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Benefits and Harms of CT Screening for Lung Cancer: A Systematic Review

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Conflicts of Interest:
All authors have completed and submitted the ICJME form for Disclosure of Potential Conflicts of Interest. Dr. Azzoli, Dr. Brawley, Dr. Byers, Dr. Colditz, Mr. Mirkin, Mr. Oliver, Dr. Smith-Bindman and Dr. Qaseem have reported no conflicts. Dr. Bach reported that he has received speaking fees from Genentech. Dr. Detterbeck reported that he was reimbursed for travel costs associated with his work on the Oncimmune advisory board, and has participated without compensation in a symposium on CT screening sponsored by Covidien. Dr.Berry reported that he is co-owner of Berry Consultants LLC which designs adaptive clinical trials for pharmaceutical companies, medical device companies and NIH cooperative groups. To the best of his knowledge none of these parties have any interest in lung cancer screening. Dr. Gould reported that he receives grant support from the National Cancer Institute. Dr. Jett reported that he has grants pending for work related to screening and early detection of lung cancer with Oncimmune and Isense. Dr. Sabichi reported her membership on the National Cancer Institute's PDQ Prevention and Screening Editorial Board and her possession of a pending patent for a test for the detection of bladder cancer. Dr. Wood reported his participation in the development of the National Comprehensive Cancer Network's clinical practice guidelines for lung cancer screening in his role as Chair of the NCCN Lung Cancer Screening Panel.

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Abstract

Context—Lung cancer is the leading cause of cancer death. Most patients are diagnosed with advanced disease, resulting in a very low five-year survival rate. Screening may reduce the risk of death from lung cancer.

Objective—A multi-society collaborative initiative (involving the American Cancer Society, the American College of Chest Physicians, the American Society of Clinical Oncology, and the National Comprehensive Cancer Network) was undertaken to conduct a systematic review of the evidence regarding the benefits and harms of lung cancer screening using low dose computed tomography (LDCT), in order to create the foundation for development of an evidence-based clinical guideline.

Data Sources—MEDLINE (OVID: 1996 to April 2012), EMBASE (OVID: 1996 to April 2012), and the Cochrane Library (April 2012).

Study Selection—Of 591 citations identified and reviewed, eight randomized controlled trials and 13 cohort studies of LDCT screening met criteria for inclusion. Primary outcomes were lung cancer mortality and all-cause mortality, and secondary outcomes included nodule detection, invasive procedures, follow-up tests, and smoking cessation.

Data Extraction—Critical appraisal using pre-defined criteria was conducted on individual studies and the overall body of evidence. Differences in data extracted by reviewers were adjudicated by consensus.

Results—Three randomized studies provided evidence on the impact of LDCT screening on lung cancer mortality, of which the National Lung Screening Trial was the most informative, demonstrating that among 53,454 enrolled, screening resulted in significantly fewer lung cancer deaths (356 vs 443 deaths; lung cancer-specific mortality, 247 vs 309 events per 100,000 person-years for LDCT and control groups, respectively; Relative Risk [RR] = 0.80, 95% Confidence Interval [CI] 0.73–0.93; Absolute Risk Reduction [ARR] = 0.33%, P=0.004). The other 2 smaller studies showed no such benefit. In terms of potential harms of LDCT screening, across all trials and cohorts, about 20% of individuals in each round of screening had positive results requiring some degree of follow-up, while approximately 1% had lung cancer. There was marked heterogeneity in this finding and in the frequency of follow-up investigations, biopsies, and the percent of surgical procedures performed in those with benign lesions. Major complications in those with benign conditions were rare.

Conclusions—LDCT screening may benefit individuals at an elevated risk for lung cancer, but uncertainty exists about potential harms and the generalizability of results.

Background

Lung cancer is the leading cause of cancer death in the United States (and worldwide), causing as many deaths as the next four most deadly cancers combined (breast, prostate, colon and pancreas).[1] Despite a slight decline since 1990 in the US, lung cancer will claim >160,000 American lives in 2012.[2] Most patients diagnosed with lung cancer today already have advanced disease (40% are stage IV, 30% are stage III), and the current five-year survival rate is only 16%.[3]

Earlier randomized controlled trials (RCT) involving chest radiographs (CXR) and sputum cytology for lung cancer screening found that these strategies detected slightly more lung cancers, smaller and more stage I tumors, but the detection of a larger number of early stage cancers was not accompanied by a reduction in the number of advanced lung cancers or lead to a reduction in lung cancer deaths.[4–14] Renewed enthusiasm for lung screening arose with the advent of low dose computerized tomography (LDCT) imaging, which is able to identify smaller nodules than can CXR.

This systematic review focuses on the evidence regarding the benefits and harms of LDCT screening for lung cancer. Other potential screening methods (e.g. CXR, sputum cytology or biomarkers, exhaled breath) are not addressed. This review is a collaborative initiative of the American Cancer Society (ACS), the American College of Chest Physicians (ACCP), the American Society of Clinical Oncology (ASCO), and the National Comprehensive Cancer Network (NCCN), and forms the basis for the clinical practice guideline of the ACCP and ASCO (Box xx – link to full guideline in box?). This work will be re-assessed when pertinent new data become available, consistent with the Institute of Medicine's recommendations for guideline development.[15]

Methods

ACS, ACCP, ASCO and NCCN assembled a panel of experts, representing the relevant clinical disciplines and the consumer's perspective. All members cleared all organizations' conflict of interest policies for participation in guideline development; none received compensation for participation. The sponsoring organizations donated staff time supported by their general administrative funds. No industry funds were used in the support of this endeavor. The panel defined a process for selection, data extraction and outcomes assessment to produce a thorough evaluation of LDCT screening relative to patient-centered outcomes, including quantifying potential benefits and harms. The target patient population for this initiative is individuals at elevated risk of developing lung cancer due to age and smoking history; and the target audience includes physicians, allied professionals and policy makers. The panel was divided into evidence review and writing sub-committees, focusing on the following key questions:

1. What are the potential benefits of screening individuals at elevated risk of developing lung cancer using LDCT?
2. What are the potential harms of screening individuals at elevated risk of developing lung cancer using LDCT?
3. Which groups are most likely to benefit or not benefit from screening?
4. In what setting is screening likely to be effective?

