JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Lung Cancer
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Lung cancer is the second most common cancer and the leading cause of cancer death in the US. In 2020, an estimated 228 820 persons were diagnosed with lung cancer, and 135 720 persons died of the disease. The most important risk factor for lung cancer is smoking. Increasing age is also a risk factor for lung cancer. Lung cancer has a generally poor prognosis, with an overall 5-year survival rate of 20.5%. However, early-stage lung cancer has a better prognosis and is more amenable to treatment.

OBJECTIVE To update its 2013 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a systematic review on the accuracy of screening for lung cancer with low-dose computed tomography (LDCT) and on the benefits and harms of screening for lung cancer and commissioned a collaborative modeling study to provide information about the optimum age at which to begin and end screening, the optimal screening interval, and the relative benefits and harms of different screening strategies compared with modified versions of multivariate risk prediction models.

POPULATION This recommendation statement applies to adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years.

EVIDENCE ASSESSMENT The USPSTF concludes with moderate certainty that annual screening for lung cancer with LDCT has a moderate net benefit in persons at high risk of lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking.

RECOMMENDATION The USPSTF recommends annual screening for lung cancer with LDCT in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation) This recommendation replaces the 2013 USPSTF statement that recommended annual screening for lung cancer with LDCT in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

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Summary of Recommendation

Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

See the Figure for a more detailed summary of the recommendation for clinicians. USPSTF indicates US Preventive Services Task Force.

Lung cancer is the second most common cancer and the leading cause of cancer death in the US. In 2020, an estimated 228 820 persons were diagnosed with lung cancer, and 135 720 persons died of the disease.[1]

The most important risk factor for lung cancer is smoking.[2,3] Smoking is estimated to account for about 90% of all lung cancer cases,[2] with a relative risk of lung cancer approximately 20-fold higher in smokers than in nonsmokers.[3] Increasing age is also a risk factor for lung cancer. The median age of diagnosis of lung cancer is 70 years.[4,5]

Lung cancer has a generally poor prognosis, with an overall 5-year survival rate of 20.5%.[1] However, early-stage lung cancer has a better prognosis and is more amenable to treatment.

Figure. Clinician Summary: Screening for Lung Cancer

What does the USPSTF recommend?	**Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years:** • Screen for lung cancer with low-dose computed tomography (CT) every year. • Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery. Grade: B
To whom does this recommendation apply?	Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. (See below for definition of pack-year.)
What's new?	The USPSTF has revised the recommended ages and pack-years for lung cancer screening. It expanded the age range to 50 to 80 years (previously 55 to 80 years) and reduced the pack-year history to 20 pack-years of smoking (previously 30 pack-years).
How to implement this recommendation?	1. **Assess risk based on age and pack-year smoking history:** Is the person aged 50 to 80 years and have they accumulated 20 pack-years or more of smoking? a. A pack-year is a way of calculating how much a person has smoked in their lifetime. One pack-year is the equivalent of smoking an average of 20 cigarettes—1 pack—per day for a year. 2. **Screen:** If the person is aged 50 to 80 years and has a 20 pack-year or more smoking history, engage in shared decision-making about screening. a. The decision to undertake screening should involve a discussion of its potential benefits, limitations, and harms. b. If a person decides to be screened, refer them for lung cancer screening with low-dose CT, ideally to a center with experience and expertise in lung cancer screening. c. If the person currently smokes, they should receive smoking cessation interventions.
How often?	• Screen every year with low-dose CT. • Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery.
What are other relevant USPSTF recommendations?	The USPSTF has made recommendations on interventions to prevent the initiation of tobacco use in children and adolescents, and on behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women. These recommendations are available at https://www.uspreventiveservicestaskforce.org
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

USPSTF indicates US Preventive Services Task Force.

USPSTF Assessment of Magnitude of Net Benefit

The US Preventive Services Task Force (USPSTF) concludes with moderate certainty that annual screening for lung cancer with LDCT has a **moderate net benefit** in persons at high risk of lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking. The moderate net benefit of screening depends on limiting screening to persons at high risk, the accuracy of image interpretation being similar to or better than that found in clinical trials, and the resolution of most false-positive results with serial imaging rather than invasive procedures.

