
Medical Policy



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Joint Medical Policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and is therefore subject to change.

***Current Policy Effective Date: 7/1/22**
(See policy history boxes for previous effective dates)

Title: Screening for Lung Cancer Using Computed Tomography Scanning or Chest Radiographs

Description/Background

There is interest in screening and early identification of lung cancer because the disease, when identified clinically, tends to have a poor prognosis. Two proposed screening methods are chest radiographs and low-dose computed tomography (CT) scans. These techniques can be used with or without computer-assisted detection (CAD). Due to biases inherent in screening studies, randomized trials that evaluate reduction in lung cancer morbidity and mortality are required to demonstrate the efficacy of screening.

Given the poor prognosis of lung cancer, there has been longstanding research interest in developing screening techniques for those at high risk. Previous studies of serial sputum samples or chest x-rays failed to demonstrate that screening improved health outcomes. More recently, there has been interest in low-dose computed tomography (CT) scanning as a screening technique, using either spiral (also referred to as helical) or electron beam (also referred to as ultrafast) CT scanning. Compared to conventional CT scans, these scans allow for the continuous acquisition of images, thus shortening the scan time and radiation exposure. A complete CT scan can be obtained within 20 seconds, or during one breath hold, in the majority of patients. The radiation exposure for this examination is greater than for that of a chest x-ray but less than for a conventional CT scan.

There are also growing applications of computer-assisted *detection* or *diagnosis* (CAD) technologies that may have an impact on the use of CT scanning or chest radiographs for lung cancer screening. Computer-assisted *detection* points out possible findings to the radiologist who then decides if the finding is abnormal. Computer-assisted *diagnosis* uses a computer algorithm to analyze features of a lesion to determine the level of suspicion and is intended to enhance the reader's diagnostic performance. These technologies may be expected to offer more benefit when used by relatively inexperienced readers and may help to standardize diagnostic performance.

Regulatory Status:

In March 2001, the U.S. Food and Drug Administration (FDA) approved the RapidScreen RS-2000 system as a computer-aided detection (CAD) system intended to identify and mark regions of interest on digitized chest radiographs. In February 2004, the FDA approved the R2 Technology ImageChecker CT system as a technique to assist in the detection of lung nodules on multidetector CT scans of the chest. The R2 Technology ImageChecker also received FDA clearance for the Temporal Comparison software module in June 2004 and for the CT-LN 1000 in July 2004. The Temporal Comparison software module provides the ability to automatically track lung nodule progression or regression over time. The ImageChecker CT-LN 1000 is used for the detection of solid nodules in the lungs. Other systems that have been developed include iCAD's Second Look CT lung and Siemens' syngo LungCARE CT. FDA product code: MYN.

Medical Policy Statement

The safety and effectiveness of low-dose CT scanning of the lung as a screening tool for lung cancer have been established. It is a useful therapeutic option for patients meeting patient selection guidelines.

Routine chest radiographs, including computer-aided detection (CAD) analysis of the x-ray, for the purpose of screening patients for lung cancer is experimental/investigational. They have not been shown to improve long-term patient clinical outcomes.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

Inclusions:

Low-dose computed tomography (CT) scanning, no more frequently than annually, may be appropriate as a screening technique for lung cancer in individuals who meet ALL of the following criteria (which are based on the results of the National Lung Screening Trial (NLST)):

- Between 50 and 80 years of age
- History of cigarette smoking of at least 20 pack-years (a "pack-year" is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked. One pack year is the equivalent of 365.24 packs of cigarettes or 7,305 cigarettes).
- Currently smoke or have quit within the past 15 years.

Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Exclusions:

- Low-dose CT scanning as a screening technique for lung cancer in all other situations where the above selection guidelines are not met.
- Routine chest radiographs when used as a screening technique for ruling out lung cancer.

Policy Guidelines (for informational purposes only):

The upper age limit for screening differs among the screening guidelines. National organizations' recommendations regarding the upper age limit for screening are as follows:

- U.S Preventive Services Task Force (USPSTF) 2013 recommendation:^{1, 2} 80 years old (based on analysis evaluating 5 independent micro-simulation models)
- National Comprehensive Cancer Network (NCCN) 2014 guideline:³ 74 years-old (based on NSLT)
- American College of Chest Physicians (ACCP) and American Society of Clinical Oncology (ASCO) 2012 joint statement:⁴ 74 years-old (based on NSLT)
- American Association for Thoracic Surgery (AATS) 2012 guideline:⁵ 79 years-old (based on several factors including that the average life expectancy is 78.6 years and that age is a risk factor for lung cancer)
- American Cancer Society (ACS) 2013 guideline:⁶ 74 years-old (based on NSLT)

Screening setting

The national organizations with recommendations on lung cancer screening all include a recommendation that the low-dose CT screening of eligible patients occurs in settings that use a multi-disciplinary approach and involve participation of a sub-specialty qualified medical team.

Chest Radiographs

Evidence from randomized controlled trials does not support the use of chest radiography as a screening technique for lung cancer. Chest radiography and sputum cytology are not considered to be valid methods for lung cancer screening at the present time.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

71250 71271 G0296

Other codes (investigational, not medically necessary, etc.):

0174T 0175T

Rationale

An initial literature search on this topic was performed by BCBSA in 2001. The policy was updated regularly with literature searches. The following is a summary of the literature on screening for lung cancer with chest x-rays or low-dose computed tomography (CT) scanning.

