Annals of Internal Medicine | Review

Screening for Lung Cancer With Low-Dose Computed Tomography: A Systematic Review to Update the U.S. Preventive Services Task Force Recommendation

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Background: Lung cancer is the leading cause of cancer-related death in the United States. Because early-stage lung cancer is associated with lower mortality than late-stage disease, early detection and treatment may be beneficial.

Purpose: To update the 2004 review of screening for lung cancer for the U.S. Preventive Services Task Force, focusing on screening with low-dose computed tomography (LDCT).

Data Sources: MEDLINE (2000 to 31 May 2013), the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through the fourth quarter of 2012), Scopus, and reference lists.

Study Selection: English-language randomized, controlled trials or cohort studies that evaluated LDCT screening for lung cancer.

Data Extraction: One reviewer extracted study data about participants, design, analysis, follow-up, and results, and a second reviewer checked extractions. Two reviewers rated study quality using established criteria.

Data Synthesis: Four trials reported results of LDCT screening among patients with smoking exposure. One large good-quality trial reported that screening was associated with significant reductions in lung cancer (20%) and all-cause (6.7%) mortality. Three small European trials showed no benefit of screening. Harms included radiation exposure, overdiagnosis, and a high rate of false-positive findings that typically were resolved with further imaging. Smoking cessation was not affected. Incidental findings were common.

Limitations: Three trials were underpowered and of insufficient duration to evaluate screening effectiveness. Overdiagnosis, an important harm of screening, is of uncertain magnitude. No studies reported results in women or minority populations.

Conclusion: Strong evidence shows that LDCT screening can reduce lung cancer and all-cause mortality. The harms associated with screening must be balanced with the benefits.

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In the United States, lung cancer is the third most common cancer among men and women and is the leading cause of cancer-related deaths (1), accounting for almost 27% of all cancer-related deaths. Current estimates suggest that almost 7% of persons born today will be diagnosed with lung cancer in their lifetime, and almost 6% will die of it (2–4). Among heavy smokers, lung cancer accounts for 33% of overall mortality (5). Seventy-five percent of patients with lung cancer present with symptoms due to incurable advanced local or metastatic disease (6).

Approximately 85% of lung cancer cases in the United States are attributable to smoking (7, 8), and a high percentage occurs in former smokers because risk continues after smoking stops (9–11). Approximately 20% of Americans currently smoke, and many more are former smokers (12); thus, lung cancer will remain a major public health problem in the United States for decades. Other persons at increased risk include older adults and those with a family history of lung cancer, chronic obstructive pulmonary disease or pulmonary fibrosis (8, 13, 14), and certain environmental (15–18) and occupational (8, 14) exposures. Some studies suggest that women are at higher risk than men with similar exposures (7, 16, 19, 20).

In 2004, the U.S. Preventive Services Task Force (USPSTF) judged the evidence about the effectiveness of lung cancer screening with chest radiography or low-dose computed tomography (LDCT) as insufficient (21). This systematic review updates evidence on the effectiveness and harms of LDCT screening for lung cancer for the USPSTF.

Methods

Key Questions and Analytic Framework

We developed and followed a standard protocol. A technical report details those methods and includes search strategies and additional evidence tables (22). Using established methods (23), the USPSTF, with input from the Agency for Healthcare Research and Quality (AHRQ), formulated key questions addressing the benefits and harms of screening for lung cancer with LDCT. Investigators created an analytic framework incorporating the key questions and outlining the patient populations, interventions, out-

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comes, and harms of LDCT screening for lung cancer (**Appendix Figure 1**, available at www.annals.org). The target population includes asymptomatic current and former adult smokers.

Data Sources and Searches

In conjunction with a research librarian, investigators searched MEDLINE (2000 to 31 May 2013), the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews (through the fourth quarter 2012), reference lists, and Scopus for relevant English-language studies and systematic reviews.

Data Extraction and Quality Assessment

For each included study, an investigator abstracted details about the patient population, study design, screening procedure, imaging assessment, analysis, follow-up, and results; data were confirmed by a second investigator. Using predefined criteria developed by the USPSTF (23), 2 investigators independently rated the quality of trials, reporting results for both comparison groups (LDCT vs. chest radiography or usual care) as good, fair, or poor; discrepancies were resolved by consensus. When studies reported findings in more than 1 article, data from the most recent publication were used unless unique data were presented in a previous publication.

Data Synthesis and Analysis

We did not perform a meta-analysis because of the substantial heterogeneity in the interventions, follow-up intervals, and quality of the trials. We created forest plots to display the findings and summarize the data qualitatively. We assessed the overall quality of the body of evidence for each key question (good, fair, or poor) using methods developed by the USPSTF on the basis of the number, quality, and size of studies; consistency of results; and directness of evidence (23).

Role of the Funding Source

This research was funded by the AHRQ under a contract to support the work of the USPSTF. Investigators worked with USPSTF members and AHRQ staff to develop and refine the scope, analytic framework, and key questions; resolve issues arising during the project; and finalize the report. Staff from the AHRQ provided project oversight; reviewed the draft report; and distributed it for peer review, which included representatives of professional societies and federal agencies. The AHRQ performed a final review of the manuscript to ensure that the analysis met methodological standards but had no role in study selection, quality assessment, synthesis, or development of conclusions. The investigators are solely responsible for the content and the decision to submit the manuscript for publication. The Department of Veterans Affairs did not have a role in the conduct of the study; the collection, management, analysis, or interpretation of data; or the preparation of the manuscript.

RESULTS

A total of 8215 abstracts was reviewed; 67 full-text articles met inclusion criteria for one of the key questions and were included (**Appendix Figure 2**, available at www.annals.org) (20, 24–89).

Trials of LDCT

We identified 7 randomized, controlled trials that reported results of LDCT screening but limited our review of effectiveness to the 4 (39, 53, 57, 60) that reported results in the intervention and control groups (**Appendix Table 1**, available at www.annals.org). The **Table** shows the demographic characteristics of study participants, screening strategies, and quality ratings. The full report describes screening programs, follow-up protocols, and procedures (22).

The NLST (National Lung Screening Trial) was a good-quality trial comparing 3 annual LDCT scans with 3 annual single-view posterior–anterior chest radiographs (53, 88). The trial was conducted at 33 U.S. sites and included asymptomatic men and women aged 55 to 74 years who were current or former (<15 years since quitting) smokers (≥30 pack-years): 26 722 were randomly assigned to LDCT and 26 732 to chest radiography.

The DANTE (Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays) trial (39, 40) was a fair-quality Italian trial comparing the addition of LDCT with usual care without LDCT. Male current or former smokers (≥20 pack-years) without significant comorbid conditions aged 60 to 74 years were included: 1276 were randomly assigned to LDCT and 1196 to usual care. All participants had a baseline clinical interview and examination, chest radiography, and 3-day sputum cytology; those in the intervention group also received LDCT. All participants were followed annually with clinical interviews and physical examinations focused on detecting lung cancer; the intervention group also received 4 annual LDCTs.

The DLCST (Danish Lung Cancer Screening Trial) (60) was a fair-quality, single-center trial comparing LDCT with no lung cancer screening. The study was planned to last 5 years, with a baseline LDCT followed by 4 annual LDCTs. The study population included healthy men and women aged 50 to 70 years who were current or former smokers (≥20 pack-years) and were able to walk up at least 36 stairs without stopping. Former smokers must have quit after age 50 years and less than 10 years before enrollment. All participants had baseline and annual pulmonary function tests and completed health questionnaires. A total of 2052 participants was randomly assigned to LDCT and 2052 to usual care.

