



Lung cancer screening: USPSTF revises its recommendation

A draft statement calls for annual screening for individuals who are between the ages of 55 and 79 years, have ≥ 30 pack-year history of smoking, and either still smoke or quit less than 15 years ago.

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The US Preventive Services Task Force (USPSTF) recently released a draft recommendation on lung cancer screening, advising annual screening with low-dose computed tomography (LDCT) for individuals at high risk for lung cancer based on age and smoking history. Once finalized, this recommendation will replace its “I” rating, which indicated that evidence was insufficient to recommend for or against screening for lung cancer.

While the wording of the new recommendation is nonspecific regarding who should be screened, the Task Force elaborates in its follow-on commentary: Screening should start at age 55 and continue through age 79 for those who have ≥ 30 pack-year history of smoking and are either current smokers or past smokers who quit < 15 years earlier.¹ The draft recommendation advises caution in screening those with significant comorbidities, as well as individuals in their late 70s. Examples of how these specifications would work in practice are included in **TABLE 1**.

Lung cancer epidemiology

Lung cancer is the second most common cancer in both men and women and the leading cause of cancer deaths in the United States,

accounting for more than 158,000 deaths in 2010.² Lung cancer is highly lethal, with $> 90\%$ mortality rate¹ and a 5-year survival rate $< 20\%$.¹ However, non-small cell lung cancer (NSCLC), which can be cured with surgical resection if caught early, is responsible for 80% of cases.³ The incidence of lung cancer increases markedly after age 50, with $> 80\%$ of cases occurring in those 60 years or older.³

Smoking causes $> 90\%$ of lung cancers,² which are preventable with avoidance of smoking and smoking cessation programs. Currently, 19% of Americans smoke and 37% are current or former smokers.¹

Evidence report

The systematic review⁴ that the new draft recommendation was based on found 4 clinical trials of LDCT screening that met inclusion criteria (**TABLE 2**). One, the National Lung Screening Trial (NLST), was a large study involving 33 centers in the United States and 53,454 current and former smokers ages 55 to 74 years. Participants had a mean age of 61.4 years and ≥ 30 pack-year history of smoking, with a mean of 56 pack-years.⁵

The study population was relatively young and healthy; only 8.8% of participants were older than 70. The researchers excluded any-

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TABLE 1

Examples of how the USPSTF lung cancer screening recommendation would work in practice

Patient	Recommendation	Rationale
60 yo with 35 pack-year history of smoking; last smoked at age 40	No screening	Quit smoking >15 years ago
55 yo with 40 pack-year history; currently smokes	Advise smoking cessation; annual LDCT through age 79, or until 15 years after quitting	Meets all criteria for annual screening
65 yo with 45 pack-year history; quit smoking at age 55	Annual LDCT for 5 years	After 5 years it will be 15 years since patient quit
70 yo with severe COPD, 40+ pack-year history	Discuss screening LDCT and risks/benefits	Older age and significant comorbidity make candidacy for lung surgery unlikely
55 yo with 20 pack-year history; smokes 1 pack per day	Advise smoking cessation; start screening at age 65 if still smoking	Does not meet ≥ 30 pack-year history

COPD, chronic obstructive pulmonary disease; LDCT, low-dose computed tomography; USPSTF, US Preventive Services Task Force.

Source: Screening for lung cancer. US Preventive Services Task Force.¹

one with a significant comorbidity that would make it unlikely that they would undergo surgery if cancer were detected.

Participants were randomized to either LDCT or chest x-ray, given 3 annual screens, and followed for a mean of 6.5 years. In the LDCT group, there was a 20% reduction in lung cancer mortality and a 7% decrease in overall mortality. This translates to a number needed to screen (NNS) of 320 to prevent one lung cancer death, which compares favorably with other cancer screening tests. Mammography has an NNS of about 1339 for women ages 50 to 59, for example, and colon cancer screening using flexible sigmoidoscopy has an NNS of 817 among individuals ages 55 to 74 years.⁴

The other 3 studies in the systematic review were conducted in other countries, and were smaller, of shorter duration, and of lower quality.⁶⁻⁸ None demonstrated a reduction in either lung cancer or all-cause mortality, and one showed a small increase in all-cause mortality.⁸ A Forest plot of all 4 studies raises questions about the significance of the decline in all-cause or lung-cancer mortality.⁴ However, a meta-analysis that deletes the one poor quality study did demonstrate a 19% decrease in lung cancer mortality, but no decline in all-cause mortality.⁹