See the **Figure**, **Table**, and eFigure in the Supplement for more information on the USPSTF recommendation rationale and assessment. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.[6]

Table. Summary of USPSTF Rationale

Rationale	Assessment
Detection	The USPSTF found adequate evidence that LDCT has sufficient sensitivity and specificity to detect early-stage lung cancer
Benefits of early detection and intervention and treatment	The USPSTF found adequate evidence that annual screening for lung cancer with LDCT in a defined population of high-risk persons can prevent a substantial number of lung cancer-related deaths
Harms of early detection and intervention and treatment	• The harms associated with LDCT screening include false-positive results leading to unnecessary tests and invasive procedures, incidental findings, short-term increases in distress due to indeterminate results, overdiagnosis, and radiation exposure • The USPSTF found adequate evidence that the harms of screening for lung cancer with LDCT are moderate in magnitude
USPSTF assessment	The USPSTF concludes with moderate certainty that annual screening for lung cancer with LDCT is of moderate net benefit for persons at high risk of lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking

Abbreviations: LDCT, low-dose computed tomography; USPSTF, US Preventive Services Task Force.

Practice Considerations

Patient Population Under Consideration

This recommendation applies to adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years.

Assessment of Risk

Smoking and older age are the 2 most important risk factors for lung cancer.[3-5] The risk of lung cancer in persons who smoke increases with cumulative quantity and duration of smoking and

with age but decreases with increasing time since quitting for persons who formerly smoked.[3] The USPSTF considers adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years to be at high risk and recommends screening for lung cancer with annual LDCT in this population.

African American/Black (Black) men have a higher incidence of lung cancer than White men, and Black women have a lower incidence than White women.[1] These differences are likely related to differences in smoking exposure (ie, prevalence of smoking) and related exposure to carcinogens in cigarettes.[7,8] The differences may also be related to other social risk factors.

Other risk factors for lung cancer include environmental exposures, prior radiation therapy, other (noncancer) lung diseases, and family history. Lower level of education is also associated with a higher risk of lung cancer.[7] The task force recommends using age and smoking history to determine screening eligibility rather than more elaborate risk prediction models because there is insufficient evidence to assess whether risk prediction model–based screening would improve outcomes relative to using the risk factors of age and smoking history for broad implementation in primary care.

Screening Tests

Low-dose computed tomography has high sensitivity and reasonable specificity for the detection of lung cancer, with demonstrated benefit in screening persons at high risk.[9-11] Other potential screening modalities that are not recommended because they have not been found to be beneficial include sputum cytology, chest radiography, and measurement of biomarker levels.[12,13]

Screening Intervals

The 2 lung cancer screening trials that showed a benefit of lung cancer screening used different screening intervals. The National Lung Screening Trial (NLST) screened annually for 3 years.[9] The Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) trial screened at intervals of 1 year, then 2 years, then 2.5 years.[11] Modeling studies from the Cancer Intervention and Surveillance Modeling Network (CISNET)[14,15] suggest that annual screening for lung cancer leads to greater benefit than does biennial screening. Based on the available evidence and these models, the USPSTF recommends annual screening.

Treatment and Interventions

Lung cancer can be treated with surgery, chemotherapy, radiation therapy, targeted therapies, immunotherapy, or combinations of these treatments.[16] Surgical resection is generally considered the current treatment of choice for patients with stage I or II non–small cell lung cancer (NSCLC).[17]

Implementation of Lung Cancer Screening

Available data indicate that uptake of lung cancer screening is low. One recent study using data for 10 states found that 14.4% of persons eligible for lung cancer screening (based on 2013 USPSTF criteria) had been screened in the prior 12 months.[18] Increasing lung cancer screening discussions and offering screening to eligible persons who express a preference for it is a key step to realizing the potential benefit of lung cancer screening.

Screening Eligibility, Screening Intervals, and Starting and Stopping Ages

As noted above, the USPSTF recommends annual screening for lung cancer with LDCT in adults aged 50 to 80 years who have at least a 20 pack-year smoking history. Screening should be discontinued once a person has not smoked for 15 years.

The NLST[9] and the NELSON trial[11] enrolled generally healthy persons, so those study findings may not accurately reflect the balance of benefits and harms in persons with comorbid conditions. The USPSTF recommends discontinuing screening if a person develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Smoking Cessation Counseling

All persons enrolled in a screening program who are current smokers should receive smoking cessation interventions. To be consistent with the USPSTF recommendation on counseling and interventions to prevent tobacco use and tobacco-caused disease,[19] persons referred for lung cancer screening through primary care should receive these interventions concurrent with referral. Because many persons may enter screening through pathways besides referral from primary care, the USPSTF encourages incorporating such interventions into all screening programs.

