Screening for Lung Cancer Using Low Dose Computed Tomography (LDCT)

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This Medical Policy document describes the status of medical technology at the time the document was developed. Since that time, new technology may have emerged, or new medical literature may have been published. This Medical Policy will be reviewed regularly and be updated as scientific and medical literature becomes available; therefore, policies are subject to change without notice.

DESCRIPTION

Note: This policy does not apply to individuals with signs and/or symptoms. In symptomatic individuals, a diagnostic work up appropriate to the clinical presentation should be undertaken, rather than screening.

Lung cancer is the leading cause of cancer related mortality in the United States and worldwide. In 2022, it is estimated that 130,180 deaths (68,820 in men and 61,360 in women) from lung cancer will occur in the United States. A new report issued by the American Lung Association (November 2021) reveals that the lung cancer five-year survival rate increased 14.5% nationally to 23.7% but remains significantly lower among

communities of color. Patients are being diagnosed at an earlier stage in their disease and living longer due to better access to care, higher screening rates and improved treatments. Screening for individuals at high risk for lung cancer has the potential to dramatically improve lung cancer survival rates by finding the disease at an earlier stage when it is more likely to be curable. Early detection, by low dose CT screening can decrease lung cancer mortality by 14 to 20 percent among high- risk populations. About 8 million Americans qualify as high-risk for lung cancer and are recommended to receive annual screening with low dose CT scans, and if half of these high-risk individuals were screened over 12,000 lung cancer deaths could be prevented.

Most lung cancers are diagnosed clinically when patients present with symptoms such as persistent cough, pain, and weight loss; unfortunately, patients with these symptoms usually have advanced lung cancer. Early detection of lung cancer is an important opportunity for decreasing mortality. Data from NLST supports using low dose CT (LDCT) of the chest to screen select patients who are at high-risk for lung cancer who have no symptoms suggestive of lung cancer. The goal of lung cancer screening is to detect disease at a stage when it is not causing symptoms and when treatment will be most successful. Screening should benefit the individual by increasing life expectancy and increasing quality of life (QOL).

Low dose computed tomography has been found to have a high sensitivity and reasonable specificity for the detection of lung cancer, with demonstrated benefit in screening persons at high-risk (i.e., asymptomatic individuals age 50 to 80, have smoked 20 pack years or more and either continue to smoke or have quit within the past 15 years). Other potential screening modalities are not recommended because they have not been found to be beneficial including sputum cytology, chest radiography, and measurement of biomarker levels.

Shared patient and physician decision making may be the best approach before deciding whether to do LDCT lung cancer screening, especially for patients with comorbid conditions. Individuals who choose to undergo lung cancer screening should enter an organized screening program at an institution with expertise in LDCT screening, with access to a multidisciplinary team skilled in the evaluation, diagnosis, and treatment of abnormal lung lesions.

While screening for lung cancer has the potential benefits of decreased morbidity and mortality from lung cancer it also has potential harms, which include:

- False-positive results, leading to unnecessary testing, unnecessary invasive procedures (including surgery), increased cost, and decreased quality of life because of mental anguish.
- False-negative results, which may delay or prevent diagnosis and treatment because of a false sense of good health.
- Futile detection of small aggressive tumors (which have already metastasized, preventing meaningful survival benefit from screening.

- Futile detection of indolent disease (i.e., overdiagnosis), which would never have harmed the patient who subsequently undergoes unnecessary therapy.
- Indeterminate results, leading to additional testing.
- Radiation exposure from serial imaging in a screening program may add to the risk of developing cancers, including lung cancer. Since screening typically occurs over several rounds and positive studies require further evaluation, the cumulative radiation dose is also important.
- Physical complications from diagnostic work-up.

To minimize the uncertainty or variation about the evaluation and management of lung nodules and to standardize report of LDCT screening results, the American College of Radiology (ACR) developed the Lung Imaging Reporting and Data System (Lung-RADS) classification system and endorses its use in lung cancer screening. Lung-RADS provides guidance to clinicians on which findings are suspicious for cancer and the suggested management of lung nodules detected on LDCT. Data suggest that the use of Lung-RADS may decrease the rate of false-positive results in lung cancer screening.

Patients with several comorbid conditions may be at greater risk than those with few or none. Therefore, the initial risk assessment before screening needs to include an assessment of functional status to determine whether patients can tolerate curative intent treatment if they are found to have lung cancer. Patients with extensive comorbidity may not be candidates for lung cancer screening, because treatment for lung cancer might not prolong survival and could cause potential morbidity and mortality.

Screening for Lung Cancer Using Low Dose Computed Tomography (LDCT) In High-Risk Asymptomatic Individuals

Clinical Context and Test Purpose
The purpose of lung cancer screening using low dose computed tomography (LDCT) is to detect disease at a stage when it is not causing symptoms and when treatment will be most successful. Screening should benefit the individual by increasing life expectancy and increasing quality of life (QOL).

LDCT is a non-contrast radiographic technique that can provide high quality, three-dimensional images of the lungs during a single breath hold with less radiation.

Populations
The relevant population of interest is high-risk asymptomatic adults with a smoking history and currently smoke or have quit smoking.

Risk assessment includes age, total cumulative exposure to tobacco smoke, and years since quitting smoking are the most important risk factors for lung cancer. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease.

