Evidence Synthesis

Number 198

Screening for Lung Cancer With Low-Dose Computed Tomography: An Evidence Review for the U.S. Preventive Services Task Force

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
5600 Fishers Lane
Rockville, MD 20857
www.ahrq.gov

Contract No. HHSA-290-2015-00011-I, Task Order No. 11

Prepared by:
RTI International–University of North Carolina at Chapel Hill Evidence-based Practice Center
Research Triangle Park, NC 27709

Investigators:
Daniel E. Jonas, MD, MPH
Daniel S. Reuland, MD, MPH
Shivani M. Reddy, MD, MSc
Max Nagle, MD, MPH
Stephen D. Clark, MD, MPH
Rachel Palmieri Weber, PhD
Chineme Enyioha, MD, MPH
Teri L. Malo, PhD, MPH
Alison T. Brenner, PhD, MPH
Charli Armstrong, BA
Manny Coker-Schwimmer, MPH
Jennifer Cook Middleton, PhD
Christiane Voisin, MSLS
Russell P. Harris, MD, MPH

AHRQ Publication No. 20-05266-EF-1
March 2021

This report is based on research conducted by the RTI International–University of North Carolina at Chapel Hill Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. HHSA-290-2015-00011-I, Task Order No. 11). The findings and conclusions in this document are those of the authors, who are responsible for its contents, and do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information (i.e., in the context of available resources and circumstances presented by individual patients).

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. AHRQ or U.S. Department of Health and Human Services endorsement of such derivative products may not be stated or implied.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Acknowledgments

The authors gratefully acknowledge the following individuals for their contributions to this project and deeply appreciate their support, commitment, and contributions: Howard Tracer, MD, AHRQ Medical Officer; Tracy Wolff, MD, MPH, Scientific Director, USPSTF Division, AHRQ; current and former members of the USPSTF; M. Patricia Rivera, MD, Professor of Medicine, Division of Pulmonary Diseases and Critical Care Medicine at UNC Chapel Hill for her expert input and her review of an earlier draft of this report; expert reviewers Deni Aberle, MD, UCLA Medical Center; Peter Bach, MD, MAPP, Memorial Sloan-Kettering Cancer Center; Tanner Caverly, MD, University of Michigan; Michael Jaklitsch, MD, Brigham and Women's Hospital; and Renda Soylemez Wiener, MD, MPH, U.S. Department of Veteran's Affairs, Boston University School of Medicine; federal partners from the Centers for Disease Control and Prevention, the National Cancer Institute, and the National Institute of Nursing Research; Sharon Barrell, MA, editor, Loraine Monroe, publications specialist; and Carol Woodell, EPC Program Manager.

Suggested Citation

Jonas DE, Reuland DS, Reddy SM, et al. Screening for Lung Cancer With Low-Dose Computed Tomography: An Evidence Review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 198. AHRQ Publication No. 20-05266-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2021.

Structured Abstract

Purpose: To systematically review the evidence on effectiveness, accuracy, and harms of screening for lung cancer with low-dose computed tomography (LDCT) for populations and settings relevant to primary care in the United States.

Data Sources: PubMed/MEDLINE, the Cochrane Library, and trial registries through May 28, 2019; reference lists of retrieved articles; outside experts; and reviewers, with surveillance of the literature through November 20, 2020.

Study Selection: English-language controlled trials of screening for lung cancer with LDCT; studies evaluating LDCT screening accuracy; studies of risk prediction models comparing benefits and harms of screening vs. the use of trial eligibility criteria or 2013 U.S. Preventive Services Task Force recommendations; trials and prospective cohort studies of treatment for Stage I lung cancer with surgery or stereotactic body radiotherapy reporting at least 5-year survival; prospective cohort and case-control studies reporting harms.

Data Extraction: One investigator extracted data and a second checked accuracy. Two reviewers independently rated quality for all included studies using predefined criteria.

Data Synthesis: This review included 223 publications. Seven randomized, controlled trials (RCTs) (described in 26 articles; 86,486 participants) evaluated lung cancer screening with LDCT; the National Lung Screening Trial (NLST) and Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) were the only RCTs that were adequately powered. The NLST found a reduction in lung cancer mortality (calculated incidence rate ratio [IRR], 0.85 [95% confidence interval {CI}, 0.75 to 0.96]) and all-cause mortality (calculated IRR, 0.93 [95% CI, 0.88 to 0.99]) with three rounds of annual LDCT screening compared with chest X-ray for high-risk current and former smokers ages 55 to 74 years. These findings indicate a number needed to screen (NNS) to prevent one lung cancer death of 323 over 6.5 years of followup. NELSON found a reduction in lung cancer mortality (calculated IRR, 0.75 [95% CI, 0.61 to 0.90]) but not all-cause mortality (calculated IRR, 1.01 [95% CI, 0.92 to 1.11]) with four rounds of LDCT screening with increasing intervals (at baseline, 1 year, 3 years, and 5.5 years) compared with no screening for high-risk current and former smokers ages 50 to 74 years. These findings indicate an NNS to prevent one lung cancer death of 130 over 10 years of followup. The sensitivity of LDCT ranged from 59 to 100 percent (13 studies; n=76,856) and was over 80 percent in most studies. The specificity ranged from 26.4 to 99.7 percent (13 studies; n=75,819) and was over 75 percent in most studies. The positive predictive value (PPV) ranged from 3.3 to 43.5 percent. The negative predictive value ranged from 97.7 to 100 percent. Evidence suggests that using the Lung-RADS™ classification system in the NLST would have increased specificity while decreasing sensitivity and increasing nodule size threshold for a positive screening result would increase PPV. Harms of screening included radiation-induced cancer (estimated 0.26 to 0.81 major cancers for every 1,000 people screened with 10 annual LDCTs), false-positive results leading to unnecessary tests and invasive procedures, overdiagnosis, incidental findings, and short-term increases in distress because of indeterminate results. For every 1,000 persons screened in the NLST, false-positive results led to 17 invasive procedures (number needed to harm, 59), resulting in less than one major complication. Using Lung-RADS could reduce false-

positive results compared with the NLST criteria; estimates suggest that using Lung-RADS could have prevented about 23 percent of all invasive procedures for false positives in the NLST. Overdiagnosis estimates ranged from a 0 to 67 percent chance that a screen-detected lung cancer was overdiagnosed. The NLST data indicate approximately four cases of overdiagnosis (and 3 lung cancer deaths prevented) per 1,000 people screened over 6.5 years. Incidental findings were common and variably defined with a wide range reported across studies (4.4% to 40.7% of people screened).

Modeling studies estimated that using risk prediction models would increase the number of screen-preventable deaths, reduce the number of participants needed to screen to prevent one lung cancer death, and reduce the number of false positive selections (i.e., selecting persons to be screened who did not have or develop lung cancer or death from lung cancer) per prevented lung cancer death compared with risk factor–based screening, when NLST-like cancer detection and mortality reductions were assumed, but the strength of evidence was low because it was largely derived from post hoc application to trial data and modeling.

Limitations: NLST and NELSON participants were younger, more highly educated, and less likely to be current smokers than the U.S. screening-eligible population, and they had limited racial and ethnic diversity. The general U.S. population eligible for lung cancer screening may be less likely to benefit from early detection compared with the NLST and NELSON participants because they face a higher risk of death from competing causes and the NLST and NELSON were mainly conducted at large academic centers, potentially limiting applicability to community-based practice. Most studies reviewed in this report (including the NLST) did not use current nodule evaluation protocols such as Lung-RADS.

Conclusions: Screening high-risk persons with LDCT can reduce lung cancer mortality and may reduce all-cause mortality but also causes false-positive results leading to unnecessary tests and invasive procedures, overdiagnosis, incidental findings, increases in distress, and, rarely, radiation-induced cancers. The evidence for benefits comes from two RCTs that enrolled participants who were more likely to benefit than the U.S. screening-eligible population and that were mainly conducted at large academic centers, potentially limiting applicability to community-based practice. Application of lung cancer screening with current nodule management protocols (e.g., Lung-RADS) might improve the balance of benefits and harms. Use of risk prediction models might improve the balance of benefits and harms, although there remains considerable uncertainty about how such approaches would perform in actual practice because current evidence does not include prospective clinical utility studies.

Table of Contents

Figures

Tables

List of Appendixes

Chapter 1. Introduction

Scope and Purpose

The U.S. Preventive Services Task Force (USPSTF) will use this report to inform an update of its recommendation on the topic of lung cancer screening. In 2013, the USPSTF recommended annual screening for lung cancer with low-dose computed tomography (LDCT) in adults ages 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years (B recommendation).[1] The USPSTF recommended that screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. This report systematically evaluates the current evidence on screening for lung cancer with LDCT for populations and settings relevant to primary care in the United States. This report also summarizes the main benefits and harms of surgical resection or stereotactic body radiotherapy (SBRT) for the treatment of early (Stage I) non-small cell lung cancer (NSCLC).

Condition Definition

Lung cancer is an abnormal proliferation of cells that originate in the lung tissues. Lung cancer has traditionally been classified into two major categories based on cell type and incorporation of immunohistochemical and molecular characteristics: (1) NSCLC, which collectively comprises adenocarcinoma, squamous cell carcinoma, and large cell carcinoma, and (2) small-cell lung cancer (SCLC), which is more aggressive and has worse survival rates.[2] The Tumor Node Metastasis staging system is used to characterize the extent of disease and determine lung cancer stage, treatment, and prognosis. **Table 1** shows an overview of staging for NSCLC. Persons with Stage I disease have lung tumors less than or equal to 4 cm, no lymph node or metastatic involvement, and the best prognosis for survival.[3] For SCLC, a simpler staging designating limited and extensive disease is used.

Etiology and Natural History

Smoking is the number one cause of lung cancer, but secondhand smoke and environmental exposures also increase risk.[4] Trends in lung cancer incidence and mortality rates have closely reflected historical patterns of smoking (but with a delay of decades).[4] In general, the prognosis for persons with lung cancer is poor; the 5-year survival rate for all stages combined was about 16 percent from 1995 to 2001, with rates varying significantly by stage at diagnosis.[5] From 2008 to 2014, reported 5-year survival rates were better, 18.6 percent for all stages combined.[3] Most patients (79%) diagnosed with lung cancer present with distant or metastatic disease; only 16 percent are diagnosed with localized (i.e., Stage 1) disease.[3]

Risk Factors

The risk of developing lung cancer is largely driven by age and smoking status. The incidence of lung cancer increases with every additional decade of life; the median age of lung cancer diagnosis is 70 years.[6, 7] Smoking is estimated to account for nearly 90 percent of all lung cancers.[8] The relative risk of lung cancer in smokers is approximately 20-fold that of nonsmokers, and risk increases with cumulative quantity and duration of smoking.[9] Secondhand smoke, which exposes nonsmokers to the components of tobacco smoke at lower concentrations, is also an established cause of lung cancer.[10, 11]

Other risk factors for lung cancer include environmental exposures, radiation therapy, other (noncancer) lung diseases, race/ethnicity,[12] and family history. Environmental exposures account for a proportionately smaller burden of lung cancer compared with tobacco (approximately 10%) and include the carcinogens radon, asbestos, polycyclic aromatic hydrocarbons (i.e., tar, soot), arsenic, and metals (e.g., beryllium, cadmium, chromium, nickel).[13, 14] Patients treated with radiation therapy are also at an increased risk of developing a primary lung cancer. In a systematic review that included 21 studies of patients with Hodgkin's lymphoma, radiation therapy was associated with an approximately five-fold increase in secondary lung cancer; the percentage of patients who received radiation therapy ranged from 48 to 100 percent in the included studies.[15] Similarly, in a meta-analysis of breast cancer patients (N=631,021), those treated with radiation therapy had a higher risk of a second lung cancer (relative risk [RR], 1.23; 95% confidence interval [CI], 1.07 to 1.43), which increased with duration of time following diagnosis.[16] Lung diseases, such as chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis, are associated with an increased risk of lung cancer, independent of age and smoking history.[17] In a subcohort analysis of the National Lung Screening Trial (NLST), lung cancer incidence increased linearly with increasing severity of COPD.[18] Cigarette smoking potentiates the risk of lung cancer in persons with other risk factors like environmental exposures, radiation therapy, and lung disease.[18-20] Finally, a family history of lung cancer is associated with a 1.7-fold increased risk of developing lung cancer (95% CI, 1.6 to 1.9), an association that is greater with two or more relatives with lung cancer and weaker in nonsmokers (odds ratio [OR], 3.6 [95% CI, 1.6 to 83] and OR, 1.4 [95% CI, 1.2 to 1.7], respectively).[21]

Prevalence and Burden

Lung cancer is the second most common cancer and the leading cause of cancer-related death in both men and women in the United States.[22] In 2017 (the most recent year with complete data) 222,500 persons in the United States were diagnosed with lung cancer, and 155,870 persons died from lung cancer, of which 84,590 were men and 71,280 were women.[22] A large majority (approximately 85%) of lung cancers are NSCLC, about 10 to 15 percent of lung cancers are SCLC, and fewer than 5 percent are lung carcinoid tumors.[23] Lung cancer incidence increases with age, and the risk is greater in men than in women. Among men, black men have the highest incidence rate of getting lung cancer, followed by white, Asian/Pacific Islander, American Indian/Alaska Native, and Hispanic men.[3] Among women, the rate is highest among white women, followed by black, American Indian/Alaska Native, Asian/Pacific Islander, and Hispanic

women.[3] Lung cancer incidence and death rates have decreased since the 1990s in both men and women because of lower rates of smoking.[3, 22]

Regarding the preventable burden of disease, a 2013 study using National Health and Nutrition Examination Survey and National Health Interview Survey (NHIS) data estimated that approximately 8.6 million Americans were eligible for lung cancer screening in 2010 according to NLST eligibility criteria (ages 55 to 74 years with at least a 30 pack-year smoking history who currently smoke or used to smoke). The study stated that if the NLST were fully implemented among this screening-eligible population, a total of 12,250 lung cancer deaths would be averted each year.[24] Others have estimated fewer lung cancer deaths would be averted. A study using data from the 2012 Health and Retirement Study evaluated comorbidities, life expectancy, smoking history, and other characteristics in the screening-eligible population and in NLST participants; it reported a lower 5-year survival rate and life expectancy in the screening-eligible persons compared with NLST participants. The authors concluded that the general U.S. population eligible for lung cancer screening is probably less likely to benefit from early detection compared with NLST participants because they face a high risk of death from competing causes, such as heart disease, diabetes, or stroke.[25]

Rationale for Screening and Screening Strategies

Lung cancer has a high prevalence, high morbidity and mortality, and better survival rates if diagnosed at an earlier stage.[3] The main rationale for screening is that it could lead to earlier detection of lung cancer when treatment is more likely to be effective. Screening is aimed at early detection of NSCLC rather than SCLC because the latter is much less common and typically spreads too quickly to be reliably detected by intermittent screening. The screening modality used in current clinical practice is LDCT. Other screening modalities that have been studied, but have not found to be beneficial, include sputum cytology, chest X-ray (CXR), and biomarkers.[26, 27]

Findings from LDCT can range from incidental pulmonary nodules to lesions suspicious for lung cancer. Multiple approaches to nodule classification that guide additional testing or surveillance are available. For example, in an effort to standardize LDCT screening results reporting, the American College of Radiology developed and endorses the Lung-RADS™ classification system (**Appendix A Table 1** and **Appendix A Table 2**).[28] Lung-RADS provides guidance to clinicians on which findings are suspicious for cancer and suggested management. Briefly, lesions in Lung-RADS categories 1 and 2 are considered benign, whereas category 3 lesions (probably benign) warrant more frequent surveillance, and category 4 lesions (suspicious) require more aggressive evaluation.

For patients with suspected lung cancer, diagnosis by the least invasive method is recommended.[29] Choosing a method to establish a diagnosis of lung cancer depends on the location of the primary lesion and potential metastatic lesions. Diagnostic techniques and procedures include sputum cytology; flexible bronchoscopy, preferred for central lesions; endobronchial ultrasound, preferred for peripheral lesions; trans-thoracic tissue needle aspiration for lesions not accessible by bronchoscopy; pleural fluid cytology or biopsy for pleural lesions;

and surgery. If results from any method are negative and clinical suspicion is high, more invasive testing is recommended.

Treatment Approaches

Lung cancer can be treated with surgery, chemotherapy, radiation therapy, newer targeted immunotherapies, and combinations of these treatments.[30] Management is determined by the presenting stage of disease and the patient's functional status, pulmonary function, medical comorbidities, and values (**Table 1** for NSCLC; **Appendix A Table 3** for SCLC). Surgical resection, lobectomy, is the treatment of choice for eligible patients with Stage I or II NSCLC and can be performed via open thoracotomy or video-assisted thoracoscopic surgery (VATS).[31] For nonsurgical candidates, SBRT is a treatment option. In the NLST and NELSON trials, 50 to 62 percent of diagnosed cancers in the LDCT screening group were Stage I and 6 to 7 percent were Stage II (**Appendix A Table 4**).[32, 33]

Clinical Practice in the United States

Several recent studies have described the uptake of lung cancer screening in the United States since the USPSTF B recommendation was issued. An analysis of data from the Cancer Control Module of the NHIS data from 2010 (before the most recent USPSTF guidelines were issued) and 2015 (after the guidelines were issued) gives some idea of screening uptake.[34] The NHIS survey used the following item as a proxy for lung cancer screening with chest computed tomography (CT): "Were any of the CAT scans of your chest area done to check for lung cancer, rather than for some other reason?" Overall, the percentage of U.S. adults older than age 40 who received CT scans for lung cancer screening was very low, although it increased from 2010 to 2015 (1.3% vs. 2.1%). Among respondents who met USPSTF-recommended age and smoking criteria, screening increased from 2.1 to 6.0 percent ($p<0.001$). The survey also found a temporal increase in screening from 2.1 to 3.8 percent among 55- to 74-year-olds who were at lower risk for lung cancer because they did not meet the eligibility criteria for smoking ($p<0.001$). Overall, the findings suggest an increase, which was large in relative terms but small in absolute terms, in use of CT screening in the U.S. population meeting eligibility criteria for lung cancer screening as well as some "unintended spillover" of screening to lower risk populations. An analysis using a 20 percent national sample of Medicare enrollees ages 55 to 77 years from January 2010 through December 2016 estimated even lower rates of LDCT screening than those estimated from NHIS.[35] More recently, however, a study using data for 10 states from the 2017 Behavioral Risk Factor Surveillance System survey found that uptake of LDCT was up to 14.4 percent, with variation across the 10 states (from 6.5% to 18.1%) and higher rates for those with insurance or COPD.[36]

A recent survey of medical directors of Federally Qualified Health Centers that serve low-income populations found that 43 percent of clinics had implemented lung cancer screening, although most reported low volume. Respondents noted that substantial implementation challenges include lack of staff time, lack of resources to systematically collect tobacco use data

and track screened populations, and substantial patient financial barriers to initial screening (for those uninsured) and followup procedures.[37]

A description of implementation of lung cancer screening in the Veterans Health Administration found that 2,106 patients underwent screening over 2 years.[38] The authors noted that screening registry data collection was labor intensive and required manual abstraction of medical record information. Of all patients screened, 56 percent had nodules that required tracking; 2 percent required further evaluation, but the findings were not cancer; and 1.5 percent had lung cancer. Incidental findings (e.g., emphysema, coronary artery calcification) were noted on LDCT scans of 40.7 percent of patients.[38, 39]

The Centers for Medicare & Medicaid Services (CMS) covers lung cancer screening, albeit with several stipulations.[40] Among these stipulations is a requirement for a written order from a provider during a lung cancer screening counseling and shared decision making (SDM) visit. Specific required elements of this visit included the use of one or more decision aids, to include benefits, harms, followup diagnostic testing, overdiagnosis, false positive rate, and total radiation exposure. Another stipulation was that CMS would cover screening only by radiologists and imaging facilities that meet certain quality standards and that collect and submit required data elements to a CMS-approved national registry for each LDCT lung cancer screening performed. Virtually all guidelines that recommend lung cancer screening, including those issued by the USPSTF, recommend that providers conduct a rigorous process of informed and SDM about the benefits and harms of lung cancer screening before initiating screening. However, given the complex nature of benefits and harms associated with screening, there is some concern that robust SDM is impractical to implement in actual practice.[37, 41, 42] Contextual Question 1 (**Appendix A**) further describes the barriers to implementing lung cancer screening and surveillance in clinical practice in the United States.

Recommendations of Other Organizations

Most guidelines on lung cancer screening now recommend screening in high-risk persons. The American Cancer Society, along with several specialty societies including the American Thoracic Society, the American College of Chest Physicians, and the American Lung Association, have issued recommendations that are similar to those of the USPSTF (**Appendix A Table 5**). The definition of high risk varies somewhat in terms of age range, smoking history, and other factors but is generally overlapping across guidelines. The National Comprehensive Cancer Network (NCCN) recommends expansion of the screening-eligible population beyond the USPSTF criteria by beginning at age 50 in those with 20 or more pack-years if they also have an additional risk factor, including a cancer history, family history, chronic lung disease (including COPD), or occupational/environmental exposures (e.g., asbestos, radon, silica). The NCCN also notes that it is reasonable to consider using the PLCOm2012 lung cancer risk calculator to assist in quantifying risk, considering a 1.3 percent threshold of lung cancer risk (over 6 years).[43] Of note, the American Academy of Family Physicians (AAFP) reviewed the USPSTF recommendation and concluded that evidence was insufficient[44] to recommend for or against screening.[45] They determined that screening cannot be recommended on the basis of a single study conducted in major medical centers.

Chapter 2. Methods

Key Questions and Analytic Framework

The scope and key questions (KQs) were developed by the Evidence-based Practice Center (EPC) investigators, USPSTF members, and Agency for Healthcare Research and Quality (AHRQ) Medical Officers. The analytic framework and KQs that guided the review are shown in **Figure 1**. Eight KQs were developed for this review:

1. a. Does screening for lung cancer with LDCT change the incidence of lung cancer and the distribution of lung cancer types and stages (i.e., stage shift)?
   b. Does screening for lung cancer with LDCT change all-cause mortality, lung cancer mortality, or quality of life?
   c. Does the effectiveness of screening for lung cancer with LDCT differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?
   d. Does the effectiveness of screening for lung cancer with LDCT differ by the number or frequency of LDCT scans (e.g., annual screening for 3 years, the protocol used in the NLST vs. other approaches)?

2. Does the use of risk prediction models for identifying adults at higher risk of lung cancer mortality improve the balance of benefits and harms of screening compared with the use of trial eligibility criteria (e.g., NLST criteria) or the 2013 USPSTF recommendations?

3. a. What is the accuracy of screening for lung cancer with LDCT?
   b. Does the accuracy of screening for lung cancer with LDCT differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?
   c. Does the accuracy of screening for lung cancer with LDCT differ for various approaches to nodule classification (i.e., those based on nodule size and characteristics)?

4. a. What are the harms associated with screening for lung cancer with LDCT?
   b. Do the harms of screening for lung cancer with LDCT differ with the use of Lung-RADS, International Early Lung Cancer Action Program (I-ELCAP), or similar approaches (e.g., to reduce false-positive results)?
   c. Do the harms of screening for lung cancer with LDCT differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?

5. a. What are the harms associated with workup or surveillance of nodules?
   b. Do the harms of workup or surveillance of nodules differ with the use of Lung-RADS, I-ELCAP, or similar approaches (e.g., to reduce false-positive results)?
   c. Do the harms of workup or surveillance of nodules differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?

6. a. What is the effectiveness of surgical resection or SBRT for the treatment of early (Stage I) non-small cell lung cancer?
   b. Does the effectiveness of surgical resection or SBRT differ for subgroups defined by age, sex, race/ethnicity, or presence of comorbid conditions?

7. a. What are the harms associated with surgical resection or SBRT for the treatment of early (Stage I) non-small cell lung cancer?
   b. Do the harms of surgical resection or SBRT differ for subgroups defined by age, sex, race/ethnicity, or presence of comorbid conditions?

8. What is the magnitude of change in all-cause and lung cancer mortality that results from a specified change in lung cancer incidence (and change in distribution of lung cancer stages [i.e., stage shift]) after screening?

In addition to addressing the KQs, this review also looked for evidence related to four contextual questions (CQs) that focused on barriers to implementing lung cancer screening and surveillance in clinical practice in the United States; the representativeness of participants, settings, and providers in randomized, controlled trials (RCTs) of lung cancer screening to corresponding individuals and institutions in the United States.; the comparability of 5-year survival rates and life expectancy of screening-eligible adults (based on NSLT criteria or USPSTF recommendations) to those of NLST participants; unintended benefits of LDCT screening for lung cancer from detecting incidental findings; and the effectiveness of smoking cessation interventions among patients receiving LDCT screening. These CQs were not a part of this systematic review. They are intended to provide additional background information. Literature addressing these questions is summarized in **Appendix A**.

Data Sources and Searches

PubMed/MEDLINE and the Cochrane Library were searched for English-language articles published from January 1, 2012, through May 28, 2019. A predefined list of search terms and Medical Subject Headings (MeSH) focused on terms that describe relevant populations, tests, interventions, outcomes, and study designs was used when applicable. The search relied primarily on the previous systematic review for the USPSTF to identify potentially relevant studies published before 2012 (we reassessed all articles included in that systematic review using the eligibility criteria).[46, 47] Complete search terms and limits are listed in **Appendix B**. ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (WHO ICTRP) were searched for unpublished literature. To supplement electronic searches, reference lists of relevant articles, systematic reviews, and studies meeting the inclusion criteria were reviewed. Studies suggested by peer reviewers or public comment respondents were reviewed and, if appropriate, incorporated into the final review. Since May 28, 2019, ongoing surveillance was conducted through article alerts and targeted searches of journals to identify major studies published in the interim that may affect the conclusions or understanding of the evidence and the related USPSTF recommendation. The last surveillance was conducted on November 20, 2020, and we identified two potentially relevant articles. One study used the LCDRAT risk prediction model using the NHIS 2013-2015. Findings were

similar to those reported by other studies assessing the LCDRAT that are included in this review.[48] The study also estimated life-years gained by screening by developing another model for risk prediction of mortality; however, the model was not externally validated in a non-NHIS cohort and was therefore not eligible for this review. The second article (also mentioned by a public commenter) was by the same authors and evaluated the LCDRAT model using NHIS 2005, 2010, and 2015.[49] It similarly estimated a greater percentage of screen-prevented lung cancer deaths across a range of risk thresholds (1.5% to 2.5%) compared with USPSTF criteria. The results of these studies would not change conclusions or the strength of evidence. All literature search results were managed using EndNote™ version 7.4 (Thomson Reuters, New York, NY).

Study Selection

Inclusion and exclusion criteria for populations, interventions, comparators, outcomes, timing, settings, and study designs were developed with input from the USPSTF (**Appendix B2**). English-language studies of adults age 18 years or older conducted in countries categorized as "very high" on the 2016 Human Development Index[50] and published in or after 2001 were included. For KQs 1 through 5 and 8 (screening and risk prediction), studies of asymptomatic adults with at least 1,000 participants were included. For KQs 6 and 7 (benefits and harms of treatment), studies among adults with Stage I NSCLC treated with surgery or SBRT (sometimes referred to as stereotactic ablative radiation, or SABR) were included. For all KQs, controlled clinical trials were eligible. Prospective cohort studies (i.e., cohort studies based on prospectively collected data that were intended to be used for evaluations relevant to this review) were also eligible for KQs on harms of screening or workup (KQs 4 and 5) and treatment (KQs 6 and 7); case-control studies were eligible for KQs on harms (KQs 4, 5, and 7).