High-quality, randomized trials that examine the effect of screening on lung cancer morbidity and mortality are necessary to determine the true impact of this technology on health outcomes. While survival from time of screening is commonly reported in screening trials, the apparent increase in survival may be confounded by one or more biases associated with screening:

- **Lead-time bias:** Lead-time refers to the length of time between when a cancer is detected by screening and when the first signs or symptoms would have appeared. If screening identifies lung cancer earlier, survival could be longer due to the lead-time rather than because of effective early treatment.
- **Length-time bias:** This bias refers to the greater likelihood that screening will detect slow-growing indolent cancers (which take longer to become symptomatic) than faster-growing, more aggressive cancer. Patients with screen-detected cancer may appear to live longer because the cancers are more indolent.
- **Over-diagnosis:** This bias occurs when screening identifies non-lethal cancer (sometimes called pseudo-disease). When this type of cancer is identified and removed, the patient appears to have benefited from screening, although the cancer would not have been fatal if left undetected.

Chest Radiographs

Several randomized trials of chest x-ray as a screening technique were published in the 1980s. The studies found that, although patients undergoing screening with chest x-ray had a higher incidence of earlier stage lung cancers, more resectable lung cancer, and improved five-year survival rate compared with the control group, there were no statistically significant differences in mortality attributable to lung cancer between the two groups.⁷

More recently, findings from an additional randomized controlled trial (RCT) that evaluated the effectiveness of screening with chest x-rays, the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial, have recently been published. Enrollment for the study was completed in 2001.⁸ Approximately 155,000 individuals were randomly assigned to receive selected screening interventions, including chest radiographs, or usual care. Smokers received chest x-rays at baseline and annually for 3 years; never-smokers were screened at entry and annually for 2 years. Baseline results were reported in 2005. Of the 77,465 patients randomly assigned to the intervention arm, 5,991 (8.9%) radiographs were suspicious for lung cancer. Of these, 206 patients underwent biopsy, and 126 cancers were diagnosed. Among these cancers, 44% were stage I. Rates of lung cancer for the initial screening ranged from 0.63% for current smokers to 0.04% in non-smokers. Results of subsequent screenings were published in 2010.⁹ Positivity rates were 7.1%, 6.6%, and 7.0%, respectively, for the first, second, and third yearly follow-up chest radiographs. Over the entire screening period, 18.5% of screened individuals had at least one positive screen. In 2011, the investigators published the main outcome data related to lung cancer screening.¹⁰ The rate of lung cancer mortality did not differ significantly in the two groups. Over 13 years of follow-up, there were a total of 1,213 lung cancer deaths in the intervention group and 1,230 lung cancer deaths in the usual care group. Cumulative lung cancer mortality rates (per 10,000 person-years of observation) were 14.0 in the intervention group and 14.2 in the control group (rate ratio [RR]: 0.99, 95% confidence interval [CI]: 0.87-1.22). There was also no benefit of screening with chest x-rays when the analysis was limited to individuals who met criteria for the National Lung Screening Trial (NLST, discussed in a subsequent section of the policy). In this subset of study participants (n=30,321), there were 316 lung cancer deaths in the intervention group and 334 lung cancer deaths in the usual care group (RR: 0.94, 95% CI: 0.81 to 1.10). The authors concluded that annual screening with chest radiographs did not reduce lung cancer mortality compared with usual care.

A 2013 Cochrane review, of evidence on lung cancer screening identified only 1 trial comparing screening with chest radiographs to no screening; this was the PLCO trial, described above.¹¹ The Cochrane review identified 5 RCTs comparing more intensive

screening with chest radiographs (with or without sputum cytology) to less intensive screening. A pooled analysis of data from 4 of these studies did not find a statistically significant difference in the risk of mortality with more intensive versus less intensive screening.

Computer-aided detection

Computer-aided detection (**CAD**) may increase the sensitivity of chest radiographs. An RCT evaluating CAD-assisted chest radiography was published by Mazzone and colleagues in 2013.¹² The study included individuals between the ages of 40 and 75 years who (1) were a current or former smoker with at least a 10 pack-year history or (2) had a first degree relative with a history of lung cancer or (3) had a diagnosis of chronic obstructive pulmonary disorder (COPD). A total of 1424 individuals were randomized, 710 to 3 annual CAD chest radiography screenings and 713 to placebo screening. The placebo intervention consisted of having the patient stand as though they were receiving a chest radiograph but no radiograph was taken. The primary study endpoint was development of symptomatic advanced stage lung cancer. After adjudication, 3 symptomatic advanced lung cancer events were identified, all in the control group. The number of events was too small for a meaningful statistical analysis of differences in primary outcome.

Several previous studies evaluated whether CAD improves diagnostic accuracy. For example, a 2010 retrospective study conducted in Europe evaluated chest radiographs from 46 individuals who had histologically proven lung cancer and 65 control patients who had no nodules larger than 5 mm in diameter identified at a CT screening that occurred within 6 weeks of the radiograph.¹³ Each radiograph was evaluated without and then with CAD findings; the OnGuard CAD system was used. CAD was not found to improve observer performance. The average sensitivity of the reviewers (2 radiologists and 4 residents) was similar without (49%) and with (51%) use of the CAD system. Observers correctly identified 27 lesions without CAD, and with CAD assistance, 3 additional malignancies were identified.

In addition, in 2009, a retrospective study identified radiographs with missed cancerous nodules and evaluated them with a CAD system (OnGuard 3.0, Riverain Medical).¹⁴ CAD correctly marked overlooked nodules in 46 of 89 (52%) patients, and there was a mean of 3.9 false positive results per image.