In March 2021, the USPSTF updated and replaced the 2013 USPSTF recommendation statement on screening for lung cancer using low dose computed tomography. On March 9, 2021, the USPSTF released the following final recommendation:

- The USPSTF's recommendation has a "B" grade and recommends annual screening with low-dose computed tomography (LDCT) in adults ages 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years.
- The USPSTF recommends discontinuing screening 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.

This updated recommendation changed the age range and pack-year eligibility criteria and recommends annual screening for lung cancer with LDCT in adults aged 50 to 80 years who have a 20 pack-year smoking history (previously was 30 pack-year smoking history) and currently smoke or have quit within the past 15 years. This recommendation did not change and continues to recommend that screening be discontinued for individuals who have 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.

Screening for lung cancer in persons at an earlier age and with fewer pack-years of smoking (i.e., 20 pack-years) may also help partially ameliorate racial disparities in screening eligibility. Data suggest that Black persons who smoke have a higher risk of lung cancer than do White persons, and this risk difference is more apparent at lower levels of smoking intensity.

The current NCCN guideline for Lung Cancer Screening Version 1.2022 recommends lung cancer screening in high- risk individual's and there are 2 groups of individuals who qualify as high- risk:

- Group 1: Individual's aged 55 to 77 years with a 30 or more pack-year history of smoking tobacco who currently smoke or, if former smoker, have quit within 15 years (category 1).
- Group 2: Individual's aged 50 years or older with a 20 or more pack-year history of smoking tobacco who are either current or former smokers with at least one additional risk factor.

Interventions

Low dose computed tomography (LDCT) has high sensitivity and acceptable specificity for detecting lung cancer in high-risk persons and is the only currently recommended screening test for lung cancer.

Most lung cancer cases are non-small cell lung cancer (NSCLC), and most screening programs focus on the detection and treatment of early-stage NSCLC. Although chest radiography and sputum cytologic evaluation have been used to screen for lung cancer, LDCT has greater sensitivity for detecting early-stage cancer.

Non–small cell lung cancer is treated with surgical resection when possible and with radiation and chemotherapy. Annual LDCT screening may not be useful for patients with life-limiting comorbid conditions or poor functional status who may not be candidates for surgery.

Comparators
Although lung cancer screening is not an alternative to smoking cessation, the USPSTF found adequate evidence that annual screening for lung cancer with LDCT in a defined population of high-risk persons can prevent a substantial number of lung cancer–related deaths.

Although chest radiography and sputum cytologic evaluation have been used to screen for lung cancer, LDCT has greater specificity and sensitivity for detecting early-stage lung cancer.

Outcomes
The magnitude of benefit to the person depends on that person's risk for lung cancer because those who are at highest risk are most likely to benefit. Screening cannot prevent most lung cancer–related deaths, and smoking cessation remains essential.

Annual screening for lung cancer with low dose computed tomography is of moderate net benefit in asymptomatic persons who are at high- risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking.

The harms associated with LDCT screening include false-negative and false-positive results, incidental findings, overdiagnosis, and radiation exposure.

Nonrandomized Trials
Of the nonrandomized screening studies, the I-ELCAP study is the largest. It included 31,567 individuals with high-risk factors from around the world, all of whom were screened with baseline and annual screening LDCT cans analyzed centrally in New York. In the I-ELCAP study is the largest, Henschke et. al. reported that a high percentage of stage I cancers (85%) were detected using LDCT, with an estimated 92% actuarial 10-year survival rate for stage I cancers resected within 1 month of diagnosis (62% of all cancers detected). Three participants with clinical stage 1 cancer who opted not to undergo treatment died within 5 years, similar to other data examining the natural history of stage I NSCLC. The authors concluded that annual screening LDCT can detect lung cancer that is curable. Limitations regarding the I-ELCAP study include that is was not randomized, the median follow-up time was only 40 months, and less than 20% of the subjects were observed for more than 5- years. Given the limited follow-up, the 10-year survival estimates may be overstated.

A study by Bach et. al. raised concern that LDCT screening may lead to overdiagnosis of indolent cases without substantially decreasing the number of advanced cases or the

overall attributable deaths from lung cancer. Although overdiagnosis did occur with LDCT in the NLST (National Lung Screening Trial), the magnitude was not large when compared with radiographic screening (83 versus 17 stage 1A bronchioloalveolar carcinoma). An analysis of the NLST data stated that 18% of lung cancers detected by LDCT seemed to be indolent. Data suggest that baseline CT scans find more indolent cancers, and subsequent annual scan find more rapidly growing cancers.

Randomized Trials

National Lung Screening Trial (NLST)
The National Lung Screening Trial (NLST) was a prospective, randomized lung cancer screening trial, sponsored by the National Institute of Health (NHI) comparing the annual screening by low does computed tomography (LDCT) scanning with annual chest x-ray for two years in 53, 454 high risk individuals at 33 United States medical centers. Participants were men and women 55 to 74 years of age with a history of at least 30 pack years of smoking, current smokers and those who had discontinued smoking within 15 years of enrollment. This trial was designed to have 90% power to detect a 21% decrease in the primary endpoint of lung cancer-specific mortality in the screened group. In 2013, the NLST researchers released their findings showed that annual screening LDCT decreased the RR of death from lung cancer by 20%. Overall, 24% of the LDCT scans and 7% of the chest radiographs performed more positive screens, an imbalance that was expected based on prior data. In each of the 3 rounds of screening, positive LDCT scan screens were determined to be actual lung cancer cases (i.e., true positive) 4%, 2% and 5% of the time, compared with 6%, 4%, and 7% of the time for positive chest radiographs.