For KQ 1 (direct evidence for health outcomes), studies that compared LDCT with CXR, no screening, or usual care were eligible. For KQ 2 (on risk prediction), externally validated models aimed at identifying persons at increased risk of lung cancer using multiple variables, including at least age and smoking history, were included. Eligible risk prediction models had to be compared to either the 2013 USPSTF recommendations or criteria used by trials showing benefit (e.g., NLST). Eligible outcomes included estimated screen-preventable lung cancer deaths or all-cause mortality, estimated screening effectiveness (e.g., number needed to screen [NNS]), and estimated screening harms. For KQ 3 (on accuracy), eligible outcomes included sensitivity, specificity, and predictive value. Because there is no single gold standard for assessing accuracy of LDCT for the diagnosis of lung cancer, comparators of subsequent diagnosis of lung cancer within 1 year (likely from repeat imagining and biopsy), biopsy, or subsequent imaging were eligible. For KQs on the harms of screening (KQ 4) or workup and surveillance (KQ 5), studies that evaluated LDCT (KQ 4) or other tests used after screening (KQ 5) were eligible; a comparison group was not required. For KQs on benefits (KQ 6) and harms (KQ 7) of treatment, studies that reported survival over at least 5 years of followup or harms were eligible.
Titles and abstracts were independently reviewed by two investigators; those marked for potential inclusion by either reviewer were retrieved for evaluation of the full text. The full texts were then independently reviewed by two investigators to determine final inclusion or exclusion. Disagreements were resolved by discussion and consensus.

Quality Assessment and Data Abstraction

Quality assessments were conducted using instruments devised for each of the included study designs and adapted for this topic. Criteria developed by the USPSTF[51] were used to evaluate randomized studies, while Cochrane's ROBINS-I tool[52] was used for nonrandomized studies, the QUADAS-2 instrument[53] was used to assess studies of diagnostic accuracy (KQ 3), and the CHARMS checklist[54] was used to assess risk prediction models (KQ 2) (**Appendix B)**. Each study was evaluated by two independent reviewers using the instrument(s) described above. Risk-of-bias ratings were translated into overall quality ratings of good, fair, or poor, using USPSTF criteria.[51] Disagreements were resolved by discussion. Only studies rated as having good or fair quality were included.

For each included study, one investigator extracted pertinent information about the methods, populations, interventions, comparators, outcomes, timing, settings, and study designs. All data extractions were checked by a second investigator for completeness and accuracy.

Data Synthesis and Analysis

Findings for each KQ were summarized in tabular and narrative format. For KQs 4 and 5, it was often unclear whether harms were directly from LDCT screening or were part of the downstream workup that follows screening. Therefore, this review reports the harms of screening and the cascade of events that follows within a combined section for KQs 4 and 5 that was stratified by outcome (e.g., radiation, overdiagnosis), specifying, when possible, if harms were directly from a particular part of the cascade. The overall strength of the evidence for each KQ was assessed as high, moderate, low, or insufficient based on the overall quality of the studies, consistency of results between studies, precision of findings, risk of reporting bias, and limitations of the body of evidence, using methods developed for the USPSTF (and the EPC program).[51] Additionally, the applicability of the findings to U.S. primary care populations and settings was assessed. Discrepancies were resolved through consensus discussion.

To determine whether meta-analyses were appropriate, the clinical and methodological heterogeneity of the studies was assessed according to established guidance.[55] The populations, tests, treatments, comparators, outcomes, and study designs were assessed qualitatively, looking for similarities and differences. The authors of this review did not conduct meta-analyses because of substantial clinical and methodological heterogeneity. For example, the trials of lung cancer screening differed in eligibility criteria (e.g., age, pack-years of smoking, years since quitting), number of screening rounds (from 2 to 5), screening intervals (e.g., annual, biennial, or escalating), thresholds for a positive screen (e.g., 4 mm, 5 mm, or based on volume), and comparators (CXR or no screening). For KQ 1, the authors of this review created forest plots to display the findings of each study by calculating incidence rate ratios (IRR), using number of events and person-years, for lung cancer incidence, lung cancer mortality, and all-cause mortality. Quantitative analyses were conducted using Stata version 14 (Stata Corp).

USPSTF Involvement

This review was funded by AHRQ. AHRQ staff and USPSTF members participated in developing the scope of the work and reviewed draft reports, but the authors are solely responsible for the content.

Expert Review and Public Comment

A draft Research Plan was posted for public comment on the USPSTF Web site from May 3, 2018 to May 30, 2018. In response to public comments, the USPSTF expanded the eligibility criteria to include SBRT and clarified terminology related to screening tests, comparators, and outcomes in the Research Plan. A final Research Plan was posted on the USPSTF's Web site on August 16, 2018. A draft report was reviewed by content experts, representatives of Federal partners, USPSTF members, and AHRQ Medical Officers. Reviewer comments were presented to the USPSTF during its deliberations and subsequently addressed in revisions of this report when appropriate. The draft report was posted for public comment. Revisions were made based on comments received, and references suggested by expert or public reviewers were evaluated for inclusion/exclusion. Revisions included the addition of a study addressing variation in accuracy by different approaches to nodule classification, clarifying that I-ELCAP changed their threshold for a positive nodule over time (from 5 mm to 6 mm), clarifying the nonlung cancers diagnosed in NLST participants, and updating the risk factors section of the introduction.

Chapter 3. Results

Literature Search

We identified 11,541 unique records and assessed 2,212 full-text articles for eligibility (**Figure 2**). We excluded 1,989 articles for various reasons, detailed in **Appendix C**, and included 223 publications. Of these, 26 publications reported eligible outcomes for the overarching question, KQ 1. Details of quality assessments of included studies and studies excluded because of poor quality are in **Appendix D Tables 1-11**.

Results by Key Question

Key Question 1

KQ 1a. Does screening for lung cancer with LDCT change the incidence of lung cancer and the distribution of lung cancer types and stages (i.e., stage shift)?

b. Does screening for lung cancer with LDCT change all-cause mortality, lung cancer mortality, or quality of life?
c. Does the effectiveness of screening for lung cancer with LDCT differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?
d. Does the effectiveness of screening for lung cancer with LDCT differ by the number or frequency of LDCT scans (e.g., annual screening for 3 years, the protocol used in the NLST, vs. other approaches)?

Summary of Included Trials

We included seven randomized, clinical trials (described in 26 articles) that evaluated lung cancer screening with LDCT (**Table 2**): NLST, Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays (DANTE), Danish Lung Cancer Screening Trial (DLCST), Italian Lung Cancer Screening Trial (ITALUNG), Lung Screening Study (LSS), the German Lung Cancer Screening Intervention Trial (LUSI), and the Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON) study.[32, 33, 56-79] All seven trials reported data on lung cancer incidence, lung cancer mortality, and all-cause mortality. Two trials conducted in the United States compared LDCT with CXR (LSS and NLST), and five trials conducted in Europe compared LDCT with no screening (DANTE, DLCST, ITALUNG, LUSI, and NELSON). Only the NLST (53,454 participants) and NELSON (15,792 participants) were adequately powered to assess for a lung cancer mortality benefit.[32, 76] Sample sizes ranged from 2,472 (DANTE) to 4,104 (DLCST) for the other five trials.[59, 62, 65, 69, 71] The age range for eligibility was similar across trials, with all ranges falling within 50 to 74 years of age. Current smokers ranged from 48 to 77 percent of the participants in each trial. The majority of participants were male in all trials (range, 56% to 100%); the DANTE trial enrolled 100 percent male participants and NELSON enrolled 84 percent males. The majority of participants were white in all trials; in the NLST, 91 percent were white, less than 5 percent were black, and less

than 2 percent were Hispanic or Latino. Six of the included trials evaluated annual screening, although the number of screening rounds varied, ranging from two (LSS) to five (DANTE, DLCST, and LUSI). NELSON evaluated four rounds of screening with increasing intervals for each round (baseline and after 1, 3, and 5.5 years). NELSON was also unique in using volumetric measurements of detected nodules and calculating volume-doubling time to define positive screening results (see KQ 3 for further details about definitions of positive tests for all trials).

Trials varied in their definition of a positive screen and in the followup evaluation process (see KQ 3 and KQs 4/5 section on false positives for details). All trials began enrollment between 2000 and 2007. Median duration of followup for lung cancer mortality (including publications describing long-term post-trial followup) ranged from 5.2 (LSS) to 12.3 (NLST) years. Compared with the prior systematic review conducted for the USPSTF, longer followup or more complete endpoint verification was available from DANTE,[61] DLCST,[67] LSS,[75] and the NLST,[63, 74] and three additional trials—NELSON,[76] ITALUNG,[62] and LUSI[59, 73]—reported data relevant to this KQ.

The NLST was rated as good quality for the main trial outcomes.[32, 57, 58] The extended post-trial followup of NLST was rated as fair quality because of using different ascertainment methods during trial years (with a verification committee) than for post-trial years (relying on registries and without a verification committee); lack of information on any post-trial screening with LDCT that may have taken place in either the LDCT or the CXR group; missing data for lung cancer incidence for 11 out of 33 centers (representing 12.4% of trial participants) that did not have a home state cancer registry available for linkages (this was not a concern for mortality outcomes because linkage to the National Death Index was available for all but 2.2% of trial participants); and, for estimates of overdiagnosis, risk of biasing estimates toward the null because the comparison group received CXR (rather than no screening test).

The main methodological limitations of the NELSON trial included risk of ascertainment bias and lacking details on potential harms of screening (e.g., further testing after screening, such as biopsies, and related harms). Ascertainment included a blinded review of medical files for 296 out of 426 (69.5%) of deceased Dutch patients with known lung cancer; the ascertainment therefore lacked blinded review for over 30 percent of deceased Dutch patients with known lung cancer and for over 80 percent of all 1,728 deaths that occurred. The limited blinded review revealed concordance of 86.1 percent among members of the independent expert committee and a sensitivity and specificity of 92.6 percent and 98.8 percent of the official death certificate for the study's primary outcome (lung cancer mortality). It was not reported whether the 296 blinded medical files reviewed were equally divided between the screening and control groups, raising additional concerns for differential bias in ascertainment. Methods used by the various registries for ascertainment were not reported. For females, there was limited reporting of some information, such as recruitment and selection for the study and adherence to the screening intervention.

We excluded one trial (the Multi-centric Italian Lung Detection [MILD] study) for poor quality;[80, 81] sensitivity analyses in **Appendix E** show results of that trial for lung cancer mortality and all-cause mortality. As in the prior report for the USPSTF, MILD was considered

to have a high risk of bias because of significant differences between the LDCT and no-screening groups at baseline, raising concerns about inadequate randomization, differential followup between groups (with less followup among the control group), high risk of measurement bias, and inability to reach its planned sample size (of 10,000 participants).

Incidence of Lung Cancer and Distribution of Lung Cancer Types and Stages

Overall, the cumulative incidence of lung cancer was higher in LDCT screening groups than in control groups for all studies except for the ITALUNG study (**Figure 3** and **Appendix E Table 2**. Adenocarcinomas were the most commonly diagnosed lung cancer type in both arms of all trials (ranging from 35% [NLST] to 68% [LUSI] of lung cancers diagnosed in LDCT arms) (**Appendix E Table 2**). All included trials reported more Stage I cancers in LDCT groups than in control groups (**Appendix E Table 2**). Most trials reported between 45 and 50 percent Stage I lung cancers in the LDCT groups; absolute between-group differences for Stage I lung cancers ranged from 8 (LSS) to 48 percent (LUSI). **Figure 4** shows the increases in early stage (I-II) and decreases in late stage (III-IV) lung cancer incidence, representing stage shift. At 6.5 years followup, the NLST reported a higher incidence of lung cancer among LDCT participants (4.1%; 1,089 lung cancers; 662 per 100,000 person-years) than among CXR participants (3.6%; 969 lung cancers; 558 per 100,000 person-years). The calculated incidence rate ratio was 1.12 (95% CI, 1.02 to 1.22). The LDCT and CXR groups had similar proportions of adenocarcinomas (35% vs. 34% of incident cancers), squamous cell carcinomas (22% vs. 22%), small cell carcinoma (13% vs. 16%), and other lung cancer types (**Appendix E Table 2**). For stage distribution, the trial reported more Stage I lung cancers in the LDCT group than the CXR group (520 vs. 289 Stage I lung cancers; 50% vs. 31% of incident lung cancers) and fewer Stage IV lung cancers (226 vs. 335; 22% vs. 36%, respectively). An extended followup of the NLST reported no statistically significant difference between groups for overall lung cancer incidence (1,701 lung cancers for the LDCT group vs. 1,681 for the CXR group; calculated incidence rate ratio of 1.01 [0.95, 1.08] **Figure 3**). For stage distribution after 11.3 years, the extended followup identified more Stage I lung cancers in the LDCT group than in the CXR group (40% vs. 27% of incident lung cancers) and fewer Stage IV lung cancers (28% vs. 36%, respectively) (**Appendix E Table 2**). The extended followup used linkages to state cancer registries and the National Death Index to ascertain outcomes beyond the original trial (rather than the same ascertainment methods used for the original trial).

Lung Cancer Mortality

Figure 5 shows the calculated IRRs for the trials that reported lung cancer mortality. Only the NLST and NELSON had sufficiently large sample sizes to detect a difference between groups. The original publication of the main results from the NLST reported a relative risk reduction in lung cancer mortality of 20.0 percent (95% CI, 6.8 to 26.7);[32] a subsequent publication with additional endpoint verification for lung cancer deaths (with approximately an additional year of followup covered, going to the prespecified endpoint) reported a relative reduction of 16 percent (95% CI, 5 to 25).[63] Over almost 7 years of followup, and over 140,000 person-years of followup in each group, the NLST found a significant reduction in lung cancer mortality with three rounds of annual LDCT screening compared with CXR (469 vs. 552 lung cancer deaths;[63] 280 per 100,000 person-years vs. 332 per 100,000 person-years; calculated IRR, 0.85 [95% CI, 0.75 to

0.96]). These findings indicate an NNS to prevent one lung cancer death of 323 over 6.5 years of followup. This calculated NNS is similar to the NNS reported by the initial NLST results publication (i.e., NNS 320 among those undergoing ≥1 screens; intention-to-screen analysis, NNS of 310 [95% CI, 190 to 840]) but is slightly different because of the incorporation of the additional endpoint verification. Analysis of extended followup data of NLST participants at 12.3 years after randomization found a similar absolute difference between groups (1,147 vs. 1,236 lung cancer deaths; RR, 0.92 [95% CI, 0.85 to 1.00]; absolute difference between groups of 3.3 [95% CI, -0.2 to 6.8] lung cancer deaths per 1,000 participants). The NELSON trial reported a reduction in lung cancer mortality for four rounds of screening with increasing intervals between LDCTs (at baseline, 1 year, 3 years, and 5.5 years). Combining NELSON data for males and females, there were 181 lung cancer deaths among participants in the screening group and 242 in the control group (calculated IRR, 0.75 [95% CI, 0.61 to 0.90]) over 10 years of followup. These findings indicate a NNS to prevent one lung cancer death of 130 over 10 years of followup. Results of the other trials were very imprecise and did not show statistically significant differences between screening with LDCT and no screening (**Figure 5**).

All-cause Mortality

Figure 6 shows the calculated IRRs for the trials that reported all-cause mortality. The NLST found a reduction in all-cause mortality with LDCT screening compared with CXR (1,912 vs. 2,039 deaths; 1,141 per 100,000 person-years vs. 1,225 per 100,000 person-years; calculated IRR of 0.93 [95% CI, 0.88 to 0.99]). To prevent one death from any cause, the NNS from the NLST was 219 (95% CI, 112 to 5,000). The other trials found no statistically significant differences between screening with LDCT and no screening, but results were imprecise (**Figure 6**). In the NELSON trial, there were more all-cause deaths in the LDCT screening group than in the control group (868 vs. 860), although the difference between groups was not statistically significant.

Quality of Life

None of the included trials assessed for potential benefits of LDCT screening on quality of life (some evaluated short-term quality of life to assess for possible psychosocial harms of screening, as described in KQ 4, but none evaluated quality of life over the longer course of the trial).

Subgroups

All included trials enrolled participants at high risk for lung cancer (based on age and smoking history). Seven publications using DLCST, LUSI, NELSON, or NLST data described subgroup analyses for at least one of the following; age, sex, race/ethnicity, smoking status and pack-years, history of COPD, and other pulmonary conditions.[63, 64, 66, 67, 73, 74, 76] A post hoc analysis of NLST data reported that 88 percent of the mortality benefit was achieved by screening the 60 percent of participants at highest risk for lung cancer death.[56] The 20 percent of participants at lowest risk accounted for just 1 percent of prevented lung-cancer deaths.[56] Other post hoc analyses of NLST data reported lung cancer mortality by sex (RR 0.73 for women vs. 0.92 for men, p=0.08), age (RR 0.82 for <65 vs. 0.87 for ≥65, p=0.60), race/ethnicity (hazard ratio [HR] 0.61 for black individuals vs. 0.86 for whites, p=0.29), and smoking status (RR 0.81 for current smokers vs. 0.91 for former smokers, p=0.40), and did not identify statistically significant differences

between groups.[63, 64, 66] A long-term followup of NLST participants at 12.3 years reported similar results for subgroups and did not identify statistically significant interactions by sex, age, or smoking status (sex: RR 0.86 for women vs. 0.97 for men, p=0.17; age: RR 0.86 for <65 years vs. 1.01 for ≥65 years, p=0.051; smoking status: RR 0.88 for current smokers vs. 1.01 for former smokers, p=0.12).[74] Both LUSI and NELSON reported a similar pattern for subgroups by sex as found in NLST that was not statistically significantly different between groups (LUSI: women, HR=0.31 [95% CI, 0.10 to 0.96] vs. men, HR=0.94 [95% CI, 0.54 to 1.61], p=0.09) or without reporting an interaction test (NELSON: women, RR 0.67 [95% CI, 0.38 to 1.14] vs. men, RR 0.76 [95% CI, 0.61 to 0.94] at 10 years of followup).[73, 76] NELSON reported analyses by age group among the men in the trial (not including the women in those analyses) but did not report interaction tests for subgroups defined by age (RRs ranged from 0.59 [95% CI, 0.35 to 0.98] for persons aged 65 to 69 years at randomization to 0.85 [95% CI, 0.48 to 1.50] for persons aged 50 to 54 years at randomization).[76] In a post hoc analysis of the DLSCT trial, age and having both COPD and greater than or equal to 35 pack-years of smoking were associated with an increased risk of death from lung cancer.[67]

Difference in Effectiveness by the Number or Frequency of LDCT Scans

Only the MILD study, which was excluded for poor quality, had a direct comparison by frequencies, comparing annual screening, biennial screening, and no screening.[82] No good- or fair-quality studies directly compared number or frequency of LDCT scans. Screening intervals were similar for all trials except for NELSON (which used increasing intervals between tests for each of its four screening rounds), with screening done annually. The number of screening rounds varied across studies; the NLST had three annual scans. Reported participation rates across studies varied somewhat but were 90 percent or greater for all studies except for ITALUNG (adherence to screening of 81% across all rounds of screening) and LSS (77% at year 1 among participants with positive baseline screen).

Key Question 2. Does the Use of Risk Prediction Models for Identifying Adults at Higher Risk of Lung Cancer Mortality Improve the Balance of Benefits and Harms of Screening Compared With the Use of Trial Eligibility Criteria (e.g., NLST Criteria) or the 2013 USPSTF Recommendations?

Summary

For benefits, four studies of three different risk prediction models (a modified version of a model developed from participants of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial [PLCOm2012], the Lung Cancer Death Risk Assessment Tool [LCDRAT], and Kovalchik model) estimating outcomes in four different cohorts reported increased screen-preventable deaths compared with the risk factor–based criteria used by the NLST or USPSTF (in the 2013 recommendations). Three studies demonstrated improved screening efficiency (determined by the NNS) of risk prediction models compared with risk factor–based screening, while one study showed mixed results. For harms, eight studies of 13 different risk prediction models (PLCOm2012, simplified PLCOm2012, Bach, Liverpool Lung Project [LLP], simplified LLP,

Knoke, Two-Stage Clonal Expansion [TSCE] incidence, TSCE Cancer Prevention Study [CPS] death, TSCE Nurses' Health Study [NHS]/Health Professionals Followup Study [HPFS] death), the Hunt Lung Cancer model, LCDRAT, COPD-LUCSS, Kovalchik model) estimating outcomes in four different cohorts reported similar numbers of false-positive selections from risk prediction with respect to lung cancer events (i.e., the risk prediction model selected people to be screened who did not have or develop lung cancer or death from lung cancer) and mixed findings for rates of false-positive selections with respect to lung cancer events when comparing risk prediction models with the risk factor–based criteria used by the NLST or USPSTF. In general, estimates of benefits and harms were consistent but imprecise, primarily because of a lack of an established risk threshold to apply the model.

Description of Included Studies

Nine good- or fair-quality studies were included, which evaluated 13 different risk prediction models.[56, 83-88] **Table 3** summarizes the predictors included in each model. The PLCOm2012 model was the most commonly evaluated model compared with risk factor–based criteria in five studies;[83, 85-87, 89] the LCDRAT model was evaluated by two studies;[84, 89] the other models were evaluated by one study each. Risk models included personal history, smoking history, family history of cancer, occupational exposures like asbestos, and lung conditions (e.g., COPD, emphysema).

The PLCOm2012 model was developed in ever-smokers in the PLCO control arm. Compared with USPSTF criteria, the PLCOm2012 model includes more personal factors (e.g., history of malignancy), more detailed smoking history, family history, and a personal history of COPD.[85] The Lung Cancer Risk Assessment Tool (LCRAT) and LCDRAT are risk models developed and validated in the control and CXR arms of the PLCO, respectively.[84] Additional eligible models for this systematic review included the Kovalchik model, the Bach model, the LLP model, simplified LLP model, the Knoke model, the Hunt Lung Cancer model, and three TSCE models predicting lung cancer incidence and death. Models included a variety of additional risk factors, such as smoking intensity (cigarettes per day);[56, 84, 85, 90, 91] occupational asbestos exposure;[90, 92] lung conditions of emphysema, COPD, and pneumonia;[56, 84, 85, 88, 92] and family history of lung cancer.[56, 84, 85, 92]

The models included in the evidence review were developed across several cohorts: smokers in the PLCO control arm,[84, 85] NLST control arm,[56] the Pittsburg Lung Screening Study,[88] the Carotene and Retinol Efficacy Trial,[90] the Liverpool Lung Project case-control study,[92] the NHS, HPFS,[93] the American Cancer Society's first Cancer Prevention Study (CPS-I), the American Cancer Society's second Cancer Prevention Study (CPS-II),[94] and the HUNT study.[95] The models were externally validated in four cohorts in the United States,[56, 83-85] one in Spain,[88] one in Norway,[95] and one in Australia.[86] Specifically, these cohorts included the NLST control (CXR) arm or pooled arms,[84, 85] smokers from the CXR and control arms of the PLCO Screening Trial 2003-2009,[56, 83-85] the NHIS 2010-2012,[84] NHIS 2015,[89] the Australian 45 and Up Study (cohort of 267,017 Medicare-eligible individuals 2006-2009),[86] the CONOR database in Norway,[95] and the Pamplona-International Early Lung Cancer Detection Program (572 individuals 2001-2013).[88] Models predicted lung cancer incidence,[85] lung cancer death,[56, 94, 96] or both.[90] The time horizon of the predictions was 1 year for the Bach model and TSCE models,[90,

[93, 94] although to obtain predictions for longer time frames, investigators repeated the risk prediction for multiple years: 5 years for the LLP model,[92] the Katki model (LCDRAT and LCRAT),[84] and the Kovalchik model;[56] 6 years for the PLCOm2012 model, the HUNT model,[95] and the Knoke model;[96] or were not reported.[88]

Outcomes were estimated by applying each risk model to the cohort (or cohorts) used for external validation. There are currently no consensus risk thresholds to deploy risk prediction models for lung cancer screening. In other words, there is not a particular 5- or 6-year calculated risk for lung cancer incidence or lung cancer death that is agreed upon as the threshold for recommending screening. Individual study investigators employed one or more of the following strategies to determine a risk threshold, which could be used to estimate benefit or harm outcomes of using a risk-based approach to screening compared with NLST or USPSTF criteria:

1. Fixed-USPSTF (or NLST) population size: select model risk threshold such that the number screened matches the number of USPSTF (or NLST) screen-eligible smokers in the United States[83-87]
2. Fixed-USPSTF effectiveness estimate: select model risk threshold such that the NNS matches the NNS of USPSTF-eligible smokers in the United States[84]
3. Stratification by risk quantiles or quintiles[56, 95]
4. Comparable or improved mortality compared with the NLST: select risk threshold at which lung cancer mortality rates were consistently lower in the CT arm vs. CXR arm of the NLST[86, 87]
5. Optimal classification based on receiver operator curve[86]
6. Risk threshold ≥2% absolute risk[86]

Twelve models demonstrated fair to good discrimination for both lung cancer incidence and lung cancer mortality. Area under the curve [AUC] ranged from 0.62 to 0.89 for eligible studies with better discrimination for lung cancer mortality than for lung cancer incidence and better discrimination in PLCO cohorts compared with the NLST or other cohorts (**Table 3**). For lung cancer mortality, the Katki model, Kovalchik model, PLCOm2012 model (full and simplified), and Bach models generally had better discrimination (and satisfactory calibration) than the other risk prediction models.[56, 83-86] For one model (COPD-Lung Cancer Screening Score [LUCSS]), the included study did not report discrimination or calibration.[88] Studies reporting discrimination or calibration for these models that did not also report eligible KQ 2 outcomes are not included in this summary.

Results of Included Studies

Studies of the PLCOm2012 Model, the Most Commonly Evaluated Model

Five studies evaluated the PLCOm2012 model using five different risk thresholds estimating outcomes over 6 years (**Table 4**).[83, 85-87, 89] Additionally, a simplified version of the PLCOm2012 model was evaluated that included age, and smoking history only.[83]

Two studies of the PLCOm2012 model calculated an increase in screen-prevented lung cancer deaths compared with the NLST criteria over 6 years using assumptions of NLST-like reduction in lung cancer mortality (20%) among smokers in the CXR arm of the PLCO.[85, 89] These two

studies also evaluated NNS to prevent one lung cancer death. One study found a reduction in NNS to prevent one lung cancer death (174 vs. 203).[85] The other study evaluated three risk thresholds (1.3%, 1.51%, and 2.19%) with NNS decreasing as the risk threshold increased (222, 207, and 169) such that the NNS was higher when using a risk prediction model for the two lowest risk thresholds compared with risk factor–based screening.[89]

Across studies of the PLCOm2012 model using a fixed-population approach to setting a risk threshold, there were a similar percentage of false-positive selections for screening and similar rates of false-positive selections for screening with respect to lung cancer deaths when compared with the USPSTF or NLST criteria (range 96.0 to 97.9%, and 37.1 to 38.1 rates, respectively). In the 45 and Up Study, the rate of false-positive selections for screening with respect to lung cancer incidence was lower compared with PLCO cohorts, but similar to false-positive rates for the risk prediction model and risk factor–based screening criteria. Additionally, a simplified version of the PLCOm2012 model including age, and smoking history only was evaluated using fixed-NLST population risk thresholds (1.19% to 1.20%) and similarly found no difference between number of false positive selections for screening or rates of false-positive selections for screening with respect to lung cancer incidence or death when compared with the NLST criteria.[83]

Using the risk threshold of at least 2 percent yielded a lower number of false-positive selections for screening and rates of false-positive selections for screening with respect to lung cancer incidence compared with USPSTF criteria in one study[86] and a lower number of false-positive selections per prevented deaths in another.[89] Studies using a risk threshold based on or close to the NLST mortality benefit (1.51%, 1.49% for optimal receiver operating characteristic curve classification) generally had similar numbers of false-positive selections, but mixed results with respect to rates of false-positive selections, depending on the cohort that was used to estimate outcomes. Two studies applied the PLCOm2012 model to cohorts of ever-smokers where the risk prediction model yielded mixed rates of false-positive selections with respect to lung cancer incidence compared with risk factor–based criteria: in the PLCO-CXR cohort, 33.8 (risk threshold ≥ 1.51%) vs. 37.3 (USPSTF criteria) and the 45 and Up Study, 28.0 for risk threshold ≥ 1.51 percent, 28.2 for risk threshold ≥ 1.49 percent, 23.7 for USPSTF criteria.[86, 87] Neither of these two studies evaluated the effect of risk prediction models on screen-prevented lung cancer deaths or NNS.