Low-Dose Spiral CT

Randomized controlled trials

Findings from a large RCT in the United States that evaluated the impact of screening with low-dose CT on lung cancer morbidity and mortality, the National Lung Screening Trial (NLST), were published in 2011. In addition, several smaller European RCTs are ongoing. There is insufficient evidence to determine whether CAD technology may improve the accuracy of CT scanning interpretation.^{15, 16} Following are descriptions of the major randomized trials evaluating CT screening:

National Lung Screening Trial

The National Lung Screening trial sponsored by the National Institutes of Health (NIH) was launched in 2002.³ By April 2004, a total of 53,454 current or former smokers from 33 sites in the United States had been randomly assigned to screening in 3 consecutive years with either a chest x-ray or low-dose spiral CT. Study eligibility included age between 55 and 74 years, a history of cigarette smoking of at least 30 pack-years and, for former smokers, quitting within the past 15 years. Individuals with a previous diagnosis of lung cancer or who had signs and/or symptoms suggestive of lung cancer were excluded. There was no study-wide diagnostic follow-up algorithm; individuals who had positive test findings were managed according to

protocols at their local center. A total of 95% of participants in the low-dose CT group and 93% in the radiography group adhered to the screening protocol.

In October 2010, the independent safety and monitoring board determined that sufficient data were available to conclude that there was a statistically significant reduction in the primary outcome, lung cancer mortality. Consequently, the trial was terminated, and study results that occurred through December 31, 2009 were analyzed and reported. During a median 6.5-year follow-up, a total of 356 of 26,722 (1.33%) participants in the low-dose CT group and 443 of 26,732 (1.66%) participants in the radiography group died of lung cancer, representing a relative risk reduction of 20% (95% CI: 6.8% to 26.7%, p=0.004) (Using intention-to-treat analysis (ITT), the absolute risk reduction was 0.33% and the number needed to screen (NNS) for 3 years with a low-dose CT to prevent one death from lung cancer was 303. The authors reported an NNS of 320 based on per-protocol data from participants who underwent at least one screen. Overall mortality, a secondary outcome, was also significantly reduced in the low-dose CT screening group. There were a total of 1,877 deaths (7.0%) in the low-dose CT group and 2,000 deaths (7.5%) in the radiography group—relative risk reduction 6.7% (95% CI: 1.2% to 13.6%, p=0.02); absolute risk reduction of 0.46% and the NNS of 219 (95% CI: 111 to 5,556).

Over all 3 screenings, the frequency of positive tests was 24.2% in the low-dose CT group and 6.9% in the radiography group. Of these, 17,497 of 18,146 (96.4%) in the low-dose CT group and 4,764 of 5,043 (94.5%) in the radiography group were false positives. The remaining 649 tests (3.6% of total positive tests) in the low-dose CT scan group and 279 (5.5% of total positive tests) in the radiography group were confirmed lung cancers. During the screening phase, a total of 39.1% of participants in the low-dose CT group and 16.0% of those in the radiography group had at least one positive screening test.

During follow-up, 1,060 lung cancers were identified in the low-dose CT group and 941 lung cancers were identified in the radiography group. The difference in the cancer rates between groups was statistically significant, with a rate ratio of 1.13 (95% CI: 6.8 to 26.7, p=0.004). In addition to the screen-detected cancers, 44 cancers in the low-dose CT group and 137 in the radiography group were diagnosed after a negative screen. Three hundred sixty-seven cancers in the low-dose CT group and 525 cancers in the radiography group were diagnosed among participants who either missed screening or who had completed their 3 screenings.

Selected data from Table 3 of the August 2011 publication³ on rates of follow-up diagnostic procedures after a positive screening result in the NSLT are shown below. Data represent all 3 screening rounds and include only cases for which diagnostic information is complete (over 97% of cases).

Table 3. Rates of Follow-up Diagnostic Procedures

	Low-dose CT (N=17,702) n (% of total sample)	Chest Radiography (N=4,953) n (% of total sample)
Imaging exam	10,246 (57.9)	3,884 (78.4)
• Chest radiography	2,547 (14.4)	1,613 (32.6)
• Chest CT	8,807 (49.8)	3,003 (60.6)
• FDG PET*/PET-CT	1,471 (8.3)	397 (8.0)
Percutaneous cytologic exam or biopsy	322 (1.8)	172 (3.5)

Bronchoscopy	671 (3.8)	225 (4.5)
Surgical procedure	713 (4.0)	239 (4.8)
• Mediastinoscopy or mediastinotomy	117 (0.7)	55 (1.1)
• Thoracoscopy	234 (1.3)	53 (1.1)
• Thoracotomy	509 (2.9)	184 (3.7)

*Positron emission tomography; (FDG, fluorodeoxyglucose)

Selected data from Table 4 of the August 2011 publication on complication rates after the most invasive screening-related diagnostic procedures are shown below. The data are from all 3 screening rounds and include only cases for which diagnostic information is complete (over 97% of cases). The frequencies of each major complication were not reported; rather the article included the total number of patients with any major complication. (Percent of total sample was calculated).