The literature search was developed and conducted by an experienced systematic reviewer using MEDLINE (OVID: 1996 to April 8, 2012), EMBASE (OVID: 1996 to April 8, 2012), and the Cochrane Library (April 20, 2012). Additional citations were gleaned from the reference lists of related papers and review articles. The literature search included MeSH and Emtree headings and related text and keyword searches in a manner that combined terms related to lung cancer, population screening and LDCT (eAppendix 1). The search was limited to published data only because it was felt that any unpublished preliminary data identified would add little to inform the primary outcomes of interest.

Studies were eligible for inclusion if they involved either a RCT using LDCT screening for lung cancer in one arm, or a non-comparative cohort study of LDCT screening, provided they reported at least one of the following outcomes: lung-cancer-specific or all-cause mortality, nodule detection rate, frequency of additional imaging, frequency of invasive

diagnostic procedures (e.g. needle or bronchoscopic biopsy, surgical biopsy, surgical resection) complications from the evaluation of suspected lung cancer, and the rate of smoking cessation or re-initiation. For lung-cancer-specific and all-cause mortality endpoints, only RCT data were considered eligible for inclusion; for other endpoints, data from the LDCT arm of both RCTs and cohort studies were included. Exclusion criteria include studies that only assessed screening among those with risk factors other than smoking (e.g. asbestos), those not published in English, and meta-analysis or case-series reports of outcomes only among patients diagnosed with lung cancer.

The above exclusion criteria were determined *a priori* and guided whether data identified by the systematic literature review was judged to have been reported in a manner appropriate for inclusion. Articles were selected and data were extracted independently by a minimum of two reviewers. At the point of abstract review, if one of two reviewers indicated that a citation may be relevant, the full text article was retrieved. Upon full text review, if there was a discrepancy among the two reviewers, a third reviewer determined eligibility and the reviewers came to consensus. In addition, the third reviewer also verified that articles deemed ineligible did not actually meet eligibility criteria. Between the three reviewers, discrepancies occurred in approximately 12% of cases and were resolved through consensus. Most notably, the small RCT by Garg et al and the smoking cessation study by Schnoll et al were originally excluded, but the decision was reversed upon further review.[16, 17] Common reasons for exclusion included the identification of narrative reviews, studies that did not involve high risk smoking populations or studies that only followed patients diagnosed with lung cancer. A full list of the studies excluded from the systematic review and the reasons for exclusion is available from the authors.

The risk of bias was assessed by a minimum of two reviewers using pre-specified criteria (eAppendix 2) and discrepancies were resolved through consensus.

The frequency of nodule detection across studies was analyzed both unadjusted and stratified by multiple study design characteristics (e.g. CT collimation, minimum smoking exposure criteria for study enrollment, stated threshold for labeling a finding “positive” or “suspicious”).

Results

Literature Search Results

Eight RCTs (Table 1)[16, 18–24] and 13 cohort studies of LDCT screening (Table 2)[25–37] were selected from 591 citations identified by the literature search (eAppendix 3). Two RCTs (LSS and DLCST) were pilot studies preceding larger trials (NLST and NELSON, respectively). Several trials are ongoing with only preliminary data currently available. Two RCTs were excluded because they lacked data on key endpoints; one RCT and several cohort studies were excluded because they involved populations at risk due to factors other than smoking or were for general population screening. The cohort study papers of the Early Lung Cancer Action Project (ELCAP) were included, but not the ELCAP case-series or meta-analysis papers. For studies reported in multiple publications, all reports were reviewed but earlier papers superseded by more mature data are not referenced.

A formal assessment of the risk of bias in the RCTs (eTable 1) discloses a low risk in NLST and DLCST, and variable results and an incomplete ability to assess the risk in other studies (often because only preliminary reports of ongoing studies are available). The risk of bias in the cohort studies is variable and often high (usually because justification of sample size, definition of a primary endpoint or funding sources was lacking).

Across the RCTs, the minimum smoking history required for enrollment ranged from 15–30 pack years (i.e. cigarette packs smoked per day multiplied by years of smoking), with a maximum time since quitting smoking ranging from 10 years to an unlimited number of years (Table 1). The lower age limit ranged from 47 to 60 years, and the upper limit from 69 to 80 years. There was greater variation in entry criteria in the cohort studies (Table 2). Thus, the underlying risk for lung cancer varies substantially. Generally speaking, the NLST, LSS and Garg studies focused on higher risk, DLCST, ITALUNG and DANTE on both higher and intermediate risk and NELSON and Depiscan on a broad range of risk among participants.[16, 18, 20–24, 38] Although estimating the average risk of all participants in any of these studies is difficult due to lack of granular data, the minimum risk level in each study can be approximated using established formulas.[39,40] Over 10 years, the risk of being diagnosed with lung cancer for participants meeting minimum entry criteria of each study, assuming they had quit smoking at time of study entry, are approximately 2% for NLST, 1% for DLSCT and considerably less than 1% for NELSON. The nodule size deemed large enough to investigate further ranged from “any size” to >5 mm; the size that triggered an invasive intervention (when specified) ranged from 6–15 mm (Tables 1, 2).

What are the Potential Benefits of Screening Individuals at Elevated Risk of Developing Lung Cancer Using LDCT?

Effect on Mortality—Three RCTs have reported the impact of LDCT screening on lung-cancer-specific mortality (Table 3). The NLST found that three annual rounds of screening (baseline, and 1and 2 years later) with LDCT resulted in a 20% relative decrease in deaths from lung cancer relative to CXR over a median of 6.5 years of follow-up (p=0.004).[22] In absolute terms, the chance of dying from lung cancer was 0.33% less over the study period in the LDCT group (87 avoided deaths over 26,722 screened participants), meaning 310 people must participate in screening to prevent one lung cancer death. Based on a slightly different denominator the NLST authors reported the number-needed-to-screen with LDCT was 320 to prevent one lung cancer death, and based on the confidence intervals overall the confidence interval on the number needed to screen ranges from xx to yy. The considerably smaller ongoing DANTE and DLST studies each compare 5 annual rounds of LDCT screening to usual care; after a median of 34 and 58 months of follow-up, no statistically significant difference in lung cancer mortality was observed in either study (Dante: RR = 0.97, 95% CI 0.71–1.32, p = 0.84); (DLST: RR = 1.15, 95% CI 0.83–1.61, p=0.43).[21]

All three studies reported on the risk of death from any cause (Table 3) between study arms, and directly or indirectly on the risk of death from any cause other than lung cancer. Only the NLST found a difference in this endpoint, with fewer deaths overall in the LDCT vs. the CXR arm (1,303 vs. 1,395 deaths per 100,000 person-years, respectively). Analyses focusing exclusively on deaths not due to lung cancer found no significant differences in any of the three studies.[22]

Effect on Smoking Behavior—No studies have evaluated whether public statements regarding LDCT screening’s benefits affect smoking behavior. Speculation exists that undergoing LDCT screening may result in justification of continued smoking, or may represent an opportunity for successful smoking cessation. Studies examining the smoking behavior of LDCT screened individuals have not found evidence that cessation or re-initiation rates are meaningfully altered by participation in screening (eTable 2).[41–43]

What are the Potential Harms of Screening Individuals at Elevated Risk of Developing Lung Cancer Using LDCT?