The MILD (Multicentric Italian Lung Detection) study was a poor-quality, single-center trial comparing annual or biennial LDCT with no lung cancer screening (57). The trial included men and women aged 49 years or older who were current or former (quit <10 years ago)

Table. **Summary of Included Randomized, Controlled Trials**

Study, Recruitment Years (Reference)	Population*	Baseline Smoking Status*	Screening Rounds, *n*	Screening Intervals, *y*	Total Median Follow-up	Follow-up After Screening Ended	Quality
LDCT vs. chest radiography							
NLST, 2002–2004 (53)	*n* = 26 722 vs. 26 732 Age: 55–74 y Men: 59%	Current: 48% vs. 48% Former: 52% vs. 52% Mean pack-years: 56	3	0, 1, 2	6.5 y (maximum, 7.4 y)†	NR but presumably 4.5 y	Good
LDCT vs. no LDCT							
DANTE, 2001–2006 (39, 40)‡	*n* = 1276 vs. 1196 Age: 60–74 y Men: 100%	Current: 56% vs. 57% Former: NR Mean pack-years: 47.3 vs. 47.2	5	0, 1, 2, 3, 4	33.7 mo (range, 1.8–79.2 mo)	NR (final results pending)	Fair§
DLCST, 2004–2006 (60)	*n* = 2052 vs. 2052 Age: 50–70 y Men: 55%	Current: 75% vs. 77% Former: 25% vs. 23% Mean pack-years: 36.4 vs. 35.9	5	0, 1, 2, 3, 4	4.8 person-years	NR	Fair‖
MILD, 2005–2011 (57)	*n* = 2376 (1190 annual, 1186 biennial) vs. 1723 Age: ≥49 y Men: 66%	Current: 68% vs. 68% vs. 90%¶ Former: 31% vs. 32% vs. 10%¶ Median pack-years: 39 vs. 39 vs. 38¶	Median number of CTs, annual vs. biennial: 5 vs. 3	Annual vs. biennial: every 12 mo (0, 1, 2, 3, 4 y) vs. every 24 mo (0, 2, 4 y)	4.4 y (maximum, 6 y)	Recruitment ended January 2011; follow-up until November 2011	Poor**

CT = computed tomography; DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays; DLCST = Danish Lung Cancer Screening Trial; LDCT = low-dose computed tomography; MILD = Multicentric Italian Lung Detection; NLST = National Lung Screening Trial; NR = not reported.
* LDCT vs. control.
† Follow-up for lung cancer mortality was 5.5 y.
‡ All participants had baseline chest radiography.
§ Unclear allocation, differences in baseline demographic characteristics, differential follow-up.
‖ Unclear allocation, differential follow-up.
¶ Annual vs. biennial vs. control.
** Inadequate randomization, differences in baseline demographic characteristics, differential follow-up.

smokers (≥20 pack-years) with no history of cancer in the previous 5 years. A total of 1190 participants was randomly assigned to annual LDCT, 1186 to biennial LDCT, and 1723 to usual care.

Effectiveness of Screening for Lung Cancer With LDCT

Participants in the DLCST and the MILD study were younger and had less smoking exposure than those in the NLST and the DANTE trial (**Table**). Lung cancer incidence and mortality and all-cause mortality were lower in the control groups of the DLCST and the MILD study than in those of the NLST and the DANTE trial (22).

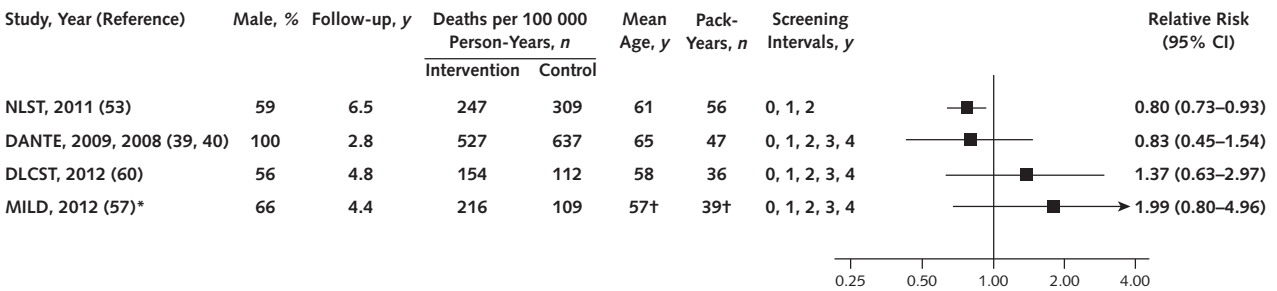
The NLST was stopped early after 6.5 years of follow-up when lung cancer mortality was reduced by 20.0% (95% CI, 6.8% to 26.7%) in the LDCT group. The reported number needed to screen (NNS) to prevent 1 lung cancer death was 320 among participants who completed 1 screening. All-cause mortality was also reduced by 6.7% (CI, 1.2% to 13.6%), with the NNS to prevent 1 death reported as 219 (53).

The DANTE trial found that, after a median follow-up of 34 months, the relative risk (RR) of lung cancer mortality among the LDCT group was 0.83 (CI, 0.45 to 1.54). All-cause mortality was equal in both groups at 3 years, with an RR of 0.85 (CI, 0.56 to 1.27) (39). These RRs were calculated with the reported person-months of follow-up appropriate for each study group (rather than the median), which was longer in the LDCT group by 657 person-months (35.7 months follow-up for the LDCT group vs. 31.5 months for the control group) (39).

In the DLCST, after a median follow-up of 4.8 years, the RRs were 1.37 (CI, 0.63 to 2.97) for lung cancer mortality and 1.46 (CI, 0.99 to 2.15) for all-cause mortality in the LDCT group (60).

In the MILD study, the RR for lung cancer mortality in the biennial LDCT group compared with the control group was 1.00 (CI, 0.34 to 2.98); the RR was 1.98 (CI, 1.57 to 2.50) in the annual LDCT group compared with the control group. All-cause mortality did not significantly differ between the combined screening groups and the control group (RR, 1.40 [CI, 0.82 to 2.38]). However, when comparing the annual LDCT group with the control group, the RR for all-cause mortality was 1.80 (CI, 1.56 to 2.07) (57). These RRs are calculated on the basis of the

Figure 1. **Trial results for lung cancer mortality.**



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; NLST = National Lung Screening Trial.
* Annual screening group compared only with control group; biennial screening group not shown.
† Median.

follow-up reported for each study group, which differed between groups (45 months for the combined LDCT group vs. 56 months for the control group).

Figures 1 and **2** show the summary results for the 4 trials.

Benefits by Subgroup

All of the trials were conducted in participants at high risk for lung cancer based on current or former smoking. However, the differences in lung cancer incidence in the control groups indicate that the studies included participants whose risk varied substantially. No trials evaluated persons at low or average risk, and, to date, none has reported findings by sex or race or ethnicity.

Other Outcomes of Lung Cancer Screening With LDCT

Seven trials and 13 cohort studies (**Appendix Table 2**, available at www.annals.org) (22) reported outcomes other than lung cancer mortality.

