Executive Summary
Screening for Lung Cancer: Chest Guideline and Expert Panel Report

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BACKGROUND: Low-dose chest CT screening for lung cancer has become a standard of care in the United States, in large part because of the results of the National Lung Screening Trial (NLST). Additional evidence supporting the net benefit of low-dose chest CT screening for lung cancer, and increased experience in minimizing the potential harms, has accumulated since the prior iteration of these guidelines. Here, we update the evidence base for the benefit, harms, and implementation of low-dose chest CT screening. We use the updated evidence base to provide recommendations where the evidence allows, and statements based on experience and expert consensus where it does not.

METHODS: Approved panelists reviewed previously developed key questions using the Population, Intervention, Comparator, Outcome format to address the benefit and harms of low-dose CT screening, and key areas of program implementation. A systematic literature review was conducted using MEDLINE via PubMed, Embase, and the Cochrane Library on a quarterly basis since the time of the previous guideline publication. Reference lists from relevant retrievals were searched, and additional papers were added. Retrieved references were reviewed for relevance by two panel members. The quality of the evidence was assessed for each critical or important outcome of interest using the Grading of Recommendations, Assessment, Development and Evaluation approach. Meta-analyses were performed where appropriate. Important clinical questions were addressed based on the evidence developed from the systematic literature review. Graded recommendations and ungraded statements were drafted, voted on, and revised until consensus was reached.

RESULTS: The systematic literature review identified 75 additional studies that informed the response to the 12 key questions that were developed. Additional clinical questions were addressed resulting in seven graded recommendations and nine ungraded consensus statements.

CONCLUSIONS: Evidence suggests that low-dose CT screening for lung cancer can result in a favorable balance of benefit and harms. The selection of screen-eligible individuals, the quality of imaging and image interpretation, the management of screen-detected findings, and the effectiveness of smoking cessation interventions can impact this balance.


KEY WORDS: guidelines; lung cancer; screening

ABBREVIATIONS: ACR = American College of Radiology; CMS = Centers for Medicare and Medicaid Services; LDCT = low-dose CT; NELSON = Nederlands-Leuvens Longkanker Screenings Onderzoek Study; NLST = National Lung Screening Trial; RCT = randomized controlled trial; SDM = shared decision-making; USPSTF = US Preventative Services Task Force

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Summary of Recommendations

Selection of Individuals for Lung Cancer Screening

1. For asymptomatic individuals age 55 to 77 who have smoked 30 pack years or more and either continue to smoke or have quit within the past 15 years, we recommend that annual screening with low-dose CT should be offered (Strong Recommendation, Moderate-Quality Evidence).

Remarks: These eligibility criteria align with the eligibility criteria for CMS coverage at the time of publication.

Remarks: Asymptomatic refers to the absence of symptoms that suggest the presence of lung cancer.

2. For asymptomatic individuals who do not meet the smoking and/or age criteria in Recommendation #1, are age 50 to 80, have smoked 20 pack years or more and either continue to smoke or have quit within the past 15 years, we suggest that annual screening with low-dose CT should be offered (Weak Recommendation, Moderate-Quality Evidence).

Remarks: These criteria align with the 2021 recommendations from the USPSTF.1

Remarks: Asymptomatic refers to the absence of symptoms that suggest the presence of lung cancer.

Remarks: Some individuals eligible by Recommendation #2 may have low net-benefit from screening and may choose not to undergo screening.

3. For asymptomatic individuals who do not meet the smoking and/or age criteria in Recommendations #1 and 2 but are projected to have a high net benefit from lung cancer screening based on the results of validated clinical risk prediction calculations and life expectancy estimates, or based on life-year gained calculations, we suggest that annual screening with low-dose CT should be offered (Weak Recommendation, Moderate-Quality Evidence).

Remarks: Augmenting the criteria outlined in Recommendations #1 and 2 with risk prediction and life-year gained calculators leads to greater equity across race and sex in eligibility for lung cancer screening and the net benefits of screening.

Remarks: Life-year gained calculators combine the results of risk prediction and life expectancy estimates into one measure.

Remarks: Examples of calculated thresholds that identify individuals with a high net benefit from lung cancer screening include:

- Life-gained: \( \geq 16.2 \) days of life-gained by screening on the Life Years Gained From Screening-CT (LYFS-CT) calculator.
- Lung-cancer death risk: \( \geq 1.33\% \) 5-year risk on the Lung Cancer Death Risk Assessment Tool (LCDRAT) calculator and \( \geq 10 \) years of life-expectancy.
- Lung-cancer incidence risk: \( \geq 2.0\% \) 5-year risk on the LCRAT calculator and \( \geq 10 \) years of life-expectancy; \( \geq 2.6\% \) 6-year risk on the Prostate, Lung, Colorectal, and Ovarian (PLCO<SUB>M2012</SUB>) calculator and \( \geq 10 \) years of life-expectancy; \( \geq 5.2\% \) 10-year risk on the Bach calculator and \( \geq 10 \) years of life-expectancy.

Remarks: The application of risk calculators or life year gained calculators to identify screen eligible individuals is more burdensome than identification using the criteria in Recommendations #1 and 2 alone. Lung cancer screening programs that choose to identify eligible individuals based on this recommendation should develop tools to support ordering providers in identifying screen eligible individuals.

Remarks: In the United States, health insurance providers may not pay for low-dose CT screening for those who do not meet the eligibility criteria listed in Recommendation #1 or 2.

Remarks: Molecular biomarkers are being developed to assist with risk prediction and/or early lung cancer detection. They have not reached a phase of evaluation to be included in this recommendation at the time of publication.
4. For individuals who have accumulated fewer than 20 pack years of smoking or are younger than age 50 or older than 80, or have quit smoking more than 15 years ago, and are not projected to have a high net benefit from lung cancer screening based on clinical risk prediction or life-year gained calculators, we recommend that low dose CT screening should not be performed (Strong Recommendation, Moderate-Quality Evidence).

5. For individuals with comorbidities that substantially limit their life expectancy and adversely influence their ability to tolerate the evaluation of screen detected findings, or tolerate treatment of an early stage screen detected lung cancer, we recommend that low-dose CT screening should not be performed (Strong Recommendation, Low-Quality Evidence).

Remarks: When an individual has a very severe comorbid condition it is easier to determine that low-dose CT screening is not indicated (eg, advanced liver disease, severe COPD with hypoventilation and hypoxia, NYHA class IV heart failure) because competing mortality limits the potential benefit, and harms are magnified. At less severe stages of comorbid conditions it can be difficult to determine if an individual’s comorbidities are significant enough that they should not receive low-dose CT screening.

Remarks: The use of a life-year gained calculator may assist clinicians with this decision by accounting for reduced life-expectancy in people at advanced age or with comorbidities.

Implementation of High-Quality Lung Cancer Screening

6. We suggest that low-dose CT screening programs develop strategies to determine whether patients have symptoms that suggest the presence of lung cancer, so that symptomatic patients do not enter screening programs but instead receive appropriate diagnostic testing, regardless of whether the symptomatic patient meets screening eligibility criteria (Ungraded Consensus-Based Statement).

Remarks: In centralized low-dose CT screening programs, the provider that communicates with the patient prior to the low-dose CT should ask about symptoms that would suggest diagnostic testing is indicated.

Remarks: In de-centralized low-dose CT screening programs, the screening program should assist the ordering provider through educational outreach and/or the provision of clinical tools (eg, reminders built into electronic medical records).