Detection of Abnormalities—LDCT identifies both cancerous and benign non-calcified nodules - the latter are often called “false positives”. Although most LDCT screening studies

have reported on nodules detected, the categorization and manner of reporting is inconsistent (e.g. it is sometimes unclear if newly identified nodules are assigned to that round, or to an earlier round if they can be retrospectively seen on an earlier LDCT). Likewise, size thresholds that would trigger an invasive work-up are variously and inconsistently reported as are the potential denominators such as per-screening round, or per-person year.

Across studies, the average nodule detection rate per round of screening was 20% (Table 5, eFigure 1), but varied from 3–30% in RCTs and 5–51% in cohort studies. Most studies reported that >90% of nodules were benign. In general there is a tendency towards lower nodule detection rates in repeat screening rounds, but the data and reporting is inconsistent (Table 5, e Figure 2). In the NLST the rate of detection did not decrease until the third round. In that round the study protocol allowed for ignoring nodules that had been present in the prior rounds. We were unable to find any relation between study features, such as smoking history of study enrollees, CT scan settings, nodule size cutoffs, and reported nodule detection rates.

Most often a detected nodule triggered further imaging, but the underlying management protocols were inconsistently reported in the studies. Whether all additional imaging tests were captured in the studies was also uncertain: reported follow-up imaging rates may be underestimated. The frequency of further CT imaging among screened individuals ranged from 1% in Veronesi to 44.6% in Sobue. The frequency of further PET imaging among screened individuals, exhibited much less variation, ranging from 2.5% in Bastarrika to 5.5% in the NLST.”.[22, 25, 28, 32] The frequency of invasive evaluation of detected nodules was generally low but varied considerably (Table 6, eFigure 3). No patterns were apparent that explained this heterogeneity. In the NLST 1.2% of patients who were not found to have lung cancer underwent an invasive procedure such as needle biopsy or bronchoscopy, while 0.7% of patients who were not found to have lung cancer had a thorocoscopy, mediastinoscopy or thoracotomy.[22] In the NELSON study these numbers were 1.2% and 0.6% respectively.[18] Invasive non-surgical procedures in patients with benign lesions were common (e.g. 73% in NLST).

Complications of Diagnostic Procedures Stemming from Screening—The only study reporting on complications resulting from LDCT screening is the NLST. Overall, the frequency of death occurring within 2 months of a diagnostic evaluation of a detected finding was 8 per 10,000 individuals screened by LDCT, and 5 per 10,000 individuals screened by CXR. Some of the deaths after a diagnostic evaluation were presumably unrelated to follow-up procedures, as 1.9 and 1.5 per 10,000 occurred within 2 months when the diagnostic evaluation involved only an imaging study. Deaths most clearly related to follow-up procedures were those occurring within 2 months when the most recent procedure was a bronchoscopy or needle biopsy (3.4 per 10,000 screened by LDCT and 2.2 per 10,000 screened by CXR). Approximately one third of the deaths occurred within 2 months of a surgical procedure in both arms, and the vast majority of these were in the patients with cancer, suggesting perhaps that the surgical procedures in those with cancer were more extensive (i.e. resection rather than biopsy; such details were not reported). The 60-day perioperative mortality for patients with lung cancer who underwent a surgical procedure was 1% for the LDCT arm and .2% for the CXR arm.

Overall, the frequency of a major complication occurring during a diagnostic evaluation of a detected finding was 33 per 10,000 individuals screened by LDCT, and 10 per 10,000 individuals screened by CXR. The rate of (presumably unrelated) complications following imaging alone was similar and low (1.1 and 1.5 per 10,000 screened); the complication rate after a bronchoscopy or needle biopsy was also low (1.5 and 0.7 per 10,000 for LDCT and CXR, respectively). The vast majority of major complications occurred after surgical

procedures, and in those patients with lung cancer. The rate of major complications in those patients with lung cancer who underwent surgery was 14%.

Focusing only on those patients who had nodules detected by LDCT that turned out to be benign, death occurred within 60 days among 0.06%, and major complications occurred among 0.36%. About half of the deaths occurred after imaging alone, whereas the majority of major complications occurred after a surgical procedure (details unknown). Calculating these numbers for an entire screened population, the risk of death or major complications following diagnostic events (including imaging) for what turns out to be a benign nodule is 4.1 and 4.5 per 10,000. This is higher than in the CXR arm (1.1 and 1.5 per 10,000).

Overdiagnosis—Overdiagnosis refers to histologically confirmed lung cancers identified through screening that would not impact the patient's lifetime if left untreated. This includes patients who are destined to die of another cause (e.g. a co-morbidity or an unexpected event).[44] Earlier studies suggested that CXR screening may have an overdiagnosis rate of roughly 25%.[45, 46] The overdiagnosis rate for LDCT screening cannot yet be estimated; NLST data shows a persistent gap of about 120 excess lung cancers in the LDCT vs. the CXR arm, but further follow-up is needed.

Radiation Exposure—The effective dose of radiation of LDCT is estimated to be 1.5 mSv per examination, but there is substantial variation in actual clinical practice. However, diagnostic chest CT (~8 mSv)[47] or PET-CT (~14 mSv)[47–49] to further investigate detected lesions rapidly increases the exposure and accounts for most of the radiation exposure in screening studies. We estimate that NLST participants received ~8 mSv per participant over the three years, including both screening and diagnostic examinations (averaged over the entire screened population). Estimates of harms from such radiation come from several official bodies and commissioned studies,[50, 51] based on dose extrapolations from atomic bombings and also many studies of medical imaging.[52, 53] Using the NLST data these models predict approximately one cancer death caused by radiation from imaging per 2500 subjects screened. Therefore, the benefit in preventing lung cancer deaths in NLST is considerably greater than the radiation risk – which furthermore only becomes manifest 10–20 years later. However, for younger individuals or those with lower risk of developing lung cancer the tradeoff would be less favorable. Preliminary modeling studies suggest that potential risks may vastly outweigh benefits in non-smokers or those ≤ age 42.[54] Further study, including the effects of ongoing annual LDCT beyond three successive years, is needed.