Radiation

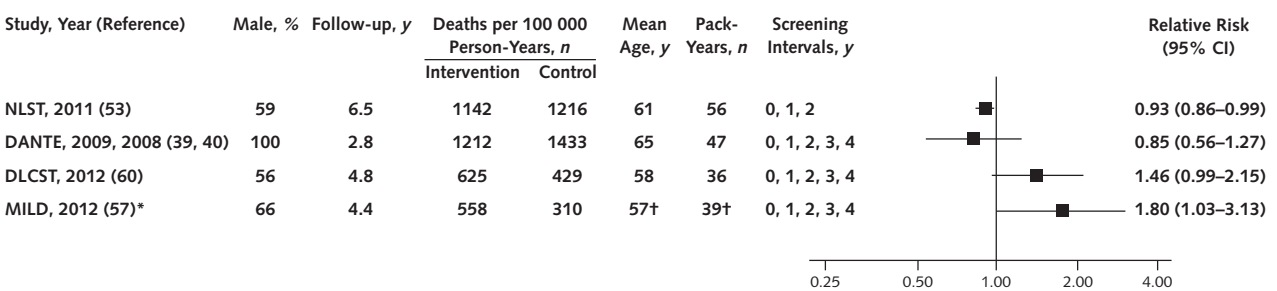
Two trials (53, 57) and 3 cohort studies (26, 67, 80, 81) reported that radiation associated with 1 LDCT ranged from 0.61 to 1.50 mSv. Only the ITALUNG study reported cumulative radiation exposure associated with screening and follow-up evaluations, which was estimated at 6 to 7 mSv for baseline LDCT and 3 subsequent annual LDCTs (49, 50).

False-Positive Findings and Follow-up Evaluations

Participants with positive results on baseline screening ranged from 9.2% to 51.0%, with calculated positive predictive values (PPVs) for abnormal screening results ranging from 2.2% to 36.0% (31, 33, 34, 37, 43, 44, 52, 59, 67, 71, 78, 80, 81, 83, 88). Positive results were lower in subsequent screenings, with PPVs for abnormal results predicting lung cancer of 4% to 42%. As nodule size increases, the PPV increases. For example, among participants in the NLST, the overall PPV for nodules 4 mm or larger identified on baseline LDCT was 3.8%, but the PPV was 0.5% for 4- to 6-mm nodules and 41.3% for those larger than 30 mm (88).

In the I-ELCAP (International Early Lung Cancer Action Program) trial, 3396 of the 21 136 participants had

Figure 2. **Trial results for all-cause mortality.**



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; NLST = National Lung Screening Trial.
* Annual screening group compared only with control group; biennial screening group not shown.
† Median.

nodules 5 mm or larger. Among 2558 participants with nodules between 5.0 and 9.0 mm, only 8 had lung cancer diagnosed within 12 months after baseline enrollment. Among 285 participants with nodules 15 mm or larger, 29.8% were diagnosed with lung cancer (89). Most abnormal results resolved after further imaging. The PPV for abnormal LDCT results with recommendations for biopsy ranged from 50% to 92% (33, 34, 39, 40, 43, 52, 53, 78, 80, 81, 83).

In the NLST, at least 1 complication occurred in association with follow-up of 245 LDCTs and 81 chest radiographies. Major complications were infrequent in both groups. Among the 649 cases of lung cancer found after a positive screening result, 73 and 23 major complications occurred in the LDCT and chest radiography groups, respectively, after an invasive procedure.

Among participants with positive results who were found not to have lung cancer, 12 and 4 major complications occurred in the LDCT and chest radiography groups, respectively. Sixteen participants in the LDCT group and 10 (all with lung cancer) in the chest radiography group died within 60 days of an invasive procedure. Whether the procedure was the cause of death is unknown (53). These procedures were only described for cases of lung cancer identified in the screening period. During follow-up, 411 cases of lung cancer were identified in the LDCT group and 662 in the chest radiography group, all probably requiring a diagnostic procedure.

False Reassurance

There is no gold standard for negative findings on screening LDCT, and sensitivity is typically determined by considering new incidents of lung cancer presenting within 1 year of a screening study as false-negative. In the 6 studies reporting this variable, sensitivity of LDCT for detecting lung cancer ranged from 80% to 100% (most often >90%), implying a false-negative rate of 0% to 20% (52, 67, 70, 71, 78, 80, 81). Raising the threshold for nodule sizes to consider positive will increase specificity for lung cancer but decrease sensitivity (89). No study evaluated the harm of false reassurance.

Overdiagnosis

No study formally reported overdiagnosis. Among 4 trials reporting results from groups with and without LDCT, the NLST suggested overdiagnosis, reporting more than 119 cases of lung cancer among 26 722 participants in the LDCT group after 6.5 years of follow-up (53). This trial also involved fewer late-stage cases of lung cancer in the LDCT group than in the chest radiography group. The 3 other trials reported more early-stage lung cancer in the LDCT groups than in the control groups but not fewer cases of advanced lung cancer (39, 40, 57, 60). However, insufficient and unequal follow-up in these studies limit the evaluation of overdiagnosis.

Psychosocial Consequences

Seven studies (27, 64, 72–74, 86, 87) evaluated psychosocial consequences among persons undergoing LDCT screening. In 2 European LDCT trials (NELSON [Dutch–Belgian Randomised Controlled Trial for Lung Cancer Screening in High-Risk Subjects] [74] and the DLCST [86, 87]), screening did not affect overall health-related quality of life or long-term anxiety. In the short term, the studies suggested increased anxiety or distress compared with baseline among participants with positive or indeterminate results (27, 64, 72, 73). Distress and fear of cancer decreased compared with baseline among those with negative results (27, 73).

Smoking Behavior

Two trials identified no differences in smoking cessation rates, relapse rates, or intensity when comparing persons randomly assigned to LDCT versus no LDCT (25, 75). In 2 trials, smoking behavior showed mixed results (comparing abnormal vs. normal findings): One showed a tendency toward smoking abstinence (25), and the other showed no difference (76). Cohort studies comparing abnormal with normal findings (24, 69) showed similar mixed results. One cohort study found that physician referral for patients with abnormal findings on LDCT increased smoking cessation rates compared with nonreferral for those with normal findings (66).

Incidental Findings

Most of the included studies reported incidental findings, but no standardized approach was available to report them. Nonpulmonary findings were common; infections and other types of cancer were also diagnosed. The NLST probably provides the best estimate of the frequency of incidental findings: 7.5% of all LDCT scans and 2.1% of all chest radiographs identified a "clinically significant" abnormality not suspicious for lung cancer (53). Coronary artery calcification was identified in approximately 50% of participants in 1 cohort study (62).

Discussion

The personal and public health consequences of lung cancer are enormous, and even a small benefit from screening could save many lives. This review found that in 1 large, good-quality trial that used 3 annual LDCTs to screen high-risk persons aged 55 to 74 years, lung cancer and all-cause mortality were reduced in the LDCT group compared with the annual chest radiography group by 20% and 7%, respectively (**Appendix Table 3**, available at www.annals.org) (53). Twenty-five percent of the overall deaths in the control group were from lung cancer in this study, highlighting the large contribution of this disease to overall mortality in this age and risk strata of the population.

