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

In 2013, the US Preventive Services Task Force (uspstf), based on the results of the National Lung Screening Trial (NLST), recommended screening high-risk patients ages 55 to 80 years who were current smokers, had a 30 pack-

[3] Primary care providers need to develop the knowledge and skills to counsel patients about the benefits and harms of screening and encourage appropriate patients at high risk for lung cancer to engage in annual low-dose CT screening.

EVIDENCE FOR SCREENING

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

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

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uspstf guidelines, because the recent expansion may help to reduce racial disparities. Additionally, the uspstf is a go-to evidence-based resource for primary care clinicians for preventive care recommendations.

Lung cancer screening rates remain critically low despite the proven benefit of screening to expand the diagnosis of early-stage, treatable lung cancer. Results from the lung cancer screening registry show that only 2% of 7.6 million patients eligible for low-dose CT under the uspstf guide-

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

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

SCREENING RECOMMENDATIONS

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

In 2013, the uspstf recommended annual lung cancer screening with low-dose CT for patients ages 55 to 80 years with a 30 pack-year smoking history and who are current smokers or have quit in the past 15 years.[3] In March 2021, this was expanded to include patients ages 50 to 80 years with a 20 pack-year smoking history who are current smokers or have quit in the past 15 years.[3] The expanded eligibility should improve racial disparities by identifying more high-risk minority and underserved patients; for example, Black patients have a higher risk of lung cancer at lower pack-years than White patients.[1] The uspstf has determined a moderate net benefit of annual screening of high-risk patients with low-dose CT.[1]

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

BENEFITS OF SCREENING

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

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

POTENTIAL HARMS OF SCREENING

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

False positives Positive results often require additional

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

ALTERNATIVES TO LOW-DOSE CT

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

COST-EFFECTIVENESS

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

UNDERUSE

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

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

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

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

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

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

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

CONCLUSION

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

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