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Lung cancer screening

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Introduction

Lung cancer is the 2nd most frequently diagnosed cancer in the United States and the leading cause of cancer death. In 2016, 224,390 new lung cancer cases were expected along with 158,080 lung cancer-related deaths.[1] Over 80% of these deaths are attributable to tobacco exposure making primary prevention the most effective cancer control strategy.[2] While the 5-year survival for early-stage lung cancers exceeds 50%, most cancers are detected at advanced stage when survival is poor.[3] Consequently, screening has been proposed as a strategy for reducing lung cancer mortality. Controlled trials have shown chest radiography and sputum cytology to be ineffective screening tests,[4] but screening with low-dose computed tomography (LDCT) can significantly reduce lung cancer mortality.[5]

This review will focus on the LDCT screening trials, particularly the National Lung Screening Trial (NLST), the subsequently issued screening guidelines, and challenges and strategies for implementing screening programs in community practice. The review begins by briefly discussing the clinical presentation, pathology, staging, treatment options, survival, and primary prevention strategies for lung cancer.

Clinical Presentation

Patients with early-stage lung cancers are usually asymptomatic, presenting with lung nodules or a mass discovered incidentally on a chest radiograph or CT scan. The clinical presentation with advanced disease is mostly related to the local tumor invasion, regional spread, distant metastasis, and paraneoplastic syndromes. These patients most commonly

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present with cough (50–75%), hemoptysis (25–50%), dyspnea (25%), and chest pain (20%).[6]

Pathology

Although recent guidelines emphasize immunohistochemical categories,[7] lung cancers have traditionally been classified histologically as small cell lung cancer (SCLC) or non-small cell lung cancer (NSCLC), with the latter group including adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Recent Surveillance, Epidemiology, and End Results Program (SEER) registry data show that adenocarcinoma (45%), squamous cell carcinoma (23%), and small cell carcinoma (13%) account for most U.S. lung cancers.[3]

Staging

Lung cancer is staged with the Tumor Node Metastasis (TNM) system.[8] The TNM system is also used for SCLC though 90% of patients with these cancers present with advanced disease.

Treatment options

Patients with early-stage NCLSC and no contraindications for surgery should undergo surgical resection.[9] Non-surgical candidates can be offered stereotactic body radiation therapy or radiofrequency ablation. Patients with early-stage cancers with high-risk features or those with ipsilateral nodal involvement should receive adjuvant chemotherapy. Patients with SCLC and clinically limited stage are candidates for curative-intent chemoradiation.[10] Treatment recommendations for more advanced-stage cancers are beyond the scope of this review.

Survival

The overall average 5-year survival of U.S. patients with lung cancer is 17.7%, however, survival varies markedly by stage at diagnosis (Figure).[3] The average 5-year survival for with localized disease is 55.2%, though only 16% of patients are diagnosed at this stage..

Cancer control strategies

Primary prevention

Smoking prevention and cessation are the best strategies for reducing lung cancer mortality and all deaths due to tobacco-related diseases.[11,12] Pharmacotherapy and behavioral interventions can help patients quit smoking.[13] However, as the prevalence of tobacco smoking continues to decrease, the incidence of lung cancer among non-smokers appears to be rising.[14] This has prompted strategies to mitigate environmental and occupational exposure to carcinogens, including second-hand smoke, radon, asbestos, arsenic, metals, fiber, dust, organic compounds, and air pollution.[15] The efficacy of these interventions in reducing lung cancer mortality is unknown.

Secondary prevention (screening)

Chest radiography and sputum cytology—These tests are not recommended for lung cancer screening, either alone or in combination, because there is no evidence that they reduce lung cancer mortality.[4]

Low-dose helical computed tomography (LDCT)—The National Lung Screening Trial (NLST), which published results in 2011, demonstrated a mortality benefit for screening high-risk individuals with LDCT lung scans (Table 1).[16] The NLST enrolled 53,454 at 33 medical centers in United States. Participants were ever smokers aged 55 to 74 years, with a minimum 30-pack year history of tobacco smoking who were currently smoking or had quit within the past 15 years. The NLST randomly assigned participants to undergo 3 rounds of annual screenings with LDCT or chest radiography.

The LDCT group had more lung cancer diagnoses than the radiography group (1060 vs. 941), and a higher proportion of lung cancers detected at stage I or II (70% vs. 56.7%). After a median 6.5 years of follow up, lung cancer mortality was 20% lower in the LDCT group compared to the radiography group, with an absolute risk reduction of 0.3 percentage points (1.33% vs. 1.66%). The number needed to screen with three rounds of LDCT to prevent one death from lung cancer was 320. Sub-group analyses suggest that women and blacks might have the greatest lung cancer mortality benefit.[17,18] Overall mortality was reduced by 6.7% in the LDCT group.