Shared Decision-making

Shared decision-making is important when clinicians and patients discuss screening for lung cancer. The benefit of screening varies with risk because persons at higher risk are more likely to benefit. Screening does not prevent most lung cancer deaths; thus, smoking cessation remains essential. Lung cancer screening has the potential to cause harm, including false-positive results and incidental findings that can lead to subsequent testing and treatment, including the anxiety of living with a lung lesion that may be cancer. Overdiagnosis of lung cancer and the risks of radiation exposure are harms, although their exact magnitude is uncertain. The decision to undertake screening should involve a thorough discussion of the potential benefits, limitations, and harms of screening.

Standardization of LDCT Screening and Follow-up of Abnormal Findings

The randomized clinical trials (RCTs) that provide evidence for the benefit of screening for lung cancer with LDCT were primarily conducted in academic centers with expertise in the performance and interpretation of LDCT and the management of lung lesions seen on LDCT. Clinical settings that have similar experience and expertise are more likely to duplicate the beneficial results found in trials.

In an effort to minimize the uncertainty and variation about the evaluation and management of lung nodules and to standardize the reporting of LDCT screening results, the American College of Radiology developed the Lung Imaging Reporting and Data System (Lung-RADS) classification system and endorses its use in lung cancer screening.[20] Lung-RADS provides guidance to clinicians on which findings are suspicious for cancer and the suggested management of lung nodules detected on LDCT. Data suggest that the use of Lung-RADS may decrease the rate of false-positive results in lung cancer screening.[21]

Additional Tools and Resources

The Centers for Disease Control and Prevention has several websites with many resources to help patients stop smoking:

- "How to Quit" resources (https://www.cdc.gov/quit)
- Smoking Cessation: Fast Facts (https://www.cdc.gov/tobacco/data_statistics/fact_sheets/cessation/smoking-cessation-fast-facts/)
- Tips From Former Smokers (https://www.cdc.gov/tobacco/campaign/tips/)

The National Cancer Institute has developed resources to help patients stop smoking (https://www.smokefree.gov). It has also developed patient and clinician guides on screening for lung cancer:

- Lung Cancer Screening (PDQ)–Patient Version (https://www.cancer.gov/types/lung/patient/lung-screening-pdq)
- Lung Cancer Screening (PDQ)–Health Professional Version (https://www.cancer.gov/types/lung/hp/lung-screening-pdq)

Other Related USPSTF Recommendations

Prevention of initiation of smoking and smoking cessation for those who smoke are the most important interventions to prevent lung cancer. The USPSTF has made recommendations on interventions to prevent the initiation of tobacco use in children and adolescents[22] and on the use of pharmacotherapy and counseling for tobacco cessation.[19]

Update of Previous USPSTF Recommendation

This recommendation replaces the 2013 USPSTF recommendation on screening for lung cancer. In 2013 the USPSTF recommended annual screening for lung cancer with LDCT in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years (abbreviated as A-55-80-30-15).[23] For this updated recommendation, the USPSTF has changed the age range and pack-year eligibility criteria and recommends annual screening for lung cancer with LDCT in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years (A-50-80-20-15). Abbreviations for screening recommendations are expanded in the **Box**.

As in the 2013 recommendation, the USPSTF recommends that screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Box. US Preventive Services Task Force Low-Dose Computed Tomographic Screening Recommendations for Lung Cancer

A-55-80-30-15

In 2013, The US Preventive Services Task Force (USPSTF) recommended annual screening for lung cancer with low-dose computed tomography (LDCT) for adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years (abbreviated as A-55-80-30-15).[23]

A-50-80-20-15

For this updated recommendation, the USPSTF has changed the age range and pack-year eligibility criteria and recommends annual screening for lung cancer with LDCT for adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years (abbreviated as A-50-80-20-15).