7. We suggest that low-dose CT screening programs develop strategies to provide effective counseling and shared decision-making visits prior to the performance of the LDCT screening exam (Ungraded Consensus-Based Statement).

Remarks: Components of the counseling and shared decision-making visit include a determination of screening eligibility (including the absence of symptoms and confirmation of overall health), the use of decision aids with information about benefits and harms of screening, a discussion about the potential CT findings and need for follow-up testing, the need for annual screening exams, confirmation of the willingness to accept treatment for a screen detected cancer, and counseling about smoking cessation.

Remarks: In centralized low-dose CT screening programs, a screening program provider may communicate with the patient prior to the low-dose CT to perform the counseling and shared decision-making visit.

Remarks: In de-centralized low-dose CT screening programs, the screening program should ensure that ordering providers are trained, and/or have the tools necessary, to deliver an effective counseling and shared decision-making visit. These tools may include decision aids, information brochures, videos, and links to electronic resources.

Remarks: Life year gained calculators, or lung cancer risk calculators combined with tools to aid life-expectancy estimation, may be useful in identifying those with a high net-benefit, those unlikely to have net-benefit, and those between these extremes where there is a closer balance of benefits to harms associated with screening. This calculation may help to tailor the discussion during the shared decision-making visit.

8. We suggest that screening programs define what constitutes a positive test on the low-dose CT based on the size of a detected solid or part-solid lung nodule, with a threshold for a positive test that is either 4 mm, 5 mm, or 6 mm in diameter (Weak Recommendation, Low-Quality Evidence).

Remarks: A positive test is defined as a test that leads to a recommendation for any additional testing other than to return for the annual screening exam.
Remarks: Screening programs should develop messages to share with providers and patients about the likelihood of having a positive test, and the meaning of the finding, particularly the low likelihood that a small solid nodule will be found to be a cancer.

Remarks: Nodule diameter is the average of long- and short-axis diameters obtained on the same sagittal, coronal, or transverse image. For part-solid nodules, nodule diameter should be based on the size of the solid component of the nodule. Nodule diameter should be measured using lung windows.

Remarks: An equivalent volumetric threshold can also be considered.

Remarks: The LungRADS structured reporting system currently uses a 6 mm threshold for a positive test on the baseline scan and 4 mm if a new nodule is found on the annual scan for solid nodules; and 6 mm on the baseline scan and any size if a new nodule is found on the annual scan for part-solid nodules.

9. We suggest that low-dose CT screening programs develop strategies to maximize compliance with annual screening exams and evaluation of screen-detected findings (Ungraded Consensus-Based Statement).

Remarks: These strategies may include education during the shared decision-making visit, communication through EHR reminders, letters, phone calls, and tools to address screening participants’ concerns about the LDCT results and follow-up plan, insurance coverage, and other questions or barriers to returning for follow-up.

10. We suggest that low-dose CT screening programs develop a comprehensive approach to lung nodule management that includes access to multidisciplinary expertise (Pulmonary, Radiology, Thoracic Surgery, Medical and Radiation Oncology), and algorithms for the management of small solid nodules, larger solid nodules, and sub-solid nodules (Ungraded Consensus-Based Statement).

Remarks: Programs without lung nodule management expertise available on site could collaborate with centers capable of high-quality lung nodule management (eg, referral, telehealth evaluation).

11. We suggest that low-dose CT screening programs develop strategies to minimize overtreatment of potentially indolent lung cancers (Ungraded Consensus-Based Statement).

Remarks: It is important to educate patients about the potential to detect an indolent lung cancer to help mitigate the psychological distress that could result from living with an indolent untreated lung cancer.

Remarks: For malignant nodules, pure ground glass is the nodule morphology on imaging that is most likely to represent an indolent cancer.

12. For individuals who currently smoke and are undergoing low-dose CT screening, we recommend that screening programs provide evidence-based tobacco cessation treatment as recommended by the US Public Health Service (Strong Recommendation, Low-Quality Evidence).

13. We suggest that low-dose CT screening programs follow the ACR/STR protocols for performing low radiation dose chest CT scans (Ungraded Consensus-Based Statement).

Remarks: An awareness of the potential for radiation related harm can help programs thoughtfully plan ways to minimize this risk through proper patient selection, the performance of the CT scan, tracking of the radiation dose being administered, and appropriate management of screen detected findings.

14. We suggest that low-dose CT screening programs use a structured reporting system to report the exam results (Ungraded Consensus-Based Statement).

Remarks: The structured reporting system should include a description of the number, location, size, and characteristics of lung nodules, guideline-based recommendations for surveillance of small lung nodules, and a description of other potentially actionable findings.

Remarks: The ACR LungRADS structured report is the most prevalent system used today. The ACR National Registry requires data to be submitted using the LungRADS categories.

15. We suggest that low-dose CT screening programs develop strategies to guide the management of non-lung nodule findings (Ungraded Consensus-Based Statement).

Remarks: Examples include coronary artery calcification, thyroid nodules, adrenal nodules, kidney and liver lesions, thoracic aortic aneurysms, pleural effusions, and parenchymal lung disease.

Remarks: A lung cancer screening program should anticipate such findings and have a system in place to address them. Examples include evidence-based
guidance within the structured report to assist the ordering provider, or centralized management of all non-lung nodule findings by the screening program. Clear communication between providers is important to prevent misunderstandings about who will assume responsibility for evaluation of these findings.

Remarks: The description of non-lung nodule findings in the structured reports should be standardized to assist with interpretation of the findings.

16. We suggest that low-dose CT screening programs develop data collection and reporting tools capable of assisting with quality improvement initiatives and reporting to the current National Registry (Ungraded Consensus-Based Statement).

Remarks: Data categories include patient eligibility criteria, imaging findings and their evaluation, results of the evaluation of imaging findings including complications, smoking cessation interventions, and lung cancer diagnoses including histology, stage, treatment, and outcomes.

Background

The benefit of cancer screening is a reduction in the number of cancer-related deaths in the group that is screened. Even within groups at high risk of developing cancer, only a fraction of those screened will benefit, whereas everyone screened is exposed to potential harms. The benefit and harms of screening differ in both frequency and magnitude. This makes it difficult to determine an acceptable balance of benefit and harms at the population level. For an individual patient, it highlights the importance of education to foster informed, value-based decisions about whether to be screened.

Even when large studies suggest that the value of the benefit of screening outweighs identified harms, the translation of this favorable balance into practice can be difficult. In lung cancer screening, the selection of screen-eligible patients, the quality of imaging and image interpretation, the management of screen-detected findings, and the effectiveness of smoking cessation interventions can impact this balance.

In this paper we provide an executive summary of the full guideline document. In the full document, we update the evidence base for the benefit, harms, and implementation of chest low-dose CT (LDCT) screening. We use this evidence base to update recommendations where the evidence allows, and update statements based on experience and expert consensus where it does not. We have updated the description of the evidence and discussion where it has changed and have maintained the text from the prior version where it did not. We have not provided updates for other forms of lung cancer screening (ie, chest radiograph, sputum analysis) because the evidence base and recommendations related to chest radiography and sputum analysis have not changed since the previous iterations of these guidelines. The intended audience for this guideline is practicing clinicians, administrators, and policy makers.

Results

Seventy-five studies were identified that met the inclusion criteria. Of these 75 studies, nine were identified to either update a prior meta-analysis or perform a new meta-analysis, six were identified to update the cohort studies of the original guideline (e-Fig 1, e-Table 2), and 61 were flagged for potential narrative synthesis. The Grading of Recommendations, Assessment, Development and Evaluation profiles for the evidence-based recommendation statements can be found in e-Tables 3-5.