Impact on Quality of Life—The impact of LDCT screening on quality of life (QOL) is unclear. We found only one study, in which 88–99% of 351 subjects reported no discomfort, but 46% reported psychological distress while awaiting results.[55] One can speculate about QOL benefits due to lower morbidity from advanced lung cancer, but there are also potential detriments due to anxiety, costs, and harms from the evaluation of both false positive scans and overdiagnosed cancers.

Which Patients are Likely to Benefit or not Benefit from LDCT Screening?

The NLST population is the only one for whom a lung cancer mortality benefit from LDCT has been demonstrated (age 55–74, ≥30 pack-years of smoking, and quit ≤15 years prior to entry). Other studies are too small, too preliminary, or too poorly designed to support meaningful conclusions. The value of LDCT screening is likely determined primarily by the risk of lung cancer versus competing causes of death. Little information exists regarding co-morbidities, but presumably the NLST participants were deemed healthy. We estimate an average risk of developing lung cancer within 10 years of ~10% for the NLST population in

the absence of screening (estimated median age 62 and ~50 pack-years of smoking). However, the risk for individual NLST participants most likely varied by more than 10-fold over that time period, from <2% to >20%, and it is unclear which groups experienced benefit.[39, 40] Further research and modeling studies are needed to provide an evidence base for refining the selection criteria for screening. Other risk factors for lung cancer are well known (e.g. family history of lung cancer, occupational exposures, personal history of lung or certain other cancers), but how these might affect selection for LDCT screening has not been studied.

In What Setting Is Screening Likely to Be Effective?

A summary (eTable 3) of the setting of the NLST (the only positive study) demonstrates that most (76%) of the NLST sites were National Cancer Institute designated cancer centers, and 82% were large academic medical centers with >400 hospital beds. We believe that all have specialized thoracic radiologists and board certified thoracic surgeons on staff. The CT scanners used in the NLST underwent ongoing extensive quality control, and the scans were interpreted by chest radiologists who underwent specific training and quality control in the interpretation of images and wording of screening LDCT findings.[48] A nodule management algorithm was included in the NLST but adherence or the setting in which nodules were managed was not mandated or tracked by the study.[48]

Most other RCTs and cohort studies of LDCT screening were conducted in facilities similar to the NLST sites: academic medical centers, large hospitals, with the involvement of relevant subspecialist services and a defined nodule management algorithm. The impact of details of the setting of LDCT screening has not been tested, but the variability in rates of false positive LDCT scans, further imaging and procedures suggests these may be important.

Discussion

This paper summarizes the systematic review conducted by a multi-society collaborative effort examining the risks and benefits of LDCT screening for lung cancer, and forms the basis of the American College of Chest Physicians and the American Society of Clinical Oncology clinical practice guideline (Box, link to full practice guideline). The guideline is based on the finding that a reasonable amount of data has been reported regarding the outcomes for LDCT screening for lung cancer and that some conclusions can be drawn regarding its risks and benefits despite many areas of uncertainty.

A recent large, high quality RCT (the NLST) found that annual LDCT screening reduced the relative risk of death from lung cancer by 20%, and the absolute risk by 0.33% in a population with a substantially elevated risk for lung cancer. Two smaller RCT's (DANTE and DLSCT) comparing LDCT to usual care found no benefit of LDCT screening, but are best interpreted as neither confirming nor contradicting the NLST findings. Because studies a recent large (N=154,901) RCT demonstrated no lung cancer mortality difference between CXR screening and usual care, the interventions in these three studies are reasonably comparable.[56]

The literature supports the conclusion that LDCT screening can lead to harm. It identifies a relatively high percentage of subjects with nodules (average ~20%), the vast majority of which are benign. The additional imaging that these nodules trigger increases radiation exposure. The rates of surgical biopsy are also variable (<1–4%) as are the percentage of surgical procedures performed for benign disease. The rate of major, and sometimes fatal, complications among those with benign conditions is low.

The unexplained heterogeneous rates of nodule detection, additional imaging and invasive procedures that occurred within the structured settings of the controlled trials of LDCT raise concerns about how easily LDCT can be more broadly implemented. There is already substantial variability in the US in the rates and complications of pulmonary needle biopsy[57] and outcomes of lung cancer surgery, being considerably better in dedicated centers (such as those conducting LDCT trials).[58, 59] Furthermore, compliance with screening is consistently lower in cohort studies than in the NLST, and could be worse with unstructured implementation, with resulting diminished benefits. Analogous concerns in breast cancer screening led to the Mammography Quality Standards Act. The position statement by the International Association for the Study of Lung Cancer recommends demonstration projects to evaluate implementation of LDCT screening, establishment of quality metrics, and multiple task forces to address the many critical areas of uncertainty.[60] Given all of these issues, performing a LDCT scan outside of a structured organized process appears to be beyond the current evidence base for LDCT lung cancer screening.

The fear associated with even a slight suspicion of lung cancer highlights the need for careful education of LDCT participants, and the need for carefully worded scan interpretations. Furthermore, even a small negative impact on smoking behavior (either lower quit rates or higher recidivism) could easily offset the potential gains from LDCT screening in a population.[61] Smoking cessation should be considered a valuable component of any screening program. Finally, in the setting of rising healthcare costs, the relative cost-effectiveness of LDCT screening compared to other interventions will be a topic of discussion and concern in policy spheres. Medicare is allowed to contemplate a preventive services cost-effectiveness before adding it to the package of preventive benefits (Medicare Improvements for Patients and Providers Act of 2008). Now that an estimate is available of effectiveness, an estimate of cost-effectiveness could be generated, but none based on study data have yet been published. Some elements of such an analysis that will be critical will be determining what the price of the component services will be, how frequently follow-up procedures will be required, and how much underlying risk of disease affects cost-effectiveness. It is likely that the test will be much less cost-effective when applied to individuals at lower risk of lung cancer, because more individuals will need to be scanned to prevent each death from the disease. Making screening available in settings without an organized approach to the evaluation and management of LDCT findings may also lower cost-effectiveness, if the frequency of interventions and procedures is higher in these settings. [61–64]