European LDCT screening trials have not shown a decrease in lung cancer mortality (Table 1).[19–22] However, these trials differed from the NLST in having smaller sample sizes, enrolling a lower-risk cohort, and in the strategies used for managing pulmonary nodules. The Dutch-Belgian Randomised Lung Cancer Screening Trial (NELSON trial) is an ongoing randomized controlled trial evaluating LDCT.[23,24] NELSON has enrolled nearly 16,000 ever smokers aged 50 to 75 years, including five-year lung cancer survivors, and randomized them to LDCT at increasing screening intervals (1, 2, and 2.5 years) vs. no screening. NELSON will assess survival, quality of life, smoking cessation, and cost effectiveness.

Screening Guidelines

In early 2014, the USPSTF gave a B recommendation to LDCT screening, implying moderate certainty of at least moderate net benefit.[25] The recommendation was based on microsimulation modeling[26] calibrated to data from the NLST and the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.[27] The simulated target population was a 100,000-person U.S. cohort born in 1950 and followed from ages 45 to 90 years. The best-case scenario was to screen annually those meeting NLST smoking criteria from ages 55 through 80. This scenario was estimated to detect 50% of cancers at an early stage, reduce lung cancer mortality by 14% (number needed to screen of 575), and avert 497 lung cancer deaths (average gain of 10.6 life-years per death averted). Harms included 67,550 false-positive test results, 910 invasive diagnostic procedures for benign lesions, and 190 (9.9%) over-diagnoses among cases of screen-detected lung cancers. Radiation exposure would result in 24 deaths.

Other professional societies also endorsed LDCT screening (Table 2), including the American Association for Thoracic Surgery (ATTS);[28] the American Cancer Society (ACS);[29] the American College of Chest Physicians (ACCP), American Society of Clinical Oncology (ASCO);[30,31] the American Lung Association (ALA);[32]; the American Thoracic Society (ATS);[33] and the National Comprehensive Cancer Network (NCCN).[34] While these guidelines routinely advised screening patients meeting NLST eligibility criteria, the ATTS and NCCN also recommended screening persons at age 50 with a ≥ 20-pack year smoking history if they had a cumulative 5-year cancer incidence risk of ≥ 5% (ATTS) or an additional risk factor for lung cancer (NCCN). However, some experts cautioned against screening patients not meeting NLST criteria given uncertainty about the balance of benefits and harms.[29,31]

Several important messages emerged across the guidelines. One was that patients should have access to high-quality, high-volume centers similar to those enrolling patients in the NLST. Screening is also not considered appropriate for those with substantial comorbidity, such as severe emphysema or cardiovascular disease, that would preclude attempting curative therapy or limit life expectancy. Lung cancer screening does not replace smoking cessation and screening programs should provide support for smoking cessation and preventing relapse. The absolute benefit of screening is small, the proportion of false positive results is high, and there are potential harms associated with invasive diagnostic procedures, radiation exposure, and incidental findings. Guidelines encouraged providers to ensure that patients are making informed decisions.

The Centers for Medicare and Medicaid Services (CMS) issued a National Coverage Determination (NCD) in early 2015 supporting annual lung cancer screening with low-dose computed tomography.[35] Appropriate beneficiaries are asymptomatic adults ages 55 to 77 meeting NLST criteria for smoking history. However, CMS also issued stringent criteria for reimbursement, including confirmation that a beneficiary met eligibility criteria and had undergone a counseling and shared decision-making visit. CMS had further stipulations regarding the qualifications and experience of the radiologists, the technical specifications of the imaging modalities, and the use of a standardized lung nodule classification and reporting system.

Shared decision making

The CMS requirement for shared decision making was unprecedented for cancer screening but an explicit acknowledgement that these decisions are preference sensitive.[36] Shared decision making is a process where a patient and provider work together to make a health care decision based on the best available evidence and the patient's values and preferences.[37,38] CMS called for informing patients about the potential benefits and risks of screening, the diagnostic testing to evaluate positive screening results, the probability of false positive tests, overdiagnosis, the total radiation exposure, the importance of adhering to annual screening, as well as the impact of a patient's ability and or willingness to undergo diagnosis and treatment on screening decisions.[35] Experts have suggested that these discussions also address tobacco harms other than lung cancer as well strategies to avoid environmental and occupational risks for lung cancer.[39]

Using decision aids is a practical strategy for supporting shared decision making. Decision aids are educational tools, which can be written, video, or web-based, that should provide objective, balanced information about the options and potential outcomes, help elicit a patient's values for these potential outcomes, and provide guidance for discussing screening decisions with a provider.[40] A Cochrane Collaboration review found that providing patients with decision aids for health treatment or screening decisions increased their engagement in decision making, increased knowledge and improved accuracy of risk perceptions, reduced decisional conflict, and increased the likelihood of making a values-congruent decision.[40] A number of lung cancer screening decision aids are available (Table 3).