Based on the published NLST results, 356 participants died of lung cancer in the LDCT arm, and 443 participants died of lung cancer in the chest radiograph arm. Thus, annual screening LDCT decreased the RR of lung cancer death by 20% in the NLST. The NSLT represents the first randomized study showing an improvement in disease-specific mortality when using a lung cancer screening program. The NLST results indicate that to prevent one death from lung cancer, 320 individuals with high-risk factors must be screening with LDCT.

Systematic Reviews
In 2019, Huang et. al. conducted a systematic review and meta-analysis to update the evidence of low dose computed tomography (LDCT) in lung cancer screening. The NELSON mortality results were presented in September 2018. Four other randomized control trials (RCTs) also reported the latest mortality outcomes in 2018 and 2019. Studies included met all of the following criteria: (1) only randomized controlled trials; (2) comparing LDCT to any other type of lung cancer screening; (3) adults, aged $\geq$ 18 years, asymptomatic with risk factor for lung cancer (current or former smokers, family history of lung cancer, underlying lung disease, or environmental exposure to toxins); (4) benefits of interest included: lung cancer mortality, all-cause mortality, early detection (stage I) rates; (5) harms of interest included: death and major complications after

invasive procedures (30–60 days post invasive procedures). Major complications were listed below: death, anaphylaxis, cardiac arrest, cerebral vascular accident/stroke, congestive heart failure, myocardial infarction, intervention-required thromboembolic complications, acute respiratory failure, respiratory arrest, bronchial stump leak requiring tube thoracostomy or other drainage for > 4 days, bronchopulmonary fistula, empyema, prolonged mechanical ventilation > 48 h postoperatively, tube placement-required hemothorax, brachial plexopathy, lung collapse, chylous fistula, injury to vital organ or vessel, wound dehiscence, and infarcted sigmoid colon. Invasive procedures included: surgery, biopsy, bronchoscopy, or fine needle aspiration cytology.

Nine randomized controlled trials (RCTs) (with multiple publications) met the inclusion criteria. These RCTs contributed to lung cancer mortality outcomes. When compared with controls (no screening or CXR), LDCT screening was associated with a statistically significant reduction in lung cancer mortality (RR 0.83, 95% CI 0.76–0.90) with no heterogeneity observed (p = 0.43, I2 = 1%). Trial sequential analysis (TSA) confirmed that the conclusion for lung cancer mortality was sufficient and no more trials were needed. Seven included trials contributed information on all-cause mortality. On the contrary, LDCT screening demonstrated no statistically significant difference in all-cause mortality (RR 0.95, 95% CI 0.90–1.00). There was no heterogeneity with this outcome (I2 = 0%). Pooled analysis of seven RCTs showed significantly greater proportions (RR 2.08, 95% CI 1.43–3.03) of early- stage cancers in LDCT groups compared to controls.

As to the harm of screening, two studies reported number of deaths after invasive procedures for diagnosis purpose. Nineteen deaths were reported after 2129 invasive procedures in persons screened by LDCT and 11 deaths were reported after 792 invasive procedures in the control group. No significant difference (RR 0.64, 95% CI 0.30–1.33¸ I2 = 0) was shown. Only one study (NLST) reported major complication rates following invasive procedures for LDCT and CXR group. The risk was higher among persons who underwent LDCT compared with CXR screening (4.1 vs 3.2 per 10,000 screened).

In the subgroup analysis according to study quality, compared with controls, LDCT screening demonstrated a statistically significant reduction in lung cancer mortality among high quality studies (RR 0.82, 95% CI 0.73–0.91). However, the same situation has not been observed in low quality studies (RR 0.87, 95% CI 0.64–1.20, I2 = 23%). This suggests that trial quality might be a potential source of heterogeneity. They furthered explored the heterogeneity on the basis of sample size and conducted a subgroup analysis based on the different sample size. A sample size that is too small reduces the power of the trial and increases the margin of error, which can render the trial meaningless. Pooled analysis of findings from seven fairly small trials (total n = 27,968) comparing LDCT with controls showed no significant difference in lung cancer mortality. While findings from two large trials (NELSON, NLST; total n = 69,276), the results of the pooled data displayed a RR of 0.80 (95% CI 0.71–0.91). In addition, regardless male or female, LDCT showed a reduction of lung cancer mortality.

Sensitivity analyses were robust. The positive association was consistent with any of these analyses. Reliability and stability of our conclusions were further confirmed.

This is the first meta-analysis of LDCT for lung cancer screening based on sufficient evidence demonstrated by trial sequential analysis (TSA) with the latest NELSON, MILD and LUSI mortality results included. NELSON trial is the only European fully powered RCT which presented its 10-year mortality findings in September 2018 at the International Association for the Study of Lung Cancer (IASLC) 19th World Conference on Lung Cancer (WCLC). In total, nine RCTs are included. Most RCTs (DANTE, DLCST, ITALUNG, LUSI, MILD, NELSON) are conducted in European countries, some trials are conducted in the USA (LSS, NLST) and China (Yang 2018). The majority of included studies are judged to be of moderate to high quality (some concerns and low risk of bias for mortality outcomes), but two studies (DANTE, MILD) are judged to be of low quality (high risk of bias for mortality outcomes). Pooled results comparing LDCT to no screening or CXR establish a survival benefit and show an increase in detection of stage I cancers. As for harms of lung cancer screening, LDCT leads to an increase in the frequency of invasive procedures but does not lead to more deaths soon after an invasive procedure compared with the control arms. The results are similar to previous meta-analyses but identified more studies, more participants and more events which enhanced the precision of the results. They also conducted trial sequential analyses which provide estimates about the reliability of current evidence and prevent premature conclusions from meta-analyses.