Supporting Evidence

Scope of Review

To update its 2013 recommendation, the USPSTF commissioned a systematic review[24,25] on the accuracy of screening for lung cancer with LDCT and the benefits and harms of screening for lung cancer. The review also assessed whether the benefits of screening vary by subgroup (eg, by race or sex) or by the number or frequency of LDCT scans and whether the harms associated with screening and the evaluation of lung nodules differ with the use of Lung-RADS, International Early Lung Cancer Action Program (I-ELCAP), or similar approaches (eg, to reduce false-positive results). In addition, the review assessed whether the use of risk prediction models for identifying adults at higher risk of lung cancer mortality improves the balance of benefits and harms of screening compared with the use of trial eligibility criteria or variants of the prior USPSTF recommendation criteria.

In addition to the systematic evidence review, the USPSTF commissioned collaborative modeling studies from CISNET[14,15] to provide information about the optimal age at which to begin and end screening, the optimal screening interval, and the relative benefits and harms of different screening strategies, including risk factor–based strategies using age, pack-year smoking history, and years since quitting smoking for former smokers, compared with modified versions of multivariate risk prediction models. The modeling studies complement the evidence that the systematic review provides.

Accuracy of Screening Tests

The USPSTF reviewed several RCTs and cohort studies that reported on the sensitivity, specificity, or predictive value of LDCT, using eventual diagnosis of lung cancer as the reference standard.[24,25] Not all of the reviewed studies reported all test accuracy data. In the studies that reported it, sensitivity ranged from 59% to 100%, specificity ranged from 26.4% to 99.7%, positive predictive value ranged from 3.3% to 43.5%, and negative predictive value ranged from 97.7% to 100%.

In the NLST[26] and NELSON trial,[11] the reported sensitivities were 93.1% and 59%, respectively, and reported specificities were 76.5% and 95.8%, respectively. Although the negative predictive values were similar for the NLST and NELSON trial (99.9% and 97.7%, respectively), the positive predictive values were very different (3.3% and 43.5%, respectively). This discrepancy is largely accounted for by the trials' differing definitions of a positive finding and screening protocols—the NELSON trial used a volumetric approach and added an indeterminate nodule result category (ie, an indeterminate finding was not considered a positive result even if it led to additional testing). The NLST used an approach of maximum diameter without an indeterminate category (ie, any nodule meeting the diameter criteria was considered a positive result).

Three retrospective studies compared how various approaches for nodule classification would alter the accuracy of LDCT.[21,27,28] The first study demonstrated that using Lung-RADS in

the NLST would have increased specificity while decreasing sensitivity.[21] The other 2 studies found that use of I-ELCAP criteria (increase in nodule size threshold to an average diameter of 5 mm, 6 mm, or larger) would increase positive predictive value.[27,28]

Benefits of Early Detection and Treatment

The USPSTF reviewed 7 RCTs that evaluated lung cancer screening with LDCT.[24,25] The NLST[9] and the NELSON trial[11] were the only trials adequately powered to detect a lung cancer mortality benefit.

The NLST, the largest RCT to date (n = 53 454), enrolled participants aged 55 to 74 years at the time of randomization who had a tobacco use history of at least 30 pack-years and were current smokers or had quit within the past 15 years. The mean pack-year smoking history in NLST participants was 56 pack-years.[9] The NELSON trial (n = 15 792) enrolled participants aged 50 to 74 years who had a tobacco use history of at least 15 cigarettes a day (three-fourths of a pack per day) for more than 25 years or 10 cigarettes a day (one-half of a pack per day) for more than 30 years and were current smokers or had quit within the past 10 years. The median pack-year smoking history in NELSON trial participants was 38 pack-years.[11]

The NLST reported a relative risk reduction in lung cancer mortality of 20% (95% CI, 6.8%-26.7%)[9]; a subsequent analysis of NLST data with additional follow-up and end point verification reported a relative risk reduction of 16% (95% CI, 5%-25%).[10] At 10 years of follow-up, the NELSON trial reported 181 lung cancer deaths among participants in the screening group and 242 in the control group (incidence rate ratio [IRR], 0.75 [95% CI, 0.61-0.90]).[11,24] The NLST also found a reduction in all-cause mortality with LDCT screening compared with chest radiography (IRR, 0.93 [95% CI, 0.88-0.99]). Results of the other trials were imprecise, without any statistically significant differences between screening with LDCT and chest radiography or no screening.[24]

Evidence on screening interval comes from the NLST and the NELSON trial and CISNET modeling studies. The NLST screened annually for 3 years.[9] The NELSON trial screened at intervals of 1 year, then 2 years, then 2.5 years.[11] The CISNET modeling studies suggest that annual screening with LDCT provides greater benefit in decreasing lung cancer mortality and in life-years gained compared with biennial screening.[14]