Translating research into practice

Generalizability of NLST

A criticism of the NLST was that participants were not representative of the general population. Less than 10% were members of minority populations; compared to the general population of tobacco users surveyed by the U.S. Census Bureau's Tobacco Use Supplement meeting study eligibility criteria, NLST participants were younger, more likely to be former smokers, and of higher socioeconomic status.[5] The lack of representativeness is problematic because minorities and people of lower socioeconomic status have the highest risk for dying from lung cancer.[41] Adherence to the screening protocol was 95% in the trial, but might be considerably lower in community settings. Furthermore, most study sites were academic medical centers. Radiologists were experienced chest CT readers who underwent training for lung nodule interpretation. The overall complication rate for diagnostic procedures following a positive screening test was only 1.4% and the 60-day operative mortality rate was just 1%. Although not derived from screening populations, previous Medicare data suggested substantially higher complication and mortality rates from invasive diagnostic procedures and lung resections.[42,43]

These issues were highlighted by the American Academy of Family Physicians (AAFP) who concluded that data were insufficient to recommend for or against LDCT screening.[44] The AAFP cited concerns about the unknown harms of expanding screening to community practice and extrapolating data from just 3 annual screens. The Medicare Evidence Development & Coverage Advisory Committee (MEDCAC), convened by CMS to review the evidence on lung cancer screening, expressed a lack of confidence that LCS screening could be effectively and safely performed in the Medicare population.[45] Meanwhile, they strongly believed that a clinically significant evidence gap remained regarding LDCT screening in the Medicare population outside a clinical trial.

Guidelines have explicitly addressed these concerns, advising that patients undergo screening only in qualified centers. The CMS recommendations also specified that screening centers contribute data to a certified national registry. Data elements included abnormal findings, diagnostic evaluations, cancer diagnoses, and treatments. Registry data will provide population-based data on practice patterns and outcomes that will help evaluate the effectiveness and safety of translating clinical trial results to community practice. Currently the ACR hosts the only certified registry.[46]

Potential harms

False positive results—In the NLST, 26% of all LDCT screening tests were positive and nearly 40% of all participants had at least one positive result.[16] However, 96.4% of the positive screening results were false positives. NLST radiologists used a 4-mm threshold to characterize nodules as abnormal. The American College of Radiology (ACR) has subsequently developed the Lung Imaging Reporting and Data System (Lung-RADS) classification scheme (Table 4) which defines suspicious solid nodules as being 8 mm or larger.[47] Investigators retrospectively applied Lung-RADS criteria to NLST images and found striking improvements in specificity.[48] Applying Lung-RADS could have reduced the false positive rate for baseline images from 26.6% to 12.8% and reduced the false positive rate for follow up exams from 21.8% to 5.3%. The tradeoff, though, was lower sensitivity--an 8.6 percentage point decrease for baseline images and a 15.2 percentage point decrease for follow-up images. The clinical consequences of potentially delaying cancer diagnoses are unknown.

Overdiagnosis—A recognized potential consequence of screening programs is overdiagnosis—finding histologically confirmed cancers that would not have been otherwise diagnosed in the absence of screening. Based on measuring volume-doubling times to identify indolent cancers, an Italian observational study estimated the over-diagnosis rate to be about 25%.[49] A study modeling NLST data estimated an overall 18.5% probability of overdiagnosis with screening detection.[50]

Radiation exposure—The radiation exposure associated with low-dose CT scanning is about 1.5 mSv per examination.[30] In contrast, the radiation exposure is about 8 mSv from a diagnostic chest CT and up to 14 mSv from a PET/CT. Although calculations are based on indirect evidence, radiation exposure from LDCT lung cancer screening has been estimated to cause one cancer death for every 2,500 screened subject over 20 years.[30] Some of this risk can be mitigated. CMS is requiring that screening centers confirm that patients are being exposed to low-dose radiation with screening chest CT scans. Applying Lung-RADS could help minimize radiation exposure from unnecessary diagnostic imaging. A retrospective analysis of NLST data also suggested that the screening interval might be lengthened following a normal baseline screen.[51]

Smoking cessation

Lung cancer screening uniquely links diagnostic testing with an effective behavioral intervention—smoking cessation. NSLT participants who were current smokers at the time of enrollment had over a 2-fold increased lung cancer mortality during follow up compared to former smokers, regardless of their screening arm.[52] Former smokers in the chest radiography screening arm who remained abstinent for 7 years had a 20% mortality reduction compared to current smokers--the same magnitude of benefit achieved with LDCT screening.