One fair-quality Italian trial involving men older than 60 years suggested that screening CT reduced lung cancer mortality, but this association was not significant (39, 40). Two European trials (1 fair-quality [60] and 1 poor-quality [57]) in lower-risk and younger patients showed no benefit of LDCT screening in reducing lung cancer mortality. In the evidence report (22), we found no data to support chest radiography for lung cancer screening, although data from the PLCO (Prostate, Lung, Colorectal, and Ovarian) Cancer Screening Trial suggested a benefit among high-risk persons and possibly high- and average-risk women (22, 56). This suggests that, if there is any benefit of chest radiography screening, the benefit of lung cancer screening with LDCT shown in the NLST may be even greater if applied to an unscreened population.

Several factors may account for differential mortality among trials. First, the European studies enrolled fewer patients and had shorter follow-up than the NLST and had inadequate power to detect a difference in lung cancer mortality. In addition, the DANTE trial had reduced power to detect a difference, because 9 patients in the control group and 16 patients in the LDCT group were diagnosed with lung cancer at baseline with chest radiography and sputum cytology. This difference also suggests possible inadequate randomization or inadequate sample size, because the baseline risk for cancer diagnosed by sputum cytology or chest radiography was nearly 2-fold higher in the LDCT group.

Second, follow-up durations among randomized groups differed in the European trials. Adjustment for actual follow-up months by group in the MILD and DANTE studies markedly changed results, with the latter suggesting a benefit of screening rather than a neutral effect. However, this difference was not significant. In addition, the DLCST investigators noted that follow-up for lung cancer in the control group was less complete than in the intervention group, but they did not provide actual follow-up time.

Third, participants in the studies showing or suggesting reduced lung cancer mortality (NLST and the DANTE trial) were older with greater smoking exposure than those in studies not showing benefit (**Table**). Of note, lung cancer incidence and mortality and overall mortality rates in the NLST and the DANTE trial were 2- to 4-fold higher than in the DLCST and the MILD study, suggesting that LDCT screening might be more beneficial in higher-risk populations. A recent modeling study supports this hypothesis, finding that the NNS to save 1 life from lung cancer over 6 years (3 years of annual screening) was 82 for high-risk participants compared with 3180 for minimally eligible NLST participants (90).

Fourth, results from the MILD study should be interpreted with caution. The trial was rated poor-quality because of inadequate randomization with systematic differences between groups and differential follow-up. Finally, differential mortality among trials may be due to different population characteristics and systems of medical care in Europe than in the United States.

The potential benefits of lung cancer screening must be weighed against potential harms. Because of the low PPV of screening LDCT, subsequent procedures are often needed for diagnosis. These procedures are usually noninvasive, such as clinical examinations, repeated CT, and positron emission tomography; however, some may be invasive, such as biopsy and surgery. In the studies that we reviewed, most invasive procedures performed were for cancer, not benign disease, with a PPV ranging from 50% to 92% in included studies. This contrasts with the high number of false-positive findings requiring further evaluation with imaging or clinical follow-up, which were predominantly done for benign disease. Screening with LDCT did not seem to reduce overall quality of life or affect smoking rates. In addition, LDCT detected many incidental findings, such as emphysema and coronary artery calcifications, but the effect of these findings was not studied.

Overdiagnosis and consequent overtreatment is a concern in lung cancer screening. The 1% to 2.7% prevalence of unrecognized lung cancer suggests a preclinical pool of lung cancer in high-risk populations. The clinical significance of these tumors is uncertain, but patients with lung cancer typically receive treatment, resulting in harm to those with nonlethal cancer. Elderly smokers have high mortality rates from causes other than lung cancer, which also increases the risk for overdiagnosis.

In the future, biomarkers and CT variables, such as volume-doubling time and nodule size, may help discriminate among biologically aggressive and indolent tumors (82, 89). Arguments against substantial overdiagnosis come from autopsy studies that report low rates of unsuspected lung cancer, as well as natural history studies showing high mortality rates among untreated patients with early-stage lung cancer (63, 91–93). Overall, the reductions in lung cancer and all-cause mortality in the NLST, despite a higher incidence of lung cancer in the LDCT group (1040 vs. 941 cases), suggest that the benefit of screening outweighs the potential harm of overdiagnosis (53).

Radiation exposure is a harm of LDCT lung cancer screening (94). For context, LDCT is associated with radiation exposure near that of mammography. Radiation-induced cancer over 10 to 20 years is particularly concerning, although none of the studies reported on this potential outcome. Radiation dose varies by body weight, CT detector and manufacturer, and the number of images obtained. In many institutions, current practice involves following nodules with LDCT rather than high-resolution CT, which substantially reduces radiation exposure. If LDCT screening becomes routine, it will be important to measure the risk for radiation-associated harms and identify methods to lower the dose.

Our review differs from a recently published systematic review of LDCT screening (95). First, our review is

more comprehensive, because we identified 8215 citations compared with 591. For example, we identified 7 studies that reported psychosocial outcomes (3 of which reported quality of life), whereas the other review identified 1 study. Second, studies published since the other review provide new data. Third, we analyzed rates of lung cancer and mortality by using the actual person-years of follow-up, which affects the effect size observed in 2 of the trials.

Our review has limitations. The NLST results may not be generalizable, because participants were younger, better educated, and less likely to be current smokers than the general U.S. population that would be eligible for LDCT screening by NLST criteria (96). The trial was conducted at mostly large academic centers. However, the large size of the trial, as well as the involvement of community health care providers in nodule management and treatment, may mitigate this concern. Furthermore, differences in population characteristics and systems of medical care and the small sample sizes used in the European studies may limit applicability to a U.S. population. Other limitations include a lack of specific information on LDCT screening in women and racial and ethnic groups. Studies of cost-effectiveness, modeling studies of radiation risk, and studies that evaluated patient perspectives on screening were not included because they were considered out of the scope of our review.

Future research to identify methods for focusing LDCT screening on persons at highest risk for disease, to improve discrimination between benign and malignant pulmonary nodules, and to find early indicators of aggressive disease is warranted. Studies have examined the role of biomarkers in these settings, and the NLST has collected biological specimens during enrollment; however, no results have yet been reported (53). New studies of risk modeling that could apply to currently screened groups, such as the Bach and Liverpool risk models, may facilitate identification of patients at higher risk who might benefit differentially from screening with LDCT (95, 97).

If LDCT screening becomes routine, the risk for harms should be measured and methods to limit them should be identified. It is also important to continue to evaluate the psychosocial consequences in patients who undergo screening, because psychological responses to screening and abnormal or normal results may differ between patients participating in research studies and the general population.

In conclusion, LDCT screening seemed to reduce lung cancer mortality. This result was driven by 1 large, good-quality study conducted in the United States in which the NNS to prevent 1 lung cancer death (among those who completed at least 1 screening) was 320 and the NNS to prevent 1 death overall was 219 over 6.5 years. These benefits compare with numbers needed to invite to screen to prevent 1 breast cancer death in mammography trials of 1339 for women aged 50 to 59 years after 11 to 20 years of follow-up (98, 99). They also compare with an NNS with flexible sigmoidoscopy of 817 to prevent 1 colon cancer death (100). Given the high number of current and former smokers in the population at risk for lung cancer, identifying and treating early-stage lung cancer with screening will hopefully clarify the balance of benefits and harms associated with screening. In addition, more work in public health to reduce smoking remains the most important approach to reducing morbidity and mortality from lung cancer.