Studies of Risk Prediction Models Reporting Benefits and Harms

For the **LCRAT and LCDRAT**, fixed-USPSTF-population, fixed-USPSTF effectiveness strategies, and comparable mortality benefit to NLST were used to select risk thresholds to apply the model to the NHIS 2010-2012 and NHIS 2015.[84, 89] Study investigators assumed NLST-like increases in lung cancer incidence and 20 percent reduction in lung cancer mortality to estimate screen-preventable deaths, NNS, false-positive selections per prevented death (also called "screening efficiency"), and overdiagnosed lung cancer per prevented death. **Kovalchik et al** developed a risk model predicting lung cancer death in the NLST control arm and applied the model to the NLST-CT arm to estimate the outcomes above.[56] Several risk thresholds were evaluated in Kovalchik et al based on risk quintiles; results for quintiles 3-5 and 4-5 corresponding to risk thresholds of 0.84 percent and 1.23 percent are shown in **Table 5**.[56]

Studies of the **PLCOm2012 model and LCDRAT model** estimated a greater number of screen-preventable lung cancer deaths than with the NLST criteria. Calculations for some studies yielded a much higher total number of estimated screen-preventable lung cancer deaths because larger national samples of smokers were used (size of sample greater than 9 million) compared with the samples used to estimate outcomes for the other models (i.e., PLCO and NLST trial arms that included ~20,000-30,000 persons).[84, 89] Kovalchik et al reported outcomes for high-risk subsets of the NLST CT screening arm, so screen-preventable lung cancer deaths were intrinsically smaller for the subset compared with the whole trial arm.

Most studies of the three risk prediction models estimated a lower NNS than screening with the NLST criteria, ranging from 29 to 136 fewer subjects screened per lung cancer death prevented. Exceptions included a study of the LCDRAT that used the PLCO-fixed effectiveness threshold, which intentionally sets the NNS equal to that achieved by the NLST criteria,[84] and one study that used a fixed-population risk threshold (1.3%) and NLST-like mortality benefit threshold (1.51%) in a more modern cohort (NHIS 2015) in which NNS was higher using the risk prediction model compared with risk factor−based criteria (222 and 207, respectively, vs. 194).[89]

Screening efficiency also improved in most cases when a risk-based approach was applied compared with the NLST criteria (range of false-positive selections per prevented lung cancer death: 64-167 for risk models vs. 108-196 for the NLST criteria). The exception was application of the PLCOm2012 model to the 2015 NHIS cohort in which risk thresholds of 1.35 percent and 1.51 percent were used; false-positive selections per prevented deaths ranged from 207 to 222 compared with 194 for USPSTF criteria.[89] For the two thresholds of LCDRAT evaluated, overdiagnosis was similar for risk-based screening and screening using the NLST criteria.

Other Studies of Risk Prediction Models Reporting Only Harms

For the remaining models included in the systematic review—the **Bach**, **LLP**, **simplified LLP**, **Knoke**, **TSCE model, HUNT Lung Cancer Model,** estimates of false-positive selections and rates of false-positive selections with respect to lung cancer incidence or death were compared with the NLST criteria using PLCO cohorts (fixed-NLST population-based risk threshold).[83, 95] In general, false-positive percentages and rates using risk-based screening were similar to screening using the NLST criteria (range of false-positive selections 97 to 98%; range of rates of false-positive selections 21 to 38%).

The **COPD-LUCSS score** predicts lung cancer incidence in subjects with COPD, including risk factors of age, body mass index, smoking in pack-years, and radiologic emphysema.[88] Using a risk threshold of COPD-LUCSS score of 7 to 10, this score had a lower number of false-positive selections for screening with respect to lung cancer incidence than the NLST criteria (86% vs. 91%).

Key Question 3. Accuracy

a. What is the accuracy of screening for lung cancer with LDCT?
b. Does the accuracy of screening for lung cancer with LDCT differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?
c. Does the accuracy of screening for lung cancer with LDCT differ for various approaches to nodule classification (i.e., those based on nodule size and characteristics)?

Summary

Fifty-three articles were eligible for this KQ.[32, 33, 38, 57-61, 64, 70, 71, 76-79, 82, 97-132] Of those, many reported information from the same study (i.e., redundant data), incomplete data, or preliminary data that were later updated in another publication. Therefore, we focused on the results from the 24 publications with the most complete data.[59, 61, 64, 76, 82, 97, 99-101, 103, 104, 107, 108, 111, 113, 115, 119, 121-123, 126, 127, 130, 131] Sensitivity of LDCT from 13 studies (76,856 total participants) ranged from 59 to 100 percent; all but three studies reported sensitivity over 80 percent. Specificity of LDCT from 13 studies (75,819 total participants) ranged from 26.4 to 99.7 percent; all but three reported specificity over 75 percent. Positive predictive value (14 studies, 77,840 participants) ranged from 3.3 to 43.5 percent. Negative predictive value (9 studies, 47,496 participants) ranged from 97.7 to 100 percent. Variability in accuracy was mainly attributed to heterogeneity of eligibility criteria, heterogeneity of screening protocols (e.g., number of screening rounds, screening intervals), heterogeneity and completeness of followup length (e.g., to identify false-negative screens), and heterogeneity in the definitions (e.g., of positive tests, indeterminate tests, false-positive test, false-negative tests). Three studies (2,211 observations) reported on reliability, finding fair to moderate reliability among radiologists.[103, 108, 113] Regarding subgroups, one study demonstrated that LDCT had higher sensitivity and lower specificity for persons 65 or older than for younger persons.[64] Three studies (73,404 participants) compared various approaches to nodule classification (Lung-RADS or I-ELCAP) using the NLST protocol as the basis for comparison.[100, 104, 107] These demonstrated that using Lung-RADS in the NLST would have increased specificity while decreasing sensitivity, and that increases in positive predictive value (PPV) are seen with increasing nodule size thresholds.

Detailed Results: Accuracy

RCTs and nonrandomized studies that reported on sensitivity, specificity, or predictive values (or provided the data that allowed us to calculate measures of accuracy) are summarized in **Tables 6** and **7**, respectively. Six RCTs[59, 61, 76, 82, 99, 101] and seven nonrandomized studies[115, 121, 123, 126, 127, 130, 131] provided sensitivity data. Sensitivity in the RCTs ranged from 59 to 95 percent. Sensitivity in the nonrandomized studies ranged from 87.7 to 100 percent, with five of the nonrandomized studies having sensitivity greater than 90 percent. Six RCTs[59, 61, 76, 82, 99, 101] and seven nonrandomized studies[111, 121, 123, 126, 127, 130, 131] provided specificity data. Specificity in the RCTs ranged from 26.4 to 99.2 percent, and specificity in the nonrandomized studies ranged from 34.0 to 99.7 percent. All but two of the nonrandomized studies[111, 130] had specificity greater than 90 percent. Nine RCTs[59, 61, 76, 82, 99, 101, 119, 122] and five nonrandomized studies[107, 111, 123, 130, 131] provided PPV data. PPV ranged from 3.3 to 43.5 percent in the RCTs and from 3.5 to 20.9

percent in the nonrandomized studies. Six RCTs[59, 61, 76, 82, 99, 101] and three nonrandomized studies[123, 130, 131] provided negative predictive value (NPV) data. NPV ranged from 97.7 to 99.9 percent in the RCTs and from 99.2 to 100 percent in the nonrandomized studies.

Among the trials that reported a reduction in lung cancer mortality, NLST and NELSON, the reported sensitivities were 93.1 and 59 percent and reported specificities were 76.5 and 95.8 percent, respectively.[76, 101] Although the NPVs were similar for the NLST and NELSON (99.9% and 97.7%, respectively), the PPVs were vastly different (3.3% and 43.5%, respectively). This difference could potentially be accounted for by the difference in screening protocols—NELSON used a volumetric approach and provided for an indeterminate nodule result category and the NLST used an approach of maximum diameter without an indeterminate category—or possibly by the prevalence of lung cancer in each of the trial settings. Alternatively, these data could represent two different positions on the same ROC curve, illustrative of tradeoffs between sensitivity and specificity.

Numerous factors may account for the variability in accuracy across studies. There was heterogeneity in the screening protocols, particularly for the number of screening LDCT scans performed, the interval between screening rounds, and threshold for a positive test. The studies also varied in terms of their followup lengths, and some had incomplete followup data. For instance, most of the nonrandomized studies did not report the length of followup after the last screening scan. As a result of differential and incomplete followup data, some studies may not have adequately captured false-positive and false-negative screens, perhaps because of an inability to ascertain complete data on the workup of screen-positive nodules or the development of interval cancers after a negative screen. As well, the definitions for positive test, indeterminate test, false-positive test, and false-negative test varied across studies. The three most common methods for defining a positive test were similar to those used by the NLST (NCN ≥4-mm maximum diameter), I-ELCAP (NCN ≥5-mm average of maximum length and width, later changed to 6 mm), or NELSON protocols (e.g., volume of NCN ≥500 mm^3).

Reliability

Three studies (2,211 observations) conducted analyses of RCT data to report reliability outcomes, finding fair to moderate reliability among radiologists.[103, 108, 113] Two of these studies calculated kappa values among radiologists; all average outcomes either had fair (kappa 0.21 to 0.40) or moderate (kappa 0.41 to 0.60) agreement levels. One study using data from three NELSON trial sites evaluated agreement among radiologists for a set of 160 nodules equally distributed across solid, part-solid with large solid component, part-solid with small solid component, and ground glass nodule definitions, finding moderate agreement (kappa 0.51 [95% CI, 0.30 to 0.68]).[113] Another study using 1990 scans from the DLCST focused on identifying emphysema (and other outcomes not eligible for this review) but also reported some outcomes eligible for this review. Specifically, it reported moderate agreement in identifying pleural nodules (kappa 0.53), centrilobular nodules (kappa 0.41), and masses (kappa 0.42), with fair agreement for subpleural/paraseptal nodules (kappa 0.24).[108] Finally, a study of data from the NELSON trial found that 22 of the 61 interval or post-screen cancers diagnosed in NELSON were, in retrospect, visible on the prior LDCT.[103] It was determined that 20 of these 22 were

detection errors (i.e., the radiologic abnormality was not detected), and the other two were detected but were misinterpreted. The study did not report kappa statistics.

Variation by Subgroups

Two studies (44,792 participants) assessed how the accuracy of LDCT varied by subgroups.[64, 126] An analysis of NLST data stratified by age of Medicare eligibility (age ≥65) demonstrated increased sensitivity (94.3% vs. 93.2%), decreased specificity (72.3% vs. 78.0%), and increased PPV (4.9% vs. 3.0%, $p < 0.001$) for Medicare-eligible participants. The increased PPV was attributed to higher cancer prevalence in this population.[64] Data from the Osaka Cancer Registry Database were stratified by sex and smoking status, finding no statistically significant differences between women and men for sensitivity (84.6% [95% CI, 65.0 to 100] vs. 90.6% [95% CI, 80.5 to 100]) or specificity (93.5% [95% CI, 92.6 to 94.4] vs. 92.1% [95% CI, 91.3 to 92.9]) or by smoking status for sensitivity (current 84.0% [95% CI, 69.6 to 98.4], former 85.7% [95% CI, 59.8 to 100], nonsmoker 100% [95% CI, NR]), or specificity (current 92.4% [95% CI, 91.6 to 93.3], former 91.5% [95% CI, 89.9 to 93.1], nonsmoker 93.5% [95% CI, 92.5 to 94.4]).[126]

Variation by Approaches to Nodule Classification

Three retrospective studies compared how various approaches to nodule classification would alter the accuracy of LDCT.[100, 104, 107] The first study (26,722 participants) was a retrospective analysis that applied Lung-RADS criteria to NLST data and found that using Lung-RADS (with Lung-RADS categories 1 and 2 considered negative results) was estimated to increase the specificity of LDCT (from 73.4% to 87.2% at baseline, $p<0.001$; from 78.2% to 94.7% after baseline, $p<0.001$) but decrease the sensitivity (from 93.5% to 84.9% at baseline, $p<0.001$; from 93.8% to 78.6% after baseline, $p<0.001$) compared with using the NLST criteria.[100] The second study (5,848 NLST participants with positive LDCT screens) evaluated how using I-ELCAP criteria and other thresholds for a positive test (e.g., 5-mm average diameter, 6 mm, etc.) alters the frequency of positive results and related outcomes compared with the NLST criteria (4-mm longest diameter).[104] The study did not report measures of accuracy, but the data reported allow for calculation of PPV and show that using a 5-mm average diameter criterion (applied to NLST data) increases the PPV (from 4% to 5.7%), as does increasing the threshold further (e.g., PPV 8.5% for 6 mm, PPV 12.2% for 7 mm). However, this analysis did not calculate other test characteristics (sensitivity, specificity, NPV) and excluded 848 nonsolid noncalcified nodules that would have otherwise met the criteria for a positive screen.[104] Similarly, the third study estimated that PPV would increase with increasing thresholds for defining a positive result (from 5-mm to 6-mm average diameter).[107]

Comparing volumetric and nonvolumetric (i.e., maximum diameter or average maximum length and width) approaches indicates that the PPV in trials using volumetric approaches to nodule classification tends to be higher than in those using nonvolumetric approaches. However, because there are no direct comparisons of these approaches, differences in study populations (e.g., lung cancer incidence) and other contributors to heterogeneity across studies may account for the differences in PPV. The NPVs are universally high using both approaches, and no trends in sensitivities or specificities are apparent.

Key Questions 4 and 5. Harms of Screening, Workup, or Surveillance

KQ 4a. What are the harms associated with screening for lung cancer with LDCT?
- b. Do the harms of screening for lung cancer with LDCT differ with the use of Lung-RADS, I-ELCAP, or similar approaches (e.g., to reduce false-positive results)?
- c. Do the harms of screening for lung cancer with LDCT differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?

KQ 5a. What are the harms associated with workup or surveillance of nodules?
- b. Do the harms of workup or surveillance of nodules differ with the use of Lung-RADS, I-ELCAP, or similar approaches (e.g., to reduce false-positive results)?
- c. Do the harms of workup or surveillance of nodules differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors?

Radiation Exposure

Nine publications reported on radiation associated with LDCT (**Table 8**).[32, 67, 111, 117, 124, 130, 133-135] Most of those reported the radiation associated with one LDCT, with ranges from 0.65 mSv to 2.36 mSv. Two of the studies evaluated the cumulative radiation exposure for participants undergoing screening with LDCT.[134, 136] Using the results of those two studies to estimate the cumulative radiation exposure for 25 years of annual screening (i.e., annual screening from age 55 to 80 as recommended by the USPSTF in 2013) yields 20.8 mSv to 32.5 mSv.

One of the two studies describing cumulative exposure reported that screened participants in the ITALUNG trial had cumulative radiation exposure of 3.3 mSv for multidetector CT (MDCT).[136] The authors estimated this would result in a lifetime risk of fatal cancer of 0.11 per 1,000 subjects for MDCT after the four screening rounds.

The other evaluated the Continuing Observation of Smoking Subjects (COSMOS) study and reported a cumulative radiation dose from LDCT and positron emission tomography (PET) CT scans (individual PET CTs had a median radiation dose 4.0 mSv) to be 13.0 mSv for women and 9.3 mSv for men after 10 years of annual screening.[134] This study also noted cumulative dosing by interval years and sex, with men averaging 3.0 mSv (range 1.9 to 27.4) after 3 years and 5.2 mSv (range 2.9 to 39.6) after 5 years and women averaging 4.2 mSv (range 2.9 to 23.3) after 3 years and 7.2 mSv (range 4.1 to 26.8) after 5 years (p values for comparison by sex not reported). This study additionally estimated lifetime attributable risk of cancer estimated with the National Research Council's Biological Effects of Ionizing Radiation VII report, which estimated the lifetime attributable risk of cancer incidence after radiation exposure for specific organs. Using this report, the estimated lifetime risk of cancer from radiation of 10 annual LDCTs was 2.6 to 8.1 major cancers per 10,000 people screened (converting to every 1,000 people screened: 0.26 to 0.81 major cancers). The study reported that men and women starting at an earlier age (50-54 years old) will have a higher number of radiation-induced major cancers (males 3.7 and females 8.1 cancers per 10,000 screened) than older (≥65 years old) participants (males 2.6 and females 5.1 cancers per 10,000 screened); no statistical testing for differences was reported. Projected risk specifically for radiation-induced lung cancer was similar, with younger patients (beginning at ages 50-54) having a higher risk than those beginning screening at age 65 years or older

(males 2.1 and females 5.5 cancers per 10,000 screened vs. 1.4 and 3.8 cancers per 10,000 screened for those 65 years or older, respectively). The authors estimated that there will be one major radiation-induced cancer (lung, stomach, colon, liver, bladder, thyroid, breast, ovaries, uterus, or leukemia) for approximately every 100 lung cancers detected by screening during the 10 years of the study.

None of the included studies provided estimates for the lifetime risk of radiation-induced cancers or fatal cancers from continuing annual screening up to age 80.

False-Positive Results and Followup Evaluations

Twenty seven publications reported false-positive rates or enough information to determine the rate of false positives, defined as any result leading to additional evaluation (repeat LDCT scan prior to next annual screening, PET scan, biopsy, etc.) that did not result in a diagnosis of cancer.[32, 38, 57-59, 64, 65, 69, 70, 76, 82, 102, 104, 107, 111, 117, 120-123, 128, 130-132, 137-139] False-positive rates varied widely across studies, most likely due to differences in definitions of positive results, such as cut-offs for nodule size (e.g., 4 mm vs. 5 mm vs. 6 mm), use of volume doubling time, and various nodule characteristics considered. We determined the false-positive rate by dividing the number of false positives by the number of individuals screened with LDCT. The range of false-positive rates overall was 7.9 to 49.3 percent for baseline screening and 0.6 to 28.6 percent for individual incidence screening rounds, although rates for some subgroups were higher (e.g., age ≥65 years) (**Table 9**). For trials, rates ranged from 7.9 to 26.9 percent for baseline screening and 0.6 to 27.2 percent for incidence screening.[32, 57, 59, 64, 76, 117, 120, 122] For cohort studies, false-positive rates ranged from 9.6 to 49.3 percent for baseline screening and 5.0% to 28.6 percent for incident screening.[38, 82, 107, 121, 128, 130, 131, 137] False-positive rates generally declined with each screening round.[64, 82, 120, 121, 128, 131]

Among the trials that found lung cancer screening mortality benefit and cohort studies based in the United States, false-positive rates were 9.6 percent to 28.9 percent for baseline and 5.0 percent to 28.6 percent for incident rounds. The NLST reported false-positive rates for baseline, year 1, and year 2 of 26.3, 27.2, and 15.9 percent, respectively.[32] The NELSON trial noted false-positive rates of 19.8 percent at baseline, 7.1 percent at year 1, 9.0 percent for males at year 3, and 3.9 percent for males at year 5.5 of screening.[76, 120] One study of 112 radiologists from 32 screening centers who each interpreted 100 or more NLST scans reported a mean false-positive rate of 28.7 percent (standard deviation 13.7, range 3.8% to 69.0%).[102] Mean rates were similar for academic (25 centers) and nonacademic (7 centers) centers (27.9% vs. 26.7%, respectively).[102] An implementation study through the Veterans Administration revealed a false-positive rate of 28.9 percent of veterans eligible for screening (58% of those who were actually screened) at baseline screening.[38] False-positive rates varied across eight study sites, ranging from 12.6 to 45.8 percent of veterans eligible for screening.[38]

Regarding whether harms of screening differ with the use of Lung-RADS, I-ELCAP, or similar approaches (KQs 4b and 5b), we found no eligible studies that directly compared Lung-RADS vs. I-ELCAP within a common set of participants. Three studies assessed how use of Lung-RADS would have affected false-positive result rates.[100, 132, 139] One found a false-positive rate among baseline results for Lung-RADS of 12.8 percent (95% CI, 12.4% to 13.2%) vs. 26.6

percent (95% CI, 26.1% to 27.1%) for the NLST approach. Another study used NLST baseline data to evaluate whether Lung-RADS category 4X improves prediction of malignancy in subsolid nodules.[132] It reported false-positive rates (i.e., upgrade of a benign nodule to category 4X) for nodules in category 3 of 7 percent (95% CI, 5% to 9%), category 4A of 7 percent (95% CI, 4% to 10%), and category 4B of 19 percent (95% CI, 13% to 24%).[132] The third stratified NLST participants by risk (using the Tammemagi lung cancer risk prediction model) and found increasing false-positive rates for increasing risk, ranging from 8.3 to 17.6 percent for baseline rates and 12.9 to 25.9 percent for cumulative rates.[139] Among studies using I-ELCAP criteria, the false-positive rate ranged from 9.6 to 16.6 percent for baseline screening to 5.0 to 28.6 percent for incident screening.[121, 128, 131]

For subgroups, one study evaluating NLST data on two annual rounds of LDCT scans found a cumulative risk of at least one false-positive test to be 33 percent.[119] It reported that after a second round of screening, smokers with more pack-years had 1.5 times the odds of a false-positive result (OR, 1.53 [95% CI, 1.08 to 2.18]). Another subgroup analysis of the NLST data found higher false-positive rates in those older than 65 years (23.5% for all participants; 22.0% vs. 27.7% for those <65 years vs. ≥65 years for all rounds, p=0.001).[64]

False-Positive Evaluations

The most detrimental harms of false-positive results occur in the workup of these nodules, which can include further imaging (LDCT, CT, or PET), biopsy, or surgical procedures. Fourteen studies reported on the evaluation of false-positive results.[32, 57, 60, 64, 99, 117-119, 121, 127, 130, 133, 135, 140] Definitions of procedures and groupings of procedures varied among studies. Among all patients screened, the percentage who had a needle biopsy for a false-positive result ranged from 0.09 to 0.56 percent (**Table 10**). Complication rates from needle biopsy for false positives ranged from 0.03 to 0.07 percent of all those screened. Surgical procedures (and surgical resections) for false positives were reported in 0.5 to 1.3 percent (0.1% to 0.5%) of all screened participants.

In the NLST, false-positive results led to invasive procedures (needle biopsy, thoracotomy, thoracoscopy, mediastinoscopy, and bronchoscopy) in 1.7 percent of those screened. Complications occurred in 0.1 percent of those screened, with major, intermediate, and minor complications occurring in 0.03 percent, 0.05 percent, and 0.01 percent, respectively, of those screened. Death in the 60 days following the most invasive procedure performed occurred in 0.007 percent of those screened.[32]

No studies directly compared the workup of nodules identified by I-ELCAP or Lung-RADS, but rates of biopsy for false positives ranged from 0.09 to 0.42 percent of all persons screened in I-ELCAP studies.[118, 121] The one study using Lung-RADS found a rate for surgical procedures (e.g., mediastinoscopy, video-assisted thoracoscopic [VATS], or thoracotomy) of 0.3 percent for false positives among all those screened.[133] An evaluation using NLST data estimated that 117 invasive procedures for false positives (23.4% of all invasive procedures for false positives from the NLST) would be prevented by using Lung-RADS criteria (preventing an invasive procedure for a false positive screening result for 0.44% of all persons screened).[100]

For subgroups, a study using the NLST data evaluating age differences for invasive procedures after false positives reported a rate of 3.3 percent of all LDCT screens for those 65 years or older and 2.7 percent of all LDCT screens in those younger than 65 (p=0.039).[64]

Overdiagnosis

Five studies specifically examined overdiagnosis,[135, 141-144] and we examined seven trials for differences in cancer incidence between LDCT and comparison groups.[32, 62, 70, 72, 76, 80, 145] Overdiagnosis is the detection of a cancer in a patient that would not have become clinically apparent in the patient's lifetime. In addition to the psychological consequences of being diagnosed with cancer, the major harm of this detection is unnecessary treatment (e.g., chemotherapy, radiation, and/or surgical resection) of something that would never have caused a problem. The presence of overdiagnosis is supported by multiple trials demonstrating an excess of early-stage cancers in the screening group without eventual catch-up of cancer cases in the comparison group in the followup period.[32, 70, 72, 80, 145] In the initial publication of NLST results, there were an excess of 119 lung cancers after three screening rounds and 6.5 years of followup (total cancers: 1,060 from the LDCT group and 941 from the CXR group).[32] The post-trial followup of NLST reported that there was no significant overall increase in lung cancer incidence at a median of 11.3 years of followup (1,701 vs. 1,681, respectively, RR, 1.01 [95% CI, 0.95 to 1.09]).[74] However, the extended post-trial followup of NLST had some important methodologic limitations for ascertaining lung cancer incidence and overdiagnosis. These included using different methods during trial years (with a verification committee) than for post-trial years (relying on registries and without a verification committee); lack of information on any post-trial screening with LDCT that may have taken place in either the LDCT or the CXR group; missing data for lung cancer incidence for 11 out of 33 centers (representing 12.4% of trial participants) that did not have a home state cancer registry available for linkages; and risk of biasing overdiagnosis estimates toward the null because the comparison group received CXR (rather than no screening test). In the NELSON trial, there were an excess of 40 lung cancers after 10 years of followup since randomization, the a priori planned followup duration (total cancers 648: 344 from LDCT group and 304 from the control group; after 11 years of followup there was an excess of 14 cancers).[76] The ITALUNG trial reported a catch-up of lung cancers in the 5 years following the end of five rounds of annual screening.[62] However, inadequate duration of followup and heterogeneity of followup duration across trials limit the evaluation of overdiagnosis.

Determining the rate of overdiagnosis in screening is challenging because calculations of excess cancers are influenced by followup periods. One modeling study using the NLST data, limited by 6.5 years of followup, reported a probability of 18.5 percent (95% CI, 5.4% to 30.6%) that any detected lung cancer by screening is overdiagnosis (for NSCLC specifically, probability 22.5% [95% CI, 9.7% to 34.3%]).[142] The study reported 1.38 cases of overdiagnosis in every 320 patients needed to screen to prevent one death from lung cancer. This study additionally modeled risk of overdiagnosis with lifetime followup after five annual screens, finding an overdiagnosis rate of 12 percent (95% CI, 7% to 15%) for all NSCLC after five annual LDCT scans with lifetime followup compared with no screening. A study using data from DLCST revealed an excess of 43 cancers (96 cancers overall and 64 screen-detected in the LDCT group vs. 53 in control group) after five annual LDCT scans and 5 years of followup, placing the estimate of

overdiagnosis at 67.2 percent (95% CI, 37.1% to 95.4%) (absolute difference of cancers divided by screen-detected cancers).[141]

One study sought to determine characteristics of potential overdiagnosis cases by evaluating volume doubling time (VDT),[135] finding about 25% of cancers are slow growing or indolent. The authors acknowledge, however, that it has also been reported that previously stable nodules can increase their rate of growth rapidly.[146] A review of the Pittsburgh Lung Screening Study (PLuSS) trial cancer cases found 17/93 (18.5%) of prevalent cancers were indolent using a cut-off VDT of >400 days and a standardized uptake value of ≤1 on the PET scan.[143] Sixteen out of the 17 (94.1%) were histologically adenocarcinomas, representing potential histologic shift.

To better determine populations at greater risk of overdiagnosis, one study evaluated overdiagnosis by COPD status in a subgroup of the NLST and found an excess of 26 adenocarcinoma-associated cancers in the COPD absent group. The authors argue that an excess of this histologic group, which is predominantly early stage, may represent a histologic shift to more indolent cancers identified by screening and not a clinically significant stage shift.[144]

Smoking Behavior

One RCT (DLCST, 4,075 participants) reported in two publications, three publications reporting on studies of participants from RCTs (NELSON, NLST, LSS, 19,426 total participants), and three cohort studies (ELCAP, Mayo Lung Project, and PLuSS, 5,537 total participants) included an evaluation of the impact of LDCT screening or screening results on smoking cessation and relapse. Evidence comparing LDCT vs. controls (no screening or CXR, depending on study) for smoking cessation or abstinence outcomes does not indicate that screening leads to false reassurance. Abnormal or indeterminate screening test results may increase cessation and continued abstinence, but normal screening test results had no influence. Regarding smoking intensity, evidence was minimal, and no study showed any influence of screening or test result on smoking intensity. Regarding smoking cessation and continued abstinence, studies showed that study participation, which could be a proxy for participation in a lung screening program, may have influenced smoking cessation. Below, we describe evidence showing the (1) impact of LDCT vs. CXR or no screening on smoking cessation and intensity (using data from RCTs); (2) impact of abnormal (true positive and false positive) or indeterminate screening results vs. normal results on smoking cessation, abstinence, and relapse (using data from RCTs and uncontrolled studies); and (3) potential impact of study participation (regardless of arm assignment or treatment) on cessation, abstinence, and relapse.