Lung cancer screening has been seen as a teachable moment when smokers are more susceptible to health messages about cessation and abstinence.[53] However, controlled screening trials have shown that screening alone will not affect smoking habits.[54–56] In contrast, abnormal LDCT findings are associated with smoking cessation.[56] NLST participants with nodules suspicious for lung cancer, particularly findings that were new or changed from a previous exam, were significantly less likely to continue smoking than participants with normal screening exams, OR = 0.66, (95% CI 0.61–0.72).[57] A clinical guideline from the Association for Treatment of Tobacco Use and Dependence and the Society for Research on Nicotine and Tobacco suggests that all smokers undergoing screening should be provided with evidence-based smoking cessation interventions.[58]

Cost-effectiveness—An estimated 7 million Americans would be eligible for lung cancer screening based on USPSTF screening criteria.[25] The total costs associated with screening could be substantial, potentially incurring $6.8 billion in Medicare expenditures over a 5-year time horizon.[59] However, analyses do suggest that lung cancer screening could provide good to moderate value.[60–62] One study based on NLST data estimated that the cost-effectiveness of screening would be $81,000 (95% CI 53,000–186,000) per quality-adjusted life-year.[6060] Estimates, though varied substantially by subgroups (Table 5).

Screening was much more cost effective in NLST participants at higher risk for dying from lung cancer. A post-hoc modeling study stratified this risk based on demographic and clinical risk factors, and found that participants in the highest 3 quintiles of lung-cancer mortality risk accounted for 88% of the mortality benefit from screening.[63] Other investigators have developed risk calculators to predict lung cancer incidence to efficiently identify the ever smokers most likely to benefit from lung cancer screening.[64–66] Table 6 shows some of the variables included in risk models. A prospective comparative analysis found that numerous lung cancer risk models more efficiently identified high-risk patients than the clinical trial eligibility criteria.[67] The best performing model, using a 6-year lung-cancer risk threshold ≥ 0.0151, could reduce the number needed to screen to prevent one lung cancer death from the 320 in NLST to 255.[66] Applying risk calculators to identify the highest-risk patients thus could make screening more cost-effective. Applying Lung-RADS criteria which raise the threshold for classifying a nodule as abnormal and applying risk models to guide biopsy decisions[68] could also make screening more cost-effective—as would successfully leveraging screening to increase smoking cessation and maintain abstinence.[62]

Implementing lung cancer screening programs

Recommendations

The American College of Chest Physicians and American Thoracic Society policy statement on lung cancer screening identified crucial components for establishing a screening program (Table 7).[69] Speakers at a lung cancer screening workshop hosted by the National Academies of Sciences, Engineering, and Medicine highlighted the importance of creating a coordinated multidisciplinary team to address screening, diagnosis, treatment, and smoking cessation.[39] They also noted the importance of having the electronic health record be able to readily identify eligible subjects; provide templates for progress notes, order sets, and radiologic reports that comply with CMS standards; track abnormal results and follow up; and transmit data to national registries.[39]Supporting meaningful shared decision making may require involving advanced practice providers, nurses, trained navigators, or health coaches who can also support smoking cessation interventions. Programs have developed tool kits that include CMS criteria for lung cancer screening, decision aids, lists of ACR-accredited screening facilities, as well as overviews of insurance coverage issues.

Uptake

The uptake of lung cancer in clinical practice has been limited. A 2014 survey of screening centers identified by the Lung Cancer Alliance Screening Centers of Excellence database found 203 screening centers.[70] However, centers were not widely distributed; 11 states had no identified screening centers and many states with high rates of lung cancer incidence and mortality had limited screening capacity, particularly in rural areas.[70] Additional concerns have been raised about having sufficient capacity for thoracic surgery.[71] Being able to provide widespread access to high-quality screening, diagnostic, and treatment centers will be essential to effectively and equitably implementing screening.

Future of lung cancer screening

Guidelines and practices will likely evolve as more data become available on optimal strategies for selecting patients and managing abnormal images. Improvements in imaging and diagnostic techniques and treatments may make the screening process safer and more cost-effective. Expected decreases in smoking rates may reduce the number of people eligible for screening.[72] Regardless, screening will require substantial resources so that the budget impact and effectiveness of community-based programs will need ongoing evaluation.

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Key Points

- Lung cancer is the leading cause of cancer death in the United States
- Over 80% of lung cancer deaths are attributed to tobacco use suggesting the importance of primary prevention
- A U.S. trial showed that screening high-risk patients with low-dose CT scans reduced lung cancer mortality by 20% compared to chest radiography.
- The U.S. Preventive Services Task Force recommends annual lung cancer screening for high-risk patients (30 pack-years, current or quit within 15 years) from age 55 to 80
- Centers for Medicare and Medicaid will cover screening but requires programs to engage patients in shared decision making, offer smoking cessation, and report data to a central registry.