The authors concluded the present meta-analysis based on sufficient evidence demonstrated by trial sequential analysis (TSA) indicates that there is significant reduction in lung cancer mortality between LDCT and other control groups. Moreover, the results of the subgroup analyses indicate that, LDCT screening has shown statistically significant mortality benefits in high quality trials, whereas low-quality trials found no significant difference. It is mandatory to identify lung cancer risk factors among the Asian population and to establish appropriate eligible criteria in the screening program for different races. The benefit of LDCT is expected to be heavily influenced by the risk of lung cancer in the different target group (smoking status, female and Asian) being screened. Due to tenuous balance of benefits and harms, medical decision making is recommended for individuals who are considering LDCT screening. More studies are warranted to optimize the approach to LDCT screening.

Summary of Evidence

Based on review of the peer reviewed medical literature which included nonrandomized, randomized controlled trials (RCTs) and systematic reviews and meta-analyses regarding low dose computed tomography (LDCT) screening for lung cancer, the findings from two of the larger trials (NELSON, NLST [National Lung Screening Trial]); total n = 69,276), resulted in pooled data displaying a risk ratio (RR) of 0.80 (95% CI 0.71–0.91) regardless male or female, LDCT showed a reduction of lung cancer mortality. The NELSON trial is the only fully powered RCT which presented its 10-year mortality findings in 2018 at the International Association for the Study of Lung Cancer (IASCL) 19th World

Conference on Lung Cancer (WCLC). Based on the meta-analysis completed in 2019 by Huang et. al., sufficient evidence has been demonstrated by these two trials as there was a significant reduction in lung cancer mortality between LDCT and other control groups. The U.S. Preventative Services Task Force (USPSTF) in 2013 found adequate evidence that annual screening for lung cancer with LDCT in a defined population of high-risk individuals can prevent a substantial number of lung cancer related deaths and the magnitude of benefit to the individual depends on that individual's risk for lung cancer because those who are at highest risk are most likely to benefit. The USPSTF concluded with moderate certainty that annual screening for lung cancer with LDCT is of moderate net benefit in asymptomatic individuals who are at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking. In March of 2021 the USPSTF replaced the 2013 USPSTF recommendation statement on screening for lung cancer. The updated recommendation lowers the recommended age to include adults 50-54 years of age and reduces the triggering level of cigarette use to 20 pack-year usage (previously 30 pack-year usage). The current NCCN guideline Lung Cancer Screening Version 1.2022 states there are two groups of individuals that qualify as high-risk and lung cancer screening is recommended: Group 1: Individuals age 55 to 77 years with a 30 or more pack year history of smoking tobacco who currently smoke, or if a former smoker have quit within 15 years; Group 2: Individuals age 50 years and older with a 20 or more pack-year history of smoking tobacco who are either current or former smokers with at least one additional risk factor. The NCCN Lung Cancer Screening Panel members feel that individuals in group 2 are also at high risk for lung cancer based on data from the NLST and other studies. The NCCN Lung Cancer Screening Panel feels that limiting the use to the NLST criteria is arbitrary and naïve, because the NLST only used age and smoking history for exclusion criteria and did not consider other well-known risk factors for lung cancer. Others share this opinion. The NCCN Lung Cancer Screening Panel feels that it is important to expand screening beyond the NLST criteria to a larger group of individuals at risk for lung cancer. Using just the narrow NLST criteria shown in group 1 of the NCCN high-risk categories (e.g., individuals aged 55-77 years with a 30 or more pack-year smoking history) only 27% of patients currently being diagnosed with lung cancer would be candidates for LDCT screening. Data suggest that the lung cancer risk for individuals with a 20 to 29 pack year smoking history is similar to that of individuals with a 30 or more pack-year history. Expanding the groups at high-risk who are candidates for screening, for example, including individuals aged 50 or more years with a 20 or more pack-year smoking history and at least one additional risk factor (other than second-hand smoke) may save thousands of additional lives. Based on the literature low dose computed tomography (LDCT) has shown high sensitivity and acceptable specificity for the detection of lung cancer in high-risk individuals, Chest radiography and sputum cytology evaluation has not shown adequate sensitivity or specificity as screening tests. Pooled results comparing LDCT to no screening or chest x-ray (CXR) establish a survival benefit and show an increase in detection of stage I cancers. Therefore, LDCT is currently the only recommended screening test for lung cancer in high-risk individuals. The evidence is sufficient to determine this technology results in meaningful improvement in the net health outcomes for those individuals at high- risk for lung cancer. Therefore, screening for lung cancer with low dose computed

tomography (LDCT) annually may be considered medically necessary for high- risk patients who meet criteria in the Policy section below.