Table 4. Complication Rates

	Low-dose CT n (% of total sample)	Chest Radiography n (% of total sample)
Lung cancer confirmed	649 (3.7%)	279 (5.2%)
At least one complication	184 (1.0%)	65 (1.3%)
At least one major complication	75 (0.4%)	24 (0.5%)
Death within 60 days after invasive diagnostic procedure	10 (0.1%)	10 (0.2%)
Lung cancer not confirmed	17,053 (96.3%)	4,674 (94.4%)
At least one complication	61 (0.3%)	16 (0.3%)
At least one major complication	12 (0.1%)	4 (0.1%)
Death within 60 days after invasive diagnostic procedure ^a	6 (<0.1%)	0 (0%)

^aThis does not include deaths among individuals who had follow-up diagnostic procedures but no invasive procedures: a total of n=5 in the low-dose CT group and n=4 in the radiography group.

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

Cancer stage was reported for cancers with a known stage; 1,040 in the low-dose CT group and 929 in the radiography group (Of the 1,040 confirmed lung cancers in the low-dose CT group, 416 (40%) were stage 1A, and 104 (10%) were stage 1B. Over half of the confirmed lung cancers identified by a positive screen (329 of 635, 52%) were stage 1A. In the radiography group, 90 of 275 confirmed cancers identified by a positive screen (32.7%) were stage 1A.

In summary, the National Lung Screening Trial was a large well-conducted trial. It found a statistically significantly lower rate of lung cancer mortality with 3 annual CT screens compared to chest radiographs; the number needed to screen (NNS) to prevent one lung cancer death was 320 (95% CI: 193 to 934). The study also found a statistically significant but modestly

lower overall mortality in low-dose CT group. There was a high rate of follow-up imaging tests but relatively low rates of invasive tests. There were few major complications reported after invasive testing, although major complications that did occur were not well-characterized. The rates of other potential complications, in particular radiation-induced cancers, are not yet known. Findings of the trial cannot be generalized to other populations, e.g., younger individuals or lighter smokers. The NLST evaluated the utility of a series of 3 annual CT screens; the efficacy of other screening regimens is not known.

In 2004, Brenner assessed the radiation risks associated with low-dose CT screening.¹⁷ The estimated doses from low-dose CT screening were 5.2 mGy + 0.9 to the lung, based on the protocol used in the National Lung Screening Trial. (This would be equivalent to at least 250 standard chest x-rays.) Brenner concluded that the radiation-related lung cancer risks for a single examination at age 55 ranges from approximately 1 per 10,000 to approximately 5 per 10,000, depending on gender and whether the person is a current or former smoker. The study estimated that there would be a 1.8% increase (95% CI: 0.5% to 5.5%) in the number of lung cancers associated with radiation from screening if 50% of all current and former smokers in the U.S. aged 50–75 years received annual CT screening. The risks of screening could be reduced by scanning less frequently or beginning screening at a later age.

Several smaller European trials that evaluate spiral CT screening are ongoing. Findings may ultimately be pooled with those from other RCTs in Europe and the United States. Each study includes a somewhat different screening population and screening regimen.

Danish Lung Cancer Screening Trial

Between 2004 and 2006, a total of 4,104 current or former smokers were randomized to screening with annual low dose CT for 5 years or no screening; lung cancer mortality is the primary outcome measure.¹⁸ After five annual rounds of screening, the mean annual participation rate was 95.5% in the screening group and 93.0% in the control group.¹⁹ The mean lung cancer detection rate was 0.83% at baseline and 0.67% for each of the 4 follow-up rounds. After a median follow-up of 4.8 years, a total of 69 lung cancers were diagnosed in the screening group and 24 in the control group; the difference between groups was statistically significant, $p < 0.001$). The number of early stage cancers diagnosed was significantly higher in the screening than the control group (48 vs. 21, $p = 0.002$). However the number of late stage cancers diagnosed was similar in the 2 groups (21 vs. 16, $p = 0.509$). As of the end of March 2010, 103 of 4,013 study participants had died, 61 (3%) in the screening group and 42 (2%) in the control group ($p = 0.059$ for overall mortality). Fifteen patients (0.73%) in the screening group and 11 patients (0.54%) in the control group died of lung cancer, $p = 0.428$). This trial did not have adequate power to examine mortality outcomes on its own, the power calculation for mortality assumed that data would be combined with that of the NELSON study (described below), another European screening trial.

Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays (DANTE) Trial

This trial, conducted in Italy, randomly assigned 2,811 male current or former smokers to receive 5 yearly spiral CT screening exams or physical examination alone. All participants had baseline chest radiographs.²⁰ Three-year findings were published in 2009.²¹ After a median of 33 months' follow-up, significantly more lung cancer was detected in the CT screening group compared to control (4.7% vs. 2.8%, respectively, $p = 0.016$). More stage-1 disease was detected by CT screening; the rate of advanced lung cancer detection was similar in the 2 groups.

ITALUNG Trial

Another Italian study randomly assigned 3,206 current or former smokers to receive four yearly low-dose CT scans or no screening.²² Participants will be followed up by cancer registry for lung cancer incidence and mortality and contacted by telephone four years after randomization. At baseline, 1,406 underwent CT screening and 426 (30%) tested positive (nodule at or greater than 5 mm). Twenty individuals were found to have lung cancer; 406 of 426 (95%) of positive screens were false-positive.