Synopsis

Lung cancer is the leading cause of cancer death in the United States. Over 80% of these deaths are attributed to tobacco use and primary prevention can effectively reduce the cancer burden. The National Lung Screening Trial (NLST) showed that low-dose CT (LDCT) screening could reduce lung cancer mortality in high-risk patients by 20% compared to chest radiography. The U.S. Preventive Services Task Force recommends annual LDCT screening for persons ages 55–80 with a 30-pack-year smoking history, either currently smoking or having quit within 15 years. The Centers for Medicare and Medicaid will cover LDCT screening though requires programs to engage patients in shared decision making, offer smoking cessation, meet stringent criteria for performing and interpreting images, and to report data to a central registry. These registry data will help determine whether community-based programs can safely, effectively, and economically implement screening.

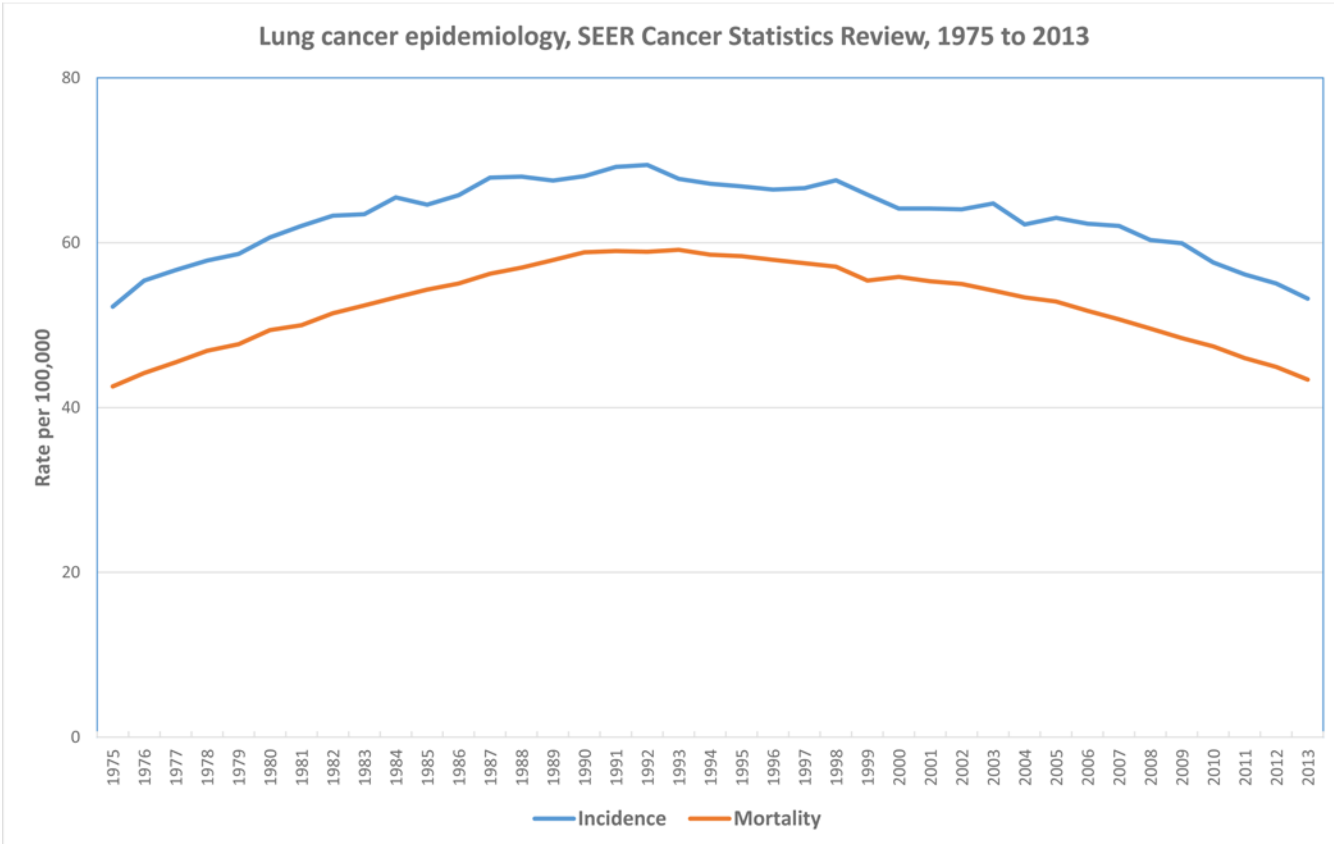

Fig. 1.