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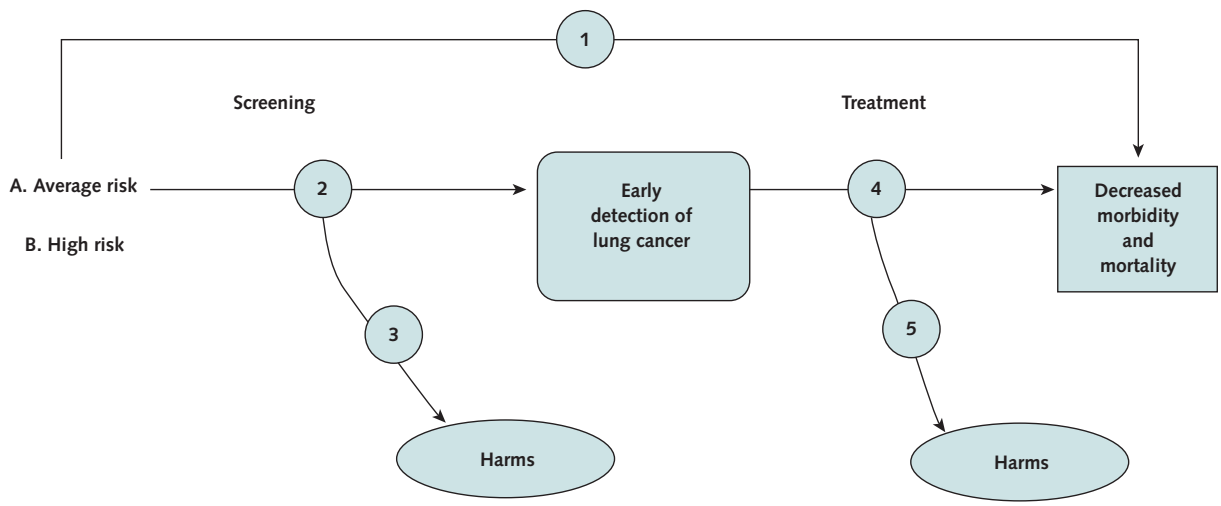
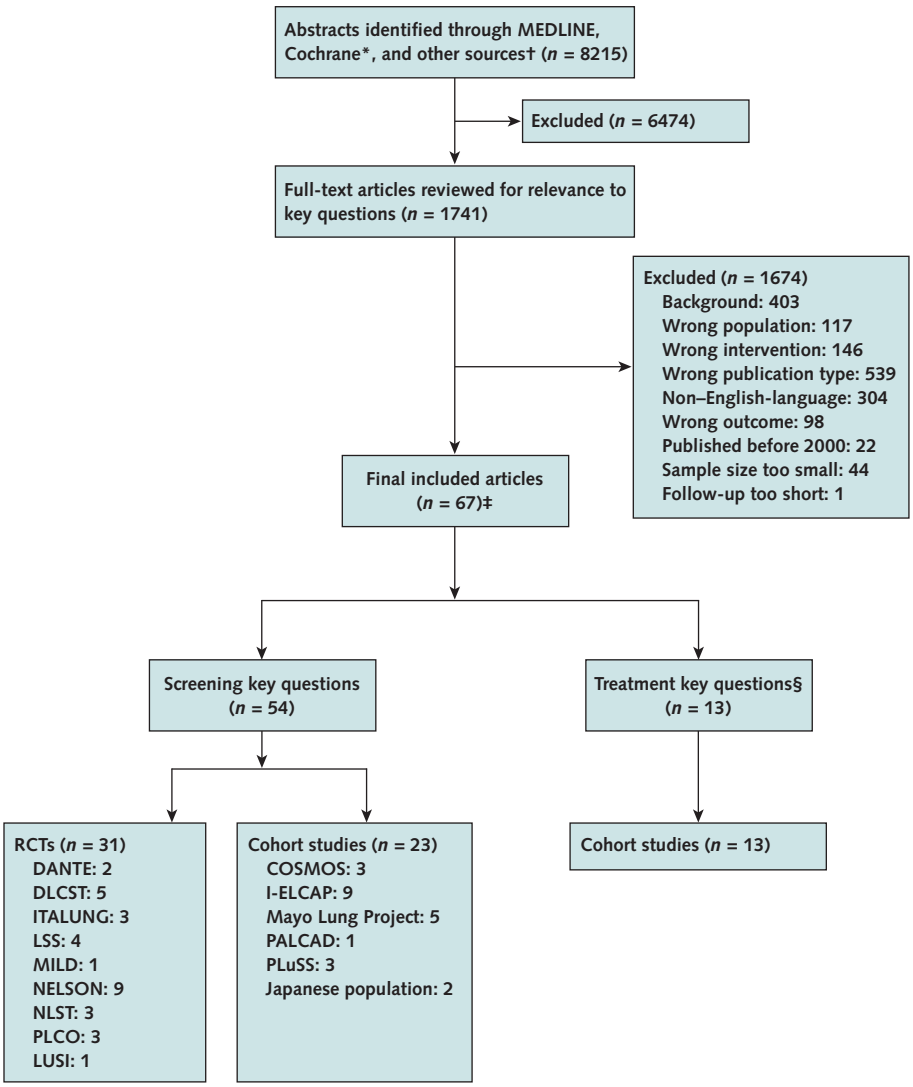
Appendix Figure 1. **Analytic framework.**



Key Questions:

1. **How effective is screening for lung cancer in reducing morbidity and mortality?**
   a. **How effective is screening in persons at average risk?**
   b. **How effective is screening in persons at higher risk for lung cancer (e.g., current or former smokers)?**
   c. **Does effectiveness differ by subgroup (e.g., sex, age, race, presence of comorbid conditions, and other lung cancer risk factors)?**
2. **What are the test characteristics (sensitivity, specificity, and predictive value) of screening tests for lung cancer?**
   a. **How do these test characteristics vary by lung cancer risk?**
   b. **How do test characteristics differ by subgroup (e.g., sex, age, and race)?**
3. **What are the harms associated with lung cancer screening, and are there ways to modify harms (e.g., unnecessary biopsies, radiation exposure, overdiagnosis, and psychosocial harms)?**
4. **How effective is surgical resection for the treatment of early (stage IA) non–small-cell lung cancer?**
5. **What are the harms associated with surgical resection of early (stage IA) non–small-cell lung cancer?**

Appendix Figure 2. **Summary of evidence search and selection.**



COSMOS = Continuing Observation of Smoking Subjects; DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays; DLCST = Danish Lung Cancer Screening Trial; I-ELCAP = International Early Lung Cancer Action Program; LSS = Lung Screening Study; LUSI = Lung Cancer Screening Intervention; MILD = Multicentric Italian Lung Detection; NELSON = Dutch–Belgian Randomised Controlled Trial for Lung Cancer Screening in High-Risk Subjects; NLST = National Lung Screening Trial; PALCAD = ProActive Lung Cancer Detection; PLCO = Prostate, Lung, Colorectal, and Ovarian; PLuSS = Pittsburgh Lung Screening Study; RCT = randomized, controlled trial.

* Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.

† Identified from reference lists or hand searching and suggested by experts.