One RCT (DLCST; described in two publications) and one report of participants from an RCT (NELSON) showed mixed results regarding smoking cessation when comparing participants who were screened with those who were not screened.[145, 147, 148] In a report of the 4,075 participants from the DLCST, the quit rate at year 1 among baseline current smokers was almost identical for the LDCT and no screening groups (11.9% vs. 11.8%, p=0.95).[145] The annual proportion of nonsmokers increased in each of the five study years but was not different across study arms (LDCT vs. no screening: baseline: 25% vs. 23%, p=0.213; year 2: 31% vs. 30%, p=0.537; year 3: 36% vs. 37%, p=0.599; year 4: 40% vs. 40%, p=0.827; year 5: 43% vs. 43%, p=0.909).[147] Conversely, in a paper reporting on 1,284 participants from the NELSON trial, both

study arms showed relatively high abstinence rates (compared with general adult population rates of 3% to 7%), but the control arm was somewhat higher (LDCT vs. no screening on smoking abstinence at 2 years–no smoking in past 7 days: 15.1% vs. 19.8%, p=0.04; fewer than five cigarettes within 2 weeks of quit date: 14.5% vs. 19.1%, p=0.04; fewer than five cigarettes since quit date: 13.9% vs. 18.7%, p=0.03).[148] This same analysis of NELSON trial participants showed no influence of LDCT screening on smoking intensity compared with no screening (reduced intensity: 53.1% vs. 53.8%, p=0.23; increased intensity: 17.7% vs. 13.8%, p=NR; remained stable: 29.2% vs. 32.4%, p=NR).[148]

One RCT (DLCST, N=3,745) and one paper reporting on screening arm participants from the NLST showed some evidence that screening results (positive or indeterminate vs. normal) may increase smoking cessation and decrease relapse.[145, 149] From the analysis of the 16,964 screening arm participants from the NLST, any false-positive result was associated with a greater point abstinence (first report of no longer smoking: HR, 1.23 [95% CI, 1.13 to 1.35]) and sustained abstinence (for at least 6 months: HR, 1.28 [95% CI, 1.15 to 1.43]) among smokers. In addition, recent quitters with at least one false-positive result were less likely to relapse than those with negative results (HR, 0.72 [95% CI, 0.54 to 0.96]).[149] Among the 3,745 DLCST participants with complete data on smoking habits, baseline smokers with positive results were more likely to quit than those with negative results (17.7% vs. 11.4%, p=0.04) and baseline ex-smokers were with positive results were less likely to relapse than those with negative results (4.7% vs. 10.6%, p<0.01).[145]

In four uncontrolled studies that compared positive or indeterminate vs. normal screening results, outcomes for smoking cessation and relapse were mixed.[150-153] A study of 2,078 ELCAP participants reported that those with negative results had higher cumulative point abstinence than those with any positive result (HR, 1.39 [95% CI, 1.01 to 1.90]; p<0.05) but did not have higher prolonged abstinence (HR, 1.34 [95% CI, 0.90 to 1.99]).[150] From the NELSON trial, a random sample of 990 male smokers with indeterminate results made more quit attempts than those with negative test results (1.9 +/- 2.7 attempts vs. 1.5 +/- 2.0 attempts, p=0.016), but there was no difference in point (12.2% vs. 10.4%, p=0.39) or prolonged (11.5% vs. 8.9%, p=0.19) abstinence.[153] Among 1,365 participants from the Mayo Lung Study, an abnormal result among baseline smokers was predictive of smoking abstinence (OR, 1.37 [95% CI, 1.12 to 1.67]; p=0.002) but not among baseline ex-smokers.[152] Among a cohort of 2,094 baseline active smokers from the PLuSS study, those who received a referral to further evaluation (e.g., additional scans) as a result of any non-normal initial LDCT result, compared with those with no referral, reported more smoking cessation. The most pronounced difference compared those with referral for results with moderate to high suspicion for cancer (delta, reported quit attempts 18.8% [95% CI, 11.1% to 26.5%]; reported quit more than 30 days, 17.7% [95% CI, 9.4% to 26.0%]; reported quit more than 30 days without relapse at 1 year 12.2% [95% CI, 4.9% to 19.5%]).[151]

Two uncontrolled studies[154, 155] reported the impact of screening (or study) participation on cessation, relapse, or motivation to quit. Among 1,473 baseline current smokers in the Mayo Lung Study, 14.9% reported abstinence at 1 year of followup, compared with 5 to 7 percent in the general population.[154] Finally, a description of reasons for study participation among 144 LSS participants and 169 NLST participants suggests that those willing to participate in a

screening program might be more open to receiving cessation counseling.[155] Both studies concluded that LDCT screening may be a "teachable moment" with regard to smoking cessation. One RCT (DLCST, N=4,075)[147] and one sample of RCT participants (NELSON, N=1,284)[148] also suggested that study participation, which could represent participation in a screening program, may, in and of itself, increase smoking cessation rates.

We did not find eligible studies reporting whether smoking behavior after LDCT differs for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors.

Psychosocial Harms

Four RCTs (DLCST, NELSON, NLST, and UK Lung Cancer Screening [UKLS] trial, 12,096 total participants), reported in six publications,[117, 156-160] one uncontrolled cohort study (PLuSS, 400 participants),[161] and two studies of participants from the screening arm of an RCT (NELSON, 630 participants;[162] UKLS, 1,589 participants[163]) included an evaluation of potential psychosocial consequences of undergoing LDCT screening for lung cancer. These studies evaluated general health-related quality of life (HRQoL; 3 studies),[156, 159, 162] anxiety (8 studies),[117, 156-162] depression (2 studies),[117, 157] distress (3 studies),[117, 159, 162] and other psychosocial consequences of LDCT screening (5 studies).[117, 158, 160, 161, 163] Taken together, there is moderate evidence to suggest that, compared with no screening, individuals who receive LDCT screening do not have worse general HRQoL, anxiety, or distress over two years of followup. Some evidence suggests differential consequences by screening result such that general HRQoL and anxiety were worse, at least in the short term, for individuals who received true-positive results compared with other screening results; distress was worse for participants who received an indeterminate screening result compared with other results. The strength of evidence is low for other psychosocial consequences, largely because of unknown consistency, imprecision, and only one or two studies assessed outcomes. The following paragraphs describe evidence for LDCT vs. no screening or CXR and for comparisons of people with different LDCT screening results (e.g., comparing those with false-positive results vs. negative results), on general HRQoL, anxiety and depression, distress, and other psychosocial consequences.

General Quality of Life

To measure general HRQoL, the NELSON trial used the SF-12 and EuroQol visual analog scale [EQ-5D VAS] questionnaires.[159] The SF-12 consists of a Physical Component Score [PCS] and a Mental Component Score [MCS]; scores range from 0 (lower level of health) to 100 (higher level of health). The EQ-5D VAS asks participants to rate their health on a scale of 0 (worst imaginable status) to 100 (best imaginable status). Regarding general HRQoL, the NELSON trial reported no statistically significant differences over 2 years of followup between individuals who had LDCT screening for lung cancer and those who were assigned to a no-screening control arm (mean PCS from the SF-12: 49.95 screening arm vs. 49.07 control arm; mean MCS from the SF-12: 52.50 screening arm vs. 51.69 control arm; mean EQ-5D VAS: 79.53 screening arm vs. 77.45 control arm; 931 participants).[159] The authors used a minimal important difference (MID) threshold of at least half of a standard deviation of the mean to determine whether the differences between assessment points were clinically relevant. Moreover, no differences in HRQoL were

observed for individuals with a negative or indeterminate result from baseline to 6 months after the second-round screening (mean PCS: 50.20 negative result vs. 49.24 indeterminate result; mean MCS: 52.70 negative result vs. 51.82 indeterminate result; mean EQ-5D VAS: 80.12 negative result vs. 78.22 indeterminate result). Similarly, findings from the NLST suggest no statistically significant differences in general HRQoL (measured using a PCS and MCS derived from the SF-36) from baseline to 6 months followup between individuals with false-positive, positive for significant incidental findings, or negative screen results.[156] Compared with those receiving negative results and after adjusting for potential confounders (e.g., baseline age, sex, race/ethnicity), regression estimates were not statistically significantly different for PCS or MCS from baseline to short-term (1 month) and long-term (6 months) followup for those receiving false-positive results (PCS baseline to 1 month: 0.46, 95% confidence limit [CL], -0.04 to 0.97; PCS baseline to 6 months: 0.30, 95% CL, -0.27 to 0.87; MCS baseline to 1 month: -0.22, 95% CL, -0.82 to 0.37; MCS baseline to 6 months: 0.03, 95% CL, -0.65 to 0.70) or significant incidental findings results (PCS baseline to 1 month: 0.13, 95% CL, -0.62 to 0.88; PCS baseline to 6 months: -0.16, 95% CL, -1.01 to 0.69; MCS baseline to 1 month: -0.04, 95% CL, -0.93 to 0.84; MCS baseline to 6 months: 0.29, 95% CL, -0.72 to 1.31). However, short-term and long-term HRQoL were worse for individuals receiving true-positive results compared with those receiving other screening results. Regression analyses revealed statistically significant changes for those receiving true-positive results compared with those receiving negative results from baseline to 1 month for MCS (-3.95, 95% CL, -5.87 to -2.04) and baseline to 6 months for PCS (-7.02, 95% CL, -8.80 to -5.24) and MCS (-4.15, 95% CL, -6.27 to -2.03) but not for baseline to 1 month for PCS (-1.18, 95% CL, -2.81 to 0.45). These findings should be interpreted with the awareness that participants in this trial received extensive counseling as part of the consent process, including information about the high risk of a false-positive screen and related followup. General HRQoL did not differ between those receiving LDCT screening and those receiving a CXR. Compared with participants randomized to receive a CXR, those who were randomized to LDCT screening did not exhibit better or worse general HRQoL (PCS baseline to 1 month: 0.07, 95% CL, -0.44 to 0.59; PCS baseline to 6 months: 0.50, 95% CL, -0.06 to 1.07; MCS baseline to 1 month: 0.23, 95% CL, -0.37 to 0.83; MCS baseline to 6 months: 0.07, 95% CL, -0.61 to 0.74).[156]

Anxiety and Depression

Some evidence suggests individuals experience short-term increases in anxiety after undergoing LDCT screening for lung cancer, but these increases tend to diminish over time. In an uncontrolled cohort study, the PLuSS,[161] participants who had an indeterminate screening result had increased state anxiety (i.e., anxiety about an event, measured using the State-Trait Anxiety Inventory [STAI]) at 1 to 2 weeks postscreen (mean [*M*]=37.7, standard deviation [*SD*]=13.8) and 6 months (*M*=37.3, *SD*=12.6) compared with baseline (*M*=34.4, *SD*=12.3), but state anxiety returned to baseline levels 12 months after screening (*M*=35.3, *SD*=13.5). For reference, a score of 39 to 40 or 54 to 55 for older adults, has been suggested for detecting clinically meaningful symptoms of state anxiety.[164] In multivariable analysis, the regression coefficient for the interaction between an indeterminate screening result and survey time (7.50; standard error [SE], 2.00) and the interaction between an indeterminate screening result and survey time squared (-1.41; SE, 0.39) were both statistically significant at $p < .001$. Analyses for trait anxiety (i.e., anxiety as a personal characteristic) did not yield any statistically significant associations for the

survey time or screening result (negative, indeterminate, or suspicious result) variables. Findings from the NLST suggest differential anxiety levels (measured using STAI Form Y-1) by screening result such that anxiety was substantially higher (worse) among individuals who received a true-positive result (1-month score: *M*=41.06, *SD*=15.10; 6-month score: *M*=37.69, *SD*=12.04) compared with those who received false-positive (1-month score: *M*=34.34, *SD*=12.58; 6-month score: *M*=33.92, *SD*=12.77), significant incidental findings (1-month score: *M*=33.83, *SD*=12.68; 6-month score: *M*=33.19, *SD*=12.41), or negative screen results (1-month score: *M*=32.67, *SD*=11.97; 6-month score: *M*=32.76, *SD*=12.36).[156] Anxiety did not differ by screening arm; compared with participants randomized to receive a CXR, those who were randomized to LDCT screening did not exhibit better or worse anxiety (STAI ratio at 1 month: 1.01, 95% CL, 0.93 to 1.10; STAI ratio at 6 months: 1.02, 95% CL, 0.93 to 1.12). Conversely, data from the DLCST did not indicate that undergoing LDCT screening for lung cancer increases the risk of receiving prescription medications for anxiety or depression during the period from baseline to 3 years followup compared with the control arm (adjusted HR: 1.00 [95% CI, 0.90 to 1.12]).[157] As the authors note, the use of prescriptions would likely identify only more severe anxiety and depression.

Distress

Research also suggests short-term increased distress levels following LDCT screening for lung cancer for individuals receiving an indeterminate result.[162] In the NELSON trial, the 15-item Impact of Events Scale (IES) was tailored to measure lung cancer–specific distress. In addition to producing a total summary score (range: 0-75), the IES yields scores for the intrusive subscale (e.g., having trouble staying asleep because pictures or thoughts about the event came to mind; range: 0-35) and avoidance subscale (e.g., trying to remove the event from memory; range: 0-40). In the short term (2 months after a baseline scan), the NELSON trial data revealed that distress levels were higher (worse) among individuals who received an indeterminate result (IES total score: *M*=8.3, *SD*=11.3) compared with those who received a negative result (IES total score: *M*=2.4, *SD*=5.5). These differences were both statistically significant ($p<.01$) and considered clinically relevant by the authors (using a MID threshold of at least half of a standard deviation of the mean),[162] although the effect was small because the average IES total score for those with indeterminate results was just 8.3 on a scale that ranges from 0 to 75. For those who received an indeterminate result, distress levels returned to near-baseline levels 2 years after baseline screening.[159] Similarly, findings from the UKLS Trial suggest higher levels of distress among individuals who undergo LDCT screening for lung cancer compared with no screening, but these effects were short term and were only among individuals with low scores at baseline (intervention arm: *M*=8.54 [95% CI, 8.44 to 8.64]; control arm: *M*=8.26 [95% CI, 8.16 to 8.36]).[117] Data from this trial also suggest differential distress levels by screening result; individuals who received a multidisciplinary team referral (indicating a major lung abnormality) reported the highest distress.

Other Psychosocial Consequences

Participants in the DLCST were assessed for other potential psychosocial consequences of LDCT screening, measured using the Consequences of Screening (COS) and Consequences of Screening in Lung Cancer (COS-LC).[158, 160] COS scales included anxiety (range of values: 0-18),

behavior (range: 0-21), dejection (range: 0-18), and sleep (range: 0-12); single items included busy to take mind off things (range: 0-3), less interest in sex (range: 0-3), and self-rated health (range: 0-4). COS-LC scales included self-blame (range: 0-15), focus on (airway) symptoms (range: 0-24), stigmatization (range: 0-12), introvert (range: 0-18), harm of smoking (range: 0-6), and anxiety (anxiety for COS-LC was the same scale used in COS plus an extra item: shocked; range: 0-21); single items included busy to take mind off things (range: 0-3), less interest in sex (range: 0-3), and self-rated health (range: 0-4). For reference, higher scores indicate more negative psychosocial consequences. Among participants with negative screening results in the LDCT screening arm and those in the control arm, mean scores significantly worsened from the prevalence round (prerandomization to study arm) to the incidence round (postrandomization) on the behavior scale (mean increase: 1.0535 screen arm, 1.1962 control arm), dejection scale (mean increase: 0.4076 screen arm, 0.5371 control arm), and sleep scale (mean increase: 1.0271 screen arm, 1.1025 control arm) and on two single items: busy to take mind off things (mean increase: 0.0539 screen arm, 0.0760 control arm) and less interest in sex (mean increase: 0.2253 screen arm, 0.1811 control arm; all $p < .01$).[160] The significantly worse scores for the three scales persisted for another three rounds of screening. At the incidence round, scores were worse for the control arm than for the LDCT screening arm for three COS scales: anxiety (*M*=1.50, *SD*=2.52 screen arm vs. *M*=1.71, *SD*=2.79 control arm), behavior (*M*=1.76, *SD*=2.85 screen arm vs. *M*=2.02, *SD*=3.04 control arm), and dejection (*M*=1.61, *SD*=2.71 screen arm vs. *M*=1.88, *SD*=2.98 control arm). Scores were also worse for the control arm for four COS-LC scales: self-blame (*M*=2.32, *SD*=3.53 screen arm vs. *M*=2.62, *SD*=3.75 control arm), focus on (airway) symptoms (*M*=3.30, *SD*=3.58 screen arm vs. *M*=3.80, *SD*=3.93 control arm), introvert (*M*=1.89, *SD*=1.76 screen arm vs. *M*=2.22, *SD*=2.96 control arm), and anxiety (*M*=1.55, *SD*=2.67 screen arm vs. *M*=1.77, *SD*=2.93 control arm). The authors note that one possible explanation for the worse psychosocial consequences in the control arm is that compared with participants in the LDCT screening arm control arm participants did not benefit from the reassurance that a normal screening result may offer. Although these differences meet the threshold for statistical significance, it is unclear whether they are clinically meaningful. Using at least a half of a standard deviation of the mean as a threshold for determining the MID,[165] we found that none of the statistically significant differences would be considered clinically meaningful.

The UKLS Trial assessed participants' satisfaction with their decision to participate in an LDCT trial using the Satisfaction with Decision Scale.[117] This six-item scale has five response categories that span from strongly disagree to strongly agree; items are summed and averaged for a total possible score ranging from 1 to 5. The authors dichotomized this score such that a score less than 5 is considered "not very satisfied" and a score of 5 is considered "very satisfied." Findings suggest decision satisfaction varied by LDCT screening result. In the short term (2 weeks after receiving scan results), 57 percent of participants who were positive for multidisciplinary team referral were very satisfied with their decision to participate in the trial, whereas 46 percent with a negative result, 44 percent with a negative result who also had an incidental finding, and 36 percent with a positive for repeat scan result were very satisfied with their decision. In the long term (10 to 27 months after recruitment), 71 percent of participants with a true-positive result were very satisfied with their decision to participate in the trial compared with 39 percent with a true-negative result, 45 percent with an incidental finding, and 41 percent with a false-positive result.

The UKLS Trial also assessed perceived concern about the LDCT scan result, which was used to represent perceived threat.[163] The authors examined whether there was an association between perceived concern and expectation-result congruence. Two weeks after they received their LDCT scan result, participants completed a questionnaire that included a single-item measure of perceived concern: "How concerned were you by your CT scan result?" Participants responded by selecting "not at all concerned," "not very concerned," "fairly concerned," or "very concerned." At baseline, participants were asked to report their expected scan result: "normal/clear scan result" (renamed "negative") or "unclear or abnormal scan result." Actual scan results were categorized as negative or positive for a repeat scan or MDT referral. Four expectation-result congruence groups were formed: (1) expected negative, (2) unexpected followup, (3) unexpected negative, and (4) expected followup. Findings indicate that although most (82%) of the 1,589 participants expected a negative result, 48 percent actually had a negative result. There was a statistically significant association between perceived concern about the LDCT scan result and expectation-result congruence ($p<.001$). Participants who received an expected negative result were statistically significantly less concerned (57% not at all concerned) about their scan result compared with those who did not have an expected negative result ($p<.001$). Participants who received an unexpected followup result reported more concern (54% fairly or very concerned) compared with those with an expected negative result (22% fairly or very concerned) and those with an unexpected negative result (36% fairly or very concerned)($p<.001$). Among those who expected a followup result, 65 percent reported they were fairly or very concerned. Younger age, those in the most deprived group (vs. the most affluent, measured using the Index of Multiple Deprivation), and those with an experience of lung cancer were more concerned about the result (all $p=.01$).

The PLuSS assessed fear of lung cancer and perceived risk of lung cancer among participants who had LDCT screening.[161] Three questions, adapted from the Psychological Consequences Questionnaire, were used to assess the effects of screening on fear. The five-point response scale ranged from "never" to "most of the time." Scores were summed to obtain a total score; higher scores suggested greater fear of cancer. Average fear of lung cancer scores varied by LDCT screening result. Fear of lung cancer scores remained fairly level over time for participants with negative screen results (*M*=7.0, *SD*=2.5 initial; *M*=7.0, *SD*=2.4 at postscreen; *M*=6.5, *SD*=2.4 at 6-month followup; *M*=6.7, *SD*=2.3 at 12-month followup) or indeterminate screen results (*M*=7.2, *SD*=2.8 initial; *M*=7.5, *SD*=2.7 at postscreen; *M*=7.1, *SD*=2.6 at 6-month followup; *M*=7.1, *SD*=2.7 at 12-month followup). Among participants with a suspicious screen result, fear of cancer increased after screening. This increase diminished over time but did not return to baseline levels by the 12-month followup survey (*M*=6.4, *SD*=2.3 initial; *M*=8.5, *SD*=2.6 at postscreen; *M*=7.4, *SD*=3.0 at 6-month followup; *M*=7.1, *SD*=2.5 at 12-month followup). The authors also highlighted that fear of lung cancer did not diminish over time for participants with a negative screen result, as might be expected, and that perhaps a negative result does not bring peace of mind. Perceived risk of lung cancer was measured by asking participants how likely they believed it was that they had or will get lung cancer. Participants indicated their risk on a scale from no chance (0%) to certain (100%). As for perceived risk of lung cancer, average scores also varied by LDCT screening result. Perceived risk of lung cancer decreased after screening for those with a negative screen result (*M*=17.1, *SD*=20.4 initial; *M*=11.2, *SD*=20.2 at postscreen; *M*=13.1, *SD*=20.8 at 6-month followup; *M*=13.1, *SD*=19.9 at 12-month followup). For those with an indeterminate result, perceived risk increased at postscreen (*M*=20.1, *SD*=25.0

compared with *M*=18.9, *SD*=22.9 initial), decreased at 6 months (*M*=14.8, *SD*=19.7), and increased to baseline levels at 12-month followup (*M*=18.9, *SD*=25.2). For those with a suspicious screening result, perceived risk nearly doubled at postscreen (*M*=34.5, *SD*=28.0 compared with *M*=18.6, *SD*=15.7 initial), then decreased at 6 months (*M*=30.3, *SD*=28.0), and increased at 12-month followup (*M*=31.2, *SD*=28.9).

Subgroups

We did not identify studies reporting whether psychosocial consequences of screening for lung cancer with LDCT differ for subgroups defined by age, sex, race/ethnicity, presence of comorbid conditions, or other lung cancer risk factors.

Incidental Findings Leading to Additional Tests and Subsequent Harms

Summary

Studies reported a wide range of screening-related incidental findings (4.4% to 40.7%) that were deemed significant and/or requiring further evaluation (**Appendix E Table 3**). Rates varied considerably in part because there was no consistent definition of what constitutes an incidental finding nor which findings were "actionable" or "clinically significant." Older age was associated with a greater likelihood of incidental findings. Common incidental findings included coronary artery calcification, aortic aneurysms, emphysema, and infectious and inflammatory processes. Other common findings were masses, nodules, or cysts of the kidney, breast, adrenal, liver, thyroid, pancreas, spine, and lymph nodes. Cancers involving the kidney, thyroid, or liver were ultimately diagnosed in 0.39 percent of NLST participants in the LDCT arm during the screening period. Incidental findings led to downstream evaluation including consultations, additional imaging, and invasive procedures with associated costs and burdens. The benefits of incidental detection of nonlung cancer conditions are uncertain.

Detailed Results

Evidence From Uncontrolled Studies

Most of the current evidence regarding incidental findings comes from uncontrolled studies because incidental findings are not easily defined for an unscreened (control) population. We found six fair-quality uncontrolled studies (n=27,237 total participants) that described rates of "significant" incidental findings in LDCT-screened populations.[38, 117, 137, 166-168] Two of these used data from trials (NLST and UKLS).[117, 166] The other four were U.S.-based cohort studies. Some of these studies reported additional data regarding followup evaluations and findings.

A study of NLST participants assigned to the LDCT screening arm (three rounds) who were enrolled at American College of Radiology Imaging Network centers (n=17,309) found that 58.7 percent of participants had one or more extrapulmonary findings, including 19.6 percent with findings categorized by radiologists as "potentially significant."[166] The frequency of these "potentially significant" abnormalities was highest for cardiovascular findings (e.g.,

atherosclerotic calcifications and aortic aneurysms) (8.5%), followed by renal (2.4%), hepatobiliary (2.1%), adrenal (1.2%), and thyroid (0.6%). These findings led to additional specialty consultations, imaging, invasive testing, and surgery. Extra-thoracic cancers, including kidney, thyroid, and liver cancers, were diagnosed in 67 (0.39%) participants during the screening period. By organ type, the ratio of malignancy to incidental LDCT lesion was highest for the thyroid (1 cancer per 14 findings) followed by kidneys (1 cancer per 37 findings).

In the United Kingdom Lung Cancer Screening Trial, among 1,994 participants screened with a single round of LDCT, the rate of significant incidental findings not related to thoracic malignancy that were referred back to the participant's general practitioner was 6.4 percent.[117]

The Veterans Health Administration Lung Cancer Screening Demonstration Project reported incidental findings at eight demonstration sites after a single round of screening. They found that 40.7 percent of participants (n=2,452) had one or more incidental findings deemed likely to require followup or further evaluation.[38] The most common findings included coronary artery calcification, emphysema, abdominal abnormalities and masses (14%), aortic dilation (8.3%), inflammatory or interstitial processes (25.4%), and thyroid nodules (2.4%). The rate of incidental findings deemed likely to need followup varied widely across the eight demonstration sites from 20.0 to 63.4 percent.

A study of 320 patients undergoing one round of LDCT screening at a tertiary U.S. lung cancer screening program reported the frequency and types of incidental findings along with additional data on subsequent evaluation that was driven by prespecified care paths.[167] If using a broad definition of incidental findings, the vast majority (94%) of the 320 patients had some type of incidental abnormality noted by radiologists in the LDCT report. These types of incidental abnormalities included calcification of coronary arteries (56%) or the aorta (21%), emphysema (50.6%), aortic dilation (8.1%), adrenal nodules (3.8%), renal cysts (2.5%), and thyroid nodules (4.7%). Using a narrower definition, we see that 15 percent of participants had incidental findings categorized as "concerning" and underwent further evaluation that included a variety of nonpulmonary subspecialty consultations, lab tests, imaging studies, and invasive procedures. Five fine-needle aspirations of thyroid nodules were performed. One patient had a total thyroidectomy that revealed a (benign) hyperplastic nodule and multinodular goiter. Evaluation of two suspicious renal masses led to diagnosis of two renal cell carcinomas (grade 3).

Another U.S. cohort study found that 14 percent of 1,520 patients assigned to three rounds of annual screening had incidental nonpulmonary findings of significance that required further evaluation.[168] The most common nonpulmonary findings (with frequency >1%) were abdominal aortic aneurysm (3.4%), adrenal masses (2.3%), indeterminate renal masses (2.2%), renal calculi (1.6%), and breast nodules (1.1%). Several nonlung cancers were eventually diagnosed including two carcinoid tumors, four renal cell cancers, three breast cancers, two lymphomas, two gastric tumors, and one pheochromocytoma.

PLuSS enrolled 3,642 participants assigned to two rounds of annual LDCT screening and followup. A total of 4.4 percent had "significant" incidental findings, which were not otherwise characterized.[137]

Evidence From RCTs

We identified one eligible controlled trial.[169] Because of concerns that LDCT could lead to overdiagnosis of thyroid cancer through increased incidental detection, the study used data from the NLST (n=53,248) to examine the association of LDCT screening and thyroid cancer risk.[169] It reported a total of 60 thyroid cancers (37 in the LDCT group vs. 23 in the CXR group), finding a significant increase in thyroid cancer incidence in the LDCT arm compared with the CXR arm during the 3 years of active screening (HR, 2.19 [95% CI, 1.07 to 4.47]) but not during subsequent years of nonimaging observation (HR, 1.08 [95% CI, 0.49 to 2.37]).

Subgroup differences. We identified one study that examined age differences in incidental findings. In this study of 26,722 participants in the LDCT screening arm of the NLST, negative screening results with "clinically significant abnormalities" were more common in the screened cohort over age 65 years compared with those under age 65 (9.2% vs. 6.9%, p< 0.0001).[64]

Key Question 6a. How Effective is Surgical Resection or SBRT for the Treatment of Early (Stage I) NSCLC?
Key Question 6b. Does Effectiveness Differ for Subgroups Defined by Age, Sex, Race/Ethnicity, or Presence of Comorbid Conditions?