Lung cancer epidemiology, SEER Cancer Statistics Review, 1975 to 2013

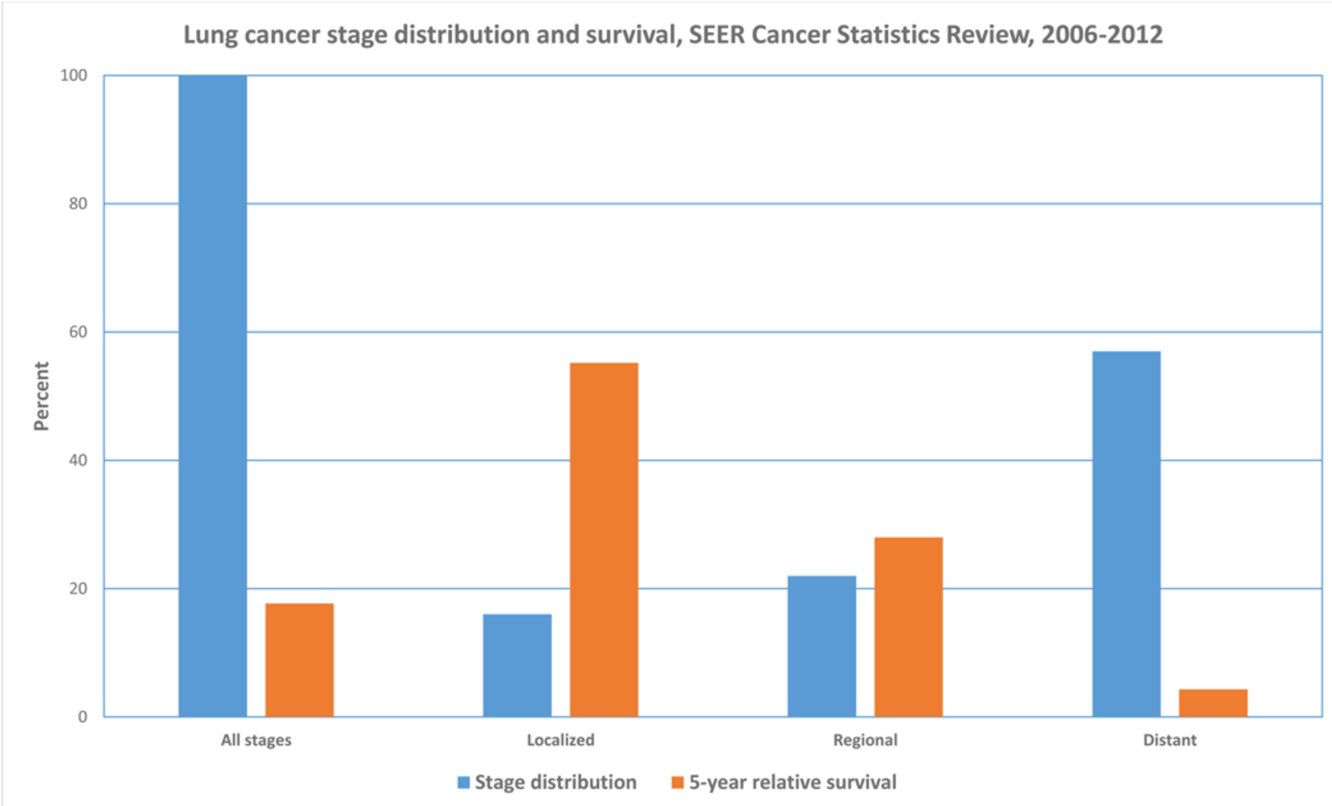

Fig. 2.
Lung cancer stage distribution and survival, SEER Cancer Statistics Review, 2006 to 2012.

Table 1.

Comparison of randomized controlled trials evaluating LDCT screening for lung cancer