Selection of Individuals for Lung Cancer Screening

The selection of individuals for lung cancer screening requires an understanding of the evidence supporting benefit from screening and describing the potential harms from screening. The decision about who to screen requires an understanding of trade-offs in the balance of benefits and harms at a population and individual level.

Benefit of Screening for Lung Cancer: Lung Cancer Mortality Reduction:

Key Question 1: What is the rate of death from lung cancer (ie, lung cancer mortality) among individuals at elevated risk of lung cancer who undergo screening with LDCT scan compared with either no screening or screening with another modality?

Four new publications from randomized controlled trials (RCTs) were identified to update the lung cancer mortality meta-analysis. The studies provide longer follow-up results for the Dutch Belgian randomized LDCT screening trial (Nederlands-Leuvens Longkanker Screenings Onderzoek Study [NELSON]), the Multicentric Italian Lung Detection (MILD) trial, the German Lung Cancer Screening Intervention (LUSI) trial, and the Lung Screening Study (LSS) than were available for the prior guideline. The study design and outcomes of these studies have been added to prior summary tables (Tables 1,2).
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Age (y)</th>
<th>Smoking History</th>
<th>Smoking Cessation (Years Since Quit)</th>
<th>Screening Interval and Duration</th>
<th>Follow-up (y)</th>
<th>Definition of Positive Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDCT scan vs CXR</td>
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<tr>
<td>LSS (NLST feasibility)</td>
<td>3,258</td>
<td>55-74</td>
<td>≥ 30 pack-years</td>
<td>&lt; 10</td>
<td>Two annual screens</td>
<td>5.2 (median)</td>
<td>≥ 4 mm</td>
</tr>
<tr>
<td>NLST</td>
<td>53,454</td>
<td>55-74</td>
<td>≥ 30 pack-years</td>
<td>≥15</td>
<td>Three annual screens</td>
<td>6.5 (median)</td>
<td>≥ 4 mm</td>
</tr>
<tr>
<td>Dépiscan</td>
<td>765</td>
<td>50-75</td>
<td>≥ 15 cigarettes/d for ≥ 20 y</td>
<td>&lt; 15</td>
<td>Three annual screens</td>
<td>NR</td>
<td>&gt; 5 mm</td>
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<tr>
<td>LDCT scan vs usual care (no screening)</td>
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<tr>
<td>DANTE</td>
<td>2,472 men</td>
<td>60-74</td>
<td>≥ 20 pack-years</td>
<td>&lt; 10</td>
<td>Five annual screens; baseline CXR for both study arms</td>
<td>8</td>
<td>&gt; 5 mm</td>
</tr>
<tr>
<td>DLCST</td>
<td>4,104</td>
<td>50-70</td>
<td>≥ 20 pack-years</td>
<td>&lt; 10</td>
<td>Five annual screens</td>
<td>10</td>
<td>&gt; 15 mm or rapid growing 5- to 15-mm nodules (&gt;25% increase in volume on 3-mo repeat CT scan)</td>
</tr>
<tr>
<td>DLCST post hoc analysis</td>
<td>4,104</td>
<td>50-70</td>
<td>≥ 20 pack-years</td>
<td>&lt; 10</td>
<td>Four annual scans</td>
<td>10.5 (mean)</td>
<td>NR</td>
</tr>
<tr>
<td>NELSON</td>
<td>15,774</td>
<td>50-75</td>
<td>≥ 15 cigarettes/d for ≥ 25 y or ≥ 10 cigarettes/d for ≥ 30 y</td>
<td>&lt;10</td>
<td>Four screening rounds; interval after baseline: 1, 2, and 2.5 y</td>
<td>10</td>
<td>Volume &gt; 500 mm³ or volume 50-500 mm³ with VDT &lt; 400 d on 3-mo repeat CT scan</td>
</tr>
<tr>
<td>ITALUNG</td>
<td>3,206</td>
<td>55-69</td>
<td>≥ 20 pack-years</td>
<td>≥10</td>
<td>Four annual screens</td>
<td>6</td>
<td>≥ 5-mm solid nodule, a ground-glass nodule ≥ 10 mm, or any part-solid nodule</td>
</tr>
<tr>
<td>MILD trial</td>
<td>4,099</td>
<td>≥ 49</td>
<td>≥ 20 pack-years</td>
<td>&lt; 10</td>
<td>Five annual screens and three biennial screens combined</td>
<td>10</td>
<td>Volume &gt; 250 mm³ or rapid growing 60-250 mm³ (&gt;25% increase in volume on 3-mo repeat CT scan)</td>
</tr>
<tr>
<td>LUSI trial</td>
<td>4,039</td>
<td>50-69</td>
<td>≥ 15 cigarettes/d for ≥ 25 y or ≥ 10 cigarettes/d for ≥ 30 y</td>
<td>&lt; 10</td>
<td>Five annual scans</td>
<td>8.8 (mean)</td>
<td>≥ 5 mm</td>
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(Continued)
Of the eight randomized controlled trials that report on lung cancer mortality\textsuperscript{4,7,10,14,17,24} only the National Lung Screening Trial (NLST)\textsuperscript{10,11} and the NELSON\textsuperscript{5} were adequately powered to answer the question of whether a mortality benefit from screening can be achieved. None of the other trials were individually powered to adequately address a mortality benefit (smaller size, screened a lower risk group than the NLST).

The meta-analysis of all included trials combined is interpreted with an understanding of the heterogeneity of the study designs and results. This revealed a statistically significant 19% relative reduction in lung cancer deaths or an absolute four fewer lung cancer deaths per 1,000 people screened (Fig 1, Table 3). The aggregate quality of the evidence of the eight RCTs\textsuperscript{4,7,10,14,17,24} reporting on lung cancer mortality was moderate (e-Table 3a).

**Key Question 2:** What is the rate of death from lung cancer (ie, lung cancer mortality) among individuals at elevated risk of lung cancer with different clinical phenotypes (sex, age, race, risk, COPD, comorbidities) who undergo screening with LDCT scan compared with either no screening or screening with another modality?

We evaluated lung cancer mortality reduction in men and women separately, combining studies where this was reported. Individual studies were not powered to detect differences between sexes. Lung cancer mortality reduction appeared to be greater among women but was significant for both men and women. Similarly, we evaluated lung cancer mortality reduction based on the starting age (50, 55, or 60 years). The results of these analyses are summarized in Table 3 and e-Figures 2-7. Limited data comparing mortality outcomes by race, smoking status, malignancy risk, and the presence of COPD were available. The aggregate quality of the evidence of the five RCTs\textsuperscript{11,17,33-35} reporting on lung cancer mortality based on clinical phenotypes was low (e-Table 3a).