Summary

No RCTs comparing surgical resection or SBRT with no treatment for stage I NSCLC were identified. Twenty-seven uncontrolled studies evaluating surgical resection (n=147,837 patients with stage I NSCLC),[170-196] including 6 from the prior review,[190-195] (**Appendix E Tables 4** and **5**) and 13 uncontrolled studies evaluating SBRT (n=8,697 patients with stage I NSCLC)[185, 196-207] (**Appendix E Tables 4** and **6**) for the treatment of stage I NSCLC were included for KQ 6 for presentation to the USPSTF; additional studies were subsequently identified in update searches and literature surveillance and are described below in the *Update Search Summary* sections. Results of those studies were similar to what was identified by the original search yield. The studies from the original search yield were uncontrolled analyses of prospectively collected data from registries or databases (e.g., National Cancer Database) or primary studies conducted at one or more institutions. Five surgical resection studies[177, 179, 181, 185, 194] and one SBRT study[185] were rated as good quality; the remaining studies were rated fair quality (**Appendix D Table 1**). Seven surgery studies[172, 181, 184, 186, 187, 191, 192] and 1 SBRT[204] study reported survival outcomes among subgroups.

The strength of evidence for the effectiveness of surgical resection and SBRT for the treatment of stage I NSCLC is moderate and low for benefit, respectively, downgrading primarily because the evidence came from uncontrolled cohort studies and for imprecision. Clinical characteristics of the NSCLC diagnoses and operability of tumors, surgical approaches, and SBRT treatment characteristics among studies and over time resulted in imprecise results, despite an overall substantial sample size for the question related to surgical resection.

Surgical Resection

Description of Included Studies

Twenty-seven studies evaluated the effectiveness of surgical resection for the treatment of stage I NSCLC. Sample sizes ranged from 540[177] to 54,350.[178] Of the 27 studies, 14 were primary studies conducted between 1983 and 2012 in the United States,[170, 172, 174, 176, 181, 182] Japan,[173, 179, 184, 191, 193, 195] the United Kingdom,[177, 181] and Italy[171] (n=16,671 stage I NSCLC patients). The remaining 13 studies were analyses of 131,166 stage I NSCLC patients in the Surveillance, Epidemiology, and End Results (SEER) database between 1988 and 2012 (k=5 studies);[175, 180, 183, 188, 192] the National Cancer Database (NCDB) between 2003 and 2012 (k=5 studies);[178, 185-187, 189] the Veteran's Affairs Informatic and Computing Infrastructure (VINCI) database between 2006 and 2015; and cancer registries in Norway (1993 to 2002),[194] and Japan (2004).[190] The SEER program and database, initiated in 1973 by the National Cancer Institute, includes data from a network of cancer registries that represent approximately one-third of the U.S. population,[208] and the NCDB is a nationwide oncology outcomes database for more than 1,500 Commission on Cancer–accredited cancer programs in the United States and Puerto Rico. The NCDB is a joint effort by the American College of Surgeons and the American Cancer Society, captures approximately 70 percent of all newly diagnosed cases of cancer in the United States, and includes over 34 million records.[209] Six of the studies[190-195] were included in the prior review.[47]

Most studies included patients with mean or median ages between 63 and 69. Exceptions included two studies of SEER data focused on patients with stage IA NSCLC who were 75 years or older[180] or who received sublobar resection (SLR),[188] and a study of patients from the United Kingdom who received wedge resection;[177] limited resections, rather than lobectomy, are often indicated for elderly patients with comorbidities or poor pulmonary reserve. The percentage of male patients in most studies ranged from 36 percent[186] to 72 percent.[171] Ninety-six percent of the patients in the analysis of VINCI data (i.e., veterans) were male.[196] Four studies had mean or median followup times of less than 3 years,[177, 185, 188, 210] five had more than 5 years of followup on average,[174, 176, 181, 187, 193] and 11 did not report mean or median length of followup.[170, 175, 178, 180, 182, 186, 189, 191, 192, 194, 195] The other 7 studies had median followup between three and five years.

Patients were enrolled based on both clinical (k=12 studies) and pathologic (k=11 studies) stage. Study populations were restricted to patients with stage I NSCLC, or they presented results for subgroups of patients defined by stage. One study did not specify type of staging,[192] two studies did not specify staging at enrollment but provided results for both clinical and pathologic staging,[190, 195] and one study categorized patients by pathologic stage when available (clinical stage, otherwise).[178] Eight of the 27 studies included only patients with stage IA NSCLC.[179, 180, 183, 184, 187-189, 192] Most studies included multiple histologic subtypes of stage I NSCLC. Four studies included only patients with adenocarcinoma, the most common subtype; three of the four studies were further restricted to stage IA adenocarcinoma NSCLC,[179, 183, 184] and the fourth was restricted to adenocarcinoma NSCLCs with lepidic features (i.e., well-differentiated, noninvasive tumor growth).[186] Three studies included only patients who received a lobectomy,[173, 175, 185] one included only patients who received SLR,[188] and one included only patients who received wedge resection.[177] All other studies included multiple surgical approaches. In one study, patients were

categorized by whether they received video-assisted thoracoscopic (VATS) or open lobectomy.[182]

Detailed Results

Long-term survival rates varied across study populations, overall and among subgroups defined by various surgical approaches and tumor characteristics in 27 studies. One fair quality study was conducted among a highly selected population of patients 75 years of age or older with stage IA NSCLC[180] and a good quality study only presented results for patients with pathologic stage I NSCLC by cardiac risk score category[181]; both are described in the subgroups section below. Of the remaining 25 studies, 14 report results for stage I NSCLC (n=139,562),[170-172, 174-178, 182, 185, 186, 191, 194, 196] 12 report results for stage IA NSCLC (n=49,741),[173, 179, 183, 184, 187-190, 192-195] and 4 report results for pathologic stage IB NSCLC (n=4,852).[173, 190, 194, 195]

Across all surgical approaches in 14 studies of stage I NSCLC, the 5-year overall survival (OS) ranged from 51 percent in a good quality Norwegian database study of 1,375 patients from 1993 to 2002[194] to 86 percent in a fair quality Japanese study of 713 patients from 1994 to 2003;[191] both studies evaluated surgical resection as the intervention (rather than specific surgical approaches). Among 54,350 patients in the NCDB from 2003 to 2006, the 5-year OS for surgical resection was 61 percent for pathologic and 57 percent for clinical stage I NSCLC.[178] In a fair quality analysis of SEER data from 2004 to 2010, the 5-year OS ranged from 53 percent to 75 percent among 16,315 stage I NSCLC patients who received lobectomy, depending on tumor size and visceral pleural invasion (VPI) status;[175] three other studies reported 5-year OS for lobectomy of 59 percent in 1,781 healthy patients matched to healthy patients who received SBRT[185] and 70 percent in both the NCDB (2003-2006; n=1,991)[186] and VA (2006-2015; n=3,620)[196] databases. Except for one analysis of SEER data from 1988 to 1997, where the 5-year OS was 58 percent among 10,761 patients, all other studies that evaluated surgical resection for stage IA NSCLC were conducted in Japan[179, 184, 190, 195] or Norway[194] where the 5-year OS rates ranged from 65 percent[194] to 86 percent.[190] The 5-year OS rates for lobectomy among 11,990 patients in the NCDB (2003-2006) and 7,989 patients in SEER (2004-2012) with stage IA NSCLC were 66 percent[187] and 71 percent,[183] respectively. All of the studies that evaluated surgical resection for pathologic stage IB NSCLC were conducted in Japan[173, 190, 195] and Norway;[194] the 5-year OS rates ranged from 42 percent among 816 Norwegian patients (1993-2002)[194] to 69 percent among 2,398 Japanese patients in 2004.[190]

Ten studies reported survival rates for different types of or approaches to surgical resection. In one US study of lobectomy for clinical stage I NSCLC (n=963) in 2002-2011, the 5-year OS rate was significantly higher among patients who received VATS (78%) than patients who received open lobectomy (68%), but the difference decreased in a propensity score–matched analysis of the data.[182] In five studies, 5-year OS rates were statistically similar between surgical approaches, although rates were generally numerically higher for lobectomy compared with SLR approaches.[176, 179, 183, 186, 193] In one of the studies (n=614), there was also no difference between lobectomy and segmentectomy with respect to 5-year recurrence-free survival rates (71% [95% CI, 64% to 78%] and 70% [95% CI, 63% to 78%], respectively).[176] The 5-year lung cancer-specific survival (LCSS) was 84 and 81 percent for lobectomy and segmentectomy, respectively, in a SEER study of 7,989 pathologic stage IA patients in 2004-2012.[183] Lobectomy outperformed

SLR in two studies; the 5-year OS rates were 66 percent[187] and 70[196] percent for lobectomy and 51 percent[187] and 56[196] percent for SLR. In one of those studies (n=3,620 VA patients), the 5-year incidence of cancer death was 23 percent for patients who received lobectomy and 32 percent for patients who received SLR.[196] Lobectomy resulted in significantly higher 5-year OS rates than specific types of SLR in two additional studies. In one study among patients 75 years and older, the 5-year OS was 50 percent for lobectomy compared with 44 percent and 39 percent for segmentectomy and wedge resection, respectively; the 5-year cancer-specific survival (CSS) was also different by surgical approach (65%, 59%, and 53%, respectively).[180] In the other study of 7,034 patients in the NCDB (2003-2011), the 5-year OS rates were 70 percent, 60 percent, and 55 percent for lobectomy, segmentectomy, and wedge resection, respectively.[189]

The 5-year OS rates were higher among stage IA than stage IB NSCLC patients in four studies,[173, 190, 194, 195] regardless of whether the tumor staging was clinical or pathologic, and ranged from 64 percent[194] to 86 percent[190] for stage IA and 42 percent[194] to 69 percent[190] for stage IB. Three studies reported 5-year survival rates by tumor size, but each study used different categories (<2 vs. 2-3 vs. 3-5 cm;[175] ≤1 vs. 1-2 cm;[189] and ≤3 vs. 3-5 vs. >5 cm[194]), making it difficult to compare them directly. However, survival rates decreased as tumor size increased in all three studies. In one of the studies (which used SEER data from 16,315 patients from 2004 to 2010), investigators further stratified by VPI status.[175] Both the 5-year OS and LCSS rates were higher among patients without VPI than patients with VPI. Among patients with tumors <2 cm, the 5-year OS and LCSS rates were 75 percent and 88 percent, respectively, for patients without VPI; the rates were lower (70 percent and 84 percent, respectively) for patients with VPI. Similarly, among patients with tumors 3-5 cm, the 5-year OS and LCSS rates were 60 percent and 72 percent, respectively, for patients without VPI; the rates were lower (53% and 66%, respectively) for patients with VPI.[175] Finally, in a multisite study of 618 patients in Japan, 5-year OS was higher among patients who met node negative criteria post-surgery (96%) than patients who did not (83%), as was 5-year recurrence-free survival (97% and 76%, respectively).[179]

Subgroups

Seven studies evaluated the effectiveness of surgical resection among subgroups of patients with stage I NSCLC; one additional study included a highly selected population based on age 75 years or older.[180] Overall survival was higher among females,[184, 186, 187, 191, 192] younger patients,[184, 186, 187, 191, 192] white patients,[186] patients without comorbidities,[172, 181, 186, 187] and non- or light smokers[184, 191] than among males, older patients, black patients, patients with comorbidities, and smokers or heavy smokers, respectively.

Five-year OS rates were higher among females than males in three studies (91% vs. 83%,[191] 85% vs.74%,[184] and 63% vs. 53%,[192] respectively); 10-year overall survival was also higher among females (85%) than males (77%) in one Japanese study between 1994 and 2003.[191] In the NCDB from 2003 to 2006, the multivariable-adjusted HRs for females compared with males were 0.78 (95% CI, 0.67 to 0.90) among 1,991 patients with lepidic adenocarcinoma[186] and 0.76 (95% CI, 0.72 to 0.80) among 11,990 patients with clinical stage IA.[187] Five- and 10-year OS rates were higher among younger patients (i.e., <67 years of age) than older patients in both Japan[184, 191] and the United States and Europe.[181, 192] In a study restricted to 1,640 patients 75 years or older with

stage IA NSCLC, the 5-year OS was 50 percent for lobectomy, 44 percent for segmentectomy, and 39 percent for wedge resection.[180] In the NCDB from 2003 to 2006, there was a 46 percent increased risk of death for every 10 years of age (adjusted HR, 1.46; 95% CI, 1.35 to 1.59).[186] In the NDCB study of 1,991 patients with lepidic adenocarcinoma (2003-2006), black patients had a 45 percent increased risk of death compared with white patients (adjusted HR, 1.45; 95% CI, 1.07 to 1.96); risk of death was nonsignificantly lower among other nonwhite patients (adjusted HR, 0.90; 95% CI, 0.60 to 1.35) than white patients.[186]

The Charleson-Deyo Comorbidity Index is a validated method of predicting mortality by weighting comorbid conditions.[211] In an analysis of 11,990 clinical stage IA patients in the NCDB diagnosed between 2003 and 2006, the multivariable-adjusted HRs for patients with Charleson-Deyo Comorbidity Index scores of 1 and ≥2 were 1.21 (95% CI, 1.14 to 1.29) and 1.56 (95% CI, 1.44 to 1.68), respectively, when compared with patients with a score of 0.[187] Adjusted HRs were similar in the 2003-2006 analysis of patients with lepidic adenocarcinoma who had Charleson-Deyo Comorbidity Index scores of 1 and 2 (compared with 0).[186] Five-year OS among patients with and without COPD was similar (73% and 74%, respectively) in a U.S. study of 724 patients conducted from 1992 to 2010.[172] As another proxy for comorbidity, the Thoracic Revised Cardiac Risk Index (ThRCRI) is a prognostic tool that aims to identify patients at increased risk of major cardiac events after surgical resection for lung cancer.[181, 212, 213] A study of 1,370 patients with pathologic stage I NSCLC who underwent surgical resection in three U.S. and European thoracic surgery units from 2000 to 2011 were evaluated according to their ThRCRI class (A: score 0 to 1; B: score 1.5 to 2.5; and C: score > 2.5).[181] Five-year OS and CSS rates decreased as ThRCRI scores increased (class A: 66% and 77%, respectively; class B: 53% and 75%, respectively; class C: 35% and 55%, respectively). Likewise, median survival decreased with ThRCRI scores (98, 68, and 60 months for classes A, B, and C, respectively).[181]

Finally, 5- and 10-year OS rates were higher among nonsmokers (5-year OS: 91%; 10-year OS: 86%)[191] and patients reporting 0 to 20 pack-years of smoking (5-year OS: 86%)[184] than among smokers (5-year OS: 83%; 10-year OS: 76%)[191] and patients reporting more than 20 pack-years of smoking (5-year OS: 71%)[184] in two Japanese studies, one of which was restricted to patients with stage 1 adenocarcinoma NSCLC.[184]

Update Search Summary: Surgery Results

Nine fair-quality studies[214-222] identified through the update search evaluated the effectiveness of surgical resection for the treatment of stage I NSCLC (**Appendix E Tables 7** and **8**). Four studies analyzed 40,288 patients from the SEER database between 2000 and 2014, ensuring at least some overlap of patients among analyses;[214, 215, 219, 221] one study analyzed 14,545 patients from the California Cancer Registry between 2007 and 2013;[216] and one study analyzed 6,905 patients from the Polish National Lung Cancer Registry between 2007 and 2013.[217] Long-term survival rates varied substantially across study populations (5-year OS: 33% to 84.6%) but were similar to what was reported by the original search yield (5-year OS: 51% to 86%). Limited evidence based on a single study[222] also supported findings from the original search yield that sicker patients (i.e., those with clinically relevant comorbidities) generally did not fare as well in terms of survival as patients without comorbidities.

SBRT

Description of Included Studies

Thirteen studies evaluated the effectiveness of SBRT, also known as stereotactic ablative radiotherapy (SABR), for the treatment of stage I NSCLC (**Appendix E Tables 4** and **6**);[185, 196-207] all studies, except one good quality study,[185] were rated as fair quality. Sample sizes ranged from 39 to 4,454. Of the 13 studies, four studies analyzed data from the NCDB for patients diagnosed and treated with SBRT from 2003 through 2014.[185, 196, 199, 200, 202] In the largest NCDB analysis, 4,454 patients were treated with SBRT. The median followup time was 50 months (95% CI, 49 to 52 months) in the entire cohort, which also included 335 radiofrequency ablation patients; 46 percent of the cohort was male and the mean age was 74 years.[202] The three other NCDB analyses were among 1,781 otherwise healthy patients with operable tumors (i.e., surgery was not contraindicated because of patient risk factors),[185] 498 patients with inoperable tumors,[200] and 127 patients who were nonagenarians (i.e., ≥90 years old) at diagnosis.[199] The mean age of the healthy patients was 76 years, and the proportion of males ranged from 43 to 46 percent in the three analyses. One additional database study included 449 patients diagnosed between 2006 and 2015 from VINCI. A majority of patients were age 60 to 79 years at diagnosis, a majority were diagnosed between 2011 and 2015, and 97 percent were male.[196] In addition to the database studies, eight primary studies were conducted between 2003 and 2014 in the United States,[197, 204] Denmark,[203] Japan,[198, 201, 205] The Netherlands,[206] and Scandinavia.[207] Sample sizes ranged from 39[206] to 772,[204] and the reported percentage of male patients ranged from 45 in Denmark[203] to 72 in Japan.[198] The mean age of patients ranged from age 72 to 79 years; one study grouped patients by age at diagnosis (<75 years, ≥75 years) where the mean ages were age 67 and 81 years, respectively and is further described in the subgroups section below.[204] One study each included patients with only operable[201] or only inoperable[207] tumors; the operability of tumors was mixed (range of percent inoperable: 62% to 85%) or not described[198, 204] in the remaining studies.

Detailed Results

The 5-year OS was 33 percent among more than 4,000 patients in the NCDB[202] but was lower among patients with inoperable tumors (n=498) (30%)[200] or who were 90 years of age or older at diagnosis (n=127) (20%).[199] In a propensity score–matched analysis of otherwise healthy patients with operable tumors receiving lobectomy or SBRT in the NCDB that was rated as good quality, the 5-year OS was 29 percent among 1,781 patients receiving SBRT. In the same study, 235 SBRT patients who refused surgery were propensity score matched to lobectomy patients, and the 5-year OS was 40 percent.[185] Among 449 veterans in the VINCI database who received SBRT, the 5-year OS was 44 percent and the 5-year unadjusted cumulative incidence of cancer death was 45 percent.[196]

The median followup time among eight primary studies evaluating SBRT for stage I NSCLC ranged from 3 years (reported as 38 months[206]) in a Dutch study of 39 patients to 7 years in a U.S. study of 65 patients.[197] Among 57 patients in Scandinavia and 100 patients in Japan with inoperable tumors, the 5-year OS ranged from 30 percent (95% CI, 18% to 42%)[207] to 42 percent (95% CI, 33% to 52%),[205] respectively. Among Japanese patients with operable tumors, the 5-

year OS ranged from 54 percent (95% CI, 41% to 65%) among 65 patients[205] to 67 percent (95% CI, 50% to 79%) among 40 patients.[201] From studies with mixed or unknown patient populations in terms of operability, the 5-yr OS ranged from 35 percent among 136 patients in Denmark[203] to 66 percent among 65 patients in the United States.[197] In the U.S. study with median followup of 7 years and a mixed patient population, the 7-year OS was 47.5 percent and the 5- and 7-year progression-free survival rates were 49.5 percent and 38.2 percent, respectively.[197] The 5-year progression-free survival was similar in a Scandinavian study (52% [95% CI, 33% to 70%]).[207]

Subgroups

One study of 772 patients treated with SABR between 2004 and 2014 at The University of Texas MD Anderson Cancer Center compared survival between patients less than 75 years of age with patients 75 years or older.[204] The median overall survival was significantly higher among younger patients (61.2 months [95% CI, 53.2 to 69.2 months]) than among older patients (47.7 months [95% CI, 39.6 to 55.9 months]). Five-year OS rates decreased with increasing age in two separate analyses; among patients with mean ages in the 70s, 80s,[204] and 90s,[199] the 5-year OS rates were 52, 40, and 20 percent, respectively.

Update Search Summary: SBRT Results

Fourteen studies (13 fair-quality studies[223-235] and 1 good-quality study[236]) identified through the update search evaluated the effectiveness of SBRT for the treatment of Stage I NSCLC (**Appendix E Tables 7** and **9**). Two studies analyzed 27,795 patients from the NCDB between 2004 and 2014;[228, 232] and one study analyzed 378 patients from the Netherlands Cancer Registry.[231] Long-term survival rates varied substantially across study populations (5-year OS: 26% to 80%) but were similar to what was reported by the original search yield (5-year OS: 20% to 67%). Although survival varied by subgroups defined by clinical and patient characteristics, differences between subgroups based on sex, age, or NSCLC T-stage were not statistically significant.

Key Question 7a. What Are the Harms Associated With Surgical Resection or SBRT for the Treatment of Early (Stage I) NSCLC? Key Question 7b. Do the Harms Differ for Subgroups Defined by Age, Sex, Race/Ethnicity, or Presence of Comorbid Conditions?

Summary

No RCTs comparing surgical resection or SBRT with no treatment for stage I NSCLC were identified. Twenty-five uncontrolled studies evaluating surgical resection (n=737,775 patients with stage I NSCLC)[170, 173, 176, 177, 179, 182, 185, 189, 196, 237-252] for the treatment of stage I NSCLC were included for KQ 7 (**Appendix E Tables 4** and **5**) for presentation to the USPSTF; additional studies were subsequently identified in update searches and literature surveillance and are described below in the *Update Search Summary* sections. Results of those studies were similar to what was identified by the original search yield. Nine of the studies from the original search yield were previously included for KQ 6,[170, 173, 177, 179, 182, 185, 189, 196, 253] three were rated

good quality,[177, 179, 185] and 22 were rated fair quality (**Appendix D Table 1**).[170, 173, 176, 182, 189, 196, 237-252] Nine of the studies were uncontrolled analyses of prospectively collected data from the NCDB from 1998 to 2010, ensuring at least some overlap of patients among analyses.[189, 239, 240, 243-245, 250-252] Likewise, there were three analyses of SEER data from 1992 to 2009 that likely included some overlap of patients.[237, 241, 247] The remaining studies were from other registries or databases (e.g., VINCI) or primary studies conducted at one or more institutions. Five surgery studies reported harms outcomes among subgroups of patients defined by age, sex, and comorbidities.[189, 239, 242, 248, 251]

An additional 31 studies (32 articles) evaluating SBRT (n=17,353 patients with stage I NSCLC)[196-198, 202-207, 237, 241, 246, 251, 254-272] were also included for KQ 7 (**Appendix E Tables 4** and **6**) for presentation to the USPSTF; additional studies were subsequently identified in update searches and literature surveillance and are described below in the *Update Search Summary* sections; results of those studies were similar to what was identified by the original search yield. One of the studies was an RCT comparing two dosing regimens of SBRT (34 Gy in 1 fraction vs. 48 Gy in four consecutive daily fractions);[263] the remaining studies were uncontrolled. All 31 studies were rated fair quality (**Appendix D Tables 1-4**). Two studies analyzed data from the NCDB from 2004 to 2014,[202, 251] and two studies analyzed data from SEER from 2001 to 2009,[237, 241] likely resulting in some patient overlap in analyses. Four SBRT studies reported harms outcomes among subgroups defined by age, sex, and comorbidities.[204, 251, 255, 261]

The strength of evidence for harms from treatment of stage I NSCLC is moderate for surgical resection and low for SBRT/SABR. Estimates of low 30- and 90-day mortality rates are reasonably consistent and precise for surgical resection, as are the estimates for specific adverse effects. For SBRT/SABR, estimates for 30- and 90-day mortality are reasonably consistently low and for specific adverse events are consistently mild to moderate. However, a majority of the SBRT/SABR studies enrolled fewer than 200 patients (i.e., are imprecise) and are clinically heterogeneous in terms of patients and treatment details. Both bodies of evidence are primarily uncontrolled studies of fair quality and may be affected by selective reporting of specific adverse events.

Harms From Surgical Resection

Description of Included Studies

Twenty-five uncontrolled studies of mostly fair quality evaluated the harms of surgical resection for the treatment of stage I NSCLC between 1983 and 2015 and were included in KQ 7 (**Appendix E Tables 4** and **5**).[170, 173, 176, 177, 179, 182, 185, 189, 196, 237-252] Sample sizes ranged from 540 patients in a good-quality study conducted in the United Kingdom from 2011 to 2012[177] to 146,908 patients in an analysis of the NCDB from 2004 to 2013.[245] Most of the studies were conducted in the United States with the exceptions of one study from Denmark,[249] one from the United Kingdom,[177] and two from Japan.[173, 179] A total of 737,775 patients with stage I NSCLC were included in the 25 studies, but there is likely overlap of indeterminant extent of patients among studies that used data from the NCDB (k=9 studies)[189, 239, 240, 243-245, 250-252] and SEER databases (k=3).[237, 241, 247] The mean or median age ranged from 65 to 69 years in most studies. One good quality study, which enrolled only patients who received wedge resection, was

conducted among patients with a median age of 72 years (interquartile ratio [IQR]: 64 to 77 years).[177] Two studies of SEER data reported median ages of 75 years, but the entire patient population also included patients receiving SBRT (who tend to be older; see below).[237, 241] Ninety-six percent of the patients in the analysis of VINCI data (i.e., veterans) were male;[196] the remaining studies were relatively balanced between males and females (range of % male: 43% to 56%). While some studies focused solely on patients who received lobectomy,[173, 182, 185, 238, 247, 249, 250] most studies included multiple types of surgical resection including lobectomy, segmentectomy, wedge resection, and pneumonectomy.

Detailed Results

The 30-day mortality rates ranged from zero in a good-quality Japanese study of 618 clinical stage IA patients[179] to 3.6 percent (95% CI, 3.06% to 4.1%) in an analysis of almost 5,000 patients in the SEER database from 1992 to 2002 who were 65 years of age or older.[247] The 30-day mortality rate for 1,386 patients receiving a pneumonectomy (i.e., surgical removal of one lung) in the NCDB from 2004 to 2013 was an outlier at 7.8 percent compared with rates of 2 percent and 1.8 percent for lobectomy (i.e., removal of a single lobe) and SLR (i.e., removal of less than a full lobe, such as wedge resection or segmentectomy), respectively.[251] The 30-day mortality rate among patients in the NCDB who delayed surgery 8 or more weeks after diagnosis was higher (2.9%) than patients who did not delay surgery (2.4%, p=0.01).[240] One study in Denmark reported a higher 30-day mortality rate among lobectomy patients who received a thoracotomy (2.9%) than patients who received VATS (1.1%, p=0.02).[249] There were no significant differences among various surgical approaches in other studies.[176, 196, 237, 238, 248, 250] Ninety-day mortality rates ranged from 2 percent in a study of VATS vs. open lobectomy[182] to 4.8 percent (95% CI, 2.7% to 7.8%) among lobectomy patients in another study of lobectomy and segmentectomy.[176] The 90-day mortality rate for 1,386 patients receiving a pneumonectomy in the NCDB from 2004 to 2013 was another outlier at 11.9 percent compared with rates of 3.5 percent and 3.3 percent for lobectomy and SLR, respectively.[251] In an analysis of over 145,000 patients in the NCDB from 2004 to 2013, the 30- and 90-day mortality rates were significantly higher (but still <4%) among patients who did not meet quality measures that included anatomical resection, surgery within 8 weeks of diagnosis, resection for cure or complete remission, or sampling of 10 or more lymph nodes.[245]

The overall perioperative morbidity (categorized as pulmonary, cardiac, neurological, and renal, but not otherwise defined) in one study comparing VATS to open lobectomy among 963 patients was 19 percent and 34 percent, respectively (p=0.0001)[182] and in another study was 46 percent and 36 percent for patients (n=899) receiving lobectomy and segmentectomy, respectively (p=0.01) (**Appendix E Table 5**).[248] Less than 30 percent of patients experienced any perioperative morbidity in a study of 800 patients (28%)[170] or acute toxicity within 60 days of surgery in 1,183 patients in a National Comprehensive Cancer Network analysis (23%).[246] Rates of specific adverse events attributed to surgical resection were generally low. The percentage of patients experiencing infection or pneumonia ranged from 3.3 percent[238] to 7 percent;[182] patients with delayed surgery experienced significantly higher rates of infection (11%) than patients without delayed surgery (6%, p=0.006).[240] Patients undergoing delayed surgery,[240] VATS lobectomy (compared with robotic lobectomy[238] or segmentectomy[248]), or who were pathologic stage IB (compared with pathologic stage IA[173]) experienced higher blood loss (sometimes

defined by need for transfusion or a return to the operating room). Three studies reported rates of bronchopleural fistulas of less than 0.5 percent.[170, 182, 238] Greater than 10 percent of patients in some studies reported cardiac arrhythmias[170, 182, 238, 240, 242] or pulmonary morbidities,[182, 238, 240, 247, 248] including air leaks.[238, 240]

Subgroups

Five studies evaluated harms of surgical resection among subgroups of patients.[189, 239, 242, 248, 251] Thirty-day mortality rates increased with increasing age in four studies. Compared with patients under 75 years, patients 75 years or older were 165 percent more likely to die within 30 days of surgery (OR, 2.65, 95% CI, 2.38 to 2.95) in a multivariable analysis of NCDB data from 2003 to 2011.[239] In another NCDB analysis, the 30- and 90-day unadjusted mortality rates for patients 55 years or younger were 0.97 percent and 1.55 percent, respectively, compared with patients 80 years or older (3.94% and 7.30%, respectively).[251] Mortality rates were higher among males than females in two studies.[189, 239] Finally, the risk of death within 30 days of surgery increased as the Charleson-Deyo Comorbidity Score increased in two studies.[189, 239] One study found no difference in mortality between "normal"- and "high"-risk patients;[242] high-risk patients were primarily identified as having predicted forced expiratory volume in 1 second and predicted diffusion capacity of the lung for carbon monoxide of 50 percent or less.