Screening for Lung Cancer Using Low Dose Computed Tomography (LDCT) in Low- Risk Asymptomatic Individuals

Age, total exposure to tobacco smoke, and years since quitting smoking are important risk factors for lung cancer. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease. The incidence of lung cancer is relatively low in persons younger than 50 years but increases with age, especially after age 60 years. In current and former smokers, age-specific incidence rates increase with age and cumulative exposure to tobacco smoke.

Smoking cessation substantially reduces a person's risk for developing and dying of lung cancer. Among persons enrolled in the National Lung Screening Trial (NLST), those who were at highest risk because of additional risk factors or a greater cumulative exposure to tobacco smoke experienced most of the benefit from screening.

The USPSTF concluded in their March 2021 recommendation update regarding lung cancer screening the following: "With moderate certainty annual screening for lung cancer with LDCT has a moderate net benefit in persons at high-risk of lung cancer based on age, total cumulative exposure to tobacco smoke and years since quitting smoking. The moderate net benefit of screening depends on limiting screening to persons at high-risk, the accuracy of image interpretation being similar to or better than that found in clinical trials and the resolution of most false-positive results with serial imaging rather than invasive procedures."

Summary of Evidence

Lung cancer screening for individuals at low risk for lung cancer are based on nonrandomized studies and observational data. Clinicians may encounter asymptomatic individuals who are interested in lung cancer screening but do not meet the criteria of being high-risk for lung cancer. Per the current society guidelines including NCCN, USPSTF and the American Chest Physicians for asymptomatic individuals who have accumulated fewer than 20 pack years of smoking or are younger than age 50 or older than age 80, or who have quit smoking more than 15 years ago, and are not projected to have a high net benefit from lung cancer screening based on clinical risk prediction or life-year gained calculators, and it is recommended that low dose CT screening should not be performed in these individuals. The evidence is insufficient to show that screening for lung cancer in these low-risk individuals would be beneficial or would outweigh the harms associated with screening for asymptomatic individuals considered at any risk other than high- risk.

Practice Guidelines and Position Statements

U.S. Preventative Services Task Force (USPSTF)

In 2021, the USPSTF updated and replaced the 2013 USPSTF recommendation statement on screening for lung cancer using low dose computed tomography. On March 9, 2021, the USPSTF released the following final recommendation:

- The USPSTF's recommendation has a "B" grade and recommends annual screening with low-dose computed tomography (LDCT) in adults ages 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years.
- The USPSTF recommends discontinuing screening 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.

National Comprehensive Cancer Network (NCCN)
Lung Cancer Screening Version 1.2022

Individuals with High Risk Factors

The NCCN Lung Cancer Screening Panel recommends lung cancer screening using LDCT for individuals with high risk factors. There are 2 groups of individuals who qualify as high risk:

- Group 1: Individual's aged 55 to 77 years with a 30 or more pack-year history of smoking tobacco who currently smoke or, if former smoker, have quit within 15 years (category 1). For the 2020 update, the NCCN Lung Cancer Screening Panel extended the upper limit of the age cutoff for lung screening up to 77 years (from 74 years) when assessing whether patients are at high risk for lung cancer. In the NLST, the entry age was as old as 74 years, but the screening age limit was actually up to 77 years, which also agrees with what CMS is recommending as the upper age limit. Initial screening with LDCT is a category 1 recommendation for group 1, because these individuals are selected based on the NLST inclusion criteria. The NCCN category 1 recommendation is based on high level evidence (e.g. randomized controlled trial) and uniform consensus among Lung Cancer Screening Panel members (>85%). Annual screening LDCT is recommended for these individuals with high risk factors based on the NLST. Annual Screening LDCT is recommended for those individuals with high risk factors based on the NLST. Annual screening LDCT is also recommended for those at high-risk with negative LDCT scans or for those whose nodules do not meet the size cutoff for more frequenting scanning or other intervention until individuals are no longer candidates for definitive treatment. Uncertainty exists about the appropriate duration of screening and the age at which screening is no longer appropriate.
- Group 2: Individual's aged 50 years or older with a 20 or more pack-year history of smoking tobacco who are either current or former smokers with at least one additional risk factor. NCCN Lung Cancer Screening Panel members expanded screening beyond the NLST criteria to a larger group of individuals at risk for lung cancer, which is described in greater detail in this section. LDCT screening is a category 2A recommendation for group 2. These additional risk factors were previously described and include personal history of cancer or lung disease, family history of lung cancer, radon exposure, and occupational exposure to carcinogen.

Note that the NCCN Lung Cancer Screening Panel does not currently believe that exposure to secondhand smoke is an independent risk factor sufficient for recommending LDCT screening, because the data are either weak or variable. The NCCN category 2A recommendation is based on lower-level evidence (e.g. nonrandomized studies, observational data, ongoing randomized trials) and uniform consensus among NCCN Lung Cancer Screening Panel members (>85%).

Individuals with Low Risk Factors

- NCCN defines individuals with low risk factors as those younger than 50 years and/or with a smoking history of less than 20 pack years. The NCCN Lung Cancer Screening Panel and the ACR do not recommend lung cancer screening for these individuals at low risk for lung cancer. This is a category 2A recommendation based on nonrandomized studies and observational data.