**Harms of Screening for Lung Cancer:** Harms in lung cancer screening are related to the performance of the screening test and the consequences of evaluating abnormal test results. Commonly discussed harms from LDCT screening include the physical and psychological consequences of identifying and evaluating lung nodules, the impact of the cumulative radiation exposure on cancer risk, and the potential for overdiagnosis and overtreatment of lung cancer. A final potential harm is the consequence of evaluating other imaging findings, unrelated to lung cancer (eg, coronary artery calcification). Little is known about whether this
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Median Age (y)</th>
<th>Male (%)</th>
<th>Median Pack-Years (%)</th>
<th>Active Smokers (%)</th>
<th>Positive Scans&lt;sup&gt;a&lt;/sup&gt; at T0</th>
<th>Positive Scans&lt;sup&gt;b&lt;/sup&gt; by End of Screening Period</th>
<th>LC Mortality, RR/HR (95% CI)</th>
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<tr>
<td>LDCT scan vs CXR</td>
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<tr>
<td>LSS (NLST feasibility)&lt;sup&gt;6&lt;/sup&gt;</td>
<td>3,258</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>RR, 1.24 (0.74-2.08)</td>
<td></td>
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<tr>
<td>NLST&lt;sup&gt;10-12&lt;/sup&gt;</td>
<td>53,454</td>
<td>61</td>
<td>59</td>
<td>48</td>
<td>48.1</td>
<td>n = 7,191 (27.3%)</td>
<td>n = 10,287 (39.1%)</td>
<td>RR, 0.85 (0.75-0.96)</td>
</tr>
<tr>
<td>Dépiscan&lt;sup&gt;13&lt;/sup&gt;</td>
<td>765</td>
<td>56</td>
<td>71</td>
<td>30</td>
<td>64</td>
<td>24%</td>
<td>RR, 0.85 (0.75-0.96)</td>
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<tr>
<td>LDCT scan vs usual care (no screening)</td>
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<td></td>
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<tr>
<td>DANTE&lt;sup&gt;14,15&lt;/sup&gt;</td>
<td>2,472</td>
<td>64.6</td>
<td>100</td>
<td>45</td>
<td>56</td>
<td>n = 199 (15.6%)</td>
<td>n = 471 (37%)</td>
<td>RR, 1.01 (0.70-1.44)</td>
</tr>
<tr>
<td>DLCST&lt;sup&gt;17,19&lt;/sup&gt;</td>
<td>4,104</td>
<td>58</td>
<td>55</td>
<td>36</td>
<td>75.3</td>
<td>n = 155 (7.6%)</td>
<td>n = 241 (11.8%)</td>
<td>RR, 1.03 (0.66-1.60)</td>
</tr>
<tr>
<td>NELSON&lt;sup&gt;5&lt;/sup&gt;</td>
<td>15,789</td>
<td>58</td>
<td>83.6</td>
<td>38</td>
<td>56.0</td>
<td>Men positive: n = 147 (2.3%)</td>
<td>Men positive: n = 467 (2.1%)</td>
<td>Men: RR, 0.76 (0.61-0.94); P = .01</td>
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<td></td>
<td>Indeterminate: n = 1,241 (19.7%)</td>
<td>Indeterminate: n = 2,069 (9.2%)</td>
<td>Women: RR, 0.67 (0.38-1.14)</td>
</tr>
<tr>
<td>ITALUNG&lt;sup&gt;24&lt;/sup&gt;</td>
<td>3,206</td>
<td>61</td>
<td>64</td>
<td>40</td>
<td>66</td>
<td>n = 426 (30.3%)</td>
<td>n = 1,044 (46.1%)</td>
<td>RR, 0.70 (0.48-1.04)</td>
</tr>
<tr>
<td>MILD trial&lt;sup&gt;7&lt;/sup&gt;</td>
<td>4,099</td>
<td>58</td>
<td>68.4</td>
<td>39</td>
<td>68.6</td>
<td>n = 335 (1.4%)</td>
<td>RR, 0.70 (0.48-1.04)</td>
<td></td>
</tr>
<tr>
<td>LUSI trial&lt;sup&gt;4&lt;/sup&gt;</td>
<td>4,052</td>
<td>55</td>
<td>64.7</td>
<td>36</td>
<td>61.9</td>
<td>n = 451 (22.2%)</td>
<td>RR, 0.74 (0.46-1.19); P = .21</td>
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<tr>
<td>UKLS&lt;sup&gt;31&lt;/sup&gt;</td>
<td>4,055</td>
<td>67</td>
<td>75</td>
<td>NR</td>
<td>39</td>
<td>n = 536 (26.9%)</td>
<td>NA</td>
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</tr>
</tbody>
</table>

CXR = chest radiograph; DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial; DLCST = Danish Lung Cancer Screening Trial; HR = hazard ratio; ITALUNG = Italian Lung Cancer Screening Trial; LC = lung cancer; LDCT = low-dose CT; LSS = Lung Screening Study; LUSI = German Lung Cancer Screening Intervention; MILD = Multi-centric Italian Lung Detection; NA = not applicable; NELSON = Nederlands-Leuvens Longkanker Screenings Onderzoek Study; NLST = National Lung Screening Trial; NR = not reported; RR = relative risk; T0 = baseline; T1 = first screen; T2 = second screen; T3 = third screen; T4 = fourth screen; UKLS = United Kingdom Lung Screening Study.

<sup>a</sup>For all randomized controlled trials, except NELSON, this represents the number of patients with positive scans. In NELSON, this represents the number of positive scans. See Table 1 for definition of positive scan in each study.

<sup>b</sup>The 1,044 refers to the total number of positive scans for T0-T4; we were unable to determine if this excludes positive results from the T0 screen.

<sup>c</sup>Single-screen trial; if follow-up imaging at 1 y was included, the value would be 1,015 (50.9%).
evaluation is more likely to be an added harm or benefit of LDCT screening.

**Death and Complications Resulting From Biopsies:**

**Key Question 3:** What is the rate of death or complications resulting from biopsies of detected lesions among individuals at elevated risk of lung cancer who undergo screening with LDCT scan compared with either no screening or screening with another modality?

Lung nodules are commonly found at the time of LDCT screening for lung cancer (Table 2). The frequency of nodule detection is affected by the criteria used to label the finding positive (e.g., nodule size, a nodule resulting in additional testing), the imaging slice thickness, the duration of screening, and the geographic location of the screening program. Procedure rates across all reviewed studies varied dramatically, in part based on study length and design (0.7%-7.6%), with a mean of 3.0% of individuals having an invasive procedure in LDCT arms from 19 studies (Fig 2).

The most serious concern is the risk of death as a result of the evaluation of a screen-detected nodule. As reported in the studies reviewed, it is difficult to determine if death soon after a procedure was the result of the procedure or was an unrelated event that occurred shortly after the procedure was performed. Limited data are available that carefully assess this (e-Fig 8, Table 4). Overall, eleven studies contributed data on major complications, showing that among individuals who underwent an invasive procedure after LDCT scan, 4.2% experienced adverse events (not including death). This evidence is summarized in Table 4 and e-Figure 9, and graded in e-Table 3b.

In summary, LDCT screening led to an increase in the frequency of invasive procedures, the number of major complications resulting from invasive procedures, and the number of deaths soon after an invasive procedure compared with control arms.

**Key Question 4:** What is the rate of death or complications resulting from biopsies of screen-detected lesions among individuals at elevated risk of lung cancer with different clinical phenotypes (sex, age, race, risk, COPD, comorbidities) who undergo screening with LDCT scan compared with either no screening or screening with another modality?

A post hoc analysis of NLST data examined overall rates of invasive procedures and complications compared with rates within high-risk subgroups. In the LDCT arm, participants with COPD (n = 4,632, defined by self-
report) were more likely than participants without COPD to undergo an invasive procedure (6.0% vs 3.8%; adjusted OR, 1.41; \( P < .01 \)) and more likely to experience any complication (1.5% vs 0.7%; adjusted OR, 1.83; \( P < .01 \)) or a serious complication (0.6% vs 0.3%; adjusted OR, 1.78; \( P < .01 \)), respectively.