	NSLT[16]	**DANTE[19]**	**DLCST[20]**	**MILD[21]**	**NELSON[73]**
Population features	United States Ages 55–74 Men and women Smoking history: ≥30 pack-years Quit ≤ 15 years	Italy Ages 60–74 Men only Smoking history: ≥20 pack-years Quit ≤ 10 years	Denmark Ages 50–70 Men and women Smoking history: ≥20 pack-years Quit ≤ 10 years	Italy Ages 55–74 Men and women Smoking history: ≥30 pack-years Quit ≤ 15 years	Netherlands/Belgium Ages 50–75 Men and women Smoking history: ≥15 pack-years Quit ≤ 10 years
Study arms: number of participants	LDCT: 26,722 CXR: 26,732	LDCT: 1,264 CXR + sputum cytology: 1,186	LDCT: 2,052 No screening: 2,052	LDCT (annual): 1190 LDCT (biennial): 1186 No screening: 1,723	LDCT: 7,915 No screening: 7,907
Statistical power	90% power to detect 21% reduction in lung cancer mortality	Unpowered	Unpowered	Unpowered	80% power to detect 20–25% reduction in lung cancer mortality
Median follow up	6.5 years	8.35 years	9.8 person years	4.4 years	Ongoing (target: 10 years)
Lung cancer mortality rate (per 100,000 person-years), risk reduction	LDCT: 247 Control: 309 RR= 0.80; 95% CI: 0.73–0.93	LDCT: 543 Control: 544 HR = 0.99; 95% CI: 0.69–1.43	LDCT: 200 Control: 190 HR = 1.03; 95% CI: 0.66–1.6	LDCT (annual): 216 LDCT (biennial): 109 Control: 109 HR = 1.52; 95% CI: 0.63–3.65	Not available
Absolute lung cancer mortality and risk reduction	LDCT: 1.3% Control: 1.6% ARR = 0.3 percentage points	LDCT: 4.7% Control: 4.6% ARI = 0.03 percentage points	LDCT: 1.90% Control: 1.85% ARI = 0.05 percentage points	LDCT (total): 0.76% Control: 0.41% ARI = 0.35 percentage points	Not available

Abbreviations: LDCT: Low-dose computed tomography; NSLT: National Lung Screening Trial; DANTE: Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays; DLCST: Danish Lung Cancer Screening Trial; MILD: Multicentric Italian Lung Detection; NELSON: Netherlands-Leuven Longkanker Screenings Network; CXR: Chest X-ray; ARR: absolute risk reduction; ARI: absolute risk increase

Table 2.

Guideline recommendations for lung cancer screening

Organization	Eligibility		Frequency	Setting	Counseling
	Age	Tobacco history			
United States Preventive Services Task Force (2013)[25]	55 to 80	≥ 30-pack year; currently smoking or quit within 15 years Screening might not be appropriate for those with substantial comorbidity	Annual	Clinical settings that have high rates of diagnostic accuracy, appropriate follow-up protocols for positive results, and clear criteria for invasive procedures	Shared decision making for screening Smoking cessation
American Cancer Society (2013)[29]	55 to 74	≥ 30-pack year; currently smoking or quit within 15 years Relatively good health	Annual	Organized screening program with expertise in screening and access to multidisciplinary team skilled in evaluating, diagnosing, and treating lung abnormalities	Informed and shared decision making for screening Smoking cessation
American Thoracic Society (2015) [33]	55 to 74	≥ 30-pack year; currently smoking or quit within 15 years	Annual	Clinical settings that have high rates of diagnostic accuracy, appropriate follow-up protocols for positive results, and clear criteria for invasive procedures	Shared decision making to allow patients to weigh trade-offs based on their personal risk profiles and make informed decision whether to screen Integrate smoking abstinence efforts into screening programs
American Association of Thoracic Surgery (2012)[28]	55 to 79	≥ 30-pack year; ever smoker regardless of time since quitting	Annual	Environments where multidisciplinary teams are available for managing indeterminate and positive findings	Use risk calculators to determine high-risk population Support smoking cessation
	50 to 79	20-pack with risk factor (5-year risk ≥ 5%)			
National Comprehensive Cancer Network[34]	55 to 74	≥ 30-pack year; currently smoking or quit within 15 years	Annual	Minimize screening risk by algorithmic management and multidisciplinary expertise	Shared decision making to include discussion of benefits and risks
	50 to 74	≥ 20-pack year; 1 additional risk factor *			
American College of Chest Physicians (2013)[31]	55 to 74	≥ 30-pack year; currently smoking or quit within 15 years Suggest not screening those with severe comorbidity	Annual	Settings that can deliver the comprehensive care provided to NLST participants	Complete description of potential benefits and harms so that the individual can decide whether to undergo screening
American Lung Association (2015)[32]	55 to 74	≥ 30-pack year; currently smoking or quit within 15 years	Annual	Link screening to accessing “best practice” multidisciplinary teams that can provide follow-up work-up and care	Develop shared decision-making toolkits Provide smoking cessation services

* Cancer history, family history, disease history (chronic obstructive pulmonary disease, pulmonary fibrosis), occupational/environmental exposures (asbestos, radon, silica, etc.)

Table 3.