‡ Studies that provided data and contributed to the body of evidence were considered included.

§ In the final report (24); not reported in this review.

Appendix Table 1. Evidence Table for Included Randomized Trials

Study, Year (Reference)	Population	CT vs. Control	Adverse Events/Harms
NLST, 2011 (53)	53 454 asymptomatic men and women, aged 55–74 y, current or former (quit ≤15 y ago) smokers with ≥30–pack-year history CT (n = 26 722) vs. chest radiography (n = 26 732) CT: Low-dose (1.5 mSv)*, multidetector, ≥4 channels Chest radiography: 1 view, PA with deep inspiration	LC incidence: 1060 (645 per 100 000 person-years) vs. 941 (572 per 100 000 person-years) LC mortality: 356 (247 per 100 000 person-years); RR, 20% (95% CI, 6.8%–27%) vs. 443 (309 per 100 000 person-years) All-cause mortality: 1877; RR, 6.7% (CI, 1.2%–14%) Additional procedures Biopsy: 656 vs. 352 Surgery, by round Baseline: 4.0% vs. 4.8% Round 1: 4.2% vs. 5.2% Round 2: 2.9% vs. 3.5% Round 3: 5.6% vs. 5.8%	CT: 16 participants died within 60 d of invasive procedure (10 had LC) Chest radiography: 10 participants died within 60 d after invasive procedure (10 had LC)
DANTE, 2009, 2008 (39, 40)	2472 asymptomatic men, aged 60–74 y, current or former smokers with ≥20–pack-year history CT (n = 1276) vs. annual clinic review (n = 1196) Mean age: 64.3 vs. 64.6 y Current smoker: 56% vs. 57% Mean pack-years: 47.3 vs. 47.2 Prior cancer (considered cured): 1.0% vs. 0.6% Respiratory comorbid condition: 35% vs. 31%; P = 0.04	LC incidence: 4.7% (n = 60) vs. 2.8% (n = 34); P = 0.02 Total cases of LC: 4.9% (n = 63) vs. 3.0% (n = 36) LC mortality: 1.6% (n = 20) vs. 1.7% (n = 20); P = 0.84 All-cause mortality: 3.6% (n = 46) vs. 3.8% (n = 45); P = 0.83 Other causes of death: 2.0% (n = 26) vs. 2.1% (n = 25); P = 0.93 Stage IA: 1.6% (n = 20) vs. 0.3% (n = 4) All stage I: 2.6% (n = 33) vs. 1.0% (n = 12); P = 0.004 Stage II: 0.3% (n = 4) vs. 0.2% (n = 2) Stage IIIA: 0.6% (n = 7) vs. 0.3% (n = 4) Stage IIIB: 0.5% (n = 6) vs. 0.3% (n = 3) Stage IV: 0.9% (n = 11) vs. 1.2% (n = 14) Additional procedures Biopsy: 7.5% (n = 96) vs. 3.0% (n = 36) VATS: 20 vs. 6; P = 0.01 Thoracotomy: 46 vs. 20; $P \leq 0.001$	CT vs. control False-positive results After VATS: 6/15 (40%) vs. 2/6 (33%) After thoracotomy: 6/41 (15%) vs. 3/20 (15%) After any major surgical procedure: 6/45 (13%) vs. 3/20 (15%)
DLCST, 2012 (60)	4104 healthy men and women, aged 50–70 y, current or former smokers with ≥20–pack-year history CT (n = 2052) vs. usual care (n = 2052) Mean age: 57.9 vs. 57.8 y Mean pack-years: 36.4 vs. 35.9 Current/former smokers: 1545/507 vs. 1579/473	LC incidence: 69 vs. 24 LC mortality: 0.7% (n = 15) vs. 0.5% (n = 11); P = 0.42 All-cause mortality: 3.0% (n = 61) vs. 2.1% (n = 42); P = 0.059 Stage I or II: 44 vs. 8 Stage III or IV: 21 vs. 16 Additional procedures Biopsy: 22 bronchoscopies, EBUSs, EUSs, or CT biopsies Surgery: 18 VATSs and/or mediastinoscopies; 3 thoracotomies, 1 with pneumonectomy Surgery screen: 7 VATSs for benign disease	1 death reported after thoracotomy for stage IA adenocarcinoma
MILD, 2012 (57)	4099 smokers, aged ≥49 y, >20 pack-years or quit <10 y ago Annual CT (n = 1190) vs. biennial CT (n = 1186) vs. usual care (n = 1723) Men: 63% to 68% Former smokers: 10% Mean pack-years: 38–39	Annual CT vs. biennial CT vs. usual care LC incidence: 34 (662 per 100 000 person-years) vs. 25 (457 per 100 000 person-years) vs. 20 (216 per 100 000 person-years) Stage IA: 59% vs. 55% vs. NR Stage IV: 17% vs. 15% vs. NR Additional procedures Biopsy: NR Surgery, CT group only: 83%–85% of cases of LC resected; 4/45 (9%) of all surgeries for benign disease	NR

CT = computed tomography; DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays; DLCST = Danish Lung Cancer Screening Trial; EBUS = endobronchial ultrasonography; EUS = endoscopic ultrasonography; LC = lung cancer; MILD = Multicentric Italian Lung Detection; NLST = National Lung Screening Trial; NR = not reported; PA = posterior–anterior; RR = relative risk; VATS = video-assisted thoracoscopic surgery.
* Whole body effective dose.