American Cancer Society (ACS)

(Accessed 2022), The American Cancer Society (ACS) lung cancer screening guideline states the following:

The most recent version of the American Cancer Society (ACS) lung cancer screening guideline (from 2018) is being taken down while we review new scientific evidence to be included in the next update. While this important update is being completed, the ACS advises that health care providers, and people at increased risk for lung cancer, follow the recently updated recommendations for annual lung cancer screening from the US Preventive Services Task Force (USPSTF), the American Academy of Family Physicians (AAFP), or the American College of Chest Physicians. These organizations recommend yearly lung cancer screening with LDCT scans for people who:

- Are 50 to 80 years old and in fairly good health, ***and***
- Currently smoke or have quit in the past 15 years, ***and***
- Have at least a 20 pack-year smoking history. (This is the number of packs of cigarettes per day multiplied by the number of years smoked. For example, someone who smoked 2 packs a day for 10 years [2 x 10 = 20] has 20 pack-years of smoking, as does a person who smoked 1 pack a day for 20 years [1 x 20 = 20].)

American College of Chest Physicians (ACCP)

In 2021, the American College of Chest Physicians (ACCP) updated their guidelines for screening for lung cancer, which includes the following updated recommendations for screening:

- For asymptomatic individuals aged 50 to 80 who have smoked 20 pack years or more and either continue to smoke or have quit within the past 15 years, we recommend that annual screening with low-dose CT should be offered.
- We suggest that low-dose CT screening programs develop strategies to maximize compliance with annual screening exams and evaluation of screen detected findings.

- For individuals who currently smoke and are undergoing low-dose CT screening, we recommend that screening programs provide evidence-based tobacco cessation treatment as recommended by the U.S. Public Health Service.

For individuals who have accumulated fewer than 20 pack years of smoking or younger than age 50 or older than 80, or have quit smoking more than 15 years ago, and are not projected to have a high net benefit from lung cancer screening based on clinical risk prediction or life-year gained calculators, we recommend that low dose CT screening should be performed. (Strong recommendation, Moderate-Quality Evidence.

PRIOR APPROVAL

Not applicable.

POLICY

Note: This policy does not apply to individuals with signs and/or symptoms. In symptomatic individuals, a diagnostic work up appropriate to the clinical presentation should be undertaken, rather than screening.

Wellmark Grandfathered Plans: For grandfathered plans refer to the member's specific benefit plan document for details on how benefits are covered under a grandfathered plan.

Wellmark ACA, QHP, Non-grandfathered and Grand-mothered Plans:

- Based on the updated USPSTF recommendation issued March 2021 (replaces the 2013 USPSTF recommendation) for lung cancer screening, this recommendation lowers the age range to include adults 50-54 years of age (i. e., 50 through 80 years of age):
    - Health insurance issuers offering non-grandfathered group or individual health insurance coverage must provide coverage without cost-sharing for this recommendation for plan years that begin on or after the date that is one year after the recommendation or guideline is issued. A recommendation or guideline by the USPSTF is considered to be issued on the last day of the month on which it publishes or otherwise releases the recommendation, therefore:
        - Wellmark will allow lung cancer screening using low dose computed tomography (LDCT) for adults 50-54 years of age when considered medically necessary for claims processed on or after 5/20/2021, **but we will apply applicable cost-sharing to this service until plan years begin on or after April 1, 2022.**
        - For plan years that begin on or after April 1, 2022, for adults 50-54 years of age when lung cancer screening using low doses computed tomography (LDCT) is considered medically necessary per Policy

criteria below, Wellmark will provide the benefits for this recommended service without cost-sharing.

***Patient selection criteria below are based on the current U.S. Preventative Services Task Force (USPSTF) Grade B recommendation*:**
Lung cancer screening utilizing low dose computed tomography (LDCT), no more frequently than annually may be considered **medically necessary** in an *asymptomatic high-risk individual* who meets **ALL** of the following criteria:

- The patient is 50 through 80 years of age; **and**
- The patient has at least a 20 pack-year history of cigarette smoking; **and**
- Currently smokes or have quit smoking within the past 15 years.

Lung cancer screening utilizing low dose computed tomography (LDCT) would be considered **not medically necessary** in an *asymptomatic high-risk individual* for the following indications:

- Once the patient has not smoked for 15 years; **or**
- A patient develops a health problem that limits life expectancy* **or** the ability to have curative lung surgery; **or**
- Not meeting the above criteria.

*This is based on a range of chest or other organ signs, symptoms or conditions which would question the member's ability to undergo non-surgical treatment if a lung cancer was discovered. For example, congestive heart failure, advanced cancer from another site or a patient with COPD who uses oxygen when ambulating, would be examples of conditions that would "substantially limit life expectancy."

For asymptomatic individuals not meeting the above criteria, including those individuals considered at low-risk for lung cancer (i.e., <50 years of age, >80 years of age, or have quit smoking more than 15 years ago), lung cancer screening using low-dose computed tomography (LDCT) is considered **not medically necessary**.

Based on the peer reviewed medical literature and society guidelines such as the National Comprehensive Cancer Network (NCCN), USPSTF and The American College of Chest Physicians, lung cancer screening using low dose computed tomography (LDCT) is not recommended whom do not meet the smoking and/or age criteria in the above criteria for high-risk individuals. Annual lung cancer screening in low-risk individuals is not projected to have a high net benefit from lung cancer screening based on clinical risk prediction or life-year gained calculators. The evidence is insufficient to show that screening would be beneficial or would outweigh the harms associated with screening for asymptomatic individuals considered at any risk other than high-risk meeting the above criteria.