Lung Cancer Screening Decision aids

Organization	Title	URL
Agency for Health Research and Quality	Lung cancer screening tools for patients and clinicians	http://effectivehealthcare.ahrq.gov/index.cfm/tools-and-resources/patient-decision-aids/lung-cancer-screening/
American Thoracic Society	Decision aid for lung cancer screening with computerized tomography (CT)	https://www.thoracic.org/patients/patient-resources/resources/decision-aid-lcs.pdf
University of Michigan	Lung cancer CT screening. Should I get screened?	http://www.shouldiscreen.com
Memorial Sloan Kettering Cancer Center	Lung cancer screening decision tool	https://www.mskcc.org/cancer-care/types/lung/screening/lung-screening-decision-tool
The Dartmouth Institute	Option Grid™ decision aid: Lung cancer screening: yes or no?	http://optiongrid.org/option-grids/grid-landing/8
National Cancer Institute	Patient and Physician Guide: National Lung Screening Trial (NLST)	https://www.cancer.gov/types/lung/research/NLSTstudyGuidePatientsPhysicians.pdf
U.S. Department of Veterans Affairs	Screening for Lung Cancer	http://www.prevention.va.gov/preventing_diseases/screening_for_lung_cancer.asp
National Comprehensive Cancer Network	Lung cancer screening	https://www.nccn.org/patients/guidelines/lung_screening/#20

Table 4.

Summary of Lung-RADS™ Classification for Baseline Screening

Category	Category Descriptor	Category	Findings	Management
Negative	No nodules and definitely benign nodules	1	No lung nodules	Continued annual screening with LDCT in 12 months
			Nodule(s) with calcification	
Benign appearance or behavior	Nodules with a very low likelihood of becoming a clinically active cancer due to site or lack of growth	2	Solid/part solid nodule(s): < 6 mm	
			Ground-glass nodule: < 20 mm	
Probably benign	Probably benign finding(s)—short-term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	Solid nodule(s): ≥ 6 to < 8 mm at baseline OR new 4 mm to < 6 mm	6 month LDCT
			Part solid nodule(s): ≥ 6 mm with solid component < 6 mm	
			Ground-glass nodule ≥ 20 mm	
Suspicious	Findings for which additional diagnostic testing and/or tissue sampling is recommended	4A	Solid nodule(s): ≥ 8 to < 15 mm	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm solid component
			Part solid nodule(s): ≥ 8 mm with solid component ≥ 6 mm to < 8 mm	
		4B	Solid nodule(s): ≥ 15 mm	Chest CT with or without contrast, PET/CT and or tissue sampling depending on the “probability of malignancy and comorbidities
			Part solid nodule(s) with solid component ≥ 8 mm	
		4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy	

Table 5.

Incremental cost-effectiveness lung cancer screening by National Lung Screening Trial subgroup

Characteristics		Number of participants	Incremental costs (U.S. $)	Incremental QALYs	Cost per QALY (U.S. $)
Sex	Male	31,446	1,683	0.0115	147,000
	Female	21,856	1,557	0.0340	46,000
Age at entry	55–59	22,773	1,541	0.0101	152,000
	60–64	16,333	1,520	0.0320	48,000
	65–69	9,504	1,900	0.0351	54,000
	70–74	4,685	1,905	0.0163	117,000
Smoking status	Former	27,643	1,661	0.0027	615,000
	Current	25,659	1,601	0.0369	43,000
Risk of lung cancer	First quintile	10,660	1,453	0.0086	169,000
	Second quintile	10,661	1,454	0.0118	123,000
	Third quintile	10,660	1,651	0.0061	269,000
	Fourth quintile	10,661	1,672	0.0515	32,000
	Fifth quintile	10,660	1,851	0.0354	52,000

Abbreviations: QALY = quality-adjusted life year

Data from Black WC, et al. New Engl J Med 2014:371:1793

Table 6.

Variables used in risk models for identifying high-risk patients

• Age
• Race/ethnicity
• Sex
• Body mass index
• Education
• Smoking status (current/former)
• Cigarettes smoked/day
• Smoking pack-years
• Age at smoking cessation
• Duration of smoking cessation
• Asbestos exposure
• Personal history of emphysema
• Personal history of malignant tumor
• Family history of lung cancer

Data from: Li K, et al. Cancer Prev Res 2015;8:777–85

Table 7.

Components necessary for a high-quality screening program: American College of Chest Physicians and American Thoracic Society [69]

Component	Explanation
Who is offered lung cancer screening	Use National Lung Screening Trial (NLST) criteria, risk calculator to identify eligible subjects
How often, and for how long, to screen	Follow NLST, U.S. Preventive Services Task Force, Centers for Medicare & Medicaid criteria
How the CT scan is performed	Perform low-dose CT scans based on technical specifications
Identifying lung nodules	Policy on size threshold to label positive screening test
Structured reporting of screening results	Use Lung-RADS
Lung nodule management algorithm	Determine criteria for performing diagnostic procedures and entering patients into surveillance
Smoking cessation	Integrate within screening program
Patient and provider education	Use standardized materials, provider education
Data collection	Annually report data on each component of screening program as well as cancers diagnosed to central data registry