Several lines of evidence suggest that screening for lung cancer in persons with fewer pack-years of smoking (ie, fewer than the 30 pack-year eligibility criterion of the 2013 USPSTF recommendation) and at an earlier age can increase the benefits of screening. As noted, the NELSON trial enrolled persons aged 50 to 74 years (about one-fourth of participants were younger than 55 years) who had accumulated fewer pack-years of smoking (half of a pack per day for more than 30 years or three-fourths of a pack per day for more than 25 years).[11] This trial provides empirical evidence for the benefit of screening for lung cancer with LDCT in persons aged 50 to 55 years and with lighter pack-year smoking histories.

The CISNET modeling studies also provided data that helped inform the pack-year eligibility criterion for lung cancer screening and the ages at which to start and stop screening. The USPSTF focused on screening programs in the 1960 birth cohort (more representative of current smoking patterns compared with earlier cohorts) that yielded lung cancer mortality reductions at least as great as the 2013 USPSTF screening program (A-55-80-30-15). For screening programs that provide this level of mortality benefit and also maximize, or come close to maximizing, both lung cancer deaths averted and life-years gained for any given level of LDCT screening, in at least 3 of the 4 CISNET models (ie, "consensus-efficient" programs), the majority (52%) have a minimum pack-year eligibility criterion of 20 pack-years. Almost all have a starting age of 50 or 55 years, and all have a stopping age of 80 years.[14,15]

Relative to the 2013 USPSTF screening program (A-55-80-30-15), CISNET modeling analyses suggest that annually screening persons aged 50 to 80 years who have at least a 20 pack-year smoking history and currently smoke or have quit within the past 15 years (A-50-80-20-15) would be associated with lung cancer mortality reduced by 13.0% vs 9.8%, with avoiding 503 vs 381 lung cancer deaths, and with 6918 life-years gained vs 4882 life-years gained per 100 000 persons in the population aged 45 to 90 years over a lifetime of screening.[14] Thus, this screening program would be associated with important reductions in lung cancer deaths and increases in life-years gained compared with the previous recommendation and is supported by new trial data and the CISNET modeling studies.

Screening for lung cancer in persons at an earlier age and with fewer pack-years of smoking (ie, 20 pack-years) may also help partially ameliorate racial disparities in screening eligibility. Data suggest that Black persons who smoke have a higher risk of lung cancer than do White persons, and this risk difference is more apparent at lower levels of smoking intensity.[7] One recent analysis of Southern Community Cohort Study participants found that 17% of Black persons who smoke were eligible for lung cancer screening based on the 2013 USPSTF eligibility criteria compared with 31% of White persons who smoke. In the same study, among persons diagnosed with lung cancer, a significantly lower percentage of Black persons who smoke (32%) were eligible for screening than were White persons (56%).[29] Data also suggest that Latinx/Hispanic persons who smoke accumulate fewer pack-years than White persons who smoke.[30,31] A strategy of annually screening persons aged 50 to 80 years who have at least a 20 pack-year smoking history and currently smoke or have quit within the past 15 years (A-50-80-20-15) would increase the relative percentage of persons eligible for screening by 87% overall—78% in non-Hispanic White adults, 107% in non-Hispanic Black adults, and 112% in Hispanic adults compared with 2013 USPSTF criteria (A-55-80-30-15).[14] Similarly, a strategy of screening persons aged 50 to 80 years who have at least a 20 pack-year smoking history and currently smoke or have quit within the past 15 years (A-50-80-20-15) would increase the relative percentage of persons eligible for screening by 80% in men and by 96% in women,[14] because they accumulate fewer pack-years than men.[32]