The evidence report included an assessment of 15 studies on the accuracy of LDCT

screening. Sensitivity varied from 80% to 100% and specificity ranged from 28% to 100%. The positive predictive value (PPV) for lung cancer ranged from 2% to 42%; however, most abnormal findings resolved with further imaging. As a result, the PPV for those who had a biopsy or surgery after retesting was 50% to 92%.⁴

Potential harms in the recommendation

Radiation exposure from an LDCT is slightly greater than that of a mammogram. The long-term effects of annual LDCT plus follow-up of abnormal findings is not fully known. There is some concern about the potential for lung cancer screening to have a negative effect on smoking cessation efforts. However, evidence suggests that the use of LDCT as a lung cancer screening tool has no influence on smoking cessation.⁴

■ **Extrapolating results.** The NLST was a well-controlled trial conducted at academic health centers, with strict procedures for conservative follow-up of suspicious lesions. A potential for harm exists in extrapolating results from such a study to the community at large, where work-ups may be more aggressive and include biopsy.

■ **Overdiagnosis.** Routine LDCT will likely result in some degree of overdiagnosis—eg,

TABLE 2
RCTs using LDCT for lung cancer screening

Study	Location (years followed)	N	Ages (years)	Quality	Lung cancer mortality RR (95% CI)	All-cause mortality RR (95% CI)
National Lung Screening Trial ⁵	33 US centers (6.5 y)	53,454	55-74 (mean, 61.4)	Good	0.80 (0.73-0.93)	0.93 (0.86-0.99)
Danish Lung Cancer Screening Trial ⁶	Denmark (2.5-3 y)	4104	50-70 (mean, 57.9)	Fair	0.83 (0.45-1.54)	0.85 (0.56-1.27)
Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial ⁷	Italy (4.8 y)	2472	60-74 (mean, 64.3)	Fair	1.37 (0.63-2.97)	1.46 (0.99-2.15)
Multicentric Italian Lung Detection ⁸	Italy (4.5 y)	4099	≥49 (median, 58)	Poor	1.99 (0.80-4.96)	1.80 (1.03-3.13)

CI, confidence interval; LDCT, low-dose computed tomography; RCT, randomized controlled trial; RR, relative risk.

detection of low-grade cancers that would either regress on their own or simply not progress—and overtreatment, with the potential for complications.

Full impact is unknown

The ultimate balance of benefits and harms of the USPSTF's lung cancer screening draft recommendation rests on some unknowns. Widespread screening is unlikely to achieve the same results as did the NLST. As already noted, those enrolled in the NLST were relatively young and had large pack-year smoking histories. The Task Force acknowledges that the 20% reduction in lung cancer mortality achieved in the NLST is unlikely to be duplicated in older patients and individuals with less significant smoking histories. Additional harms will likely accrue if suspicious findings are more aggressively pursued than they were in this study. The potential harms, as well as benefits, from incidental findings on chest LDCT scans are also unknown.

■ **The number of screenings.** The potential for benefits beyond 3 screenings is also unknown, as the USPSTF's projections in such cases are based on modeling. The degree of overdiagnosis is not fully understood, nor is the harm that could result from the accumulated radia-

tion of what could be an annual LDCT for 25 years. The harm/benefit ratio will become clearer with time and can then be compared with other medical interventions.

■ **Financial burden.** While it may appear to some that the draft recommendation would unfairly benefit smokers by allowing them to undergo free annual CT screening, patients are likely to incur significant financial obligations as a result of doing so. The Affordable Care Act mandates that the annual LDCT screening would have to be offered with no patient cost sharing, but follow-up CTs for questionable findings, biopsies, and treatment will all be subject to deductibles and copayments.

Recommendations of others

Other organizations have adopted recommendations on lung cancer screening similar to the USPSTF proposal. These include the American Association for Thoracic Surgery, American Cancer Society, American College of Chest Physicians, American Lung Association, American Society of Clinical Oncology, and American Thoracic Society. Most apply to those ages 55 to 74 years and use other inclusion criteria of the NLST. Some stipulate that patients should be in good enough health to benefit from early detection, and most include a reference to the quality of the centers

at which screening should occur. The American Academy of Family Physicians is currently considering what its recommendation on lung cancer screening will be.

Final USPSTF recommendation expected soon

Noticeably absent from the news coverage

of the proposed USPSTF recommendation was the word “draft.” The Task Force has now collected public comments about its proposed recommendation and will be considering potential changes to the wording. Publication of the final recommendation is expected in December—shortly after press time. **JFP**

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