Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the
Blue Cross Blue Shield Association

Title: Screening for Lung Cancer Using CT Scanning

Professional
Original Effective Date: June 5, 2012
Revision Date(s): December 27, 2012; April 26, 2013; December 31, 2013; October 1, 2014; February 10, 2015; April 28, 2015; January 1, 2016; April 13, 2016; October 1, 2016; May 10, 2017; February 18, 2019; February 9, 2021; September 1, 2021
Current Effective Date: September 1, 2021

Institutional
Original Effective Date: June 5, 2012
Revision Date(s): December 27, 2012; April 26, 2013; December 31, 2013; October 1, 2014; February 10, 2015; April 28, 2015; January 1, 2016; April 13, 2016; October 1, 2016; May 10, 2017; February 18, 2019; February 9, 2021; September 1, 2021
Current Effective Date: September 1, 2021

DESCRIPTION

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. 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.

BACKGROUND

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 10-20 seconds, or during 1 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-aided detection or diagnosis (CAD) technologies that may have an impact on the use of CT scanning or chest radiographs for lung cancer screening. Computer-aided detection points out possible findings to the radiologist who then decides if the finding is abnormal. Computer-aided detection 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. Both of 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.

POLICY

A. Low-dose computed tomography (CT) scanning, no more frequently than annually, may be considered **medically necessary** as a screening technique for lung cancer in individuals who meet ALL of the following criteria*:

1. Between 50 and 80 years of age (see Policy Guidelines); **AND**
2. History of cigarette smoking of at least 20 pack-years
   Number of pack years = (number of cigarettes smoked per day × number of years smoked) ÷ 20 (1 pack has 20 cigarettes)
   A pack year is defined as twenty cigarettes smoked every day for one year; **AND**
3. If former smoker, quit within the previous 15 years.

*Patient selection criteria are based on the National Lung Screening Trial (NLST) and the US Preventive Services Task Force (USPSTF) 2021 recommendation.

B. Low-dose CT scanning is considered **experimental / investigational** as a screening technique for lung cancer in all other situations.

Policy Guidelines

1. This policy does not apply to individuals with signs and/or symptoms of lung disease. In symptomatic individuals, a diagnostic work-up appropriate to the clinical presentation should be undertaken, rather than screening.
2. *Computed Tomography (CT) Scanning*
   The upper age limit for screening differs among the screening guidelines. National organizations' recommendations regarding the upper age limit for screening are as follows:
   a. USPSTF 2013 recommendation[1,2]: 80 years old (based on analysis evaluating 5 independent microsimulation models)
   b. National Comprehensive Cancer Network (NCCN) 2017 guideline[3]: 74 years old (based on NLST)
   c. American College of Radiology: 80 years old (based on USPSTF)
   d. American College of Chest Physicians (ACCP) and American Society of Clinical Oncology (ASCO) 2012 joint statement[4]: 74 years old (based on NSLT)
   d. 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)
   e. American Cancer Society (ACS) 2013 guideline[6]: 74 years old (based on NSLT)
   f. Centers for Medicare and Medicaid Services (CMS) 2015 Decision Memo[7]: 77 years (based on maximum age at the third round of screening in the NSLT)
3. *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.
4. *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.

RATIONALE

The MEDLINE literature was reviewed through December 26, 2014. The following is a summary of the literature on screening for lung cancer with chest radiographs 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.

Overdiagnosis: 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 radiograph as a screening technique were published in the 1980s. The studies found that, although patients undergoing screening with chest radiograph had a higher incidence of earlier stage lung cancers, more resectable lung cancer, and improved 5-year survival rate compared with the control group, there were no statistically significant differences in mortality attributable to lung cancer between the 2 groups.[8]

More recently, findings from an additional randomized controlled trial (RCT) that evaluated the effectiveness of screening with chest radiographs, the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial became available. Enrollment for the study was completed in 2001 and screening was completed in 2006.[9] Approximately 155,000 individuals were randomly assigned to receive selected screening interventions, including chest radiographs, or usual care. Smokers received chest radiographs 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, 5991 (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 nonsmokers. Results of subsequent screenings were published in 2010.[10] 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 1 positive screen. In 2011, the investigators published the main outcome data related to lung cancer screening.[11] The rate of lung cancer mortality did not differ significantly in the 2 groups. Over 13 years of follow-up, there were a total of 1213 lung cancer deaths in the intervention group and 1230 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 to 1.22). There was also no benefit of screening with chest radiographs when the analysis was limited to individuals who met criteria for the National Lung Screening Trial (NLST; discussed in a following subsection). 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, previously described.[12] 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.