Simulation studies suggest that risk prediction models to determine eligibility for lung cancer screening could be associated with reduced lung cancer deaths and the number of participants needed to screen to prevent 1 lung cancer death. The CISNET modeling studies commissioned by the USPSTF thus compared the benefits and harms of screening programs based on risk prediction models vs risk factor–based screening (ie, using age and smoking history). The risk prediction models used were modified versions of the PLCOm2012 model,[33] the Lung Cancer Death Risk Assessment Tool (LCDRAT) model,[34] and the Bach model,[35] limited to age, sex (for those models that include sex as a variable,

such as the LCDRAT and Bach models), smoking intensity, and smoking duration (and setting other potential variables such as race, education, body mass index, personal history of cancer, or family history of lung cancer to their reference value). Because age is an important risk factor for lung cancer, these risk prediction models shifted screening to persons of older age and increased the number of lung cancer deaths averted, but screening occurs at older ages when there are fewer years to be gained. Thus, some risk prediction model–based screening programs were associated with slightly increased life-years gained, while some were not or were associated with even slightly decreased life-years gained. Risk prediction models also were associated with increased the number of over diagnosed lung cancers, which are more common in older individuals.[14]

It is possible that the use of a more complex risk prediction model to determine eligibility might impose a barrier to wider implementation and uptake of lung cancer screening, a service that currently has low uptake. Currently, there are no studies that have prospectively compared the use of USPSTF criteria considering age, pack-year smoking history, and number of years since quitting vs risk prediction models as criteria for lung cancer screening, so it is uncertain whether using a risk prediction model would improve lung cancer detection and clinical outcomes. The International Lung Screening Trial (ILST), a prospective cohort study that is comparing the accuracy of the PLCOm2012 model against the 2013 USPSTF criteria for detecting lung cancer, may provide some evidence regarding this issue.[36] In summary, determining eligibility for lung cancer screening using more complex risk prediction models may represent an implementation barrier, and there is currently insufficient evidence to assess whether risk prediction model–based screening would improve outcomes relative to simply using the risk factors of age and smoking history.

Harms of Screening and Treatment

Harms of screening can include false-positive results leading to unnecessary tests and invasive procedures, overdiagnosis, radiation-induced cancer, incidental findings, and increases in distress or anxiety.

The NLST reported false-positive rates of 26.3% for baseline, 27.2% for year 1, and 15.9% for year 2.[9] The NELSON trial reported false-positive rates of 19.8% at baseline, 7.1% at year 1, 9.0% for males at year 3, and 3.9% for males at year 5.5 of screening.[11,37] An implementation study through the Veterans Health Administration revealed a false-positive rate of 28.9% of veterans eligible for screening (58% of those who were actually screened) at baseline.[38] Both of these studies were conducted prior to the use of the Lung-RADS protocol for nodule classification, the use of which may reduce false-positives, albeit at the cost of some false-negatives. One retrospective study assessed how use of Lung-RADS would have changed the false-positive result rate in the NLST and found a false-positive rate among baseline results for Lung-RADS of 12.8% (95% CI, 12.4%-13.2%) vs 26.6% (95% CI, 26.1%-27.1%) for the NLST approach.[21]

The further workup of false-positive results can result in significant harms such as additional imaging, biopsy, or surgical procedures. Fourteen studies reported on the evaluation of false-positive results. Among all patients screened, the percentage who had a needle biopsy for false-positive results ranged from 0.09% to 0.56%. Complication rates from needle biopsy for false-positive results ranged from 0.03% to 0.07% of all patients screened. Surgical procedures for false-positive results were reported in 0.5% to 1.3% of all screened participants.[24]

In the NLST, false-positive results led to invasive procedures (needle biopsy, thoracotomy, thoracoscopy, mediastinoscopy, and bronchoscopy) in 1.7% of patients screened. Complications occurred in 0.1% of patients screened, and death in the 60 days following the most invasive procedure performed to evaluate a false-positive result occurred in 0.007% of those screened.[9] One study estimated that the use of Lung-RADS criteria would have prevented 23.4% of invasive procedures due to false-positive results.[21]

In the CISNET modeling studies, the false-positive rate varied based on screening eligibility criteria. Relative to the 2013 USPSTF criteria (A-55-80-30-15), the 2021 USPSTF criteria (A-50-80-20-15) would result in 2.2 vs 1.9 false-positive results per person over a lifetime of screening.[14] Note that screening programs that start at younger ages or use a lower pack-year eligibility screen a larger total number of persons.