Other questions regarding the generalizability of available findings also remain, such as the extent to which reported findings will generalize from the clinical studies to the broader community, and the extent to which one can extrapolate from studies with only a few rounds of screening to an approach that could cover many years of screening. It is possible to speculate that benefits of screening could be enhanced if screening were continued for longer periods, but the risks could be amplified as well. Careful studies are also needed to explore how LDCT screening might affect individuals who are unlike those already studied or who are screened in settings unlike those where previous studies have been conducted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Peter B. Bach had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1

Randomized Controlled Trials Identified in the Search of the Literature

Study	Number of Participants				Screening with LDCT			Study Duration			Number of Screens			Participant Characteristics		
	Randomized		% Screened or Followed at Baseline by Trial Arm		Collimation (mm)	Nodule Size (mm) Warranting Work up (↑ Imaging, Diagnostic Tests)	Was a Diagnostic Protocol in Place?	Years of Accrual	Planned Years of Follow-up from Baseline	Planned	Completed (at last report)	Conducted Annually?	Male	Age Range	Smoking History Eligibility (current or former)	
	LDCT	Control	LDCT	Control											Pack Years[a]	Years since quit
LDCT versus Usual Care (no screening)																
NELSON 2009 [18]	7,907 [b]	7,915 [b]	95%	100%	0.75	≥ 4.6 / > 9.8	Yes [c]	2004-NR [b]	10	3	2	No [d]	84%	50–75	> 15	≤ 10
DLCST 2012 [19,38]	2,052	2,052	100%	100%	0.75 [e]	≥ 5 / > 15	Yes	2004–06	10	5	5	Yes	55%	50–70	≥ 20	< 10 [f]
ITALUNG 2009 [20]	1,613	1,593	87%	100%	1–1.25	≥ 5 / ≥ 8 [h]	Yes	-	-	4	1	Yes	65%	55–69	≥ 20	< 10
DANTE 2009 [21]	1,276 [j]	1,196 [j]	91%	85%	5	Any/ ≥ 6 [i]	Yes [c]	2001–06	-	5	5 [j]	Yes	100%	60–74	≥ 20	< 10
Garg 2002 [16]	92 [k]	98 [k]	100%	100%	5	Any / > 10	Yes [c]	2001-NR [k]	-	2	1	Yes	75%	50–80	≥ 30	- [L]
LDCT versus Chest X-Ray																
NLST 2011 [22,65]	26,722	26,732	98%	97%	≤ 2.5	≥ 4	Yes [m]	2002–04	> 7	3	3	Yes	59%	55–74	≥ 30	≤ 15
LSS 2005 [23,66]	1,660	1,658	96%	93%	5	Any [n]	No	2000	2	2 [o]	2	Yes	59%	55–74	≥ 30	< 10
Depiscan 2007 [24]	385	380	86% [p]	77%	1–1.5	> 5 / ≥ 10	Yes	2002–04	-	3	1	Yes	71%	47–76	≥ 15	< 15

Note: - = Not Reported, The column heading Nodule Size (mm) Warranting Work-up indicates first the largest size nodule warranting additional imaging, and second the largest size nodule warranting diagnostic testing

[a] Pack-years is defined as the number of cigarettes packs (20 cigarettes per pack) smoked per day multiplied by the number of years smoked.

[b] Randomization is ongoing with a target accrual of 16000 participants.

[c] A protocol was reported, however specific details on adherence or deviation from the protocol or actual procedures used were not reported.

[d] Planned screening at years 1,2, and 4.

[e] Collimation = 16 × 0.75 mm

[f] Former smokers had to have quit after the age of 50 years and less than 10 years ago.

[j] The median follow-up was 33.7 months and only 161 participants (6.5% of those screened or followed at baseline) had 5 or more years of follow-up. Baseline data are mainly reported

[k] Target accrual of 400 participants in total was planned

[L] Study does not specify a maximum time since quitting.

[m] "…trial radiologists developed guidelines for diagnostic follow-up, but no specific evaluation approach was mandated." 22

[n] The size of the non calcified nodule to warrant further imaging was increased to ≥ 4 at year 1 to reflect evolving practice..

[o] In the original design, one screen was planned, however, it was later amended to 2 screens (baseline and 1 repeat)

[p] Six patients randomized to chest X-ray crossed over to receive LDCT at baseline.

Table 2

Cohort Studies of LDCT Identified in the Search of the Literature

Study	Number of Participants		LDCT		Was a Diagnostic Protocol in Place?	Study Duration		Number of Screens			Participant Characteristics			
	Enrolled in Study	% Screened at Baseline	Collimation (mm)	Nodule Size (mm) Warranting Work up (↑ Imaging / Diagnostic Tests)		Years of Accrual	Planned Years of Follow-up from Baseline	Planned	Completed (at last report)	Conducted Annually?	Male	Age Range (or Lower Limit)	Smoking History Eligibility (current or former)	
													Pack Years[a]	Years since quit
Veronesi 2008 [25, 67]	5,201 [b]	- [b]	2.5	> 5 / > 8 [l]	Yes	2004–05	-	5	2	Yes	66%	≥ 50	≥ 20	<10
Wilson 2008 [26]	3,755	97%	2.5	Any / ≥ 10 [g]	No	2002–06	3	2	2	Yes	51%	50–79	≥ 12.5 [n]	<10
Menezes 2010 [27]	3,352 [b]	- [b]	1–1.25	≥ 5 / ≥ 15	Yes	2003–07	-	6	6	Yes	46%	50–80	≥ 10	-
Sobue 2002 [28]	1,682	96%	10	Any	Yes [o]	1993–98	-	~10 [f]	~10	No [h]	88%	40–79	≥ 20	-
Swenson 2005 [29, 68,69]	1,520	100%	5	Any / > 8 [c]	Yes	1999	5	5	5	Yes	52%	50–85	≥ 20	<10
Pastorino 2003 [30]	1,035	100%	10	> 5	Yes	2000–01	-	5	2	Yes	71%	50–84	≥ 20	-
Henschke 2001 [31, 70]	1,000	-	10	Any / ≥ 6 [i]	Yes [j]	1993–98	10 [m]	3	3	Yes	54%	≥ 60	≥ 10	-
Bastarrika 2005 [32]	911 [b]	- [b]	8 [d]	≥ 5 / ≥ 10 [l]	Yes	-	-	2	2	Yes	74%	≥ 40	≥ 10	-
Diederich 2004 [33, 71, 72]	817	100%	5	Any / > 10 [e]	Yes	1995–99	6 [f]	6	6	Yes	72%	40–78	≥ 20	-
Novello 2005 [34]	520	99%	8.8	≥ 5 / > 11	Yes	2001	-	5	3	Yes	73%	54–79	≥ 20	< 10
Callol 2007 [35]	482	97%	10	≥ 5 / >10	Yes	2001–04	-	2	2	No [k]	65%	50–73	> 10	< 0.5
MacRedmond 2006 [36, 73]	449	100%	10	Any / ≥ 10	Yes	-	2	2	2	Yes	50%	50–74	≥ 10	-
Picozzi 2005 [37]	60	100%	10 [p]	Any / ≥ 10 [e]	Yes	2000–01	3	3	3	Yes	78%	57–78	≥ 20	-