Netherlands-Leuven Longkanger Screenings Onderzoek (NELSON) Trial

This study, conducted in the Netherlands and Belgium, randomly assigned current or former smokers to CT screening or no screening.^{23, 24} The screening intervention consisted of a CT scan at baseline and at 1 and 3 years after baseline. For the 3 screening rounds, and 2 years additional follow-up, the sensitivity of low-dose CT screening was 84.6% (95% CI, 79.6% to 89.2%), and the specificity was 98.6% (95% CI, 98.5% to 98.8%). (25) A total of 187 of 7155 participants (3%) were diagnosed with screening-detected lung cancer, and another 49 were diagnosed with interval cancers, 34 in the first year after screening and 15 in the second year. The primary outcome of the trial is lung cancer mortality reduction after 10 years. Mortality results are expected in 2015 or 2016.²⁶

A total of 1,466 participants in the NELSON trial participated in a related quality-life-study; 733 were randomized to the screening arm and 733 to the control arm.²⁷ They were given questionnaires before randomization, 2 months after the first screening round, and 2 years after baseline (6 months after the second screening round). The questionnaire response rate was 1,288 (88%) at baseline and 931 (79%) 2 years later. No statistically significant differences between the screened and control groups were found in scores on any quality-of-life measures at 2 years. The authors interpreted this finding as suggesting that lung cancer screening did not negatively impact quality of life.

German Lung Cancer Screening Intervention trial (LUSI)

This study randomized 4,052 heavy smokers age 50-69 years old to screening with 5 annual CT scans or a control group that is not being screened.²⁸ Baseline screening findings were reported in 2012. A total of 2,029 participants received a first-round CT scan. The baseline scan was negative for 1,488 of participants (73%). The remaining 540 suspicious screens led to 31 biopsies (biopsy rate 1.5%) and 22 confirmed lung cancers (cancer detection rate 1.1%).

Systematic Reviews

In 2012, Bach and colleagues published a systematic review of literature on CT screening for lung cancer.²⁹ The study identified 8 RCTs and 13 cohort study; the NLST was the largest RCT. Across studies, approximately 20% of participants in each round of screening had positive findings resulting in follow-up, and about 1% had lung cancer. There was heterogeneity across studies in the rate of positive findings and the type and frequency of follow-up investigations. The authors noted that the NLST trial was the only study to date that has found a significant lung cancer mortality benefit associated with low-dose CT screening. Other studies were described as too small, too poorly designed, or else the final results were not yet available. Another systematic review, published in 2014 by Fu et al, identified 9 RCTs evaluating CT screening in current and former smokers.³⁰ NLST remains the study with the largest sample size, by far. In a meta-analysis of 4 RCTs, the pooled lung cancer specific mortality favored low-dose CT over chest radiography or usual care (odds ratio, 0.84; 95% CI, 0.74 to 0.96). As previously noted, a number of the European trials are ongoing and do not yet have final mortality data.

A pair of studies funded by the Agency for Healthcare Research and Quality was published in 2013. Humphrey et al conducted a systematic review of evidence for the update of the USPSTs recommendation on lung cancer screening.³¹ The review identified 4 trials focusing on low-dose CT screening in current and former smokers; the 4 trials consisted of the NLST and 3 European trials. The authors did not pool study findings. They noted that the 3 European trials were underpowered, and follow-up was not long enough to evaluate screening effectiveness.

In addition, a study modeling benefits and harms of various approaches to screening was published.² The modeling study evaluated models that varied screening programs by age of the participants, pack-years, years since quitting, and frequency of screening. The authors found that several possible approaches to screening and did not identify an approach that was clearly the “best” in terms of trade-offs between benefits and harms. One approach that was supported by the study was annual screening between the ages of 55 and 80 years for individuals with at least 30 pack-years of smoking and no more than 15 years since quitting for former smokers. This program is similar to the NLST eligibility criteria, except the maximum screening age is 80 years rather than 74. Using this approach, the analysis estimated that 37 eligible individuals would need to be screened to prevent one death from lung cancer. The published modeling study did not report on models in which screening ended at age 74 years (or 75), but the lead author stated in personal communication that these models had been tested and were inferior in terms of numbers of deaths prevented.

SUMMARY OF EVIDENCE

The evidence on computed tomography (CT) screening for lung cancer includes several randomized controlled trials (RCTs), some of which are still ongoing. The largest RCT, the National Lung Screening Trial (NLST) was a multicenter trial published in 2011. This was a high-quality trial that reported a decrease in both lung cancer mortality and overall mortality in a high-risk population screened with 3 annual low-dose computed tomography (CT) scans compared to chest radiographs. There is considerable uncertainty regarding the optimal length and interval of screening. Thus, screening for lung cancer with low-dose CT annually for 3 years may be considered medically necessary for high-risk patients who meet criteria of the NLST and investigational otherwise.

SUPPLEMENTAL INFORMATION

Clinical Input Received through Physician Medical Societies and Academic Medical Centers

In response to requests by BCBSA, input was received through 2 Physician Specialty Societies and 3 Academic Medical Centers in late 2011. All of the reviewers agreed with the medically necessary policy statement, with the exception that one reviewer did not think the criterion limiting CT scanning to once a year for 3 years should be included. The reviewers were split on the issue of whether screening with CT scanning should be considered investigational for all other asymptomatic individuals who did not meet criteria in the medically necessary statement. No studies were cited in support of screening other individuals with low-dose CT, but several reviewers mentioned the 2011 version of the National Comprehensive Cancer Network (NCCN) guideline.

