, for a condition that would not have caused a problem in the patient's lifetime.[17] The actual overdiagnosis rate is difficult to ascertain from trials because of the limited follow-up time.[1] However, one study reviewed data from 4.5 years of follow-up from the last screens in the NLST and found an estimated overdiagnosis rate of 18.5%; with 9 years of follow-up, the rate dropped to 3%.[17]

Radiation exposure Another risk of undergoing low-dose CT is radiation exposure and radiation-induced cancer. One study estimated the lifetime risk of cancer from the radiation of 10 annual low-dose CTs to be 0.26 to 0.81 major cancers per 1,000 people.[6]

SHARED DECISION-MAKING

A shared decision-making discussion between the clinician and patient before low-dose CT is an important component of lung cancer screening. This discussion must include the eligibility, benefits, limitations, risks, and potential harms of lung cancer screening with low-dose CT. It also should include the need for annual screenings or other follow-up testing.[11] Following the discussion, the patient would decide whether to undergo screening. Additionally, patients must be willing and able to go through treatment if they are diagnosed with lung cancer.[18]

TABLE 2. Lung-RADS scoring version 1.1[14]

Lung-RADS score	Category descriptor	Management	Risk of malignancy
0	Incomplete	Additional CT images and/or comparison to prior chest CT is needed	n/a
1	Negative	Annual screening with low-dose CT in 12 months	<1%
2	Benign appearance or behavior	Annual screening with low-dose CT in 12 months	<1%
3	Probably benign	Low-dose CT in 6 months	1% to 2%
4A	Suspicious	Low-dose CT in 3 months; consider PET/CT if ≥8mm solid component to the nodule	5% to 15%
4B	Very suspicious	Chest CT, PET/CT, and/or biopsy. Consider low-dose CT in 1 month for new, large nodules on annual screening low-dose CT for potentially infectious/inflammatory conditions	>15%
4X			
S	Other	As appropriate for the specific finding	n/a

A decision aid (www.shouldiscreen.com) may be used as an adjunct to a shared decision-making visit and may improve the quality of the visit.[19,20] It should be noted that for reimbursement, the Centers for Medicare and Medicaid Services (CMS) requires completion of a shared decision-making visit before low-dose CT screening.[20] CMS also requires clinicians to provide smoking cessation counseling during these visits.[11]

ALTERNATIVES TO LOW-DOSE CT

Alternatives to low-dose CT for lung cancer screening include chest radiography, sputum cytology, and biomarkers. However, studies using these methods have not shown reduced mortality and thus are not recommended.[1] In the 1970s, a large randomized controlled trial found no mortality benefit when comparing usual care with chest radiography with sputum cytology every 4 months.[21] More recently, from 1993 to 2001, nearly 155,000 trial participants were randomized to either annual chest radiography or usual care for 4 years; no reduction in lung cancer mortality was found over a 13-year follow-up.[22] More research is necessary on serum and blood-based biomarkers to aid in diagnosing lung cancer. One promising study found that biomarkers may be useful in the diagnosis of lung cancer in conjunction with low-dose CT.[23]

COST-EFFECTIVENESS

Although there is a cost to lung cancer screening with low-dose CT, including up to $6.8 billion in Medicare expenditures over 5 years, it may provide a good to moderate value.[2] The commonly accepted threshold for the cost-effectiveness of an intervention in the United States is less than $100,000 per quality-adjusted life-year (QALY).[24] Using data from the NLST, the estimated cost-effectiveness of low-dose CT screening is $81,000 per QALY.[2] A comparative analysis of NLST, CMS, and 2013 USPSTF criteria found that all three are cost-effective.[24] The USPSTF criteria was the most beneficial but also the most expensive of the three.[24]

UNDERUSE

Despite the USPSTF recommending lung cancer screening with low-dose CT since 2013, screening rates remain low across the country.[3] In 2016, only 2% of eligible smokers underwent screening.[3] Poor knowledge of screening on the parts of clinicians and patients contributes to these low rates, pointing to the necessity of clinician and patient education.[3,25] Many clinicians are unaware of the eligibility criteria for lung cancer screening; some still order chest radiographs for their high-risk patients.[25] Having to complete a shared decision-making visit also is a barrier because of lack of clinician time.[3]

Most eligible patients will agree to lung cancer screening if their clinician recommends it. One study found that high-risk smokers age 55 years and older are concerned about developing lung cancer, and more than 80% would agree to screening with low-dose CT.[26] Another study found that 52% of current and former smokers are aware of lung cancer screening, and more than 80% of those who have not had previous screening would undergo a low-dose CT if recommended by their healthcare provider.[12]

TABLE 3. Potential incidental findings on low-dose CT[15,16]

Pulmonary
- COPD (39% to 50% of incidental findings)
- Interstitial lung abnormalities (16%)—smoking-related interstitial fibrosis, idiopathic pulmonary fibrosis, desquamative interstitial pneumonia, respiratory bronchiolitis interstitial lung disease
- Infection (6.1%)—bacterial or viral infection, tuberculosis, nontuberculous mycobacterial infection

Pleural
- Plaques (3.8%)
- Effusion (1.2%)

Mediastinal
- Cardiovascular—coronary artery calcification (56% to 80%), aortic calcification (20.6%), thoracic aortic dilation (8.1%), aortic aneurysm (0.38% to 3.4%)
- Thyroid—nodules (4.7%)
- Mediastinal masses (less than 1%)—thymic hyperplasia, cyst, lipoma
- Lymph nodes (1.6%)—mediastinal or hilar lymphadenopathy due to infection, edema, sarcoidosis, fibrosis, lymphoma, or metastases
- Esophagus—dilation due to achalasia, scleroderma, other inflammatory causes; diffuse wall thickening due to infectious or inflammatory causes; lesions (Esophageal evaluation is limited on low-dose CT due to lack of distension and contrast.)

Upper abdominal
- Malignancy (0.5%)—renal, pancreatic, hepatocellular, adrenal
- Nonmalignant—renal cysts (2.5%), nephrolithiasis (1.3%), cholelithiasis

CONCLUSION

Annual low-dose CT has been shown to reduce lung cancer mortality by 20% but remains underused.[4] Primary care providers have an opportunity to improve lung cancer screening rates by becoming familiar with current recommendations and encouraging patients at high risk for lung cancer to undergo annual low-dose CT. Most current and former smokers will agree to screening if their clinician recommends it. Advertisements promoting lung cancer screening, similar to those for breast and colon cancer screening, also may improve patients' awareness and knowledge of screening. An understanding of Lung-RADS is essential when reviewing the results of a low-dose CT. Nonprimary care or subspecialty clinicians may not be in a position to provide recommendations to patients about lung cancer screening. However, they may contribute to improving screening rates and patient outcomes by recognizing high-risk patients and referring them to an appropriate clinician to discuss screening. **JAAPA**

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