**Surgery and Nonsurgical Procedures for Benign Disease:**

**Key Question 5:** What is the rate of surgery for benign disease among individuals at elevated risk of lung cancer who undergo screening with LDCT scan compared with either no screening or screening with another modality?

The rate of surgical procedures for benign disease varied across studies. The rate of surgery (any surgical resection by thoracotomy or video-assisted thoracoscopic surgery) for benign disease was 4.7 per 1,000 screened in those screened by LDCT scan (17 studies\(^{1,10,11,13,14,18,25,27,31,36,38-45} \)). In the LDCT arms, 22.0% of surgeries were performed for benign disease (e-Table 3b, Fig 3, Table 4). In the LDCT arm, 37.0% of nonsurgical procedures were performed for benign disease (e-Fig 10). Nonsurgical procedures were defined as needle biopsies and bronchoscopies.

**Psychosocial Impact:**

**Key Question 6:** What is the psychosocial impact (including distress, anxiety, depression, and quality of life) on individuals at elevated risk of developing lung cancer who undergo screening with LDCT scan and are found to have a screen-detected lung nodule compared with either no screening or no nodule detected on LDCT screening?
Three randomized trials and two observational cohort studies examined the potential for an adverse psychological impact among those patients found to have a screen-detected nodule.46-50 In summary, these trials suggest that finding a screen-detected nodule may transiently increase distress but does not adversely affect anxiety levels or quality of life.

Overdiagnosis:

**Key Question 7:** What is the rate of overdiagnosis among individuals at elevated risk of lung cancer who undergo screening with LDCT scan compared with either no screening or screening with another modality?

The debate about the impact of overdiagnosis is in part related to how it is defined. Traditionally, overdiagnosis has been defined as the discovery of a cancer that is so indolent that it is clinically insignificant. Alternatively, one may extend this definition to include any lung cancer diagnosed, whether indolent or aggressive, in a patient with a comorbid condition that leads to their death before the cancer would have affected their well-being.

Investigators from the NLST concluded that among all LDCT screen-detected tumors, 18.5% (95% CI, 5.4-30.6) were overdiagnosed and 78.9% (95% CI, 62.2-93.5) of lepidic predominant adenocarcinomas detected by LDCT scan were overdiagnosed.51 By contrast, a post hoc analysis of overdiagnosis in the Danish Lung Cancer Screening Trial (DLCST) estimated the overdiagnosis rate to be 67.2% (95% CI, 37.1%-95.4%).21

Cost-effectiveness:

**Key Question 8:** What is the cost-effectiveness of LDCT screening of individuals at elevated risk of lung cancer compared with either no screening or screening with another modality?

By most currently used standards in the United States, LDCT screening is considered cost-effective. The most robust study using data collected directly from the NLST found a cost per quality-adjusted life year of $81,000.52 Results from a systematic review that included data from 13 studies found that cost-effectiveness estimates for LDCT screening range from $18,452 to $66,480 per life year gained and $27,756 to $243,077 per quality-adjusted life year gained.53

Cost-effectiveness of LDCT screening could vary substantially as it is implemented in real-world settings depending on patient selection, false-positive rate, and rates of invasive procedures. The cost of evaluating and managing other findings on the LDCT scan has not been completely factored into cost-effectiveness analyses.54,55

### Figure 2 – Number of invasive procedures per number of screened individuals over the period of screening (low-dose CT scan). DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial; MILD = Multi-centric Italian Lung Detection.
TABLE 4  Summary of Biopsies in Included Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Nonsurgical Biopsies/Procedures</th>
<th>No. of Nonsurgical Biopsies/Procedures With Benign Results</th>
<th>No. of Surgical Procedures</th>
<th>No. of Surgical Procedures With Benign Results</th>
<th>No. of Complications From Invasive Procedures</th>
<th>No. of Deaths After Invasive Procedures$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDCT scan vs CXR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSS (NLST feasibility)$^b$</td>
<td>29</td>
<td>16 (55.1%)</td>
<td>46</td>
<td>18 (39.1%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>NLST$^{10-12}$</td>
<td>993</td>
<td>293</td>
<td>673</td>
<td>164 (24.4%)</td>
<td>84$^b$</td>
<td>16</td>
</tr>
<tr>
<td>Dépiscan$^{13}$</td>
<td>NR</td>
<td>NR</td>
<td>9</td>
<td>3 (33.3%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>LDCT scan vs usual care (no screening)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DANTE$^{14,15}$</td>
<td>NR</td>
<td>NR</td>
<td>90</td>
<td>17 (18.9%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>DLCST$^{17,19}$</td>
<td>NR</td>
<td>NR</td>
<td>25</td>
<td>7 (28.0%)</td>
<td>4$^c$ (0.2%)</td>
<td>NR</td>
</tr>
<tr>
<td>NELSON$^d$</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>ITALUNG$^{24}$</td>
<td>38</td>
<td>1 (2.6%)</td>
<td>38</td>
<td>4 (10.5%)</td>
<td>NR</td>
<td>6 (3.7%)</td>
</tr>
<tr>
<td>MILD trial$^{27, d}$</td>
<td>NR</td>
<td>NR</td>
<td>45</td>
<td>4 (8.9%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>LUSI trial$^e$</td>
<td>90</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>UKLS$^{31}$</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

CXR = chest radiograph; DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial; DLCST = Danish Lung Cancer Screening Trial; ITALUNG = Italian Lung Cancer Screening Trial; LDCT = low-dose CT; LSS = Lung Screening Study; LUSI = German Lung Cancer Screening Intervention; MILD = Multi-centric Italian Lung Detection; NELSON = Nederlands-Leuvens Longkanker Screenings Onderzoek Study; NLST = National Lung Screening Trial; NR = not reported; UKLS = United Kingdom Lung Screening Study.

$^a$Deaths after invasive procedures refers to mortality after and invasive follow-up procedure that was initiated by screening. In the NLST and ITALUNG, it is reported as death within 60 d of invasive procedure.

$^b$Major complications include the following: acute respiratory failure, anaphylaxis, bronchopulmonary fistula, cardiac arrest, cerebral vascular accident/stroke, congestive heart failure, death, hemothorax requiring tube placement, myocardial infarction, respiratory arrest, bronchial stump leak requiring tube thoracostomy or other drainage for > 4 d, wound dehiscence, empyema, injury to vital organ or vessel, prolonged mechanical ventilation over 48 h postoperatively, thromboembolic complications requiring intervention, chylous fistula, brachial plexopathy, lung collapse, and infarcted sigmoid colon.

$^c$Major complications include empyema and myocardial infarction.

$^d$Data reported in the 5-y MILD follow-up publication$^{36}$ are included here. Although the 10-y follow-up publication$^{35}$ reports on the number of surgical procedures and number of these procedures with benign results, it is not possible to determine if the reported data are for the cumulative 10 y, or if data represents procedures for years 5 through 10.
Radiation Exposure From the LDCT Scan: Although an LDCT scan is a noninvasive procedure, patients are exposed to ionizing radiation during the scan. Patients enrolled in a lung cancer screening program may undergo many LDCT scans during long-term enrollment, and diagnostic CT scans and fluorodeoxyglucose PET/CT scans for the evaluation of screen-detected findings.