PRACTICE GUIDELINES AND POSITION STATEMENTS

National Comprehensive Cancer Network (NCCN)

The Version 1.2022 lung cancer screening guideline from the National Comprehensive Cancer Network has the following recommendations regarding screening with low-dose CT:

- Screening is recommended for high-risk individuals, age 55-77 years-old, at least a 30 pack-year history of smoking, and smoking cessation no more than 15 years ago. These criteria are based on the National Lung Screening Trial.
- Screening is also recommended for high-risk individuals aged 50 years and older with at least a 20 pack-year history of smoking and one additional risk factor for lung cancer (other than second-hand smoke). This recommendation is based on non-randomized studies and observational data.
- For individuals who test negative on the initial screen, the NCCN recommends annual screens for an additional 2 years and then they recommend considering further annual screens until the patient is no longer eligible for definitive treatment. The guideline notes: “there is uncertainty about the appropriate duration of screening and the age at which screening is no longer appropriate.”³

American College of Radiology (ACR)

In 2014, The American College of Radiology (ACR) published a position statement strongly supporting lung cancer screening with low-dose CT for high-risk patients between the ages of 55 and 80 years with at least a 30 year pack-history of smoking.³² The statement also described the ACR Lung Cancer Screening Center designation to increase the likelihood that lung cancer screening will take place at sites that offer high-quality low dose CT screening programs.

American Cancer Society (ACS)

In January 2013, American Cancer Society (ACS) website published guidelines on lung cancer screening with low-dose CT. They state that patients who meet all of the following criteria, which are based on National Lung Screening Trial (NLST) criteria, may be candidates for screening:

- 55 to 74 years old;
- Otherwise in good health;
- At least a 30 pack-year smoking history; AND
- Current smokers or quit smoking within the last 15 years.

For patients who meet the above criteria and choose screening, screening is recommend annually until age 74 for individuals who otherwise remain healthy. In addition, the ACS recommends that screening only take place in facilities with the correct type of computed tomography (CT) scans, experience performing low-dose CT scans for lung cancer screening and a team of specialists that can provide appropriate care.⁶

American College of Chest Physicians (ACCP)/American Society of Clinical Oncology (ASCO)

In May 2012, the American College of Chest Physicians (ACCP) and American Society of Clinical Oncology (ASCO) issued a joint statement on CT screening for lung cancer. This statement was confirmed by the ACCP in May 2013. The statement included the following recommendations:

- For smokers and former smokers aged 55 to 74 years 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 computed tomography (LDCT) 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 National Lung Screening Trial (NLST) participants. (Grade of recommendation: 2B.)

- For individuals who have accumulated fewer than 30 pack years of smoking or are either younger than 55 years or older than 74 years, or individuals who quit smoking more than 15 years ago, and for individuals with severe comorbidities that would preclude potentially curative treatment, limit life expectancy, or both, we suggest that CT screening should not be performed. (Grade of recommendation: 2C.)^{4, 29}

The 2013 guideline noted that most effective duration or frequency of screening remains unknown.

American Association for Thoracic Surgery (AATS)

In 2012, the American Association for Thoracic Surgery (AATS) published guidelines for lung cancer screening. The guidelines recommend “annual lung cancer screening with low-dose computed tomography screening for North Americans from age 55 to 79 years with a 30 pack-year history of smoking. Long-term lung cancer survivors should have annual low-dose computed tomography to detect second primary lung cancer until the age of 79 years. Annual low-dose computed tomography lung cancer screening should be offered starting at age 50 years with a 20 pack-year history if there is an additional cumulative risk of developing lung cancer of 5% or greater over the following 5 years. Lung cancer screening requires participation by a subspecialty-qualified team.”⁵

U.S. Preventive Services Task Force Recommendations

On March 9, 2021, the USPSTF published updated recommendations on screening for lung cancer. ¹ The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. The recommendation was given a “B” recommendation, defined as “high certainty that the net benefit is substantial or the ability or willingness to have curative lung surgery”.

Government Regulations

National/Local:

National Coverage Determination (NCD) for Lung Cancer Screening with Low Dose Computed Tomography (LDCT) (210.14). Implementation date: 1/4/16.

CAG-00439R, decision summary: Screening for lung cancer with LDCT. Date published February 10, 2022

For purposes of Medicare coverage of lung cancer screening with LDCT, beneficiaries must meet all of the following eligibility criteria:

- Age 50 – 77 years;
- Asymptomatic (no signs or symptoms of lung cancer);
- Tobacco smoking history of at least 20 pack-years (one pack-year = smoking one pack per day for one year; 1 pack = 20 cigarettes);
- Current smoker or one who has quit smoking within the last 15 years; and

- Receive a written order for lung cancer screening with LDCT. Written orders for lung cancer LDCT screenings must be appropriately documented in the beneficiary's medical records, and must contain the following information:
 - Beneficiary date of birth;
 - Actual pack – year smoking history (number);
 - Current smoking status, and for former smokers, the number of years since quitting smoking;
 - Statement that the beneficiary is asymptomatic (no signs or symptoms of lung cancer); and
 - National Provider Identifier (NPI) of the ordering practitioner.

Counseling and Shared Decision Making Visit

Before the beneficiary's first lung cancer LDCT screening, the beneficiary must receive a counseling and shared decision-making visit that meets all of the following criteria, and is appropriately documented in the beneficiary's medical records:

- Must be furnished by a physician (as defined in Section 1861(r)(1) of the Social Security Act) or qualified non-physician practitioner (meaning a physician assistant, nurse practitioner, or clinical nurse specialist as defined in §1861(aa)(5) of the Social Security Act), and
- Must include all of the following elements:
 - Determination of beneficiary eligibility including age, absence of signs or symptoms of lung cancer, a specific calculation of cigarette smoking pack-years; and if a former smoker, the number of years since quitting;
 - Shared decision making, including the use of one or more decision aids, to include benefits and harms of screening, follow-up diagnostic testing, over-diagnosis, false positive rate, and total radiation exposure;
 - Counseling on the importance of adherence to annual lung cancer LDCT screening, impact of comorbidities and ability or willingness to undergo diagnosis and treatment;
 - Counseling on the importance of maintaining cigarette smoking abstinence if former smoker; or the importance of smoking cessation if current smoker and, if appropriate, furnishing of information about tobacco cessation interventions; and
 - If appropriate, the furnishing of a written order for lung cancer screening with LDCT.