Note: - = Not Reported, The column heading Nodule Size (mm) Warranting Work-up indicates first the largest size nodule warranting additional imaging, and second the largest size nodule warranting diagnostic testing

[a] Pack-years, defined as number of cigarettes packs smoked per day multiplied by the number of years smoked.

[b] The total number of participants enrolled was not reported, only the total number scanned at baseline, thus compliance with screening at baseline cannot be determined

[c] The following change to the protocol was reported: nodules < 4mm were initially followed with repeat CT at 6 months, but was then changed to 12 months (repeat screening)

[d] 297 participants were studied with a single slice helical scanner at a collimation of 8 mm and to precisely characterize any pulmonary nodule then same day high resolution CT. For the remaining 614 patients, a four-row multi-slice helical CT scanner was used – collimation = 1.25 mm.

[e] Nodules < 10 mm underwent repeat screening while nodules ≥ 10 were referred for biopsy

[f] Screening was discontinued after at least one normal annual repeat scan in participants < 55 years old

[g] The following change to the protocol was reported: All patients with non-calcified nodules at baseline were referred to additional imaging, at repeat screening only nodules ≥ 4 mm were referred.

[h] Bi-annual

[i] Nodules ≤ 5 mm = follow-up with high dose CT, nodules 6–10 mm assessment of the possibility for biopsy, ≥ 11 mm = referred to pulmonary physician for biopsy

[j] The workup protocol was not rigid and could be adjusted.

[k] Semi-annual.

[l] Diagnostic work-up was a referral to PET scan.

[m] Planned follow-up of those with malignant disease.

[n] At least one-half pack per day for at least 25 years.

[o] Referred to thin slice CT

[p] In the last round of screening 14 participants were scanned according to a different protocol including collimation = 3 mm.

Table 3

Mortality due to All Causes, Lung Cancer, and All Causes other than Lung Cancer in Randomized Trials

Study	Compared with	Number of Participants Screened or Followed		Median Follow-up (months)	P-Value on endpoint	Mortality							
						% With Events (n)		Rate of Events per 100,000 Person-years		Relative Risk (95% CI)	Rate Ratio	Absolute Difference	Number Needed to Screen to Prevent One Event
		LDCT	Control			LDCT	Control	LDCT	Control				
All Cause Mortality													
DANTE 2009 [21]	Usual Care	1,276	1,196	34	0.84	3.6% (46)	3.8% (45)	-	-	0.97 [a,b] (0.80–1.20)	-	0.2%	635
NLST 2011 [22]	CXR	26,722	26,732	78	0.004	7.0% (1,877)	7.5% (2,000)	1,303 [b]	1,395 [b]	0.93 (0.86–0.99)	0.93 [b]	0.5%	219
DLCST 2012 [19]	Usual Care	2,052	2,052	58	0.428	3.0% (61)	2.0% (42)	-	-	1.19 (1.01–1.40)	-	- 1.0%	-
Lung Cancer Specific Mortality													
DANTE 2009 [21]	Usual Care	1,276	1,196	34	0.83	1.6% (20)	1.7% (20)	-	-	0.97 [a,b] (.71–1.32)	-	0.1%	954
NLST 2011 [22]	CXR	26,722	26,732	78	0.02	1.3% (356)	1.7% (443)	247	309	0.80 (0.73 –0.93)	0.80 [b]	0.3%	320
DLCST 2012 [19]	Usual Care	2,052	2,052	58	0.059	0.7% (15)	0.5% (11)	-	-	1.15 (0.83–1.61)	-	- 0.2%	-
Mortality not due to Lung Cancer													
DANTE 2009 [21]	Usual Care	1,276	1,196	34	0.93	2.0% (26)	2.1% (25)	-	-	0.99 [b] (0.75–1.30)	-	0.1% [b]	1898 [b]
NLST 2011 [22]	CXR	26,722	26,732	78	0.51	5.7% (1521)	5.8% (1557)	1,056 [b]	1,086 [b]	0.99 [b] (0.95–1.02)	0.97 [b]	0.1% [b]	755 [b]
DLCST 2012 [19]	Usual Care	2,052	2,052	58	0.08	2.2% (46)	1.5% (31)	-	-	1.20 [b] (1.00–1.44)	-	- 0.7% [b]	-

Note: - = Not Reported.