<u>Computer-Aided Detection</u>
CAD may increase the sensitivity of chest radiographs. An RCT evaluating CAD-assisted chest radiography was published by Mazzone et al in 2013.[13] 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 patients stand as though they were receiving a chest radiograph, but no radiograph was taken. The primary study end point 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.[14] 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).[15] 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
<u>Randomized Control Trials</u>
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, 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.[16,17] 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 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 radiograph 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, the absolute risk reduction was 0.33% and the number needed to screen (NNS) for 3 years with a low-dose CT to prevent 1 death from lung cancer was 303. The authors reported an NNS of 320 based on per-protocol data from participants who underwent at least 1 screen. Overall mortality, a secondary outcome, was also significantly reduced in the low-dose CT screening group. There were a total of 1877 deaths (7.0%) in the low-dose CT group and 2000 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 5556).

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 4764 of 5043 (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 1 positive screening test.

During follow-up, 1060 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. A total of 367 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 publication[3] on rates of follow-up diagnostic procedures after a positive screening result in the NSLT are shown next. Data represent all 3 screening rounds and include only cases for which diagnostic information is complete (over 97% of cases).

Table 1. 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)

CT: computed tomography; FDG: fluorodeoxyglucose; PET: positron emission tomography.

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 2. 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*	6 (<0.1)	0 (0)

CT: computed tomography.
[a]This 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.[18] The estimated doses from low-dose CT screening were 5.2±0.9 mGy to the lung, based on the protocol used in NLST. (This would be equivalent to at least 250 standard chest radiographs.) 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 to 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 (DLCST)

Between 2004 and 2006, a total of 4104 current or former smokers were randomized to screening with annual low-dose CT for 5 years or no screening; lung cancer mortality was the primary outcome measure.[19] After 5 annual rounds of screening, the mean annual participation rate was 95.5% in the screening group and 93.0% in the control group.[20] 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 4013 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 next), 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 2811 male current or former smokers to receive 5 yearly spiral CT-screening exams or physical examination alone. All participants had baseline chest radiographs.[21] The study was initiated in 2001, and recruitment was completed in 2006. Three-year findings were published in 2009.[22] After a median of 33 months' follow-up, significantly more lung cancer was detected in the CT screening group compared with 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 3206 current or former smokers to receive 4 yearly low-dose CT scans or no screening.[23] Participants will be followed up by cancer registry for lung cancer incidence and mortality and contacted by telephone 4 years after randomization. At baseline, 1406 underwent CT screening, and 426 (30%) tested positive (nodule at or >5 mm). Twenty individuals were found to have lung cancer; 406 of 426 (95%) of positive screens were false positive.

Netherlands-Leuvens 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.[24,25] The screening intervention consisted of a CT scan at baseline and 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%).[26] 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.[27]

A total of 1466 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.[28] 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 1288 (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 4052 heavy smokers age 50 to 69 years old to screening with 5 annual CT scans or a control group that is not being screened.[29] Baseline screening findings were reported in 2012. A total of 2029 participants received a first-round CT scan. The baseline scan was negative for 1488 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%). Of these 22 cancers, 18 (82%) were stage I, one was stage II, and 3 were stage III. There was 1 interval cancer.

Systematic Reviews

In 2012, Bach et al published a systematic review of literature on CT screening for lung cancer.[30] The study identified 8 RCTs and 13 cohort studies; 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.[31] 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.[32] 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 modelling benefits and harms of various approaches to screening was published.[2] The modelling study evaluated models that varied screening programs by age of the participants, packyears, 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 modelling 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 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 CT scans compared with chest radiographs. There is considerable uncertainty regarding the optimal length and interval of screening. Thus, screening for lung cancer with low-dose CT annually may be considered medically necessary for high-risk patients who meet criteria and investigational otherwise.

CLINICAL INPUT FROM PHYSICIAN MEDICAL SOCIETIES AND ACADEMIC MEDICAL CENTERS

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received through 2 Physician Specialty Societies and 3 Academic Medical Centers after this policy was approved in October 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

The Version 1.2016 lung cancer screening guideline from the National Comprehensive Cancer Network (NCCN) has the following recommendations regarding screening with low-dose CT:

- Screening is recommended for high-risk individuals, age 55 to 74 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 1 additional risk factor for lung cancer (other than second-hand smoke). This recommendation is based on nonrandomized 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]

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.[33] 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.
In January 2013, the 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 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 CT scans, experience performing low-dose CT scans for lung cancer screening and a team of specialists that can provide appropriate care.[6]

In May 2012, American College of Chest Physicians (ACCP) and American Society of Clinical Oncology 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 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.)"[4,30]

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

In 2012, American Association for Thoracic Surgery 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 U.S. Preventive Services Task Force published updated recommendations on screening for lung cancer.[1] The task force recommended annual screening for lung cancer with low-dose CT in adults between the ages of 50 and 80 years who have at least a 20 pack-year smoking history and who either currently smoke or quit smoking within the past 15 years. Moreover, the statement includes the recommendation that screening be discontinued when individuals have not smoked for at least 15 years, when they develop a health problem substantially limiting life expectancy, or when they are no longer willing or able 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."