The risk of ionizing radiation to an individual undergoing LDCT screening depends on the age at which screening begins, sex, number of CT scans received, and exposure to other sources of ionizing radiation, particularly other medical imaging tests. Assessing the risks to patients from ionizing radiation from lung cancer screening is challenging because of limited data that rely on modeling, and the unknown effects of estimated effective doses < 100 mSv (single exposure or cumulative). The average estimated effective dose of one LDCT scan in the NLST was 1.5 mSv.10

Considerations When Assessing the Balance of Benefit and Harms

Clinical Lung Cancer Risk and Screening Benefit Assessment Tools:

Key Question 9: What is the rate of lung cancer detection when clinical risk assessment tools are applied for the selection of individuals at elevated risk of lung cancer for LDCT screening compared with the use of the NLST or US Preventative Services Task Force (USPSTF) criteria?

The ability to predict which individuals are at high risk for developing lung cancer, or could gain high life years (benefit) from lung cancer screening, is limited when using dichotomized age and smoking history criteria. More precise accounting of age, smoking history, and additional lung cancer risk factors may improve risk or benefit prediction and screening efficiency, while reducing racial/ethnic/sex disparities in eligibility for screening.

There are two kinds of prediction models. Risk models predict lung cancer incidence (eg, Bach, LCRAT, PLCO_M2012) or lung cancer death (eg, LCDRAT).56-58 A benefit model (eg, LYFS-CT) calculates the life years gained by undergoing lung cancer screening.59 These five models have been shown to have improved discriminatory ability compared with other models,60 and are available through websites61-64 or as downloadable Excel files (Microsoft Inc).65,66 Risk models incorporate major lung cancer risk factors, including age, sex, race/ethnicity, presence of COPD, smoking intensity, smoking duration, and smoking quit time. Benefit models also include factors that influence life expectancy.

---

**Study or Subgroup** | **Prevalence IV, Random, 95% CI** | **Prevalence IV, Random, 95% CI**
--- | --- | ---
Aberle 2011 | 0.2437 [0.2114, 0.2760] | 
Bastarrika 2005 | 0.1667 [-0.1316, 0.4650] | 
Blanchon 2007 | 0.3333 [0.0254, 0.6412] | 
Callol 2007 | 0.3333 [-0.0438, 0.7104] | 
DANTE (Infante 2015) | 0.1889 [0.1080, 0.2698] | 
Diederich 2004 | 0.2667 [0.0429, 0.4905] | 
Field 2016 | 0.1026 [0.0073, 0.1979] | 
Gohagan 2004 | 0.3913 [0.2502, 0.5324] | 
Lopes Pegina 2013 | 0.1053 [0.0077, 0.2029] | 
MacRedmond 2006 | 0.2000 [-0.1506, 0.5506] | 
MILD (Pastorino 2012) | 0.0889 [0.0058, 0.1720] | 
Ostrowski 2019 | 0.3120 [0.2485, 0.3755] | 
Pastorino 2003 | 0.2143 [0.0624, 0.3662] | 
Saghir 2012 | 0.2800 [0.1040, 0.4560] | 
Sobue 2002 | 0.2857 [0.0924, 0.4790] | 
Veronesi 2008 | 0.1389 [0.0736, 0.2042] | 
Wilson 2008 | 0.3415 [0.2388, 0.4442] | 
Total (95% CI) | 0.2195 [0.1720, 0.2670] | 

**Heterogeneity:** $\chi^2 = 50.41, df = 16 (P < .0001); I^2 = 68\%$

**Test for overall effect:** $z = 9.06 (P < .00001)$

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Figure 3 – Number of surgical procedures for benign disease per total procedures: low-dose CT scan. DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial. MILD = Multi-centric Italian Lung Detection.
A fundamental question when applying these models is whether the identification of patients for screening based on a risk score rather than age, pack-year, and quit-year cutoffs would lead to changes in patient or cancer phenotype that would affect the balance of benefit and harms of screening. The risk models include variables that impact nodule presence, the risk of nodule evaluation, the risk of lung cancer treatment, survival after lung cancer treatment, and overall survival. In particular, risk models, when used in isolation, choose people at older ages with more comorbidities than USPSTF criteria.

Although use of risk calculators might increase the number of preventable deaths, they may not appreciably increase the life years gained in a population when used in the absence of an additional life expectancy criterion. In contrast, adding a life expectancy criterion or defining eligibility based on benefit models of life years gained, could optimize the life years gained by screening in a population. Life gained models choose somewhat older, but healthier, people than USPSTF criteria.

Risk of harms generally increases with age and the number and severity of comorbidities. Therefore, an individual’s life expectancy could serve as a proxy for the risk of harms from screening. Life expectancy is primarily driven by age, comorbidities, and smoking history. People with limited life expectancy may be less likely to benefit, and more likely to be harmed by lung cancer screening, even if deemed to have high lung cancer risk.

The application of life year-gained models requires a days-of-life-gained threshold, whereas the application of risk models should include both a risk threshold and a life expectancy threshold. In the absence of clinical trials that evaluate outcomes on enrollment based on model thresholds, a conservative approach to their application would be to establish thresholds that would be considered preference insensitive. Individuals who exceed such a threshold would have such an estimated high lung cancer mortality benefit from screening that even high levels of concern about the harms of screening would not outweigh this benefit (e-Fig 11).

Minimizing Disparities: Among patients enrolled in the NLST, individuals who currently smoke and Black subjects experienced the highest lung cancer mortality and the greatest benefit from LDCT screening. However, minorities and those with low socioeconomic status (who are more likely to be currently smoking) often experience disparities in receiving appropriate preventive health care. LDCT screening has been slow to be implemented and is underused nationally despite coverage by private and public insurers. Lower rates of screening uptake have been found among minorities, those with a lower educational status, and individuals with low socioeconomic status. As screening is implemented more widely, outreach to underserved populations to ensure that eligible individuals receive LDCT screening will be of critical importance to prevent disparities. Little work has been done to establish the most effective strategies.

Current age and smoking history-based eligibility criteria engender disparities with respect to race/ethnicity, sex, smoking intensity, and years since quitting, and for special populations such as people living with HIV (see Rivera et al for a comprehensive review). By reducing the age and the pack-years eligibility for screening from 55 to 50 and 30 to 20 years of age, respectively, as in the USPSTF draft recommendations, more Blacks will be eligible for screening, which may partially eliminate this particular disparity.

Reducing disparities by improving equity requires managing people with equal net benefit from screening as equally as possible. Because risk of lung cancer or lung cancer death (paired with life expectancy), or life years gained from screening, more directly attempt to estimate the net benefit from screening, use of risk or benefit calculators could improve equity by applying the same threshold to everyone regardless of race/ethnicity, sex, or any other factor accounted for by the calculators. Use of risk calculators may increase eligibility for Blacks relative to Whites and therefore increase the number of lung cancer cases detected relative to Whites. Use of benefit calculators may increase the life years gained for Blacks relative to Whites.

Impact of Comorbidity and Quality of Life: Compared with NLST participants, a US-representative sample meeting NLST eligibility are older, more likely to currently smoke, and more likely to have comorbidities. Older people or people with more comorbidities may be more likely to have a serious harm from screening and may have a higher mortality risk from surgical resection. Moreover, older people and those with more comorbidities will have fewer life years gained from screening. Therefore, when considering screening on an individual basis, balancing the risk of developing lung cancer with the risk of dying of competing causes of death is critical.

These considerations are especially important for people with COPD. COPD confers a much higher risk of lung
cancer but also confers a higher risk of competing mortality and a higher risk for treatment-related harms (eg, complications from biopsy or surgical resection). People with mild to moderate COPD may experience large health gains with screening because of the increased lung cancer risk and still reasonable life expectancy, whereas those with more advanced COPD, in particular those with severe COPD and poor functional status, may have limited net benefit from LDCT screening.