Policy Guidelines
A pack-year is a way to calculate the amount a person has smoked in their lifetime. It is calculated by multiplying the number of packs of cigarettes smoked per day by the

number of years the person has smoked. For example, 1 pack year is equivalent of smoking an average of 20 cigarettes, 1 pack per day for 1 year and so on.

The decision to undertake screening should involve a discussion of its potential benefits, limitations, and harms.

If a person decides to be screened, referral for lung cancer screening with low-dose CT should be to a center with experience and expertise in lung cancer screening.

If the person currently smokes, they should receive smoking cessation interventions.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 71271 Computed tomography, thorax, low dose for lung cancer screening, without contrast material(s)

SELECTED REFERENCES

- Mahadevia PJ, Fleisher LA, Frick KD, Eng J, Goodman SN, Powe NR. Lung cancer screening with helical computed tomography in older adult smokers. A decision and cost-effective analysis. JAMA 2002;289(3)313-322.
- Gohagan J, Marcus P, Fagerstrom R, Pinsky P, Kramer B, Prorok P; Writing Committee, Lung Screening Study Research Group. Baseline findings of a randomized feasibility trial of lung cancer screening with spiral CT scan vs chest radiograph: the Lung Screening Study of the National Cancer Institute. Chest. 2004 Jul;126(1):114-21.
- Institute for Clinical Systems Improvement (ICSI). Computed tomography screening for lung cancer. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); February 2001. ICSI Technology Assessment Report #52.
- ECRI. Computed tomography for lung cancer screening. Plymouth Meeting (PA): ECRI Health Technology Assessment Information Service; 2005 Jan. (Health Technology Forecast Report).
- ECRI. Helical computed tomography (CT) for lung cancer screening. Plymouth Meeting (PA): ECRI Health Technology Assessment Information Service; 2004 July. TARGET [database online].
- Swensen SJ, Jett JR, Hartmen TE et al. CT screening for lung cancer: five-year prospective experience. Radiology. 2005 Apr;235(1):259-65.
- Henschke CI, Yankelevitz DF, Miettinen OS. Computed Tomographic Screening for Lung Cancer: The Relationship of Disease Stage to Tumor Size. Arch Intern Med 2006; 166:321-25.

- Lindell RM, Hartman TE, Swensen SJ et al. Five-year Lung Cancer Screening Experience: CT Appearance, Growth Rate, Location, and Histologic Features of 61 Lung Cancers. Radiology. 2007 Feb;242(2):555-62.
- The Early Lung Cancer Action Program Investigators. Survival of Patients with Stage I Lung Cancer Detected on CT Screening. N Engl J Med. 2006; 355:1763-1771.
- Bach PB, Jett JR, Pastorino U et al. Computed Tomography Screening and Lung Cancer Outcomes. JAMA. 2007; 297:953-961.
- Black C, de Verteuil R, Walker S, Ayres J, Boland A, Bagust A, Waugh N.
- Population screening for lung cancer using computed tomography, is there evidence of clinical effectiveness? A systematic review of the literature. Thorax, 2007 Feb;62(2):131-8.
- American Society of Clinical Oncology (ASCO) 45th Annual Meeting: Abstract CRA 1502. Presented May 30, 2009.
- Bach PB, Silvestri GA, Hanger M et al. Screening for Lung Cancer. ACCP Evidence-based clinical practice guidelines (2nd edition). Chest. 2007 Sep; 132 (3 Suppl) 69S-77S.
- 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.
- 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.
- Croswell JM, Baker SG, Marcus PM et al. Cumulative incidence of false-positive test results in lung cancer screening. Ann Intern Med 2010; 152(8):505-12.
- National Lung Cancer Screening Trial Research Team; Aberle DR, Adams AM, Berg CD et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 2011; 365(5):395-409.
- 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.
- American Cancer Society. Lung Cancer (non-small cell). Last revised July 2011. Last accessed September 2011.
- ECRI Institute. Professional societies endorse low-dose CT scans for lung cancer screening in high-risk patients. Plymouth Meeting (PA): ECRI Health Technology Assessment Information Service; 2012 August 1. [Health Technology Trends].
- Bach PB, Mirkin JN, Oliver TK, et al. Benefits and harms of CT screening for lung cancer: a systematic review. JAMA. 2012 Jun 13;307(22):2418-29.
- 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 Apr;67(4):296-301.
- U.S. Preventative Services Task Force (USPSTF) Screening for Lung Cancer Recommendation Statement. 2013
- American Cancer Society, Lung Cancer Screening Guidelines. Updated 2018.