Written Orders for Subsequent Annual Lung Cancer Screenings with LDCT

For subsequent annual lung cancer LDCT screenings, the beneficiary must receive a written order for lung cancer LDCT screening. The written order may be furnished during any appropriate visit with a physician (as defined in Section 1861(r)(1) of the Social Security Act) or qualified non-physician practitioner (meaning a physician assistant, nurse practitioner, or clinical nurse specialist as defined in Section 1861(aa)(5) of the Social Security Act).

If a physician or qualified non-physician practitioner elects to provide a lung cancer screening counseling and shared decision making visit before a subsequent annual lung cancer LDCT screening, the visit must meet all of the criteria described above for a counseling and shared decision making visit.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

References

1. United States Preventive Services Task Force (USPSTF). Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement March 9, 2021. Available online at:[http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening?ds=1&s=lung cancer.de Koning HJ., Meza R, Plevritis SK. Benefits and Harms of Computed Tomography Lung Cancer Screening Programs for High-Risk Populations AHRQ Publication No. 13-05196-EF-2. accessed March 2022.](http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening?ds=1&s=lung%20cancer.de%20Koning%20HJ.,%20Meza%20R,%20Plevritis%20SK.Benefits%20and%20Harms%20of%20Computed%20Tomography%20Lung%20Cancer%20Screening%20Programs%20for%20High-Risk%20Populations%20AHRQ%20Publication%20No.%2013-05196-EF-2.%20accessed%20March%202022.)
3. National Comprehensive Cancer Network. Lung Cancer Screening. Clinical practice guidelines in oncology, V1.2022. Available online at: http://www.nccn.org/professionals/physician_gls/PDF/lung_screening.pdf . Last accessed March 2022.
4. Detterbeck FC, Mazzone PJ, Naidich DP et al. Screening for lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2013; 143(5 Suppl):e78S-92S.
5. Jaklitsch MT, Jacobson FL, Austin JH et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. J Thorac Cardiovasc Surg 2012; 144(1):33-8.
6. American Cancer Society. Can non-small cell lung cancer be found early? July 2013. Available online at: <http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-detection>. Last accessed March 2022.
7. Patz EF, Goodman PC, Bepler G. Screening for lung cancer. N Engl J Med 2000; 343(22):1627-33.
8. National Cancer Institute, Division of Cancer Prevention. Lung Cancer Screenings. Available online at: <http://www.cancer.net/research-and-advocacy/asco-care-and-treatment-recommendations-patients/lung-cancer-screening>. Last accessed December 2019.
9. Hocking WG, Oken MM, Winslow SD et al. Lung cancer screening in the randomized prostate, lung, colorectal and ovarian (PLCO) cancer screening trial. J Natl Cancer Inst 2010; 102(10):722-31.
10. Oken MM, Hocking WG, Kvale PA et al. Screening by chest radiograph and lung cancer mortality: The prostate, lung, colorectal and ovarian (PLCO) randomized trial. JAMA 2011; 306(17):1865- 73.
11. Manser R, Lethaby A, Irving LB et al. Screening for lung cancer. Cochrane Database Syst Rev 2013; 6:CD001991.
12. Mazzone PJ, Obuchowski N, Phillips M et al. Lung cancer screening with computer aided detection chest radiography: design and results of a randomized, controlled trial. PLoS One 2013; 8(3):e59650.
13. de Hoop B, De Boo DW, Gietema HA et al. Computer-aided detection of lung cancer on chest radiographs: effect on observer performance. Radiology 2010; 257(2):532-40.
14. White CS, Flukinger T, Jeudy J et al. Use of a computer-aided detection system to detect missed lung cancer at chest radiography. Radiology 2009; 252(1):273-81.