**Molecular Biomarkers:**

**Key Question 10:** What is the rate of lung cancer detection when molecular biomarker results are applied to the selection of individuals at elevated risk of lung cancer for LDCT screening compared with the use of the NLST or USPSTF criteria?

There is growing interest in investigating the use of molecular biomarkers to improve the sensitivity and specificity of lung cancer screening eligibility criteria. An accurate molecular biomarker could identify individuals who are more likely to benefit from lung cancer screening and/or reduce the harms of LDCT screening. No applicable studies comparing molecular biomarkers with NLST or USPSTF criteria were found that could be included in the systematic review for this guideline. Further research in this field has the potential to optimize and expand the impact of lung cancer screening.

**Frequency and Duration of LDCT Screening for Lung Cancer:** Models indicate that as the age to begin screening is increased, lung cancer mortality reduction decreases. Concomitantly, the number of scans (and the radiation-induced lung cancer cases) decreases by a similar amount. As the age to end screening is increased, the lung cancer mortality reduction and the number of scans increases slightly.

NELSON has brought the interval between scans into greater focus (NELSON used LDCT scan at baseline and 1, 3, and 5.5 years). The stage shift for screen-detected cancer cases was less favorable for the 2.5-year interval than the 1-year interval; for both screen-detected and interval cancer cases, stage IIB-IV accounted for 15% in the 1-year interval and 35% in the 2.5-year interval.

**Implementation of High-Quality Lung Cancer Screening**

To optimize the net benefit from LDCT screening, it is critical that high-quality screening programs are developed. Several papers have outlined phases of program development, implementation considerations, and key program components. Each program needs to develop approaches to screening that fit their local environment. Programs require plans for who to screen; how to identify and schedule appropriate patients; how to conduct a shared decision-making (SDM) visit; how to perform the LDCT scan; how to communicate the results of the LDCT scan; how to manage abnormal findings; how to assure compliance with annual screening; how to incorporate smoking cessation guidance; and how to collect, report, and use data for program improvement.

We have attempted to develop recommendations that are applicable regardless of program design. In the remarks of some of the recommendations, we comment on implementation within a spectrum of program structures ranging from decentralized to centralized. We do not recommend one program structure over the other, recognizing that local resources and health system designs will influence the structure, and trade-offs of quality and access must be considered. In this section, we describe some of the evidence available to help guide the implementation of high-quality programs, regardless of their structure.

**Lung Cancer Symptoms:** New symptoms that are poorly explained (eg, coughing, hemoptysis, shortness of breath, chest pain, unintentional weight loss, hoarseness, bone pains, headaches, vision changes) should make one consider lung cancer in the proper clinical setting. Symptoms and signs related to paraneoplastic syndromes (confusion, nausea, constipation, weakness, clubbing) may also be part of the initial presentation. Individuals who present with these symptoms should have diagnostic testing performed unrelated to their screening eligibility.

**Counseling and SDM Visits:** One of the requirements for Medicare coverage of lung cancer screening is that a beneficiary has a "lung cancer screening counseling and shared decision-making (SDM) visit." The visit is to include the following: determination of eligibility for lung cancer screening; SDM, using decision aids with information about benefits and harms of screening, follow-up testing, false-positive rate, and radiation exposure; counseling on the need for repeated annual screening and possible diagnostic testing and treatment; and counseling on smoking cessation or maintaining abstinence. The goal of SDM is to inform individuals about the trade-offs of screening vs not screening and to help them make a choice that is aligned with their preferences and values. Decision aids are usually print or
video materials that provide information for patients, often in graphic and/or numerical formats, that may help aid individual decision-making.

A systematic review of the effects of SDM interventions on breast, colorectal, and prostate cancer screening found that SDM typically improves knowledge and decisional conflict, but has limited impact on intentions to screen or screening utilization.95 In individuals who currently smoke and were eligible for LDCT screening, one RCT examined the impact of providing a decision aid through tobacco quit lines vs usual care.96 This RCT found that the decision aid improved knowledge and reduced decisional conflict but did not change screening intentions or behaviors. Observational studies suggest that an SDM visit may improve screening knowledge and lead to high levels of patient satisfaction whether in-person or telephonic, and that diverse populations think decision aids are useful and able to increase patient knowledge about LDCT screening and its trade-offs.97-100

Detailed initial presentations of information during SDM may not be feasible for lung cancer screening in routine primary care practice.101,102 Lack of time is a consistent barrier to SDM in primary care101 and has been reported as a potential barrier to SDM for LDCT screening.103,104 In health systems with decentralized programs, or for patients not able to make a visit to a centralized program’s screening coordinator, creative models of SDM and streamlined SDM tools may be necessary. By estimating each patient’s lung cancer risk and considering life expectancy, or estimating life year gains, physicians can more accurately inform their patients about the net benefit of CT screening for them personally.101

Lung Nodule Size: Threshold for a Positive Result: Key Question 11: What is the stage distribution of lung cancer, the rate of death from lung cancer (ie, lung cancer mortality), and the portion of positive scans, among individuals at elevated risk of lung cancer who undergo annual screening with LDCT scan with a 4-mm nodule size threshold for defining a positive LDCT scan compared with other definitions of a positive LDCT scan?

In lung cancer screening, the lung cancer mortality rate, stage distribution, and portion of positive scans may depend on the size of pulmonary nodules deemed appropriate for follow-up or further investigation. Nine LDCT screening trials have published results related to these outcomes. The trials varied in the size of nodules found on LDCT scans that were defined as positive, ranging from $\geq 4$ mm in the NLST and Lung Screening Study (LSS) to $\geq 5$ mm for solid nodules in the Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial (DANTE), German Lung Cancer Screening Intervention (LUSI) trial, Italian Lung Cancer Screening Trial (ITALUNG), and United Kingdom Lung Screening Study (UKLS), to size and growth based on volumetric measurements in the Multi-centric Italian Lung Detection (MILD) trial, Danish Lung Cancer Screening Trial (DLCST), and NELSON (Table 1).

Given the challenge with compliance in real-world implementation and the available data, it is not clear that altering the size threshold will maintain the same lung cancer mortality benefit. This may be dependent on local characteristics of a program and the screened population. The aggregate quality of evidence of the six studies informing this statement is low (e-Table 4).

Maximizing Compliance With Annual Screening: For a screening program to be effective, participants must return for yearly follow-up screening if they continue to meet eligibility criteria. Furthermore, when positive findings are discovered, compliance with follow-up testing is important. Many of the available clinical trials had high adherence rates for repeat screens. Generalizing these high adherence rates is problematic for several reasons. Patients in these studies received their scans at no cost. Patients enrolled in the NLST were better educated, were > 90% White, had a higher socioeconomic status, and were more likely to have previously smoked compared with the population of Americans eligible for screening. Patients with these attributes are far more likely to adhere to their screening regimen.111-113

Poor adherence can substantially reduce the efficacy of screening. The Cancer Intervention and Surveillance Modeling Network modeled lung cancer mortality benefit when patient adherence varied and found that if adherence dropped to 46%, the mortality benefit from screening was reduced by one-half.114

One observational study suggested that the addition of a nurse navigator to a screening program can improve compliance with annual screening, as does the provision of reminders to screening participants.115 Given the potential for poor adherence with annual testing in the demographic eligible for LDCT screening, it is important that patients are informed about the value of annual testing, and that further research is performed to better understand the
factors that influence compliance, which can then be used in the development of tools to assist screening programs.