Determining the rate of overdiagnosis in screening trials is challenging because the duration of follow-up affects the calculation of excess, potentially over diagnosed, cancers in the screening vs control groups. Initially, the NLST reported 119 additional lung cancers (1060 total cancers with LDCT vs 941 with chest radiography) after 3 screening rounds and 6.5 years of follow-up (IRR, 1.12 [95% CI, 1.02-1.22]).[9,24] With extended follow-up, the NLST found no statistically significant difference between groups for overall lung cancer incidence; however, this study had some methodological limitations, including use of a different ascertainment method during posttrial follow-up, lack of information on any posttrial screening that may have occurred in either the LDCT or chest radiography group, and missing data.[39] In the NELSON trial, 40 excess lung cancers (344 cancers in the LDCT group vs 304 in the control group) were reported in the LDCT group after the a priori planned 10 years of follow-up; after 11 years of follow-up, there was an excess of 14 cancers with LDCT.[11]

In the CISNET modeling studies, which account for lifetime follow-up, the 2013 USPSTF screening program (A-55-80-30-15) would result in 6.3% of screen-detected cases of lung cancer being over diagnosed lung cancers vs 6.0% lung cancers being overdiagnoses with the 2021 screening program (A-50-80-20-15).[14]

In the 9 publications reporting on radiation exposure associated with LDCT,[24] the radiation exposure associated with 1 LDCT scan ranged from 0.65 to 2.36 mSv. For context, average annual background radiation exposure in the US is 2.4 mSv. Two of the studies estimated the cumulative radiation exposure for participants undergoing screening with LDCT. Using estimated radiation exposure from screening and follow-up evaluations and estimates of the risk of radiation-induced cancer deaths, the Italian Lung Cancer Screening Trial (ITALUNG) estimated a lifetime risk of fatal cancer of 0.11 cases per 1000 persons for LDCT after the 4 screening rounds,[40] and the Continuing Observation of Smoking Subjects study estimated a lifetime risk of 2.6 to 8.1 major cancers per 10 000 persons screened after 10 rounds of annual screening.[41]

The CISNET modeling studies found that lifetime estimates of radiation-related lung cancer deaths varied by eligibility criteria for screening. Relative to the 2013 USPSTF recommendation (A-55-80-30-15), the 2021 USPSTF recommendation (A-50-80-20-15) would be associated with an estimated 38.6 vs 20.6 radiation-related lung cancer deaths per 100 000 persons in the total population aged 45

to 90 years, or 1 death caused for every 13.0 vs 18.5 lung cancer deaths avoided by screening.[14]

When comparing LDCT groups vs control groups for smoking cessation or abstinence outcomes, evidence does not indicate that screening leads to lower rates of smoking cessation or continued abstinence or to higher rates of relapse. Several studies suggest that, compared with no screening, individuals who receive LDCT screening do not have worse health-related quality of life, anxiety, or distress over 2 years of follow-up. However, screening participants who receive true-positive or indeterminate results may experience worse health-related quality of life, anxiety, or distress in the short-term.[24]

Studies reported a wide range of screening-related incidental findings that were deemed significant or required further evaluation (4.4% to 40.7%), in part because of inconsistent definitions of what constitutes an incidental finding and which findings were clinically significant.[24] Older age was associated with a greater likelihood of incidental findings. Common incidental findings included coronary artery calcification, aortic aneurysms, emphysema, and infectious and inflammatory processes. Other common findings were masses, nodules, or cysts of the kidney, breast, adrenal gland, liver, thyroid, pancreas, spine, and lymph nodes. Cancers involving the kidney, thyroid, or liver were ultimately diagnosed in 0.39% of NLST participants in the LDCT group during screening.[42]

Incidental findings led to downstream evaluation, including consultations, additional imaging, and invasive procedures with associated costs and burdens. The benefits of incidental detection of nonlung cancer conditions and the balance of benefits and harms of incidental findings on LDCT screening remain uncertain.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from July 7, 2020, to August 3, 2020. Most comments generally agreed with the draft recommendation, although some requested broadening the eligibility criteria for lung cancer screening and others mentioned that additional risk factors for lung cancer other than smoking exist or that lung cancer can occur in persons who never smoked. In response, the USPSTF acknowledges that there are risk factors for lung cancer other than smoking; however, current evidence does not support the incorporation of these risk factors as determinants of eligibility for lung cancer screening. The USPSTF also acknowledges that lung cancer can occur in persons who never smoked or among persons who currently smoke or formerly smoked who do not meet screening eligibility criteria. Nevertheless, smoking is the major risk factor for lung cancer, all trials of screening for lung cancer have been conducted among persons who smoke or were former smokers, and trial and modeling data support the current USPSTF recommendation as offering a reasonable balance of benefits and harms.