15. Goo JM, Lee JW, Lee HJ et al. Automated lung nodule detection at low-dose CT: preliminary experience. *Korean J Radiol* 2003; 4(4):211-6.
16. Wormanns D, Fiebich M, Saidi M et al. Automatic detection of pulmonary nodules at spiral CT: clinical application of a computer-aided diagnosis system. *Eur Radiol* 2002; 12(5):1052-7.
17. Brenner DJ. Radiation risks potentially associated with low-dose CT screening for adult smokers for lung cancer. *Radiology* 2004; 231(2):440-5.
18. Pedersen JH, Ashraf H, Dirksen A et al. The Danish randomized lung cancer CT screening trial - overall design and results of the prevalence round. *J Thoracic Oncol* 2009; 4(5):608-14.
19. Saghir Z, Dirksen A, Ashraf H et al. CT screening for lung cancer brings forward early disease. The randomized Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. *Thorax* 2012; 67(4):296-301.
20. Infante M, Lutman FR, Cavuto S et al. Lung cancer screening with spiral CT: baseline results of the randomized DANTE trial. *Lung Cancer* 2008; 59(3):355-63.
21. Infante M, Cavuto S, Lutman FR et al. A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE Trial. *Am J Respir Crit Care Med* 2009; 180(5):445-53.
22. Lopes PA, Picozzi G, Mascalchi M et al. Design, recruitment and baseline results of the ITALUNG trial for lung cancer screening with low-dose CT. *Lung Cancer* 2009; 64(1):34-40.
23. van Iersel CA, de Koning HJ, Draisma G, et al. Risk-based selection from the general population in a screening trial: selection criteria, recruitment and power for the Dutch-Belgian randomized lung cancer multi-slice CT screening trial (NELSON). *Int J Cancer*. 2007;120(4):868-874. PMID
24. van Klaveren RJ, Oudkerk M, Prokop M et al. Management of lung nodules detected by volume CT screening. *N Engl J Med* 2009; 361(23):2221-9.
25. Horeweg N, Scholten ET, de Jong PA, et al. Detection of lung cancer through low-dose CT screening (NELSON): a prespecified analysis of screening test performance and interval cancers. *Lancet Oncol*. Nov 2014;15(12):1342-1350. PMID 25282284
26. Field JK, Hansell DM, Duffy SW et al. CT screening for lung cancer: countdown to implementation. *Lancet Oncol* 2013; 14(13):e591-600.
27. van den Bergh KA, Essink-Bot ML, Borsboom GJ et al. Long-term effects of lung cancer computed tomography screening on health-related quality of life: the NELSON study. *Eur Respir J* 2011; 38(1):154-61.
28. Becker N, Motsch E, Gross ML et al. Randomized study on early detection of lung cancer with MSCT in Germany: study design and results of the first screening round. *J Cancer Res Clin Oncol* 2012; 138(9):1475-86.
29. Bach PB, Mirkin JN, Oliver TK et al. Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA* 2012; 307(22):2418-29.
30. Fu C, Liu Z, Zhu F, et al. A meta-analysis: is low-dose computed tomography a superior method for risky lung cancers screening population? *Clin Respir J*. Oct 13 2014. PMID 25307063
31. Humphrey LL, Deffebach M, Pappas M et al. Screening for lung cancer with low-dose computed tomography: a systematic review to update the US Preventive services task force recommendation. *Ann Intern Med* 2013; 159(6):411-20.
32. Kazerooni EA, Armstrong MR, Amorosa JK, et al. ACR CT Accreditation Program and the Lung Cancer Screening Program Designation. *J Am Coll Radiol*. NoCMS0 2014. PMID 25455196

33. CMS final decision memo for Screening for Lung Cancer with Low Dose Computed Tomography (LDCT) (CAG-00439N). Available at <http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274>. (Accessed March 2022).
34. Blue Cross Blue Shield Association. Screening for Lung Cancer Using CT Scanning. Medical Policy Reference Manual. Policy #6.01.30 Issue 2:2015, original policy date 9/27/05, last review date 2/12/15. Archived November 2015.
35. HAYES Directory Assessment. Low-Dose Helical (Spiral) Computed Tomography for Lung Cancer Screening. Lansdale, PA: HAYES, Inc. April 4, 2013, updated March 2017. Archived May 2018.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through March 2022, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
5/15/03	5/15/03	4/1/03	Joint policy established
6/21/05	6/21/05	5/23/05	Routine maintenance
5/1/07	2/10/07	2/10/07	Routine maintenance
3/1/09	12/908	12/31/08	Routine maintenance
7/1/11	4/19/11	5/3/11	<ul style="list-style-type: none"> • Policy title changed from “Spiral CT Scanning for Lung Cancer Screening” to “Screening for Lung Cancer Using CT Scanning or Chest Radiographs (Spiral or Helical CT)”. • Added codes 0174T and 0175T to policy, in addition to NOC code 76497.
11/1/12	8/21/12	8/21/12	Routine update. Policy status unchanged. This policy replaces the policy, “Computer Aided Detection and Algorithm Analysis of Digital Image Data for Malignant Pulmonary Lesion Detection.”
5/1/14	2/18/14	2/28/14	Policy status changed to established for specified indications. References and new Hayes rating added. Removed NOC code from policy.
1/1/15	10/24/14	11/3/14	Added new code, S8032 - Low-dose computed tomography for lung cancer screening for services beginning 10/1/14.
2/5/15	2/17/15	2/17/15	Updated Medicare section to reflect CMS coverage determination to cover this screening service effective 2/5/15. Updated rationale and references.
5/1/16	2/16/16	2/16/16	Routine maintenance. Updated references. Added G0296 & G0297 payable for Medicare.
5/1/17	2/21/17	2/21/17	Routine maintenance, S8032 deleted. CMS/MDHHS sections updated.
5/1/18	2/20/18	2/20/18	Routine maintenance.
5/1/19	2/19/19		Routine maintenance
5/1/20	2/18/20		Routine maintenance. Updated references. No change in policy status.

5/1/21	2/16/21		Routine maintenance. Code G0297 deleted. No change in policy status.
7/1/21	4/20/21		MPS adjusted to align with USPSTF changes in age and amount of pack per year smoking history.
7/1/22	4/19/22		Added code 71271 to policy, no change in policy status, routine policy maintenance.

Next Review Date: 2nd Qtr. 2023

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: SCREENING FOR LUNG CANCER USING CT SCANNING OR CHEST
RADIOGRAPHS (SPIRAL OR HELICAL CT)

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered; criteria apply.
BCNA (Medicare Advantage)	See government section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.