**Managing Screen-Detected Lung Nodules:** Given the frequency with which lung nodules are identified on LDCT screening examinations, the knowledge that most screen-detected nodules are benign, and the implications of nodule management decisions on the benefit and harms of screening, nodule management strategies are a critical component of LDCT screening.

As previously described in the harms section, despite the high rate of identifying lung nodules, clinical trials have reported a low rate of procedures for lung nodules, major complications from procedures, and death potentially related to procedures. Most of the trials that informed this section were performed at large institutions with experience in lung nodule management, tools available to assess lung nodules, and a nodule evaluation system in place. By contrast, surveys indicate that systems and processes of care to facilitate nodule evaluation have not been consistently adopted in US medical facilities.117,118 Studies that include more diverse practice settings have reported higher and more variable rates of biopsy and complications during incidental nodule management.68,119

**Incorporating Smoking Cessation Into Lung Cancer Screening:**

**Key Question 12:** What is the rate of smoking cessation among individuals who currently smoke, are at elevated risk of lung cancer, and who receive smoking cessation counseling as part of an LDCT screening program, compared with those who do not receive smoking cessation counseling, and compared with those who do not participate in LDCT screening?

LDCT screening represents a potential teachable moment to counsel individuals who currently smoke about smoking cessation. The Centers for Medicare and Medicaid Services (CMS) policy requires smoking cessation counseling to be delivered at the time of LDCT screening. Based on a meta-analysis of four trials,120-123 those undergoing LDCT screening appear to have higher smoking quit rates than those in usual care arms (risk ratio, 1.22; 95% CI, 1.03-1.44; \( P = .04 \)) (e-Table 5, Fig 4). A prior systematic review suggested that patients with a screen-detected nodule are more likely to quit smoking than patients with negative screening results.124

The most effective intervention to promote smoking cessation in the setting of lung cancer screening is currently unknown and is an area of active research.125,126 There are well-established smoking cessation interventions that have been studied in other settings that provide a basis for establishing a smoking cessation component to a lung cancer screening program.127,128

**Lung Cancer Screening Program Personnel**

A high-quality lung cancer screening program requires a diverse group of health care personnel, components, and processes to maximize the net benefit of screening (e-Table 6). Key professional groups, including the American College of Radiology (ACR), the American College of Chest Physicians, the American Lung Association, and the American Thoracic Society, have identified several essential components of lung cancer screening programs.90,129

**LDCT Parameters**

Appropriate technique is necessary to ensure that LDCT scans are obtained in a manner that produces high-quality images while minimizing patient exposure to ionizing radiation. Images should be optimized to avoid artifacts and provide high spatial resolution while maintaining a CT dose volume index \( \leq 3.0 \) mGy for average-size patients, adjusted accordingly for larger or smaller patients. To maintain a standardized approach

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>LDCT Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio, IV, Random, 95% CI</th>
<th>Risk Ratio, IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashraf 2014</td>
<td>299</td>
<td>1,545</td>
<td>240</td>
<td>1,579</td>
<td>30.2%</td>
<td>1.27 [1.09, 1.49]</td>
<td></td>
</tr>
<tr>
<td>Brain 2017</td>
<td>115</td>
<td>759</td>
<td>79</td>
<td>787</td>
<td>20.0%</td>
<td>1.51 [1.15, 1.97]</td>
<td></td>
</tr>
<tr>
<td>Pistelli 2019</td>
<td>258</td>
<td>1,239</td>
<td>231</td>
<td>1,383</td>
<td>29.7%</td>
<td>1.25 [1.06, 1.46]</td>
<td></td>
</tr>
<tr>
<td>van der Aalst 2010</td>
<td>88</td>
<td>641</td>
<td>99</td>
<td>640</td>
<td>20.2%</td>
<td>0.89 [0.68, 1.16]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>4,184</strong></td>
<td></td>
<td><strong>4,389</strong></td>
<td></td>
<td>100.0%</td>
<td><strong>1.22 [1.03, 1.44]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: \( \hat{\tau}^2 = 0.02; \chi^2 = 8.26; df = 3 (P = .04); I^2 = 64\% \)

Test for overall effect: \( z = 2.29 (P = .02) \)

Figure 4 – Risk of smoking cessation in patients enrolled in LDCT screening programs vs usual care. LDCT = low-dose CT.
to LDCT screening, a dedicated LDCT protocol should be developed and reviewed annually by the supervising radiologist, medical physicist, and radiology technologist.

**Structured Radiology Reporting**

The ACR and Society of Thoracic Radiology Practice Parameter for the Performance and Reporting of Lung Cancer Screening Thoracic Computed Tomography provides guidance about how to report the LDCT screening examination. Current CMS requirements include the use of a standardized lung nodule identification, classification, and reporting system for all lung cancer screening LDCT scans and participation in a CMS-approved registry. The ACR hosts the only national data registry, which accepts data on imaging findings based on the LungRADS system, making this a practical choice for most programs. The structured report categorizes lung nodules based on size/risk, provides recommendations for surveillance intervals for small nodules, and can be used to report other incidental findings.

**Managing Other Findings**

A chest CT scan does not image only the lungs, but everything from the lower neck to the upper abdomen. The cohort eligible for LDCT screening, based on smoking history and age, has been shown to frequently have comorbidities. As such, it is not surprising that many LDCT screening scans reveal potentially actionable findings (other than pulmonary nodules). The value of what amounts to screening for other findings is undefined; the balance of benefits and harms of lung cancer screening is impacted by these other findings and the appropriateness of further investigation. Professional organizations have developed general guidelines for many of these other findings (e-Table 7).

It may be practical to organize incidental findings into three categories: not clinically relevant, possibly clinically relevant, and concerning (e-Table 8). These can be thought of in terms of next steps that might be considered: no investigation is necessary (in the context of annual screening), further investigation may be indicated (clinical judgment), and therapeutic intervention is likely to be indicated. These categories are developed with an awareness of formal guidelines for investigation and treatment of relevant conditions (e-Table 7).

**Data Collection, Reporting, and Review**

Data collection, reporting, and review help screening programs reflect on their performance, and design and implement plans for improvement. Similarly, data reporting and review help inform the screening community and policy makers about the current state of lung cancer screening, aspects of screening that would benefit from additional research, and the policy level support required to expand access to high-quality screening. Data collection and reporting to a national registry is currently mandated by the CMS. The only available national registry is run by the ACR.

Data on testing performed for the management of lung nodules and incidental findings may help programs make improvements to internal care pathways, and garner support for program infrastructure. Data collection requirements from the CMS and the ACR national registry can be found in e-Tables 9 and 10. Soon, process and outcome quality indicators will be available to further guide programs about the collection and use of their data.

**Summary**

In this document, we have provided an update of the evidence related to the benefit and harms of lung cancer screening, and evidence that assists programs with selecting individuals to screen and implementing high-quality LDCT screening. Based on this review, we have developed recommendations where evidence allowed and consensus-based statements in areas that we think warranted comment despite a lack of high-quality evidence. Future updates to this guideline are planned, with literature reviews every 3 months and editing of the guideline when new evidence suggests recommendations and suggestions should change.

**Acknowledgments**

The e-Figures and e-Tables can be found in the Supplemental Materials section of the online article.

**References**


among african american adult smokers. JAMA Oncology. 2019;5(9):1318-1324.