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS

G0296	Counseling visit to discuss need for lung cancer screening (LDCT) using low dose CT scan (service is for eligibility determination and shared decision making)
71271	CT, thorax, low dose for lung cancer screening without contrast material

ICD-10 Diagnoses

F17.210	Nicotine dependence, cigarettes, uncomplicated
F17.211	Nicotine dependence, cigarettes, in remission
F17.213	Nicotine dependence, cigarettes, with withdrawal
F17.218	Nicotine dependence, cigarettes, with other nicotine-induced disorders
F17.219	Nicotine dependence, cigarettes, with unspecified nicotine-induced disorders
Z12.2	Encounter for screening for malignant neoplasm of respiratory organs
Z87.891	Personal history of nicotine dependence

REVISIONS

06-05-2012	Effective for Institutional providers 30 days after the Revision Date.
	Policy added to the bcbsks.com web site.
12-27-2012	In Coding section: Corrected nomenclature for CPT codes 71250, 0174T, 0175T
04-26-2013	Updated Description section.
	In the Policy section: ▪ In Item A, removed "for 3 consecutive years," to read "Low-dose computed tomography (CT) scanning, nor more frequently than annually may be considered medically necessary…"
	Updated Rationale section.
	Updated Reference section.
12-31-2013	In Coding section: ▪ Added ICD-10 Diagnosis *(Effective October 1, 2014)*
	Updated Reference section.
10-01-2014	Updated Description section.
	In the Policy section: ▪ In Item A, 1, removed "74" and added "80" to read, "Between 55 and 80 years of age …" ▪ In Item , 2, added "and the US Preventive Services Task Force (USPSTF) 2013 recommendation" to read, "Patient selection criteria are based on the National Lung Screening trial (NLST) and the US Preventive Services Task Force (USPSTF) 2013 recommendation."

	In the Policy Guidelines section: ▪ Added "The upper age limit for screening differs among the screening guidelines," in paragraph 2. ▪ In Item 2, a., added "USPSTF 2013 recommendation(1,2): 80-years old (based on analysis evaluating 5 independent microsimulation models)" ▪ In Item 2, removed "The optimal frequency of CT screening is not known. However, the recommendation to screen selected individuals is based on the NLST, which screened individuals annually for 3 consecutive years," and, "Sources: National Comprehensive Cancer Network (NCCN) 2013 guideline (1); American Cancer Society (ACS) 2012 interim guidance (2); American College of Chest Physicians (ACCP) and American Society of Clinical Oncology (ASCO) 2012 joint statement (3); American Association for Thoracic Surgery (AATS) 2012 guideline (4)."
	Updated Rationale section.
	Updated Summary section.
	In Coding section: ▪ Added HCPCS code S8032. ▪ Added ICD-10 codes F17.200-F17.299.
	Updated Reference section.
02-10-2015	In Coding section: ▪ Removed CPT/HCPCS codes 17250, 0174T, and 0175T.
04-28-2015	Updated Description section.
	In Policy section: ▪ In Policy Guidelines, Item 2, removed ", frequency and duration of screening for individuals who otherwise meet screening criteria", to read "The upper age limit for screening differs among the screening guidelines. National organizations' recommendations regarding the upper age limit for screening are as follows:" ▪ In Policy Guidelines, Item 2 b, removed "2014" and added "2015" ▪ In Policy Guidelines, added Item 2 c, "American College of Radiology: 80 years old (based on USPSTF)" ▪ In Policy Guidelines, added Item 2 f, "Centers for Medicare and Medicaid Services (CMS) 2015 Decision Memo(7): 77 years (based on maximum age at the third round of screening in the NSLT)"
	Updated Rationale section.
	Updated References section.
01-01-2016	In Coding section: ▪ Added HCPCS codes: G0296 and G0297.
04-13-2016	Updated Rationale section.
	Updated References section.
10-01-2016	In Coding section: ▪ Removed HCPCS code: S8032
05-10-2017	In Policy section: ▪ In Policy Guidelines Item 2 b, removed "2015" and added "2017" to read, "National Comprehensive Cancer Network (NCCN) 2017 guideline[3]: 74 years old (based on NLST)"
	Updated References section.
02-18-2019	Policy published 01-16-2019 with an effective date of 02-18-2019.
	In Coding section: ▪ Removed ICD-9 codes. ▪ Removed ICD-10 codes: F17.200, F17.201, F17.203, F17.208, F17.209, F17.220, F17.221, F17.223, F17.228, F17.229, F17.290, F17.291, F17.293, F17.298, F17.299.
	Policy reviewed; no other revisions made.
02-09-2021	In Coding section