Update Search Summary: Surgery Results

Four fair-quality studies[217, 220, 273, 274] identified through the update search evaluated harms of surgical resection for the treatment of stage I NSCLC between 2017 and 2018 and were included for KQ7 (**Appendix E Tables 7** and **8**). One study analyzed 6,905 patients from the Polish National Lung Cancer Registry from 2007 to 2013,[217] and another analyzed 9,508 patients from the SEER database from 2000 to 2009.[273] Estimates of 30- and 90-day mortality and perioperative morbidity (when reported) were reasonably consistent and precise, and they were similar to the original search yield's findings for surgical resection.

Harms From SBRT

Description of Included Studies

Thirty-one fair quality studies described in 32 articles evaluated SBRT/SABR (n=17,353 patients with stage I NSCLC)[196-198, 202-207, 237, 241, 246, 251, 254-272] for the treatment of stage I NSCLC between 1998 and 2015 and were included for KQ 7 (**Appendix E Tables 4** and **6**). Sample sizes ranged from 30 patients in a single institution study in Italy[262] to 8,216 in an analysis of the NCDB from 2004 to 2013;[275] most studies enrolled fewer than 200 patients. One of the studies was a fair-quality RCT comparing two dosing regimens of SBRT (34 Gy in one fraction vs. 48 Gy in four consecutive daily fractions);[263] the remaining studies were uncontrolled. While most studies were conducted in North America, there were a few conducted in Europe[203, 206, 207, 254, 256, 262, 267, 270] and Asia.[198, 205, 255, 268] The mean or median age of patients receiving SBRT/SABR was between 70 and 79, and the percentage of male patients ranged from 37 percent to 97 percent. Treatment-related toxicity and adverse events were evaluated using the Common Toxicity Criteria for Adverse Events version 3 or 4 in 18 studies. Adverse events were graded according

to severity (grade 1: mild; grade 2: moderate; grade 3: severe or medically significant; grade 4: life-threatening consequences; grade 5: death related to adverse event).[276] Clinical toxicities were also graded using Radiation Therapy Oncology Group (RTOG) criteria[277] in two studies.[262, 263]

Detailed Results

Nine studies reported 30-day mortality rates of 0 to 2 percent;[196, 198, 203, 237, 246, 251, 258, 265, 266] 90-day mortality rates were similar (range: 0% to 3%) in nine studies.[196, 198, 203, 237, 241, 251, 258, 265, 266] The most commonly reported adverse events were radiological toxicity, pulmonary toxicity and respiratory disorders, fatigue, pain, and dermatologic adverse events. The RCT comparing two SBRT dosing regimens reported that a majority of reported adverse events were grade 2 (i.e., moderate);[263] the incidence of grade 2 toxicities ranged from 9 percent[271] to 31 percent[206]in the other studies, and the common toxicities were dyspnea, esophageal pain, chest wall pain, and coughing. The range of grade 3 (i.e., severe) toxicities was 0 percent to 13 percent in 13 studies; the most common grade 3 toxicities reported were pulmonary toxicities, fatigue, chest wall pain, and dermatitis.[197, 203, 205, 206, 255, 260, 262-264, 268, 269, 271, 272] Seven studies reported no grade 4 (i.e., life threatening) adverse events.[197, 206, 207, 255, 264, 267, 269, 271] Among six studies that reported patients who experienced a grade 4 adverse event,[205, 207, 262, 263, 265, 268, 272] the highest incidence rate was 5 percent (dyspnea among patients with medically inoperable tumors)[268] and the most commonly reported toxicity was pulmonary in nature. One study reported a death due to hemoptysis in a patient older than 75 years of age,[204] and two studies each reported a single death due radiation pneumonitis.[256, 260]

Thirteen studies reported data related to rib fractures;[197, 204, 207, 254, 256, 258, 260, 261, 263, 264, 267, 268, 271] most were grade 1 (i.e., mild) or 2 (i.e., moderate) according to the Common Toxicity Criteria for Adverse Events or RTOG criteria. The overall incidence of any rib fracture ranged from 0[271] to 37 percent.[261] In the study reporting the highest overall incidence, 17 of 46 patients reported 41 fractured ribs and the median time to a fractured rib after SBRT was 21 months (range: 7 to 40 months).[261] In the RCT comparing dosing regimens, 18 percent of patients receiving 34 Gy in one fraction and only 2 percent of patients receiving 48 Gy in four fractions at 12 Gy per fraction experienced an "injury" that included fracture.[263] Nineteen studies reported data related to radiation pneumonitis.[197, 204, 205, 207, 237, 246, 254-256, 258-260, 263, 264, 266, 267, 270-272] As many as 75% of patients experienced grade 1 radiation pneumonitis[197] and as described above, only two patients experienced grade 5 (i.e., fatal) radiation pneumonitis.[256, 260] The rate of grade 2, 3, or 4 (i.e., moderate severity to life-threatening) radiation pneumonitis in all of the studies was less than 12 percent.

Subgroups

Four SBRT studies reported harms outcomes among subgroups defined by age, sex, and comorbidities.[204, 251, 255, 261] Thirty- and 90-day unadjusted mortality rates did not substantially differ by age in one study of over 8,000 patients in the NCDB,[251] and rates of grade 2 or 3 (i.e., moderate or severe) adverse events did not differ by age (<75 years, ≥75 years) in a study of 772 U.S.-based patients.[204] In one Japanese study, females experienced numerically higher rates of grade 2 or higher radiation pneumonitis than males (16% vs. 13%, respectively; adjusted OR 1.30 [95% CI, 0.53 to 3.10]).[255] In a small study of 46 patients, females were significantly more

likely to experience rib fractures (adjusted OR 4.43), but the CI was very wide (1.68 to 11.69).[261] In that same study, patients with diabetes or COPD were less likely to experience rib fractures (OR 0.51 [95% CI, 0.09 to 2.88) for diabetes and OR 0.97 [95% CI, 0.28 to 3.39] for COPD) but not significantly so.[261]

Update Search Summary: SBRT Results

Twenty-nine studies (28 fair-quality studies[224-230, 232-234, 236, 278-295] and 1 good-quality study[236]) identified through the update search evaluated the effectiveness of SBRT for the treatment of stage I NSCLC between 2006 and 2019 (**Appendix E Tables 7** and **9**). Two studies analyzed 27,795 patients from the NCDB from 2004 to 2014,[228, 232] one analyzed 99 patients from the Amsterdam Cancer Registry from 2002 to 2007,[289] one study analyzed 55 patients from the RTOG 0236 uncontrolled clinical trial,[279] and one RCT (the CHISEL trial) analyzed 66 patients.[293] Estimates of 30- and 90-day mortality from the update search yield were reasonably consistently low and for specific adverse events were consistently mild to moderate. The most commonly reported adverse events were radiological toxicity, pulmonary toxicity and respiratory disorders, fatigue, chest wall pain, and dermatologic adverse events. These findings matched those of the original search yield, and studies from the update search yield were subject to the same limitations. Studies identified in the update search did not report enough information to determine whether most included patients experienced adverse events.

Key Question 8. What Is the Magnitude of Change in All-Cause and Lung Cancer Mortality That Results From a Specified Change in Lung Cancer Incidence (and Change in Distribution of Lung Cancer Stages [i.e., Stage Shift]) After Screening?

The NLST results indicate that an absolute increase in lung cancer incidence of 0.5 percent (4.1% vs. 3.6% of participants) and the associated absolute increase in Stage I lung cancers of 19 percent (50% vs. 31% of incident lung cancers) and absolute decrease in Stage IV lung cancers of 14 percent (22% vs. 36% of incident lung cancers) after three annual rounds of screening with LDCT (compared with CXR) were associated with 52 fewer lung cancer deaths and 84 fewer all-cause deaths per 100,000 person-years.[32, 63] Attributing the changes in lung cancer and all-cause mortality to this particular change in lung cancer incidence assumes the approach to workup of lung cancers and subsequent treatments (surgical interventions) used in the NLST.

The NELSON results indicate that an absolute increase in lung cancer incidence of 0.6 percent (5.2% vs. 4.6% of participants) and the associated absolute increase in Stage I lung cancers of 27 percent (41% vs. 14% of incident lung cancers) and absolute decrease in Stage IV lung cancers of 19 percent (27% vs. 46% of incident lung cancers) after four rounds of screening with LDCT using a volumetric method (compared with no screening) were associated with 83 fewer lung cancer deaths per 100,000 person-years, but not fewer all-cause deaths.[76] Attributing the changes in lung cancer to this particular change in lung cancer incidence assumes the approach to workup of lung cancers and subsequent treatments (surgical interventions) used in NELSON.

Chapter 4. Discussion

Summary of Evidence

Table 11 provides a summary of the main findings in this evidence review organized by KQ along with a description of consistency, precision, quality, limitations, strength of evidence, and applicability.

Evidence for Benefit and Harms of Screening

For benefits of screening, the good-quality NLST demonstrated a reduction in lung cancer mortality and all-cause mortality with three rounds of annual LDCT screening compared with CXR. Its results indicate an NNS of 323 to prevent one lung cancer death over 6.5 years of followup. The fair-quality NELSON trial also demonstrated a reduction in lung cancer mortality, but not all-cause mortality, with four rounds of LDCT screening with increasing intervals; its results indicate a NNS of 130 to prevent one lung cancer death over 10 years of followup. Harms of screening include false-positive results leading to unnecessary tests and invasive procedures, overdiagnosis, incidental findings, short-term increases in distress because of indeterminate results, and, rarely, radiation-induced cancer (estimated 0.26 to 0.81 major cancers for every 1,000 people screened with 10 annual LDCTs). For every 1,000 persons screened in the NLST, false-positive results led to 17 invasive procedures. Overdiagnosis estimates ranged from a 0 to 67 percent chance that a screen-detected lung cancer was overdiagnosed. The NLST data indicate approximately four cases of overdiagnosis (and 3 lung cancer deaths prevented) per 1,000 people screened (for 3 rounds of annual screening and 6.5 years of followup). Incidental findings were common and variably defined with a wide range reported across studies (4.4% to 40.7%). Common incidental findings were coronary artery calcification; aortic aneurysms; emphysema; infectious and inflammatory processes; and masses, nodules, or cysts of the kidney, breast, adrenal, liver, thyroid, pancreas, spine, and lymph nodes. Incidental findings led to consultations, additional imaging, and invasive procedures. To further underscore the downstream impact of incidental findings, a study of patients undergoing one round of LDCT screening in the Cleveland Clinic screening program estimated a 1-year cost of screening based on Medicare reimbursement of $817 per patient, of which 46 percent was attributed to evaluation and treatment of incidental findings.[167]

The NLST and NELSON results are generally applicable to high-risk current and former smokers ages 50 to 74 years, but participants were younger, more highly educated, less likely to be current smokers than the U.S. screening-eligible population, and had limited racial and ethnic diversity (91% white; <5% black; <2% Hispanic or Latino). The general U.S. population eligible for lung cancer screening may be less likely to benefit from early detection compared with the NLST and NELSON participants because they face a high risk of death from competing causes, such as heart disease, diabetes, or stroke.[25] A study using data from the 2012 Health and Retirement Study (a national survey of adults 50 years or older) evaluated comorbidities, life expectancy, smoking history, and other characteristics in the screening-eligible population and in NLST participants; it reported a lower 5-year survival rate and life expectancy in the screening-

eligible persons compared with NLST participants (87% vs. 93%, p<0.001 and 18.7 years vs. 21.2 years, respectively).[25] NELSON did not allow people with any of the following to be enrolled in the trial: moderate or severe health problems and an inability to climb two flights of stairs; weight over 140 kg; or current or past renal cancer, melanoma, or breast cancer.
The NLST was mainly conducted at large academic centers, potentially limiting its applicability to community-based practice (e.g., because of challenges with implementation [Contextual Question 1 in **Appendix A**], level of multidisciplinary expertise). Many of the trial centers are well recognized for expertise in thoracic radiology as well as cancer diagnosis and treatment.[32] Community centers may be less equipped for screening programs and for treatment of lung cancers identified by screening. For example, the NLST publication noted that mortality associated with surgical resection of lung cancer was much lower in the trial than that reported for the U.S. population (1% vs. 4%).[32, 296]

Regarding pack-years of smoking among trial participants, NLST required a minimum of 30 pack-years for enrollment, whereas NELSON had a lower threshold for eligibility. Specifically, it required that participants smoked either (1) more than 15 cigarettes a day for more than 25 years or (2) more than 10 cigarettes a day for over 30 years, which roughly translate to about 19 pack-years and 15 pack-years, respectively. Among participants enrolled in the study, the median number of pack-years smoked was 38 (interquartile ratio 29.7 to 49.5). The trials enrolled current smokers or those who had quit within 10 years (NELSON) or 15 years (NLST).
Most studies reviewed in this report (including NLST) did not use current nodule evaluation protocols such as Lung-RADS (endorsed by the American College of Radiology). A study included in this review estimated that Lung-RADS would reduce false-positive results compared with NLST criteria and that about 23 percent of all invasive procedures for false-positive results from the NLST would have been prevented by using Lung-RADS criteria.[100] A recent publication developed an infographic to show the outcomes of screening 1,000 persons (with 3 annual screens) if Lung-RADS had been used in the NLST:[297]

- 779 persons would have normal results
- 180 persons would have at least one abnormal result requiring a followup LDCT at 3 or 6 months but no lung cancer diagnosis (false-positive screens)
  - 13 of those 180 would require an invasive procedure to rule out lung cancer
  - 0.4 (1 in 2,500 screened) would have a major complication from an invasive procedure
  - 0.2 (1 in 5,000 screened) would die within 60 days of an invasive procedure from any cause
- 41 persons would be diagnosed with lung cancer
  - 4 cases represent overdiagnosis
  - 3 cases represent lung cancer deaths prevented because of screening

The infographic did not address some important harms, including those from incidental findings. Application of lung cancer screening with (1) current nodule management protocols and (2) the use of risk prediction models might improve the balance of benefits and harms, although the strength of evidence supporting this possibility was low. There remains considerable uncertainty about how such approaches would perform in actual practice because the evidence was largely derived from post hoc application of criteria to trial data (for Lung-RADS) and from modeling

studies (for risk prediction) and does not include prospective clinical utility studies. When applied to current clinical practice, lung cancer screening programs have demonstrated significant variation, even within a single institution type (e.g., the Veterans Health Administration demonstration project reported a wide range of false-positive rates [12.6% to 45.8% of veterans eligible for screening] and incidental findings deemed likely to need followup [20.0% to 63.4%] across eight study sites).[38]

Risk prediction models are an alternative to risk factor–based selection of participants for lung cancer screening and aim to improve identification of those most likely to benefit and to avoid screening those least likely to develop and die from lung cancer. Several models have been developed that incorporate multiple risk factors into regression-based models that predict an absolute risk of lung cancer incidence or mortality. Subjects meeting a specified risk threshold could be offered screening.

The 2013 USPSTF recommendations for lung cancer screening identify subjects appropriate for screening using risk factors of age and smoking history. Some studies suggested that even among persons meeting these criteria there is a broad range of risk of lung cancer incidence and mortality. An analysis of NLST data reported that about 90 percent of the mortality benefit was achieved by screening the highest 60th percentile at risk.[56] Additionally, some studies have noted that persons not meeting USPSTF criteria (due to age or lower cumulative pack-years) may benefit from lung cancer screening, in part due to loss of information from dichotomizing smoking history and not accounting for other known risk factors for lung cancer such as African American race, COPD, radiation treatment, family history, and occupational exposures.[298, 299]

Studies included in this evidence review found that risk prediction models increased the number of screen-preventable deaths. In most cases, they also reduced the number of participants needed to screen to prevent one lung cancer death (i.e., increased efficiency of screening), and reduced the number of false-positive selections for screening per prevented lung cancer death compared with risk factor–based screening, when NLST-like cancer detection and mortality reductions were assumed. The exception is one study of the PLCOm2012 model applied to a more contemporary cohort (NHIS 2015) where risk thresholds of 1.3 percent and 1.51 percent result in a higher NNS and number of false-positive selections for screening per prevented death.[89] These risk thresholds were developed using the PLCO study, which enrolled patients from 1993 to 2001. The number of smokers in the United States has decreased since that time, which is reflected in the NHIS dataset, suggesting fixed population methods can lead to different thresholds across different cohorts due to underlying differences in patient demographics, smoking behavior, and other risk factors. Overall, the results of the risk prediction studies suggest that lung cancer screening benefits may be improved and harms might be reduced if participants could be selected based on risk prediction calculations,[56, 84, 85] with re-evaluation of risk thresholds over time.

The studies comparing risk prediction model–guided screening with risk factor–based screening have limitations. First, studies reporting increased screen-preventable deaths and reduced NNS with risk prediction models assumed NLST-like benefits from screening to estimate outcomes.[84, 85] Related to the aforementioned applicability issues, lung cancer screening in routine clinical practice and screening that targets persons who would not have been eligible for the NLST may

not result in similar detection of screen-preventable cancers and mortality benefits as found in the trial. Second, no studies included in this systematic review evaluated life-years gained by using risk prediction models; only screen-prevented deaths were reported. At older ages, while screening may increase the number of deaths averted, the competing risk of death from other conditions may attenuate improvements in life-years gained. The collaborative decision analysis that is being conducted for the USPSTF addresses this issue. Third, almost all risk prediction models were studied by retrospectively applying models to previously conducted cohort studies or trials.

An important challenge related to the use and evaluation of risk prediction models is the lack of established risk thresholds to implement individualized risk prediction–based screening in practice. The decision to offer LDCT screening to an individual would be contingent on whether the absolute risk of lung cancer incidence or mortality falls above a prespecified cut-off. The included studies used a variety of approaches to estimating risk thresholds, most commonly a USPSTF- or NLST-fixed population screening size. With this approach, the risk threshold is set where the same number of persons would undergo LDCT as those who would be identified by a risk factor–based approach, implying that the absolute number of participants screened by USPSTF criteria is considered an acceptable number of persons to screen.

Another approach was to determine the risk threshold above which there was evidence of mortality benefit from the NLST trial. Two studies of the PLCOm2012 models using this risk threshold (≥1.51%) reported the number of false-positive selections for screening and specificities from which rates of false-positive selections were calculated. It is important to note that "false positive" for KQ 2 refers to the model performance with respect to the models selecting persons to be screened who did not have or develop lung cancer events (diagnosis or death), not with respect to LDCT results. While the overall percentage of false-positive selections for screening was similar for risk prediction model- and risk factor–based screening approaches, the PLCOm2012 model had a lower rate of false-positive selections than the USPSTF criteria in the U.S.-based PLCO cohort (33.8% vs. 37.3%) compared with an Australian study in which the model has a higher rate of false-positive selections vs. USPSTF criteria (28.0% vs. 23.7%). A greater percentage of the U.S. study had a 6-year lung cancer incidence ≥1.51% than the Australian study (35% vs. 25%), suggesting that the underlying risk of the population may affect evaluation of the model and model performance in different populations.

The accompanying decision analysis evaluates three risk prediction models captured by the systematic review that are publicly available and accessible: the PLCOm2012, LCDRAT, and Bach models.[300] The decision analysis uses simplified versions of all three of these models restricted to age, sex, and smoking covariates because jointly simulating other risk factors (e.g., race/ethnicity, family history, medical comorbidities) was not possible due to the lack of well-calibrated and validated lung cancer natural history models incorporating all covariates, accounting for their correlation and time trends. While the CISNET group has extended the Smoking History Generator to consider other covariates, the new Risk Factor Generator is still being evaluated and validated.

Accuracy of Screening With LDCT

The previous evidence review for the USPSTF included one trial and five cohort studies reporting sensitivity (from 80 to 100%) and two trials and five cohort studies reporting specificity (from 28 to 100%).[46] This review includes the studies from the prior review in addition to more recently published studies. In this review, the vast majority of studies reported sensitivity over 80 percent and specificity over 75 percent. NPVs were universally high (range: 97.7% to 100%), but PPVs showed more variation across studies (range: 3.3% to 43.5%). Variability in accuracy was mainly attributed to heterogeneity of eligibility criteria, screening protocols (e.g., number of screening rounds, screening intervals), heterogeneity and completeness of followup length (e.g., to identify false-negative screens), and heterogeneity in the definitions (e.g., of positive tests, indeterminate tests, false-positive test, false-negative tests). Some studies focused on the number of positive scans or nodules rather than on the number of participants with a positive scan, making it challenging to calculate accuracy metrics.

Few studies used the nodule classification approach recommended by American College of Radiology (i.e., Lung-RADS). Studies comparing various approaches to nodule classification reported that using Lung-RADS in the NLST would have increased specificity while decreasing sensitivity and that increases in PPV are seen with increasing nodule size thresholds. The included studies provide limited evidence on whether volumetric or nonvolumetric approaches yield greater accuracy because there are no direct comparisons of these approaches; differences in study populations (e.g., lung cancer incidence) and other contributors to heterogeneity across studies may account for the higher PPVs that tend to be reported in studies using volumetric approaches.

Benefits and Harms of Surgery and SBRT for Stage I NSCLC

The effectiveness of screening for lung cancer with LDCT relies on identification of Stage I NSCLC and subsequent successful surgical removal. This review found a range of 5-year OS across studies from 33 to 86 percent for Stage I NSCLC. The included studies indicate that OS may be higher for lobectomy than SLR surgical approaches; Stage IA than Stage IB tumors; smaller than larger tumors; and for patients who are female, younger, nonsmokers, or have fewer comorbidities than patients who are male, older, smokers, or sicker. Harms of surgery include mortality (30-day mortality rates: 4% or less in most studies; 90-day mortality: 2% to 5% in most studies). Less than one-third of patients in most studies experienced treatment-related adverse events. Common adverse events included pulmonary events (e.g., air leak, pleural effusion) and cardiac arrhythmias.

Across the included studies there was substantial clinical heterogeneity of factors that are related to outcomes. NSCLC staging has changed over time (including definition of Stage I and tumor size criteria) and varied across studies, and studies varied in use of clinical or pathologic requirements for eligibility (i.e., some identified/enrolled participants based on clinical staging and others based on pathologic staging). Among studies that collected data on both clinical and pathologic staging, some upstaging after surgical resection often occurred (e.g., 20% of patients were upstaged in SEER[196]). Variation in surgical approaches over time may also be associated with patient outcomes, with worse outcomes for open surgery than for minimally invasive

approaches such as VATS resection. Use of lobectomy vs. limited/sublobar resection may be associated with patient outcomes, but patients who receive limited resections are often older and sicker.

SBRT is an emerging treatment technology that has not yet been standardized in terms of treatment protocols related to dose, frequency, and duration. Studies reported a wide range of 5-year OS (from 20% to 80%) and harms. Harms included 30- and 90-day mortality (rates ranged from 0% to 3%), pulmonary toxicities, respiratory disorders (including dyspnea), chest wall pain, fatigue, dermatologic reactions, rib fractures, and others. Adverse events were experienced by a majority of those treated with SBRT, but most were of mild or moderate severity. Variation in 5-year OS was likely related to clinical characteristics, such as age, comorbidities, and operability of tumors.

Limitations of the SBRT evidence include small sample sizes, often reporting only short-term survival outcomes (e.g., 2- or 3-year OS), lack of pathologic confirmation of lung cancer diagnosis and stage, and lack of comparison groups. Some studies of SBRT that were included for KQ 7 (harms) were excluded from KQ 6 because they only reported survival outcomes at timepoints less than 5 years.[237, 241, 254-258, 260, 263, 264, 266-268, 271, 272] We excluded additional short-term studies that would have been eligible for KQ 6 if they had longer followup; these studies were not eligible for KQ 7 either (because they did not report on harms).[301-313] Regarding pathologic confirmation of diagnosis and stage, it was often lacking in studies of SBRT because patients had not undergone surgical resection.

The evidence summarized in this review for surgery and SBRT generally comes from uncontrolled studies. No RCTs compared surgical resection with SBRT (the STARs, ROSEL, and ROG 1021 RCTs were all stopped early due to poor accrual). Investigators acknowledged how difficult it is to compare surgical resection with SBRT, primarily because SBRT was typically performed when surgery was contraindicated, and many performed propensity-score matched analyses. We did not include the evidence from comparative analyses, however, because it was beyond the scope of this review and instead reported on the absolute rates for eligible outcomes reported by the studies, which are not necessarily comparable across groups or studies.

Limitations

This review has limitations. The limitations of the included studies are discussed above in Results and Discussion. Here we focus on limitations of this review. We excluded non-English language articles. We excluded studies with sample size less than 500 or 1,000 for some KQs to focus on the best evidence. Doing so omitted some smaller studies that reported on harms of screening. For example, a study of 351 participants in the NELSON trial examined discomfort of LDCT scanning and waiting for the LDCT results.[314] Most participants (88% to 99%) reported experiencing no discomfort related to the LDCT scan, but about half reported at least some discomfort from waiting for the result (46%) and dreading the result (51%).

The KQ on risk prediction models (KQ 2) was focused on how well risk prediction models perform vs. current recommended risk factor–based criteria for lung cancer screening, with respect to estimated screen-preventable deaths or all-cause mortality, screening effectiveness (e.g., number needed to screen), and screening harms (e.g., false-positive screens). To be included in this review, a risk prediction model was required to be externally validated, include known lung cancer risk factors of age and smoking history, and compare outcomes with either USPSTF or screening criteria from a trial showing benefit (e.g., NLST). KQ 2 complements the decision analysis report[300] by evaluating previously published studies that apply risk prediction models to cohorts or representative samples of the U.S. population rather than simulated populations.

For accuracy, some included studies did not report accuracy metrics; rather, when sufficient data were reported, we calculated sensitivity, specificity, PPV, and NPV from the study data. This approach introduces uncertainty into these statistics and may account for variability (e.g., because it was sometimes uncertain whether data were number of nodules, number of LDCTs, or number of people).

Future Research Needs

The NLST and NELSON used different approaches to screening (for both screening intervals and definitions of positive tests). Additional research evaluating effectiveness and implementation of the volumetric approach used in NELSON vs. the approach used in the NLST, Lung-RADS, and other nodule management approaches could be useful to inform screening programs.

The optimal screening intervals for LDCT screening and optimal ages to start and stop screening could be important areas of future research. No good- or fair-quality trials directly compared different screening intervals. The 2013 USPSTF recommendation to screen every year from age 55 to 80 for everyone who meets risk-based criteria is relatively intensive. Longer intervals between LDCTs could be considered (e.g., perhaps longer intervals or stopping completely after some number of normal scans). The NELSON trial provides some empirical evidence of lung cancer mortality benefit with a less than annual screening interval.