[a] Based on count data

[b] Calculated by authors

Table 5

Nodule Detection in CT Screening

Study	Number of Participants Screened	% Compliance from Randomization/ Enrollment	Round of Screening [a]	% Participants with Non Calcified Lung Nodules Over Study Threshold [b] (n)	% Participants with Lung Cancer Nodules (n)	% Participants with Benign Nodules (n)	% Nodules not Lung Cancer	% of Participants Diagnosed with Lung Cancer Over Entire Study Period [c]
LDCT versus Usual Care (no screening)								
NELSON 2009 [18]	7,557	95%	Baseline	21% (1570)	0.9% (70)	20% (1500)	96% (1500)	1.6% (124)
	7,289	92%	Year 1	8% (570)	0.7% (54)	7% (516)	91% (516)	
DLCST 2009 [19,38]	2,047	100%	Baseline	9% (179)	0.8% (17)	8% (162)	91% (162)	3.4% (70)
	1,976	96%	Year 1	-	0.6% (11)	-	-	
	1,944	95%	Year 2	-	0.7% (13)	-	-	
ITALUNG 2009 [20]	1,406	87%	Baseline	30% (426)	1.5% (20)	29% (406)	95% (406)	1.5% (20)
DANTE 2009 [21]	1,276	91%	Baseline	18% (226)	3.7% (47)	14% (179)	79% (179)	4.7% (60)
Garg 2002 [16]	92	100%	Baseline	3% (3)	2.2% (2)	1% (1)	33% (1)	2.2% (2)
LDCT versus Chest X-Ray								
NLST 2011 [22,65]	26,309	98%	Baseline	27% (7191)	1.0% (270)	26% (6921)	96% (6921)	4.0% (1060)
	24,715	92%	Year 1	28% (6901)	0.6% (168)	27% (6733)	98% (6733)	
	24,102	90%	Year 2	17% (4054)	0.9% (211)	16% (3843)	95% (3843)	
LSS 2005 [23,66]	1,629	96%	Baseline	19% (316)	1.8% (30)	18% (286)	91% (286)	2.5% (40)
	1,398	86%	Year 1	26% (360)	0.6% (8)	25% (352)	98% (352)	
Depiscan 2007 [24]	336	87%	Baseline	24% (81)	2.4% (7)	22% (74)	91% (74)	2.4% (8)
Cohort Studies of LDCT								
Veronesi 2008 [25, 67]	5,201 [d]	100%	Baseline	11% (560)	1.1% (54)	10% (506)	90% (506)	1.8% (92)
	4821	93%	Year 1	10% (500)	0.4% (19)	10% (481)	96% (481)	
Wilson 2008 [26]	3,642	97%	Baseline	41% (1477)	1.5% (53)	39% (1424)	96% (1424)	2.2% (80)
	3,423	89%	Year 1	42% (1450)	0.7% (24)	42% (1426)	98% (1426)	
Menezes 2010 [27]	3,352 [d]	100%	Baseline	18% (600)	1.3% (44)	17% (556)	93% (556)	1.9% (65)
	2,686	80%	Year 1	10% (259)	0.4% (10)	9% (249)	96% (249)	

Study	Number of Participants Screened	% Compliance from Randomization/ Enrollment	Round of Screening [a]	% Participants with Non Calcified Lung Nodules Over Study Threshold [b] (n)	% Participants with Lung Cancer Nodules (n)	% Participants with Benign Nodules (n)	% Nodules not Lung Cancer	% of Participants Diagnosed with Lung Cancer Over Entire Study Period [c]
	669	20%	Year 2	11% (70)	0.9% (6)	10% (64)	91% (64)	
Sobue 2002 [28]	1,611	96%	Baseline	12% (186)	0.9% (14)	11% (172)	93% (172)	2.2% (36)
	1,180	70%	Year 0.5 [e]	7% (83)	0.3% (3)	7% (80) [f]	96% (80)	
	891	53%	Year 1 [e]	7% (60)	0.6% (5)	6% (55) [f]	92% (55)	
Swenson 2005 [68,69]	1,520	100%	Baseline	51% (780)	2% (31)	49% (749)	96% (749)	4.5% (68)
	1,464	97%	Year 1	13% (191)	0.2% (3)	13% (188)	98% (188)	
	NR	NR	Year 2	-	-	-	-	
Pastorino 2003 [30]	1,035	100%	Baseline	19% (199)	1.1% (11)	18% (188)	95% (188)	2.1% (22)
	996	96%	Year 1	10% (99)	1.1% (11)	9% (88)	89% (88)	
Henschke 2001 [31,70]	1,000	100%	Baseline	23% (233)	2.7% (27)	21% (206)	88% (206)	3.6% [g] (36)
	841	84%	Year 1	3% (30) [g]	0.6% (7) [g]	2% (23) [g]	77% (23)	
	343	34%	Year 2					
Bastarrika 2005 [32]	911 [d]	100%	Baseline	14% (131)	1.3% (12)	13% (119)	91% (119)	1.5% (14)
	424	47%	Year 1	-	0.5% (2)	-	-	
Diederich 2004 [33,71, 72]	817	100%	Baseline	46% (378)	1.3% (11)	45% (367)	97% (367)	1.8% (15)
	668	82%	Year 1	11% (73)	-	-	-	
	549	67%	Year 2	5% (25)	-	-	-	
Novello 2005 [34]	519	99%	Baseline	22% (114)	1% (5)	21% (109)	96% (109)	2.3% (12)
	NR	NR	Year 1	5% (26)	0.6% (3)	5% (23)	88% (23)	
	NR	NR	Year 2	5% (16)	0.6%(3)	3% (13)	81% (13)	
Callol 2007 [35]	466	97%	Baseline	21% (98)	0.2% (1)	21% (97)	98% (97)	1.1% (5)
	406	84%	Year 2 [h]	2% (9)	1% (4)	1% (5)	56% (5)	
MacRedmond 2006 [36, 73]	449	100%	Baseline	-	0.4% (2)	-	-	1.3% (6)
	413	92%	Year 1	-	0.7% (3)	-	-	
Picozzi 2005 [37]	60	100%	Baseline	33% (20)	1.7% (1)	32% (19)	95% (19)	3.3% (2)

Study	Number of Participants Screened	% Compliance from Randomization/ Enrollment	Round of Screening [a]	% Participants with Non Calcified Lung Nodules Over Study Threshold [b] (n)	% Participants with Lung Cancer Nodules (n)	% Participants with Benign Nodules (n)	% Nodules not Lung Cancer	% of Participants Diagnosed with Lung Cancer Over Entire Study Period [c]
	45	75%	Year 1	18% (8)	2.2% (1)	16% (7)	88% (7)	
	42	70%	Year 2	12% (5)	0% (0)	12% (5)	100% (5)	

Note: - = Not Reported.

[a] The majority of studies do not present results beyond the 2nd repeat screening, please see Table 1 for information on the number of planned screens completed.

[b] Data are reported according to the nodule size warranting imaging workup in each study reported in Tables 1 and 2.

[c] Includes interval cancers and those detected by symptoms or other causes over multiple screens with the number screened at baseline as the denominator.

[d] The total number **of participants** enrolled was not reported, only the total number scanned at baseline.

[e] Scans were conducted twice per year

[f] Reviewer calculation.

[g] ELCAP reported cumulative nodule detection data for two followup rounds of screening. Total participants screened in both followup rounds of screening is used as the denominator.

[h] The first repeat scan was conducted 2 years after the initial baseline scan.