Appendix Table 2. Included Cohort Studies

Study, Year (Reference)	Population	Intervention vs. Control	Adverse Events/Harms	Duration of Follow-up
LSS, 2005 (34)	3318 men and women, aged 55–74 y, current or former (quit <10 y ago) smokers with ≥30–pack-year history CT (n = 1660) vs. PA CXR (n = 1658) At 1 y: 1398 vs. 1317	Screening-detected LC: 38/40 vs. 16/20 Stage I: 48% vs. 40% Additional procedures Bronchoscopy at 1 y: 14 vs. 8 Biopsy/resection at 1 y: 18 vs. 10 Surgery: NR vs. NR	Participants with complications related to follow-up: 6 LDCT tracheobronchitis: 1 LDCT complications: 3 Pneumothorax: 1 Incision infection: 1 Pneumonia/ARDS: 1 CXR DVT: 2	NR
ITALUNG, 2009 (44)	1613 participants, aged 64 y (range, 55–69 y), ≥20 pack-years within the past 10 y CT (n = 1406) vs. usual care (n = 1593)	639 nodules in 426 participants LC: 20 (1 with 2 primary) NSCLC: 86% Stage I: 10 Stage IA: 8 Additional procedures: 16 FNA biopsies in 15 participants 12 FNA biopsy specimens positive for LC, 2 indeterminate (later LC), 1 benign 17 cases of cancer surgically resected in 16 participants; 1 resection for a benign lesion (101) Mean collective effective dose: 8.75–9.36 Sv Mean effective dose per patient over 4 y: 6.26.8 mSv* Mean number of radiation-induced cases of cancer: 0.12–0.33 per 1000 patients (0.12–0.13 per 1000 men; 0.31–0.33 per 1000 women)	NR Radiation dose	3 y
NELSON, 2009, 2010, 2011, 2007, 2009, 2012 (74–79)	15 822 asymptomatic men and women; mean age, 59 y (SD, 6); smoking history of 15 cigarettes/d for >25 y or >10 cigarettes/d for >30 y and if former smoker quit ≤10 y ago CT (n = 7907) vs. no screening (n = 7915) Women: 16%	LC diagnosis: 1.6% (n = 127) vs. NR Overall positive scan: 2.7% (n = 209) vs. NR Additional procedures Biopsy: 3.2% (n = 247) bronchus, 0.2% (n = 16) FNA Surgery: 2% (n = 153), 0.6% (n = 45) for benign disease	29% of VATS or other surgeries for benign nodules	2 y
PLCO, 2011 (56)	154 901 men and women, aged 55–74 y, smokers, current or former (quit <15 y ago) smokers with ≥30–pack-year history CXR (n = 77 445) vs. usual care (n = 77 456) Men: 50 vs. 50 White: 86 vs. 85 Current smokers: 10 vs. 10 Former smokers: 42 vs. 42 Never smokers: 45 vs. 44 NLST-eligible: 20 vs. 21 Family history: 11 vs. 11	LC incidence: 20.1 vs. 19.2 per 10 000 person-years LC mortality: RR, 0.99 (95% CI, 0.87–1.22) Stage IA: 32% vs. 27% Stage IV: 22% vs. 55% Additional procedures Biopsy: NR Surgery: NR	54 persons without LC had a complication of a diagnostic follow-up procedure, including pneumothorax, atelectasis, and infection Adverse events in the usual care group: NR	Median 12 y
COSMOS, 2008 (80, 81)	5200 asymptomatic men and women, aged >50 y, current or former (quit <10 y ago) smokers with ≥20–pack-year history Median pack-years: 44 Mean age: 57.7 y Men: 64% Current smokers: 80%	LDCT only Cases of cancer diagnosed at baseline: 55 Cases of cancer diagnosed at 1 y: 13 Incidence: 13 Stage I: 66% Additional procedures Biopsy: 101 (86 malignant, 15 benign) Surgery: 62 (first year), 46 (second year)	Benign lesions diagnosed at surgery (false-positive): 15 patients (14% of surgical cases) Major postoperative illness: 4/86	NR
Toyoda et al, 2008 (70)	18 070 current smokers from Osaka between 1998 and 2000 recommended to have LDCT and sputum cytology LDCT (n = 4689) vs. CXR (n = 13 381)	Sensitivity Overall: 89% Smokers: 84% Nonsmokers: 100% Adenocarcinoma LDCT: 100% Nonadenocarcinoma: 62% Women: 85% Men: 91%		

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Appendix Table 2—**Continued**

Study, Year (Reference)	Population	Intervention vs. Control	Adverse Events/Harms	Duration of Follow-up
		Specificity LDCT: 93% CXR: 97% LDCT baseline: 91% LDCT annual: 96% Men LDCT: 92% Women: 94% Smokers: 92% Nonsmokers: 94%	NR	NR
Tsushima et al, 2008 (71)	2486 high-risk men (70% ever smokers) and medium-risk women (11% ever smokers) Mean age: 51 y Women: 39%	LDCT multislice only Negative: 2132 Seminegative: 140 Patients with nodules: 354 (14%) Semipositive: 111 Positive: 103 HRCT: 183 Cases of cancer: 7 Cases of cancer in nonsmoking women: 3/7	NR	NR
Henschke et al, 2004 (37)	ELCAP 1 (CXR): 1000 men and women, aged ≥60 y, with ≥10–pack-year smoking history; women: 46% ELCAP 2: 1968 men and women, aged ≥40 y, with ≥1–pack-year smoking history; median age: 59 y; women: 52%; median pack-years: 32	CXR Baseline† Nodules: 368 LC: 79 Interval: 2 Screening-detected: 77 Stage I: 75 Adenocarcinoma: 65 Repeated screening‡ Nodules: 254 (6%) LC: 29 Interval: 1 Stage I: 27 Adenocarcinoma: 17	NR	2–3 y
Henschke et al, 2006 (20)	14 435 asymptomatic men and women, aged ≥40 y, current or former smokers 6296 women vs. 8139 men Median age: 67 y Median pack-years: 47	LDCT only LC cases: 156 LC mortality: NR Stage I: 139 Surgery: Resection: 375 Lobectomy: 284 Wedge: 60 Segmentectomy: 21 Bilobectomy: 10	Not resectable; underwent radiation, chemotherapy, or both; or received no treatment: 29	46 mo
Henschke et al, 2006 (41)	31 567 asymptomatic adults, aged >40 y, with a history of smoking or occupational exposure with increased risk for secondhand smoke Median age: 61 y Median pack-years: 30	LDCT only Baseline Concerning nodule: 13% (n = 4186) LC prevalence: 1.3% (n = 405) Interval cancer without nodule: 5/27 381 Annual New nodules: 5% (n = 1460) LC prevalence: 0.3% (n = 74) Cases of LC: 484 Additional procedures Biopsy (baseline): 535 Surgery: 411 Death during surgery: 0.5%	Baseline Cancer: 405 Biopsy: 535 Annual cancer: 74	NR
Shemesh et al, 2006 (62)	4250 high-risk smokers ELCAP population	CXR only CAC score 2: 1544 (36%) Positive CAC: 2706 (64%) Frequency of positive CAC: 66% in former smokers vs. 62% in current smokers	NR	NR
Menezes et al, 2010 (52) Wagnetz et al, 2012 (83)	3352 asymptomatic men and women, aged ≥50 y, ≥10–pack-year smoking history Median age: 60 y (range, 50–83) Median pack-years: 30 Women: 54%	CT only LC: 44 (13% previous) Stage I: 42/65 Stage II: 4 Stage III/IV: 10	NR	≥1 y

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Appendix Table 2—**Continued**

Study, Year (Reference)	Population	Intervention vs. Control	Adverse Events/Harms	Duration of Follow-up
		Additional procedures Biopsy: 78 (Menezes et al, 2010 [52]), 127 (Wagnetz et al, 2012 [83]) Surgery: 48		
Liu et al, 2011 (43)	3348 (1994–2002) and 3582 (2003–2009) government workers, aged ≥40 y 1994–2002: 70% nonsmokers 2003–2009: 71% nonsmokers	Single-slice CT (1994–2002 cohort) only Cumulative incidence: 0.9% Screening-detected cases of cancer with 1 interval cancer: 36 Nodules ≥5 mm: 6.2% Stage I: 67% 5-y lung survival: 75% 16 MDCT (2003–2009 cohort) only LC diagnosis: 0.9% Cases of cancer with no interval cancer: 34 Nodule ≥5 mm: 9.8% Stage I: 91% 5-y LC survival: 95%	Rate of surgery for benign nodules: 18% (1994–2002) and 8.1% (2003–2009)	NR
LUSI, 2012 (26)	4052 men and women, aged 50–69 y, ≥25 y of ≥15 cigarettes/d or ≥30 y of ≥10 cigarettes/d current or former (quit <10 y ago) smokers Aged 50–54 y: 46% Aged 60–69 y: 28% Men: 2622 Women: 1430 Current smokers: 62%	LDCT only LC incidence: 22 Stage IV: 1 Additional procedures Biopsy: 31 Surgery: 8 VATSs, 11 thoracotomies	9 biopsies of benign nodules, resulting in 1 bronchoscopy, 3 VATSs, 5 thoracotomies	NR
Mayo Lung Project, 2005 (67)	1520 men and women, aged >50 y, current or former (quit <10 y ago) smokers with ≥20–pack-year history Men: 788 Women: 732 Current smokers: 61% Median pack-years: 45 (range, 20–230)	CT only Prevalent/incident or interval LC any stage: 31/35 Stage IA: 20/16 Stage IB: 2/1 Stage IIA: 4/4 Stage IIB: 0/2 Stage IIIA: 2/4 Stage IIIB: 0/2 Stage IV: 1/0 Unknown: 0/2 SCLC: 2/6 Mortality LC: 9 (of 5481.5 person-years) All-cause: 48 Additional procedures 15 surgeries for benign nodules (no deaths) among 13 patients	1 postoperative death (patient with LC)	4 y (≈6000 person-years)
PLuSS, 2008 (27, 84)	3642 men and women, current or former (quit <10 y ago) smokers with ≥0.5–pack/d history for 25 y Mean age: 59 y Men: 51% Women: 49% Mean pack-years: 47 Current smokers: 60%	CT only LC incidence: 2.2% (CI, 1.7%–2.2%) Stage I: 58% Stage II: 17% Stage III: 30% Stage IV: 7% Additional procedures Biopsy: NR Surgery: 28 resections for suspected LC returned nonmalignant diagnoses, 3 lobectomies for benign nodules	19 participants with resections for benign nodules despite not meeting ELCAP criteria for biopsy	3 y from initial LDCT