Studies on how current nodule management approaches and risk prediction performs in clinical practice are needed. Possible next steps in evaluating risk prediction models for lung cancer screening include prospective evaluation compared with risk factor–based criteria, further research into appropriate risk thresholds, and implementation studies of lung cancer risk prediction models in clinical practice. The recently published CHEST guidelines on lung cancer screening noted that it is uncertain whether applying risk prediction models would lead to changes in patient or cancer phenotype that would affect the balance of benefits and harms of screening because the risk models include variables that affect nodule presence, risk of nodule evaluation, risk of lung cancer treatment, survival after lung cancer treatment, and overall survival.[315]

Research into biomarkers combined with LDCT could potentially improve the efficiency of lung cancer screening. Biomarkers related to detection of lung cancer could include protein antigens or antibodies, cell-free DNA, mRNA, and miRNA (noncoding RNA that regulates translation or degradation).[26] Biomarkers could potentially be used to identify high-risk candidates for screening with LDCT, as is currently under study in the Early Cancer detection test-Lung cancer Scotland (ECLS) study.[316] Biomarkers are in early stages of development, with work being done on evaluating the ability of biomarkers to discriminate between persons with and without the disease, rather than prospectively detecting persons with early disease.[26]

Three ongoing trials conducted in Japan, China, and the United Kingdom were identified in this review.[117, 317, 318] The Japanese randomized trial for evaluating the efficacy of low-dose thoracic CT screening for lung cancer in people with a smoking history of less than 30 pack-years (JECS study) plans to include 17,500 subjects in each arm.[317] Participants will be randomized to LDCT in Years 1 and 6 or to CXR in Year 1. Participants in both arms are also encouraged to have annual CXR for lung cancer screening. The primary outcomes are the sensitivity and specificity of the screening modalities in the first year, and secondary outcomes include the lung cancer stage and incidence, harms of screening, and mortality over 10 years. An RCT in China randomized 6,717 participants with at least 20 pack-years of smoking to LDCT screening every 2 years for three rounds or to standard care.[318] The primary aim is to evaluate detection of lung cancer, and the secondary aim is to evaluate lung cancer–specific mortality. The UKLS pilot randomized 4,055 people; the full trial is expected to randomize another 28,000 participants from seven centers.[117] Enrollment into UKLS was based on a risk questionnaire (Liverpool Lung Project risk model version 2) for people 50 to 75 years of age, to identify those at high risk of developing lung cancer (≥5% over 5 years). Although the UKLS has reported some preliminary findings from its pilot phase that are described in this evidence report (e.g., for accuracy, false-positive results, and possible psychosocial harms), assessment of health and mortality outcomes is ongoing and will be reported after followup of 10 years.

Conclusion

Screening high-risk persons with LDCT can reduce lung cancer mortality and may reduce all-cause mortality, but it also causes false-positive results leading to unnecessary tests and invasive procedures, overdiagnosis, incidental findings, short-term increases in distress (from indeterminate results), and, rarely, radiation-induced cancers. The evidence for benefits comes from two RCTs that enrolled participants who were more likely to benefit than the U.S. screening-eligible population and that were mainly conducted at large academic centers, potentially limiting applicability to community-based practice. Application of lung cancer screening with current nodule management protocols (e.g., Lung-RADS) might improve the balance of benefits and harms. Use of risk prediction models might improve the balance of benefits and harms, although there remains considerable uncertainty about how such approaches would perform in actual practice because current evidence does not include prospective clinical utility studies.

References

1. Moyer VA. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014 Mar 04;160(5):330-8. doi: 10.7326/m13-2771. PMID: 24378917.
2. Travis WD, Brambilla E, Nicholson AG, et al. The 2015 World Health Organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. *J Thorac Oncol*. 2015 Sep;10(9):1243-60. doi: 10.1097/JTO.0000000000000630. PMID: 26291008.
3. National Cancer Institute Surveillance, Epidemiology, and End Results Program. Cancer stat facts: lung and bronchus cancer. National Cancer Institute; n.d. https://seer.cancer.gov/statfacts/html/lungb.html. Accessed December 28, 2020.
4. National Cancer Institute. A snapshot of lung cancer. National Cancer Institute. https://www.cancer.gov/types/lung. Accessed Oct 19, 2016.
5. National Cancer Institute. Non-small cell lung cancer treatment (PDQ®)–health professional version. National Cancer Institute; 2016. https://www.cancer.gov/types/lung/hp/non-small-cell-lung-treatment-pdq. Accessed Oct 19, 2016.
6. American Cancer Society Medical and Editorial Team. Key statistics for lung cancer. Atlanta, GA American Cancer Society; 2017. https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/key-statistics.html. Accessed October 23, 2017.
7. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. *CA Cancer J Clin*. 2015 Jan-Feb;65(1):5-29. doi: 10.3322/caac.21254. PMID: 25559415.
8. Alberg AJ, Brock MV, Ford JG, et al. Epidemiology of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*. 2013 May;143(5 Suppl):e1S-e29S. doi: 10.1378/chest.12-2345. PMID: 23649439.
9. Samet JM. Health benefits of smoking cessation. *Clin Chest Med*. 1991 Dec;12(4):669-79. PMID: 1747986.
10. Hackshaw AK, Law MR, Wald NJ. The accumulated evidence on lung cancer and environmental tobacco smoke. *BMJ*. 1997 Oct 18;315(7114):980-8. PMID: 9365295.
11. U.S. Department of Health and Human Services. The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, ; 2006.
12. Aldrich MC, Mercaldo SF, Sandler KL, et al. Evaluation of USPSTF lung cancer screening guidelines among African American adult smokers. *JAMA Oncol*. 2019 Jun 27doi: 10.1001/jamaoncol.2019.1402. PMID: 31246249.
13. Krewski D, Lubin JH, Zielinski JM, et al. Residential radon and risk of lung cancer: a combined analysis of 7 North American case-control studies. *Epidemiology*. 2005 Mar;16(2):137-45. PMID: 15703527.
14. Straif K, Benbrahim-Tallaa L, Baan R, et al. A review of human carcinogens--Part C: metals, arsenic, dusts, and fibres. *Lancet Oncol*. 2009 May;10(5):453-4. PMID: 19418618.

15. Ibrahim EM, Kazkaz GA, Abouelkhair KM, et al. Increased risk of second lung cancer in Hodgkin's lymphoma survivors: a meta-analysis. *Lung*. 2013 Feb;191(1):117-34. doi: 10.1007/s00408-012-9418-4. PMID: 23053567.
16. Grantzau T, Overgaard J. Risk of second non-breast cancer after radiotherapy for breast cancer: a systematic review and meta-analysis of 762,468 patients. *Radiother Oncol*. 2015 Jan;114(1):56-65. doi: 10.1016/j.radonc.2014.10.004. PMID: 25454172.
17. Brenner DR, Boffetta P, Duell EJ, et al. Previous lung diseases and lung cancer risk: a pooled analysis from the International Lung Cancer Consortium. *Am J Epidemiol*. 2012 Oct 01;176(7):573-85. doi: 10.1093/aje/kws151. PMID: 22986146.
18. Hopkins RJ, Duan F, Chiles C, et al. Reduced expiratory flow rate among heavy smokers increases lung cancer risk. Results from the National Lung Screening Trial-American College of Radiology Imaging Network Cohort. *Ann Am Thorac Soc*. 2017 Mar;14(3):392-402. doi: 10.1513/AnnalsATS.201609-741OC. PMID: 28076701.
19. Saracci R. The interactions of tobacco smoking and other agents in cancer etiology. *Epidemiol Rev*. 1987;9:175-93. PMID: 3315716.
20. American Cancer Society Medical and Editorial Content Team. Non-small cell lung cancer risk factors. Atlanta, GA: American Cancer Society; 2016. https://www.cancer.org/cancer/non-small-cell-lung-cancer/causes-risks-prevention/risk-factors.html. Accessed October 23, 2017.
21. Lissowska J, Foretova L, Dabek J, et al. Family history and lung cancer risk: international multicentre case-control study in Eastern and Central Europe and meta-analyses. *Cancer Causes Control*. 2010 Jul;21(7):1091-104. doi: 10.1007/s10552-010-9537-2. PMID: 20306329.
22. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. *CA Cancer J Clin*. 2017 Jan;67(1):7-30. doi: 10.3322/caac.21387. PMID: 28055103.
23. American Cancer Society Medical and Editorial Team. About non-small cell lung cancer. Atlanta, GA: American Cancer Society; 2019. https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html. Accessed March 18, 2019.
24. Ma J, Ward EM, Smith R, et al. Annual number of lung cancer deaths potentially avertable by screening in the United States. *Cancer*. 2013 Apr 01;119(7):1381-5. doi: 10.1002/cncr.27813. PMID: 23440730.
25. Howard DH, Richards TB, Bach PB, et al. Comorbidities, smoking status, and life expectancy among individuals eligible for lung cancer screening. *Cancer*. 2015 Dec 15;121(24):4341-7. doi: 10.1002/cncr.29677. PMID: 26372542.
26. Hirales Casillas CE, Flores Fernandez JM, Padilla Camberos E, et al. Current status of circulating protein biomarkers to aid the early detection of lung cancer. *Future Oncol*. 2014 Jun;10(8):1501-13. doi: 10.2217/fon.14.21. PMID: 25052758.
27. 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 Nov 02;306(17):1865-73. doi: 10.1001/jama.2011.1591. PMID: 22031728.
28. American College of Radiology. Lung CT screening reporting and data system ACR.org: American College of Radiology; n.d. https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads. Accessed March 7, 2019.
29. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-

based clinical practice guidelines. *Chest*. 2013 May;143(5 Suppl):e142S-e65S. doi: 10.1378/chest.12-2353. PMID: 23649436.
30. Ettinger DS, Akerley W, Borghaei H, et al. Non-small cell lung cancer, version 2.2013. *J Natl Compr Canc Netw*. 2013 Jun 01;11(6):645-53; quiz 53. PMID: 23744864.
31. Yan TD, Black D, Bannon PG, et al. Systematic review and meta-analysis of randomized and nonrandomized trials on safety and efficacy of video-assisted thoracic surgery lobectomy for early-stage non-small-cell lung cancer. *J Clin Oncol*. 2009 May 20;27(15):2553-62. doi: 10.1200/jco.2008.18.2733. PMID: 19289625.
32. Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011 Aug 04;365(5):395-409. doi: 10.1056/NEJMoa1102873. PMID: 21714641.
33. 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*. 2014 Nov;15(12):1342-50. doi: 10.1016/s1470-2045(14)70387-0. PMID: 25282284.
34. Huo J, Shen C, Volk RJ, et al. Use of CT and chest radiography for lung cancer screening before and after publication of screening guidelines: intended and unintended uptake. *JAMA Intern Med*. 2017 Mar 1;177(3):439-41. doi: 10.1001/jamainternmed.2016.9016. PMID: 28135349.
35. Nishi S, Zhou J, Kuo YF, et al. Use of lung cancer screening with low-dose computed tomography in the Medicare population. *Mayo Clin Proc Innov Qual Outcomes*. 2019 Mar;3(1):70-7. doi: 10.1016/j.mayocpiqo.2018.12.003. PMID: 30899910.
36. Zahnd WE, Eberth JM. Lung cancer screening utilization: a behavioral risk factor surveillance system analysis. *Am J Prev Med*. 2019;57(2):250-5. doi: 10.1016/j.amepre.2019.03.015.
37. Zeliadt SB, Hoffman RM, Birkby G, et al. Challenges implementing lung cancer screening in federally qualified health centers. *Am J Prev Med*. 2018 Apr;54(4):568-75. doi: 10.1016/j.amepre.2018.01.001. PMID: 29429606.
38. Kinsinger LS, Anderson C, Kim J, et al. Implementation of lung cancer screening in the Veterans Health Administration. *JAMA Intern Med*. 2017 Mar 01;177(3):399-406. doi: 10.1001/jamainternmed.2016.9022. PMID: 28135352.
39. Redberg RF, O'Malley PG. Important questions about lung cancer screening programs when incidental findings exceed lung cancer nodules by 40 to 1. *JAMA Intern Med*. 2017 Mar 1;177(3):311-2. doi: 10.1001/jamainternmed.2016.9446. PMID: 28135358.
40. Centers for Medicare & Medicaid Services. Proposed decision memo for screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439N). Baltimore, MD: U.S. Centers for Medicare & Medicaid Services; 2014. https://www.cms.gov/medicare-coverage-database/details/nca-proposed-decision-memo.aspx?NCAId=274 Accessed Nov 20, 2017.
41. Brenner A, James S, Malo TL, et al. Analysis of patient-provider conversations to assess quality of shared decision making about lung cancer screening. SciAbstracts: Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill; 2018.
42. Reuland DS, Cubillos L, Brenner AT, et al. A pre-post study testing a lung cancer screening decision aid in primary care. *BMC Med Inform Decis Mak*. 2018 Jan 12;18(1):5. doi: 10.1186/s12911-018-0582-1. PMID: 29325548.

43. Network NCC.Network NCC, ed Clinical Practice Guidelines in Oncology: Lung Cancer Screening, Version 1.2020. 2019. https://www.nccn.org/professionals/physician_gls/pdf/lung_screening.pdf. Accessed June 19, 2019.
44. American Academy of Family Physicians. Clinical Preventive Service recommendation: lung cancer. American Academy of Family Physicians; 2017. http://www.aafp.org/patient-care/clinical-recommendations/all/lung-cancer.html. Accessed Nov 20, 2017.
45. Seehusen DA. Should family physicians routinely screen for lung cancer in high-risk populations? No: the USPSTF's recommendation for lung cancer screening is overreaching. *Am Fam Physician*. 2014 Jul 15;90(2):73d-4d. PMID: 25077590.
46. Humphrey L, Deffebach M, Pappas M, et al. Screening for lung cancer: systematic review to update the U.S. Preventive Services Task Force Recommendation. Evidence Syntheses, No. 105. Report No.: 13-05188-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; July 2013. PMID: 24027793.
47. Humphrey LL, Deffebach M, Pappas M, et al. Screening for lung cancer with low-dose computed tomography: a systematic review to update the US Preventive Services Task Force recommendation. *Ann Intern Med*. 2013 Sep 17;159(6):411-20. doi: 10.7326/0003-4819-159-6-201309170-00690. PMID: 23897166.
48. Cheung LC, Berg CD, Castle PE, et al. Life-gained-based versus risk-based selection of smokers for lung cancer screening. *Ann Intern Med*. 2019 Oct 22doi: 10.7326/M19-1263. PMID: 31634914.
49. Cheung LC, Katki HA, Chaturvedi AK, et al. Preventing lung cancer mortality by computed tomography screening: the effect of risk-based versus U.S. Preventive Services Task Force eligibility criteria, 2005-2015. *Ann Intern Med*. 2018 Jan 2doi: 10.7326/M17-2067. PMID: 29297008.
50. Jahan S. Human development report 2016: human development for everyone. The United Nations Development Programme. New York, NY: 2016. http://hdr.undp.org/sites/default/files/2016_human_development_report.pdf
51. U.S. Preventive Services Task Force. Appendix VI. Criteria for assessing internal validity of individual studies. 2015. In Procedure Manual [cited 5/17/2017]. Rockville, MD: U.S. Preventive Services Task Force. 2015. Available from: https://www.uspreventiveservicestaskforce.org/Page/Name/appendix-vi-criteria-for-assessing-internal-validity-of-individual-studies. ClinicalTrials.gov Identifier:
52. Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016 Oct 12;355:i4919. doi: 10.1136/bmj.i4919. PMID: 27733354.
53. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011 Oct 18;155(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009. PMID: 22007046.
54. Moons KG, de Groot JA, Bouwmeester W, et al. Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the CHARMS checklist. *PLoS Med*. 2014 Oct;11(10):e1001744. doi: 10.1371/journal.pmed.1001744. PMID: 25314315.
55. West SL, Gartlehner G, Mansfield AJ, et al. Comparative effectiveness review methods: clinical heterogeneity. Agency for Healthcare Research and Quality. 10-EHC070-EF.

Rockville (MD): 2010. PMID: 21433337. https://www.ncbi.nlm.nih.gov/pubmed/21433337
56. Kovalchik SA, Tammemagi M, Berg CD, et al. Targeting of low-dose CT screening according to the risk of lung-cancer death. *N Engl J Med*. 2013 Jul 18;369(3):245-54. doi: 10.1056/NEJMoa1301851. PMID: 23863051.
57. Church TR, Black WC, Aberle DR, et al. Results of initial low-dose computed tomographic screening for lung cancer. *N Engl J Med*. 2013 May 23;368(21):1980-91. doi: 10.1056/NEJMoa1209120. PMID: 23697514.
58. Aberle DR, DeMello S, Berg CD, et al. Results of the two incidence screenings in the National Lung Screening Trial. *N Engl J Med*. 2013 Sep 05;369(10):920-31. doi: 10.1056/NEJMoa1208962. PMID: 24004119.
59. Becker N, Motsch E, Gross ML, et al. Randomized study on early detection of lung cancer with MSCT in Germany: results of the first 3 years of follow-up after randomization. *J Thorac Oncol*. 2015 Jun;10(6):890-6. doi: 10.1097/jto.0000000000000530. PMID: 25783198.
60. Becker N, Motsch E, Gross ML, et al. Randomized study on early detection of lung cancer with MSCT in Germany: study design and results of the first screening round. *J Cancer Res Clin Oncol*. 2012 Sep;138(9):1475-86. doi: 10.1007/s00432-012-1228-9. PMID: 22526165.
61. Infante M, Cavuto S, Lutman FR, et al. Long-term follow-up results of the DANTE Trial, a randomized study of lung cancer screening with spiral computed tomography. *Am J Respir Crit Care Med*. 2015 May 15;191(10):1166-75. doi: 10.1164/rccm.201408-1475OC. PMID: 25760561.
62. Paci E, Puliti D, Lopes Pegna A, et al. Mortality, survival and incidence rates in the ITALUNG randomised lung cancer screening trial. *Thorax*. 2017 Sep;72(9):825-31. doi: 10.1136/thoraxjnl-2016-209825. PMID: 28377492.
63. Pinsky PF, Church TR, Izmirlian G, et al. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. *Cancer*. 2013 Nov 15;119(22):3976-83. doi: 10.1002/cncr.28326. PMID: 24037918.
64. Pinsky PF, Gierada DS, Hocking W, et al. National Lung Screening Trial findings by age: Medicare-eligible versus under-65 population. *Ann Intern Med*. 2014 Nov 04;161(9):627-33. doi: 10.7326/m14-1484. PMID: 25199624.
65. Saghir Z, Dirksen A, Ashraf H, et al. CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT. *Thorax*. 2012 Apr;67(4):296-301. doi: 10.1136/thoraxjnl-2011-200736. PMID: 22286927.
66. Tanner NT, Gebregziabher M, Hughes Halbert C, et al. Racial differences in outcomes within the National Lung Screening Trial. Implications for widespread implementation. *Am J Respir Crit Care Med*. 2015 Jul 15;192(2):200-8. doi: 10.1164/rccm.201502-0259OC. PMID: 25928649.
67. Wille MM, Dirksen A, Ashraf H, et al. Results of the randomized Danish Lung Cancer Screening Trial with focus on high-risk profiling. *Am J Respir Crit Care Med*. 2016 Mar 01;193(5):542-51. doi: 10.1164/rccm.201505-1040OC. PMID: 26485620.
68. Schabath MB, Massion PP, Thompson ZJ, et al. Differences in patient outcomes of prevalence, interval, and screen-detected lung cancers in the CT arm of the national lung

screening trial. *PLoS One*. 2016;11(8):e0159880. doi: 10.1371/journal.pone.0159880. PMID: 27509046.
69. Gohagan JK, Marcus PM, Fagerstrom RM, et al. Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest X-ray screening for lung cancer. *Lung Cancer*. 2005 Jan;47(1):9-15. doi: 10.1016/j.lungcan.2004.06.007. PMID: 15603850.
70. Gohagan J, Marcus P, Fagerstrom R, et al. 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. doi: 10.1378/chest.126.1.114. PMID: 15249451.
71. 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 Sep 1;180(5):445-53. doi: 10.1164/rccm.200901-0076OC. PMID: 19520905.
72. Infante M, Lutman FR, Cavuto S, et al. Lung cancer screening with spiral CT: baseline results of the randomized DANTE trial. *Lung Cancer*. 2008 Mar;59(3):355-63. doi: 10.1016/j.lungcan.2007.08.040. PMID: 17936405.
73. Becker N, Motsch E, Trotter A, et al. Lung cancer mortality reduction by LDCT screening-Results from the randomized German LUSI trial. *Int J Cancer*. 2020 Mar 15;146(6):1503-13. doi: 10.1002/ijc.32486. PMID: 31162856.
74. Black WC, Chiles C, Church TR, et al. Lung cancer incidence and mortality with extended follow-up in the National Lung Screening Trial National Lung Screening Trial Writing Team (1). *J Thorac Oncol*. 2019 Jun 13;14(10):1732-42. doi: 10.1016/j.jtho.2019.05.044. PMID: 31260833.
75. Doroudi M, Pinsky PF, Marcus PM. Lung cancer mortality in the Lung Screening Study Feasibility Trial. *JNCI Cancer Spectr*. 2018 Jul;2(3):pky042. doi: 10.1093/jncics/pky042. PMID: 31360863.
76. de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med*. 2020 Feb 6;382(6):503-13. doi: 10.1056/NEJMoa1911793. PMID: 31995683.
77. Ru Zhao Y, Xie X, de Koning HJ, et al. NELSON lung cancer screening study. *Cancer Imaging*. 2011 Oct 03;11 Spec No A:S79-84. doi: 10.1102/1470-7330.2011.9020. PMID: 22185865.
78. Walter JE, Heuvelmans MA, de Jong PA, et al. Occurrence and lung cancer probability of new solid nodules at incidence screening with low-dose CT: analysis of data from the randomised, controlled NELSON trial. *Lancet Oncol*. 2016 Jul;17(7):907-16. doi: 10.1016/s1470-2045(16)30069-9. PMID: 27283862.
79. Xu DM, Gietema H, de Koning H, et al. Nodule management protocol of the NELSON randomised lung cancer screening trial. *Lung Cancer*. 2006 Nov;54(2):177-84. doi: 10.1016/j.lungcan.2006.08.006. PMID: 16989922.
80. Pastorino U, Rossi M, Rosato V, et al. Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. *Eur J Cancer Prev*. 2012 May;21(3):308-15. doi: 10.1097/CEJ.0b013e328351e1b6. PMID: 22465911.
81. Pastorino U, Silva M, Sestini S, et al. Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy. *Ann Oncol*. 2019 Jun 5doi: 10.1093/annonc/mdz169. PMID: 31168572.

82. Sverzellati N, Silva M, Calareso G, et al. Low-dose computed tomography for lung cancer screening: comparison of performance between annual and biennial screen. *Eur Radiol*. 2016 Nov;26(11):3821-9. doi: 10.1007/s00330-016-4228-3. PMID: 26868497.
83. ten Haaf K, Jeon J, Tammemagi MC, et al. Risk prediction models for selection of lung cancer screening candidates: a retrospective validation study. *PLoS Med*. 2017 Apr;14(4):e1002277. doi: 10.1371/journal.pmed.1002277. PMID: 28376113.
84. Katki HA, Kovalchik SA, Berg CD, et al. Development and validation of risk models to select ever-smokers for CT lung cancer screening. *JAMA*. 2016 Jun 07;315(21):2300-11. doi: 10.1001/jama.2016.6255. PMID: 27179989.
85. Tammemagi MC, Katki HA, Hocking WG, et al. Selection criteria for lung-cancer screening. *N Engl J Med*. 2013 Feb 21;368(8):728-36. doi: 10.1056/NEJMoa1211776. PMID: 23425165.
86. Weber M, Yap S, Goldsbury D, et al. Identifying high risk individuals for targeted lung cancer screening: independent validation of the PLCOm2012 risk prediction tool. *Int J Cancer*. 2017 Jul 15;141(2):242-53. doi: 10.1002/ijc.30673. PMID: 28249359.
87. Tammemagi MC, Church TR, Hocking WG, et al. Evaluation of the lung cancer risks at which to screen ever- and never-smokers: screening rules applied to the PLCO and NLST cohorts. *PLoS Med*. 2014 Dec;11(12):e1001764. doi: 10.1371/journal.pmed.1001764. PMID: 25460915.
88. de-Torres JP, Wilson DO, Sanchez-Salcedo P, et al. Lung cancer in patients with chronic obstructive pulmonary disease. Development and validation of the COPD Lung Cancer Screening Score. *Am J Respir Crit Care Med*. 2015 Feb 1;191(3):285-91. doi: 10.1164/rccm.201407-1210OC. PMID: 25522175.
89. Landy R, Cheung LC, Berg CD, et al. Contemporary implications of U.S. Preventive Services Task Force and risk-based guidelines for lung cancer screening eligibility in the United States. *Ann Intern Med*. 2019 Jun 4doi: 10.7326/M18-3617. PMID: 31158854.
90. Bach PB, Kattan MW, Thornquist MD, et al. Variations in lung cancer risk among smokers. *J Natl Cancer Inst*. 2003 Mar 19;95(6):470-8. PMID: 12644540.
91. Khera N, Holland JC, Griffin JM. Setting the stage for universal financial distress screening in routine cancer care. *Cancer*. 2017 Nov 01;123(21):4092-6. doi: 10.1002/cncr.30940. PMID: 28817185.
92. Cassidy A, Myles JP, van Tongeren M, et al. The LLP risk model: an individual risk prediction model for lung cancer. *Br J Cancer*. 2008 Jan 29;98(2):270-6. doi: 10.1038/sj.bjc.6604158. PMID: 18087271.
93. Meza R, Hazelton WD, Colditz GA, et al. Analysis of lung cancer incidence in the nurses' health and the health professionals' follow-up studies using a multistage carcinogenesis model. *Cancer Causes Control*. 2008 Apr;19(3):317-28. doi: 10.1007/s10552-007-9094-5. PMID: 18058248.
94. Hazelton WD, Clements MS, Moolgavkar SH. Multistage carcinogenesis and lung cancer mortality in three cohorts. *Cancer Epidemiol Biomarkers Prev*. 2005 May;14(5):1171-81. doi: 10.1158/1055-9965.EPI-04-0756. PMID: 15894668.
95. Markaki M, Tsamardinos I, Langhammer A, et al. A validated clinical risk prediction model for lung cancer in smokers of all ages and exposure types: a HUNT study. *EBioMedicine*. 2018 May;31:36-46. doi: 10.1016/j.ebiom.2018.03.027. PMID: 29678673.