Table 6

Frequency of Follow-up Imaging and Surgical Biopsies/Procedures for Detected Nodules

Study	Number of Particpants Randomized	% of Screened Arm with Nodules at Baseline	% of Nodules at Baseline that are Benign	% of Screened Arm Undergoing Additional Diagnostic CT	% of Screened Arm Undergoing Additional PET	% of Screened Arm Undergoing Non-Surgical Biopsy/Procedure	% of Non-Surgical Procedures with Benign Final Result	% of Screened Arm Undergoing Surgical Biopsy/Procedure	% of Surgical Procedures with Benign Final Result
LDCT versus Chest X-Ray									
NELSON 2009 [18]	15,822 [a]	**21**% (1570)	96% (1500)	-	0	3.4% (257)	54% (138)	2.0% (153)	**30% (45)**
DLCST 2009 [38]	4,104	**9**% (179)	91% (162)	-	-	_ [b]	_ [b]	(1.2%) (25) [b]	**(32%) (8)** [b]
ITALUNG 2009 [20]	3,206	**30**% (426)	95% (3843)	-	4.2% (59)	1.1% (16)	6% (1)	1.1% (16)	**6% (1)**
DANTE 2009 [21, 74]	2,811 [c]	**18**% (226)	79% (179)	-	4.5% (57)	-	-	5.6% (72)	**24% (17)**
Garg 2002 [16]	190	**3**% (3)	33% (1)	3.3% (3)	-	-	-	-	-
LDCT versus Usual Care (no screening)									
NLST 2011 [22]	53,454	**25**% (6561)	96% (6291)	33% (8807)	5.5% (1471)	1.5% (402)	73% (293)	2.6% (673)	**24% (164)**
LSS 2005 [23, 66]	3,318	**19**% (316)	91% (286)	-	-	_ [b]	_ [b]	(3.3%) (53) [b]	**(43%) (23)** [b]
Depiscan 2007[24]	765	**24**% (81)	91% (74)	-	-	0.9% (3)	-	3.3% (11) [b]	**27% (3)**[b]
Cohort Studies									
Veronesi 2008 [25, 67]	5,201	**11**% (560)	90% (506)	1% (54)	3% (157)	1.9% (101)	15% (15)	2.0% (106)	**14% (15)**
Wilson 2008 [26]	3,755	**41**% (1477)	96% (1424)	-	-	-	-	2.3% (82)	**34% (28)**
Menezes 2010 [27]	3,352	**18**% (600)	93% (556)	-	-	2.3% (78)	21% (16)	-	-
Sobue 2002 [28]	1,682	**12**% (186)	93% (172)	44.6% (719)	-	3.0% (50)	58% (29)	1.2% (21)	**29% (6)**
Swenson 2005 [68, 69]	1,520	**51**% (780)	96% (749(	-	-	-	-	2.6% (39)	**21% (8)**
Pastorino 2003 [30]	1,035	**19**% (199)	95% (188)	9.2% (95)	4.1% (42)	_ [b]	_ [b]	(2.7%) (28) [b]	**(21%) (6)** [b]
Henschke 2001 [31, 70]	1,000	**23**% (233)	88% (206)	-	-	3.6% (36)	6% (2)	-	-
Bastarrika 2005 [32]	911	**16**% (143)	92% (131)	0% (0)	2.5% (23)	0.7% (6)	17% (1)	1.4% (13)	**0% (0)**
Diederich 2004 [33, 71, 72]	817	**46**% (378)	97% (367)	-	-	_ [b]	_ [b]	(1.8%) (15) [b]	**(27%) (4)** [b]
Novello 2005 [34]	520	**22**% (114)	96% (109)	-	-	-	-	-	-
Callol 2007 [35]	482	-	-	-	-	-	-	1.5% (7)	**29% (2)**

Study	Number of Particpants Randomized	% of Screened Arm with Nodules at Baseline	% of Nodules at Baseline that are Benign	% of Screened Arm Undergoing Additional Diagnostic CT	% of Screened Arm Undergoing Additional PET	% of Screened Arm Undergoing Non-Surgical Biopsy/Procedure	% of Non-Surgical Procedures with Benign Final Result	% of Screened Arm Undergoing Surgical Biopsy/Procedure	% of Surgical Procedures with Benign Final Result
MacRedmond 2006 [36, 73]	449	-	-	-	-	-	-	0.9% (4)	**25% (1)**
Picozzi 2005 [37]	60	**33**% (20)	95% (19)	-	5% (3)	-	-	-	-

[a] Randomization is ongoing with a target accrual of 16000 participants.

[b] Values apply to any invasive procedure (surgical or non-surgical)

[c] The median follow-up was 33.7 months and only 161 participants (6.5% of those screened or followed at baseline) had 5 or more years of follow-up. Baseline data are mainly reported

The role of CT screening for lung cancer: Recommendations from the American College of Chest Physicians and the American Society of Clinical Oncology[1]

Recommendation 1	For smokers and former smokers who are age 55 to 74 and who have smoked for 30 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 over both annual screening with chest radiograph or no screening, but only in settings that can deliver the comprehensive care provided to NLST participants. Grade of recommendation: 2B
Remark 1	*Counseling should include a complete description of potential benefits and harms, as outlined in Tables 1 and 2, so the individual can decide whether or not to undergo LDCT screening.*
Remark 2	*Screening should be conducted in a center similar to those where the National Lung Screening Trial was conducted, with multi-disciplinary coordinated care and a comprehensive process for screening image interpretation, management of findings, and evaluation and treatment of potential cancers.*
Remark 3	*A number of important questions about screening could be addressed if individuals who are screened for lung cancer are entered into a registry that captures data on follow-up testing, radiation exposure patient experience, and smoking behavior.*
Remark 4	*Quality metrics should be developed such as those in use for mammography screening, which could help enhance the benefits and minimize the harm for individuals who undergo screening.*
Remark 5	*Screening for lung cancer is not a substitute for stopping smoking. The most important thing patients can do to prevent lung cancer is not smoke.*
Remark 6	*The most effective duration or frequency of screening is not known.*
Recommendation 2	For individuals who have accumulated fewer than 30 pack years of smoking or are either younger than age 55 or older than 74, or individuals who quit smoking more than 15 years ago, and for individuals with severe comorbidities that would preclude potentially curative treatment and/or limit life expectancy, we suggest that CT screening should not be performed. Grade of recommendation: 2C.

[1]Full text of the ACCP and ASCO evidence based practice guideline on the role of CT screening for lung cancer is available in the online appendix.