ARDS = acute respiratory distress syndrome; CAC = coronary artery calcification; COSMOS = Continuing Observation of Smoking Subjects; CT = computed tomography; CXR = chest radiography; DVT = deep venous thrombosis; ELCAP = Early Lung Cancer Action Program; FNA = fine-needle aspiration; HRCT = high-resolution computed tomography; LC = lung cancer; LDCT = low-dose computed tomography; LSS = Lung Screening Study; LUSI = Lung Cancer Screening Intervention; MDCT = multidetector row computed tomography; NELSON = Dutch–Belgian Randomised Controlled Trial for Lung Cancer Screening in High-Risk Subjects; NLST = National Lung Screening Trial; NR = not reported; NSCLC = non–small-cell lung cancer; PA = posterior–anterior; PLCO = Prostate, Lung, Colorectal, and Ovarian; PLuSS = Pittsburgh Lung Screening Study; RR = relative risk; SCLC = small-cell lung cancer; VATS = video-assisted thoracoscopic surgery.
* Whole body effective dose.
† Positive result: 1 solid/part-solid nodule ≥5 mm; semipositive result: <5-mm noncalcified nodule.
‡ Any new or growing nodule; interval cancer = LC diagnosis within 1 y of prior CT; n = 4538.

Appendix Table 3. Summary of Evidence

Studies (Publications)	Design	Limitations	Consistency	Applicability	Overall Quality
How effective is screening for lung cancer with LDCT in reducing mortality and morbidity?					
6 studies (8 publications)	RCTs	Only 4 studies report findings in both the LDCT and non-LDCT groups. Thus, the base of data is limited. Among these, 3 RCTs evaluating LDCT had short follow-up and were underpowered; 1 study had inadequate randomization and differential follow-up.	Low	High	Fair
Findings: One good-quality trial (n = 53 454) of high-risk participants with good generalizability showed that LDCT compared with chest radiography conducted over 3 screenings reduced lung cancer mortality by 20% and all-cause mortality by 6.7%. Three smaller (n = 2472, 4099, and 4104) European trials of fair- and poor-quality included high-risk participants and showed no benefit associated with LDCT screening vs. no LDCT screening. Meta-analysis of 3 fair- or good-quality trials showed an RR of lung cancer mortality of 0.81 (95% CI, 0.72–0.91) and an RR of all-cause mortality of 1.02 (CI, 0.78–1.33). No trials reported data on LDCT lung cancer screening in women or in different racial or ethnic populations.					
What are the harms associated with lung cancer screening with LDCT, and are there ways to modify harms (e.g., unnecessary biopsies, radiation exposure, overdiagnosis, and psychosocial harms)?					
20 studies (40 publications)	RCTs; cohort	Variable methods of determining sensitivity and specificity. Harms variably reported among the studies.	High	High	Fair
Findings: Radiation: Two RCTs and 3 cohort studies reported that radiation associated with 1 LDCT scan ranged from 0.6–1.5 mSv. One study reported cumulative radiation exposure associated with its screening program, estimated at 6–7 mSv. False-positive examinations and follow-up evaluations: Positive examinations at baseline screening ranged from 9.2%–51.0% (of participants) with calculated PPVs for abnormal scans ranging from 2.2%–36%; most were resolved with further imaging. Positive examinations were lower in subsequent screenings with PPVs for abnormal scans predicting lung cancer of 4%–42%; most were resolved with further imaging. PPVs for abnormal LDCT scans with recommendations for biopsy ranged from 50%–92%. False reassurance: Sensitivity of LDCT ranged from 80%–100%, implying a false-negative rate of 0%–20%. The harms of false reassurance were not evaluated in any study. Procedures: In the NSLT, during the *screening* period, 99 and 53 needle biopsies, 303 and 92 bronchoscopies, and 673 and 234 surgeries were performed in the LDCT and chest radiography groups, respectively. These numbers are reported by scan, not participant. Procedure complications during the screening period, as reported in the NLST, were low. At least 1 complication occurred in association with 245 LDCT and 81 chest radiography screenings. Major complications from procedures were related to 85 LDCT and 27 chest radiography screenings. Among the LDCT group, 16 deaths occurred within 60 d of the most invasive procedure; 10 occurred in the chest radiography group. Overdiagnosis: Not formally reported in any study. It was suggested in 1 trial of LDCT compared with no LDCT that showed an excess of 119 cases of lung cancer among approximately 26 000 participants after 6.5 y of follow-up. Three RCTs with limited follow-up reported more early-stage lung cancer in LDCT-screened groups than among controls but not a smaller number of cases of advanced lung cancer. Psychosocial consequences: Five studies showed that LDCT screening did not substantially affect overall health-related quality of life. Most studies reported no long-term difference in anxiety among participants, although 3 studies suggested increased short-term anxiety among those with positive or indeterminate results. Distress was decreased among persons with negative results (compared with baseline) in 1 trial. Smoking behavior: Three RCTs identified no differences in smoking cessation rates, smoking relapse rates, or smoking intensity between LDCT and no LDCT screening groups. In RCTs, smoking behavior among participants with abnormal scans and those with normal scans showed mixed results, with 1 study showing a tendency toward smoking abstinence among those with abnormal scans. Mixed results were also seen in cohort studies. One cohort study suggested that physician referral for patients with abnormal screening LDCT may result in higher smoking cessation rates. Incidental findings: There was no standardized approach to reporting incidental findings. Among LDCT studies, nonpulmonary lung findings were common; infections and other types of cancer were also diagnosed. Coronary artery calcification was identified in approximately 50% of participants in 1 cohort study evaluating CT scans retrospectively. COPD was also commonly identified.				

COPD = chronic obstructive pulmonary disease; CT = computed tomography; LDCT = low-dose computed tomography; NLST = National Lung Screening Trial; PPV = positive predictive value; RCT = randomized, controlled trial; RR = relative risk.