	▪ Deleted HCPCS code G0297 ▪ Added CPT code 71217
09-01-2021	In Policy section: ▪ Replaced "55" with "50" in Item A.1. ▪ Replaced "30" with "20" in Item A.2. ▪ Replaced "2013 recommendation" with "2021 recommendation"
	Updated Rationale section
	Updated References section

REFERENCES

1. United States Preventive Services Task Force (USPSTF). Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement December 31, 2013; http://www.uspreventiveservicestaskforce.org/uspstf13/lungcan/lungcanfinalrs.htm#summary. Accessed December 2, 2014.
2. United States Preventive Services Task Force (USPSTF). Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement March 9, 2021; https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening. Accessed July 2, 2021
3. HJ. de Koning, R Meza, SK Plevritis. Benefits and Harms of Computed Tomography Lung Cancer Screening Programs for High-Risk Populations AHRQ Publication No. 13-05196-EF-2. July 2013; http://www.uspreventiveservicestaskforce.org/uspstf13/lungcan/lungcanmodeling.pdf. Accessed December 2, 2014.
4. National Comprehensive Cancer Network. Lung Cancer Screening. Clinical practice guidelines in oncology, V1.2017.
5. 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. May 2013;143(5 Suppl):e78S-92S. PMID 23649455
6. 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. Jul 2012;144(1):33-38. PMID 22710039
7. American Cancer Society. Can non-small cell lung cancer be found early? July 2013; http://www.cancer.org/cancer/lungcancer-non-smallcell/detailedguide/non-small-cell-lung-cancer-detection. Accessed December 2, 2014.
8. Centers for Medicare and Medicare Services (CMS). Decision Memo for Screening for lung cancer with Low Dose Computed Tomography (LDCT) (CAG-00439N) 2015; http://www.cms.gov/medicare-coveragedatabase/details/nca-decision-memo.aspx?NCAId=274. Accessed February 4, 2015.
9. Patz EF, Goodman PC, Bepler G. Screening for lung cancer. N Engl J Med. 2000;343(22):1627-1633.
10. National Cancer Institute, Division of Cancer Prevention. Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial. http://prevention.cancer.gov/programs-resources/groups/ed/programs/plco. Accessed December 2, 2014.
11. 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):722-731.

12. 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):1865-1873.
13. Manser R, Lethaby A, Irving LB, et al. Screening for lung cancer. Cochrane Database Syst Rev. 2013;6:CD001991. PMID 23794187
14. 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. PMID 23527241
15. de Hoop B, De Boo DW, Gietema HA, et al. Computer-aided detection of lung cancer on chest radiographs: effect on observer performance. Radiology. Nov 2010;257(2):532-540. PMID 20807851
16. 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):273-281.
17. Goo JM, Lee JW, Lee HJ, et al. Automated lung nodule detection at low-dose CT: preliminary experience. Korean J Radiol. 2003;4(4):211-216.
18. 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):1052-1057.
19. Brenner DJ. Radiation risks potentially associated with low-dose CT screening for adult smokers for lung cancer. Radiology. 2004;231(2):440-445.
20. 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):608-614.
21. 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. Apr 2012;67(4):296-301. PMID 22286927
22. 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):355-363.
23. 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):445-453.
24. 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.
25. 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.
26. 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):2221-2229.
27. 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
28. Field JK, Hansell DM, Duffy SW, et al. CT screening for lung cancer: countdown to implementation. Lancet Oncol. Dec 2013;14(13):e591-600. PMID 24275132
29. 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):154-161. PMID

30. 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. Sep 2012;138(9):1475-1486. PMID 22526165
31. Bach PB, Mirkin JN, Oliver TK, et al. Benefits and harms of CT screening for lung cancer: a systematic review. Jama. Jun 13 2012;307(22):2418-2429. PMID 22610500
32. 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
33. 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. Sep 17 2013;159(6):411-420. PMID 23897166
34. Kazerooni EA, Armstrong MR, Amorosa JK, et al. ACR CT Accreditation Program and the Lung Cancer Screening Program Designation. J Am Coll Radiol. Nov 20 2014. PMID 25455196

Other References

1. Blue Cross and Blue Shield of Kansas, Radiology Liaison Committee, February 2013; February 2015.
2. Blue Cross and Blue Shield of Kansas, Surgery Liaison Committee, August 2013.