Some comments suggested the use of more complex risk prediction models to determine eligibility for lung cancer screening. In response, the USPSTF clarified language that use of these risk prediction models might make implementation more difficult, and that there are currently no lung cancer screening trials prospectively comparing USPSTF eligibility criteria with risk prediction models. The USPSTF also added a reference to the ILST, a prospective cohort study addressing this issue.

In response to comments, the USPSTF also added information about the currently low uptake of lung cancer screening and data on the effect of the current recommendation on eligibility for screening in Latinx/Hispanic persons. Last, the USPSTF added and updated resources and website links in the Additional Tools and Resources section.

How Does the Evidence Fit With Biological Understanding?

Lung cancer is a proliferation of malignant cells that originate in lung tissue. Smoking is the strongest risk factor for lung cancer. Older age is also associated with increasing incidence of lung cancer. Lung cancer is classified into 2 major categories based on cell type and immunohistochemical and molecular characteristics: NSCLC, which collectively comprises adenocarcinoma, squamous cell carcinoma, and large cell carcinoma, and small cell lung cancer. Screening is aimed at early detection of NSCLC rather than small cell lung cancer because the latter is much less common and typically spreads too quickly to be reliably detected at an early, potentially curable stage by screening.

Currently, 79% of patients present with lung cancer that has spread to regional lymph nodes or metastasized to distant sites. Only 17% of patients present with localized disease. Patients with localized disease have a 59% 5-year survival rate, compared with 32% for those with regional spread and 6% for those with distant metastases.[1] By leading to earlier detection and treatment, screening for lung cancer can give patients a greater chance for cure.

Research Needs and Gaps

- Implementation research addressing how best to increase the uptake of lung cancer screening discussions in clinical practice is needed, particularly among the populations at higher risk of death from lung cancer or populations that are socially and economically disadvantaged.
- Research is needed to evaluate whether, as lung cancer screening is implemented in more diverse community settings, including among racial/ethnic minorities, among populations socially and economically disadvantaged (for whom smoking prevalence and lung cancer incidence is higher), and in settings that screen greater numbers of women, the balance of benefits and harms differs from those observed in RCTs.
- Research to identify biomarkers that can accurately identify persons at high risk is needed to improve detection and minimize false-positive results.
- Research to identify technologies that can help more accurately discriminate between benign and malignant lung nodules is needed.
- Research is needed on the benefits and harms of using risk prediction models to select patients for lung cancer screening, including whether use of risk prediction models represents a barrier to wider implementation of lung cancer screening in primary care.

Recommendations of Others

The American Association for Thoracic Surgery recommends annual lung cancer screening with LDCT for North Americans aged 55 to 79 years with a 30 pack-year history of smoking. It also recommends offering annual lung cancer screening with LDCT starting at

age 50 years to persons with a 20 pack-year smoking history if there is an additional cumulative risk of developing lung cancer of 5% or greater over the following 5 years.[43]

The American Cancer Society recommends annual lung cancer screening with LDCT for persons aged 55 to 74 years who are in fairly good health, have at least a 30 pack-year smoking history, and currently smoke or have quit within the past 15 years. It also recommends smoking cessation counseling for current smokers, shared decision-making about lung cancer screening, and that screening be conducted in a high-volume, high-quality lung cancer screening and treatment center.[44]

The American College of Chest Physicians suggests that annual screening with LDCT should be offered to asymptomatic smokers and former smokers aged 55 to 77 years who have smoked 30 pack-years or more and either continue to smoke or have quit within the past 15 years. It also recommends that screening not be performed for individuals with comorbidities that adversely influence their ability to tolerate the evaluation of screen-detected findings or tolerate treatment of an early-stage screen-detected lung cancer or that substantially limit their life expectancy.[45]

The National Comprehensive Cancer Network recommends annual screening for lung cancer with LDCT in persons aged 55 to 77 years who have at least a 30 pack-year smoking history and currently smoke or have quit within the past 15 years or in persons 50 years or older who have at least a 20 pack-year smoking history and have at least 1 additional risk factor for lung cancer.[46]

The American Academy of Family Physicians has concluded that the evidence is insufficient to recommend for or against screening for lung cancer with LDCT in persons at high risk of lung cancer based on age and smoking history.[47]

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