- National Cancer Institute, National Lung Screening Trial (NLST), NCI Press Release, NIH Funded Study Shows 20 Percent Reduction in Lung Cancer Mortality with Low Dose CT Compared to Chest X-Ray.
- 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, Michael T. Jaklitsch, M.D. et al. The Journal of Thoracic and Cardiovascular Surgery, Volume 144, Number 1. July 2012. PMID 22710039
- The American Society of Clinical Oncology (ASCO), The Role of CT Screening for Lung Cancer in Clinical Practice. The Evidence Based Practice Guideline of the American College of Chest Physicians and the American Society for Clinical Oncology. Peter B. Back, M.D., et al. May 2012.
- UpToDate. Screening for Lung Cancer. Mark E. Deffebach, M.D., Linda Humphrey, M.D. Topic last updated April 3, 2018.
- Peter B. Bach M.D., MAPP; Joshua N. Mirkin BA. Et. al. Benefits and Harms of CT Screening for Lung Cancer; A Systemic Review. JAMA May 20, 2012, Vol 307, No 22
- American Lung Association. Providing Guidance on Lung Cancer Screening to Patients and Physicians, April 23, 2012. Also available at
- ECRI Health Technology Forecast. Computed Tomography with Computer-Aided Detection for Lung Cancer Screening. Published December 2013, Updated February 2015. Also available at https://www.ecri.org
- National Comprehensive Cancer Network (NCCN) Lung Cancer Screening Version 1.2022.
- American Academy of Family Physicians. Lung cancer clinical recommendations.
- Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) 210.14 Lung Cancer Screening with Low Dose Computed Tomography (LDCT).
- National Cancer Institute. Lung Cancer Screening PDQ.
- Detterback F, Mazzone P, Naidich D, Back P. Screening for Lung Cancer – Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2013;14395) (Suppl):e78S-e92S
- Bach PB, Mirkin JN, Oliver TK, et. al. Benefits and harms of CT screening for lung cancer: a systematic review. JAMA 2012 Jun 13;307(22):2418-29
- California Technology Assessment Forum (CTAF). Low Dose Spiral Computerized Tomography (LDSCT) Screening for Lung Cancer. Technology Assessment October 19, 2011. Available at www.ctaf.org
- 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 Apr;67(4):296-301
- American Thoracic Society/American College of Chest Physicians. An official American Thoracic Society/American College of Chest Physicians policy statement: Implementation of low dose computed tomography lung cancer

screening programs in clinical practice.Am J Respir Crit Care Med 2015 Oct 1:192(7):881-91. PMID 26426785
- American College of Chest Physicians. Diagnosis and Management of Lung Cancer 3rd ed. American College of Chest Physicians Evidence Based Clinical Practice Guidelines, Screening for Lung Cancer. Chest 2013;143(5) (Suppl):e78S-e92S
- American College of Radiology (ACR)/Society of Thoracic Radiology (STR) Practice parameters for the performance and reporting of lung cancer screening thoracic computed tomography (CT) 2014.
- Centers for Disease Control (CDC) Lung Cancer.
- UpToDate. Preventative Care in Adults: Recommendations. H Nancy Sokol M.D., Topic last updated May 4, 2016.
- Humphrey LL, Deffebach M, Pappas M. et. al. Screening for lung cancer with low dose computed tomography: a systematic review to update the US Preventative Services Task Force recommendation. Ann Intern Med 2013 Sep 17;159(6):411-20. PMID 23897166
- Manser R. Lethaby A, Irving LB, et. al. Screening for lung cancer. Cochrane Database Syst Rev 2013 Jun 21;(6):CD001991. PMID 23794187
- Gould M. Lung cancer screening with low dose computed tomography. N Engl J Med 2014; 371:1813-20
- Mazzone P, Silvestri G, Patel S, et. al. Screening for Lung Cancer: CHEST Guideline and Expert Panel Report. CHEST 2018.01.016
- Kovalchik S, Tammemagi M, Berg C, et.al. Targeting of Low Dose CT Scanning According to the Risk of Lung-Cancer Death. N Engl J Med 2013; 369:245-54
- Rampinelli C, De Marco P, Origgi D, et. al. Exposure to low dose computed tomography for lung cancer screening and risk of cancer: secondary analysis of trial data and risk-benefit analysis. BMJ 2017;356: j347
- Huang KL, Wang SY, Lu WC, et. al. Effects of low dose computed tomography on lung cancer screening: a systematic review, meta-analysis and trial sequential analysis. BMC Pulmonary Medicine (2019) 19:126
- UpToDate. Screening for Lung Cancer. Mark E. Deffebach M.D., Linda Humphrey M.D. Topic last updated January 22, 2021
- American Cancer Society Cancer Facts and Figures 2021. Also available at https://www.cancer.org
- United States Preventative Services Task Force (USPSTF). Lung Cancer Screening Recommendation issued March 9, 2021. Also available at https://www.uspreventativeservicestaskforce.org
- Mazzone P, Silvestri G, Souter L, et. al. the American College of Chest Physicians updated their guidelines on Screening for Lung Cancer. Chest 2021;160(5):e427-e494
- American Lung Association Lung Cancer Facts. Accessed February 2022
- Snowill T, Yang H, Griffin E, et. al. Low-dose computed tomography for lung cancer screening in high-risk populations: a systematic review and economic evaluation. Health Technol Assess 2018 Nov;22(69):1-276

- De Koning HJ, van der Aalst CM, de Jong PA, et. al. Reduced lung cancer mortality with volume CT screening in randomized trial. N Engl J Med. 2020;382(6):503-513
- Cancer Facts and Figures 2022. American Cancer Society

POLICY HISTORY

Date	Reason	Action
February 2022	Annual Review	Policy Revised
April 2021	Interim Review	Policy Revised
February 2021	Annual Review	Policy Revised
February 2020	Annual Review	Policy Revised
February 2019	Annual Review	Policy Renewed
February 2018	Annual Review	Policy Revised
February 2017	Annual Review	Policy Revised
February 2016	Annual Review	Policy Renewed
March 2015	Annual Review	Policy Revised
April 2014	Reinstated Policy	Policy Revised
April 2013	Interim Review	Policy Retired
September 2012	Annual Review	Policy Renewed
September 2011	Annual Review	Policy Revised
October 2010	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
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