96. Knoke JD, Burns DM, Thun MJ. The change in excess risk of lung cancer attributable to smoking following smoking cessation: an examination of different analytic approaches using CPS-I data. *Cancer Causes Control*. 2008 Mar;19(2):207-19. doi: 10.1007/s10552-007-9086-5. PMID: 17992575.
97. Field JK, Duffy SW, Baldwin DR, et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. *Thorax*. 2016 Feb;71(2):161-70. doi: 10.1136/thoraxjnl-2015-207140. PMID: 26645413.
98. Horeweg N, van der Aalst CM, Vliegenthart R, et al. Volumetric computed tomography screening for lung cancer: three rounds of the NELSON trial. *Eur Respir J*. 2013 Dec;42(6):1659-67. doi: 10.1183/09031936.00197712. PMID: 23845716.
99. Lopes Pegna A, Picozzi G, Falaschi F, et al. Four-year results of low-dose CT screening and nodule management in the ITALUNG trial. *J Thorac Oncol*. 2013 Jul;8(7):866-75. doi: 10.1097/JTO.0b013e31828f68d6. PMID: 23612465.
100. Pinsky PF, Gierada DS, Black W, et al. Performance of Lung-RADS in the National Lung Screening Trial: a retrospective assessment. *Ann Intern Med*. 2015 Apr 07;162(7):485-91. doi: 10.7326/m14-2086. PMID: 25664444.
101. Pinsky PF, Gierada DS, Nath H, et al. ROC curves for low-dose CT in the National Lung Screening Trial. *J Med Screen*. 2013;20(3):165-8. doi: 10.1177/0969141313500666. PMID: 24009092.
102. Pinsky PF, Gierada DS, Nath PH, et al. National lung screening trial: variability in nodule detection rates in chest CT studies. *Radiology*. 2013 Sep;268(3):865-73. doi: 10.1148/radiol.13121530. PMID: 23592767.
103. Scholten ET, Horeweg N, de Koning HJ, et al. Computed tomographic characteristics of interval and post screen carcinomas in lung cancer screening. *Eur Radiol*. 2015 Jan;25(1):81-8. doi: 10.1007/s00330-014-3394-4. PMID: 25187382.
104. Yip R, Henschke CI, Yankelevitz DF, et al. CT screening for lung cancer: alternative definitions of positive test result based on the national lung screening trial and international early lung cancer action program databases. *Radiology*. 2014 Nov;273(2):591-6. doi: 10.1148/radiol.14132950. PMID: 24955929.
105. Yankelevitz DF, Yip R, Smith JP, et al. CT screening for lung cancer: Nonsolid nodules in baseline and annual repeat rounds. *Radiology*. 2015 Nov;277(2):555-64. doi: 10.1148/radiol.2015142554. PMID: 26101879.
106. Henschke CI, Yip R, Smith JP, et al. CT screening for lung cancer: part-solid nodules in baseline and annual repeat rounds. *AJR Am J Roentgenol*. 2016 Dec;207(6):1176-84. doi: 10.2214/ajr.16.16043. PMID: 27726410.
107. Henschke CI, Yip R, Yankelevitz DF, et al. Definition of a positive test result in computed tomography screening for lung cancer: a cohort study. *Ann Intern Med*. 2013 Feb 19;158(4):246-52. doi: 10.7326/0003-4819-158-4-201302190-00004. PMID: 23420233.
108. Wille MM, Thomsen LH, Dirksen A, et al. Emphysema progression is visually detectable in low-dose CT in continuous but not in former smokers. *Eur Radiol*. 2014 Nov;24(11):2692-9. doi: 10.1007/s00330-014-3294-7. PMID: 25038853.
109. Zhao YR, Heuvelmans MA, Dorrius MD, et al. Features of resolving and nonresolving indeterminate pulmonary nodules at follow-up CT: the NELSON study. *Radiology*. 2014 Mar;270(3):872-9. doi: 10.1148/radiol.13130332. PMID: 24475806.

110. Gierada DS, Pinsky PF, Duan F, et al. Interval lung cancer after a negative CT screening examination: CT findings and outcomes in National Lung Screening Trial participants. *Eur Radiol*. 2017 Aug;27(8):3249-56. doi: 10.1007/s00330-016-4705-8. PMID: 28050695.
111. Crucitti P, Gallo IF, Santoro G, et al. Lung cancer screening with low dose CT: experience at Campus Bio-Medico of Rome on 1500 patients. *Minerva Chir*. 2015 Dec;70(6):393-9. PMID: 25700151.
112. Wang Y, van Klaveren RJ, de Bock GH, et al. No benefit for consensus double reading at baseline screening for lung cancer with the use of semiautomated volumetry software. *Radiology*. 2012 Jan;262(1):320-6. doi: 10.1148/radiol.11102289. PMID: 22106357.
113. van Riel SJ, Sanchez CI, Bankier AA, et al. Observer variability for classification of pulmonary nodules on low-dose CT images and its effect on nodule management. *Radiology*. 2015 Dec;277(3):863-71. doi: 10.1148/radiol.2015142700. PMID: 26020438.
114. Heuvelmans MA, Oudkerk M, de Bock GH, et al. Optimisation of volume-doubling time cutoff for fast-growing lung nodules in CT lung cancer screening reduces false-positive referrals. *Eur Radiol*. 2013 Jul;23(7):1836-45. doi: 10.1007/s00330-013-2799-9. PMID: 23508275.
115. Tammemagi MC, Schmidt H, Martel S, et al. Participant selection for lung cancer screening by risk modelling (the Pan-Canadian Early Detection of Lung Cancer [PanCan] study): a single-arm, prospective study. *Lancet Oncol*. 2017 Nov;18(11):1523-31. doi: 10.1016/s1470-2045(17)30597-1. PMID: 29055736.
116. McWilliams A, Tammemagi MC, Mayo JR, et al. Probability of cancer in pulmonary nodules detected on first screening CT. *N Engl J Med*. 2013 Sep 5;369(10):910-9. doi: 10.1056/NEJMoa1214726. PMID: 24004118.
117. Field JK, Duffy SW, Baldwin DR, et al. The UK Lung Cancer Screening Trial: a pilot randomised controlled trial of low-dose computed tomography screening for the early detection of lung cancer. *Health Technol Assess*. 2016 May;20(40):1-146. doi: 10.3310/hta20400. PMID: 27224642.
118. Wagnetz U, Menezes RJ, Boerner S, et al. CT screening for lung cancer: implication of lung biopsy recommendations. *AJR Am J Roentgenol*. 2012 Feb;198(2):351-8. doi: 10.2214/ajr.11.6726. PMID: 22268177.
119. Croswell JM, Baker SG, Marcus PM, et al. Cumulative incidence of false-positive test results in lung cancer screening: a randomized trial. *Ann Intern Med*. 2010 Apr 20;152(8):505-12, w176-80. doi: 10.7326/0003-4819-152-8-201004200-00007. PMID: 20404381.
120. van Klaveren RJ, Oudkerk M, Prokop M, et al. Management of lung nodules detected by volume CT scanning. *N Engl J Med*. 2009 Dec 3;361(23):2221-9. doi: 10.1056/NEJMoa0906085. PMID: 19955524.
121. Menezes RJ, Roberts HC, Paul NS, et al. Lung cancer screening using low-dose computed tomography in at-risk individuals: the Toronto experience. *Lung Cancer*. 2010 Feb;67(2):177-83. doi: 10.1016/j.lungcan.2009.03.030. PMID: 19427055.
122. 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 Thorac Oncol*. 2009 May;4(5):608-14. doi: 10.1097/JTO.0b013e3181a0d98f. PMID: 19357536.

123. Tsushima K, Sone S, Hanaoka T, et al. Radiological diagnosis of small pulmonary nodules detected on low-dose screening computed tomography. *Respirology*. 2008 Nov;13(6):817-24. doi: 10.1111/j.1440-1843.2008.01379.x. PMID: 18811880.
124. Veronesi G, Bellomi M, Scanagatta P, et al. Difficulties encountered managing nodules detected during a computed tomography lung cancer screening program. *J Thorac Cardiovasc Surg*. 2008 Sep;136(3):611-7. doi: 10.1016/j.jtcvs.2008.02.082. PMID: 18805261.
125. Lopes Pegna A, 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 Apr;64(1):34-40. doi: 10.1016/j.lungcan.2008.07.003. PMID: 18723240.
126. Toyoda Y, Nakayama T, Kusunoki Y, et al. Sensitivity and specificity of lung cancer screening using chest low-dose computed tomography. *Br J Cancer*. 2008 May 20;98(10):1602-7. doi: 10.1038/sj.bjc.6604351. PMID: 18475292.
127. Veronesi G, Bellomi M, Mulshine JL, et al. Lung cancer screening with low-dose computed tomography: a non-invasive diagnostic protocol for baseline lung nodules. *Lung Cancer*. 2008 Sep;61(3):340-9. doi: 10.1016/j.lungcan.2008.01.001. PMID: 18308420.
128. Henschke CI, Yankelevitz DF, Libby DM, et al. Survival of patients with stage I lung cancer detected on CT screening. *N Engl J Med*. 2006 Oct 26;355(17):1763-71. doi: 10.1056/NEJMoa060476. PMID: 17065637.
129. Henschke CI, Yip R, Miettinen OS. Women's susceptibility to tobacco carcinogens and survival after diagnosis of lung cancer. *JAMA*. 2006 Jul 12;296(2):180-4. doi: 10.1001/jama.296.2.180. PMID: 16835423.
130. Swensen SJ, Jett JR, Hartman TE, et al. CT screening for lung cancer: five-year prospective experience. *Radiology*. 2005 Apr;235(1):259-65. doi: 10.1148/radiol.2351041662. PMID: 15695622.
131. Henschke CI, Yankelevitz DF, Smith JP, et al. CT screening for lung cancer assessing a regimen's diagnostic performance. *Clin Imaging*. 2004 Sep-Oct;28(5):317-21. doi: 10.1016/j.clinimag.2004.05.001. PMID: 15471661.
132. Chung K, Jacobs C, Scholten ET, et al. Lung-RADS category 4X: Does it improve prediction of malignancy in subsolid nodules? *Radiology*. 2017 Jul;284(1):264-71. doi: 10.1148/radiol.2017161624. PMID: 28339311.
133. Walker BL, Williamson C, Regis SM, et al. Surgical outcomes in a large, clinical, low-dose computed tomographic lung cancer screening program. *Ann Thorac Surg*. 2015 Oct;100(4):1218-23. doi: 10.1016/j.athoracsur.2015.04.112. PMID: 26209493.
134. 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 Feb 8;356:j347. doi: 10.1136/bmj.j347. PMID: 28179230.
135. Veronesi G, Maisonneuve P, Bellomi M, et al. Estimating overdiagnosis in low-dose computed tomography screening for lung cancer: a cohort study. *Ann Intern Med*. 2012 Dec 4;157(11):776-84. doi: 10.7326/0003-4819-157-11-201212040-00005. PMID: 23208167.
136. Mascalchi M, Belli G, Zappa M, et al. Risk-benefit analysis of X-ray exposure associated with lung cancer screening in the Italung-CT trial. *AJR Am J Roentgenol*. 2006 Aug;187(2):421-9. doi: 10.2214/ajr.05.0088. PMID: 16861547.

137. Wilson DO, Weissfeld JL, Fuhrman CR, et al. The Pittsburgh Lung Screening Study (PLuSS): outcomes within 3 years of a first computed tomography scan. *Am J Respir Crit Care Med*. 2008 Nov 1;178(9):956-61. doi: 10.1164/rccm.200802-336OC. PMID: 18635890.
138. van't Westeinde SC, Horeweg N, Vernhout RM, et al. The role of conventional bronchoscopy in the workup of suspicious CT scan screen-detected pulmonary nodules. *Chest*. 2012 Aug;142(2):377-84. doi: 10.1378/chest.11-2030. PMID: 22302298.
139. Pinsky PF, Bellinger CR, Miller DP, Jr. False-positive screens and lung cancer risk in the National Lung Screening Trial: implications for shared decision-making. *J Med Screen*. 2018 Jun;25(2):110-2. doi: 10.1177/0969141317727771. PMID: 28929865.
140. Infante M, Chiesa G, Solomon D, et al. Surgical procedures in the DANTE trial, a randomized study of lung cancer early detection with spiral computed tomography: comparative analysis in the screening and control arm. *J Thorac Oncol*. 2011 Feb;6(2):327-35. doi: 10.1097/JTO.0b013e318200f523. PMID: 21178639.
141. Heleno B, Siersma V, Brodersen J. Estimation of overdiagnosis of lung cancer in low-dose computed tomography screening: a secondary analysis of the Danish Lung Cancer Screening Trial. *JAMA Intern Med*. 2018 Oct 1;178(10):1420-2. doi: 10.1001/jamainternmed.2018.3056. PMID: 30276415.
142. Patz EF, Jr., Pinsky P, Gatsonis C, et al. Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA Intern Med*. 2014 Feb 01;174(2):269-74. doi: 10.1001/jamainternmed.2013.12738. PMID: 24322569.
143. Thalanayar PM, Altintas N, Weissfeld JL, et al. Indolent, potentially inconsequential lung cancers in the Pittsburgh Lung Screening Study. *Ann Am Thorac Soc*. 2015 Aug;12(8):1193-6. doi: 10.1513/AnnalsATS.201412-577OC. PMID: 26107281.
144. Young RP, Duan F, Chiles C, et al. Airflow limitation and histology shift in the National Lung Screening Trial. The NLST-ACRIN Cohort Substudy. *Am J Respir Crit Care Med*. 2015 Nov 1;192(9):1060-7. doi: 10.1164/rccm.201505-0894OC. PMID: 26199983.
145. Ashraf H, Tonnesen P, Holst Pedersen J, et al. Effect of CT screening on smoking habits at 1-year follow-up in the Danish Lung Cancer Screening Trial (DLCST). *Thorax*. 2009 May;64(5):388-92. doi: 10.1136/thx.2008.102475. PMID: 19052048.
146. Hasegawa M, Sone S, Takashima S, et al. Growth rate of small lung cancers detected on mass CT screening. *Br J Radiol*. 2000 Dec;73(876):1252-9. doi: 10.1259/bjr.73.876.11205667. PMID: 11205667.
147. Ashraf H, Saghir Z, Dirksen A, et al. Smoking habits in the randomised Danish Lung Cancer Screening Trial with low-dose CT: final results after a 5-year screening programme. *Thorax*. 2014 Jun;69(6):574-9. doi: 10.1136/thoraxjnl-2013-203849. PMID: 24443174.
148. van der Aalst CM, van den Bergh KA, Willemsen MC, et al. Lung cancer screening and smoking abstinence: 2 year follow-up data from the Dutch-Belgian randomised controlled lung cancer screening trial. *Thorax*. 2010 Jul;65(7):600-5. doi: 10.1136/thx.2009.133751. PMID: 20627916.
149. Clark MA, Gorelick JJ, Sicks JD, et al. The relations between false positive and negative screens and smoking cessation and relapse in the National Lung Screening Trial: implications for public health. *Nicotine Tob Res*. 2016 Jan;18(1):17-24. doi: 10.1093/ntr/ntv037. PMID: 25746779.

150. Anderson CM, Yip R, Henschke CI, et al. Smoking cessation and relapse during a lung cancer screening program. *Cancer Epidemiol Biomarkers Prev*. 2009 Dec;18(12):3476-83. doi: 10.1158/1055-9965.epi-09-0176. PMID: 19959698.
151. Styn MA, Land SR, Perkins KA, et al. Smoking behavior 1 year after computed tomography screening for lung cancer: Effect of physician referral for abnormal CT findings. *Cancer Epidemiol Biomarkers Prev*. 2009 Dec;18(12):3484-9. doi: 10.1158/1055-9965.epi-09-0895. PMID: 19959699.
152. Townsend CO, Clark MM, Jett JR, et al. Relation between smoking cessation and receiving results from three annual spiral chest computed tomography scans for lung carcinoma screening. *Cancer*. 2005 May 15;103(10):2154-62. doi: 10.1002/cncr.21045. PMID: 15825210.
153. van der Aalst CM, van Klaveren RJ, van den Bergh KA, et al. The impact of a lung cancer computed tomography screening result on smoking abstinence. *Eur Respir J*. 2011 Jun;37(6):1466-73. doi: 10.1183/09031936.00035410. PMID: 21148233.
154. Cox LS, Clark MM, Jett JR, et al. Change in smoking status after spiral chest computed tomography scan screening. *Cancer*. 2003 Dec 1;98(11):2495-501. doi: 10.1002/cncr.11813. PMID: 14635086.
155. Taylor KL, Cox LS, Zincke N, et al. Lung cancer screening as a teachable moment for smoking cessation. *Lung Cancer*. 2007 Apr;56(1):125-34. doi: 10.1016/j.lungcan.2006.11.015. PMID: 17196298.
156. Gareen IF, Duan F, Greco EM, et al. Impact of lung cancer screening results on participant health-related quality of life and state anxiety in the National Lung Screening Trial. *Cancer*. 2014 Nov 01;120(21):3401-9. doi: 10.1002/cncr.28833. PMID: 25065710.
157. Kaerlev L, Iachina M, Pedersen JH, et al. CT-Screening for lung cancer does not increase the use of anxiolytic or antidepressant medication. *BMC Cancer*. 2012 May 23;12:188. doi: 10.1186/1471-2407-12-188. PMID: 22621716.
158. Rasmussen JF, Siersma V, Pedersen JH, et al. Psychosocial consequences in the Danish randomised controlled lung cancer screening trial (DLCST). *Lung Cancer*. 2015 Jan;87(1):65-72. doi: 10.1016/j.lungcan.2014.11.003. PMID: 25433982.
159. 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 trial. *Eur Respir J*. 2011 Jul;38(1):154-61. doi: 10.1183/09031936.00123410. PMID: 21148229.
160. Aggestrup LM, Hestbech MS, Siersma V, et al. Psychosocial consequences of allocation to lung cancer screening: a randomised controlled trial. *BMJ Open*. 2012;2(2):e000663. doi: 10.1136/bmjopen-2011-000663. PMID: 22382119.
161. Byrne MM, Weissfeld J, Roberts MS. Anxiety, fear of cancer, and perceived risk of cancer following lung cancer screening. *Med Decis Making*. 2008 Nov-Dec;28(6):917-25. doi: 10.1177/0272989x08322013. PMID: 18725404.
162. van den Bergh KA, Essink-Bot ML, Borsboom GJ, et al. Short-term health-related quality of life consequences in a lung cancer CT screening trial (NELSON). *Br J Cancer*. 2010 Jan 5;102(1):27-34. doi: 10.1038/sj.bjc.6605459. PMID: 19935789.
163. Dunn CE, Edwards A, Carter B, et al. The role of screening expectations in modifying short-term psychological responses to low-dose computed tomography lung cancer screening among high-risk individuals. *Patient Educ Couns*. 2017 Aug;100(8):1572-9. doi: 10.1016/j.pec.2017.02.024. PMID: 28274672.

164. Julian LJ. Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). *Arthritis Care Res (Hoboken)*. 2011 November;63(S11):S467-S72. doi: 10.1002/acr.20561|.
165. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. *Med Care*. 2003 May;41(5):582-92. doi: 10.1097/01.MLR.0000062554.74615.4C. PMID: 12719681.
166. Nguyen XV, Davies L, Eastwood JD, et al. Extrapulmonary findings and malignancies in participants screened with chest CT in the National Lung Screening Trial. *J Am Coll Radiol*. 2017 Mar;14(3):324-30. doi: 10.1016/j.jacr.2016.09.044. PMID: 28259326.
167. Morgan L, Choi H, Reid M, et al. Frequency of incidental findings and subsequent evaluation in low-dose computed tomographic scans for lung cancer screening. *Ann Am Thorac Soc*. 2017 Sep;14(9):1450-6. doi: 10.1513/AnnalsATS.201612-1023OC. PMID: 28421812.
168. Swensen SJ, Jett JR, Sloan JA, et al. Screening for lung cancer with low-dose spiral computed tomography. *Am J Respir Crit Care Med*. 2002 Feb 15;165(4):508-13. doi: 10.1164/ajrccm.165.4.2107006. PMID: 11850344.
169. O'Grady TJ, Kitahara CM, DiRienzo AG, et al. Randomization to screening for prostate, lung, colorectal and ovarian cancers and thyroid cancer incidence in two large cancer screening trials. *PLoS One*. 2014;9(9):e106880. doi: 10.1371/journal.pone.0106880. PMID: 25192282.
170. Scheel PJ, 3rd, Crabtree TD, Bell JM, et al. Does surgeon experience affect outcomes in pathologic stage I lung cancer? *J Thorac Cardiovasc Surg*. 2015 Apr;149(4):998-1004.e1. doi: 10.1016/j.jtcvs.2014.12.032. PMID: 25636526.
171. Guerrera F, Errico L, Evangelista A, et al. Exploring stage I non-small-cell lung cancer: development of a prognostic model predicting 5-year survival after surgical resectiondagger. *Eur J Cardiothorac Surg*. 2015 Jun;47(6):1037-43. doi: 10.1093/ejcts/ezu410. PMID: 25391390.
172. Zhai R, Yu X, Shafer A, et al. The impact of coexisting COPD on survival of patients with early-stage non-small cell lung cancer undergoing surgical resection. *Chest*. 2014 Feb;145(2):346-53. doi: 10.1378/chest.13-1176. PMID: 24008835.
173. Nakamura H, Saji H, Kurimoto N, et al. Impact of intraoperative blood loss on long-term survival after lung cancer resection. *Ann Thorac Cardiovasc Surg*. 2015;21(1):18-23. doi: 10.5761/atcs.oa.13-00312. PMID: 24583702.
174. Su S, Scott W, Allen M, et al. Patterns of survival and recurrence after surgical treatment of early stage non-small cell lung carcinoma in the ACOSOG Z0030 (ALLIANCE) trial. J Thorac Cardiovasc Surg; 2014. p. 747-52: Discussion 52-3.
175. Lakha S, Gomez JE, Flores RM, et al. Prognostic significance of visceral pleural involvement in early-stage lung cancer. *Chest*. 2014 Dec;146(6):1619-26. doi: 10.1378/chest.14-0204. PMID: 25032521.
176. Landreneau RJ, Normolle DP, Christie NA, et al. Recurrence and survival outcomes after anatomic segmentectomy versus lobectomy for clinical stage I non-small-cell lung cancer: a propensity-matched analysis. *J Clin Oncol*. 2014 Aug 10;32(23):2449-55. doi: 10.1200/jco.2013.50.8762. PMID: 24982447.

177. Mediratta N, Shackcloth M, Page R, et al. Should males ever undergo wedge resection for stage 1 non-small-cell lung cancer? A propensity analysis. *Eur J Cardiothorac Surg*. 2014 Aug;46(2):267-73; discussion 73. doi: 10.1093/ejcts/ezt603. PMID: 24420371.
178. Khullar OV, Gillespie T, Nickleach DC, et al. Socioeconomic risk factors for long-term mortality after pulmonary resection for lung cancer: an analysis of more than 90,000 patients from the National Cancer Data Base. *J Am Coll Surg*. 2015 Feb;220(2):156-68.e4. doi: 10.1016/j.jamcollsurg.2014.10.009. PMID: 25488349.
179. Tsutani Y, Miyata Y, Nakayama H, et al. Sublobar resection for lung adenocarcinoma meeting node-negative criteria on preoperative imaging. *Ann Thorac Surg*. 2014 May;97(5):1701-7. doi: 10.1016/j.athoracsur.2014.02.024. PMID: 24679941.
180. Razi SS, John MM, Sainathan S, et al. Sublobar resection is equivalent to lobectomy for T1a non-small cell lung cancer in the elderly: a surveillance, epidemiology, and end results database analysis. *J Surg Res*. 2016 Feb;200(2):683-9. doi: 10.1016/j.jss.2015.08.045. PMID: 26490227.
181. Brunelli A, Ferguson MK, Salati M, et al. Thoracic revised cardiac risk index is associated with prognosis after resection for stage I lung cancer. *Ann Thorac Surg*. 2015 Jul;100(1):195-200. doi: 10.1016/j.athoracsur.2015.03.103. PMID: 26004925.
182. Stephens N, Rice D, Correa A, et al. Thoracoscopic lobectomy is associated with improved short-term and equivalent oncological outcomes compared with open lobectomy for clinical Stage I non-small-cell lung cancer: a propensity-matched analysis of 963 cases. *Eur J Cardiothorac Surg*. 2014 Oct;46(4):607-13. doi: 10.1093/ejcts/ezu036. PMID: 24603446.
183. Zhao ZR, Situ DR, Lau RWH, et al. Comparison of segmentectomy and lobectomy in Stage IA adenocarcinomas. *J Thorac Oncol*. 2017 May;12(5):890-6. doi: 10.1016/j.jtho.2017.01.012. PMID: 28111235.
184. Maeda R, Yoshida J, Ishii G, et al. Influence of cigarette smoking on survival and tumor invasiveness in clinical stage IA lung adenocarcinoma. *Ann Thorac Surg*. 2012 May;93(5):1626-32. doi: 10.1016/j.athoracsur.2012.01.005. PMID: 22421592.
185. Rosen JE, Salazar MC, Wang Z, et al. Lobectomy versus stereotactic body radiotherapy in healthy patients with stage I lung cancer. *J Thorac Cardiovasc Surg*. 2016 Jul;152(1):44-54.e9. doi: 10.1016/j.jtcvs.2016.03.060. PMID: 27131846.
186. Cox ML, Yang CJ, Speicher PJ, et al. The role of extent of surgical resection and lymph node assessment for clinical stage I pulmonary lepidic adenocarcinoma: an analysis of 1991 patients. *J Thorac Oncol*. 2017 Apr;12(4):689-96. doi: 10.1016/j.jtho.2017.01.003. PMID: 28082103.
187. Speicher PJ, Gu L, Gulack BC, et al. Sublobar resection for clinical stage IA non-small-cell lung cancer in the United States. *Clin Lung Cancer*. 2016 Jan;17(1):47-55. doi: 10.1016/j.cllc.2015.07.005. PMID: 26602547.
188. Fernandez FG, Crabtree TD, Liu J, et al. Sublobar resection versus definitive radiation in patients with stage IA non-small cell lung cancer. *Ann Thorac Surg*. 2012 Aug;94(2):354-60; discussion 60-1. doi: 10.1016/j.athoracsur.2011.12.092. PMID: 22429673.
189. Khullar OV, Liu Y, Gillespie T, et al. Survival after sublobar resection versus lobectomy for clinical stage IA lung cancer: an analysis from the national cancer data base. *J Thorac Oncol*. 2015 Nov;10(11):1625-33. doi: 10.1097/jto.0000000000000664. PMID: 26352534.

190. Sawabata N, Miyaoka E, Asamura H, et al. Japanese lung cancer registry study of 11,663 surgical cases in 2004: demographic and prognosis changes over decade. *J Thorac Oncol*. 2011 Jul;6(7):1229-35. doi: 10.1097/JTO.0b013e318219aae2. PMID: 21610521.
191. Maeda R, Yoshida J, Ishii G, et al. Long-term survival and risk factors for recurrence in stage I non-small cell lung cancer patients with tumors up to 3 cm in maximum dimension. *Chest*. 2010 Aug;138(2):357-62. doi: 10.1378/chest.09-3046. PMID: 20435660.
192. Chang MY, Mentzer SJ, Colson YL, et al. Factors predicting poor survival after resection of stage IA non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2007 Oct;134(4):850-6. doi: 10.1016/j.jtcvs.2007.03.044. PMID: 17903494.
193. Okada M, Koike T, Higashiyama M, et al. Radical sublobar resection for small-sized non-small cell lung cancer: a multicenter study. *J Thorac Cardiovasc Surg*. 2006 Oct;132(4):769-75. doi: 10.1016/j.jtcvs.2006.02.063. PMID: 17000286.
194. Strand TE, Rostad H, Moller B, et al. Survival after resection for primary lung cancer: a population based study of 3211 resected patients. *Thorax*. 2006 Aug;61(8):710-5. doi: 10.1136/thx.2005.056481. PMID: 16601091.
195. Goya T, Asamura H, Yoshimura H, et al. Prognosis of 6644 resected non-small cell lung cancers in Japan: a Japanese lung cancer registry study. *Lung Cancer*. 2005 Nov;50(2):227-34. doi: 10.1016/j.lungcan.2005.05.021. PMID: 16061304.
196. Bryant AK, Mundt RC, Sandhu AP, et al. Stereotactic body radiation therapy versus surgery for early lung cancer among US veterans. *Ann Thorac Surg*. 2018 Feb;105(2):425-31. doi: 10.1016/j.athoracsur.2017.07.048. PMID: 29198624.
197. Sun B, Brooks ED, Komaki RU, et al. 7-year follow-up after stereotactic ablative radiotherapy for patients with stage I non-small cell lung cancer: results of a phase 2 clinical trial. *Cancer*. 2017 Aug 15;123(16):3031-9. doi: 10.1002/cncr.30693. PMID: 28346656.
198. Matsuo Y, Chen F, Hamaji M, et al. Comparison of long-term survival outcomes between stereotactic body radiotherapy and sublobar resection for stage I non-small-cell lung cancer in patients at high risk for lobectomy: A propensity score matching analysis. *Eur J Cancer*. 2014 Nov;50(17):2932-8. doi: 10.1016/j.ejca.2014.09.006. PMID: 25281527.
199. Arnold BN, Thomas DC, Rosen JE, et al. Effectiveness of local therapy for stage I non-small-cell lung cancer in nonagenarians. *Surgery*. 2017 Sep;162(3):640-51. doi: 10.1016/j.surg.2017.04.025. PMID: 28697883.
200. Koshy M, Malik R, Weichselbaum RR, et al. Increasing radiation therapy dose is associated with improved survival in patients undergoing stereotactic body radiation therapy for stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2015 Feb 1;91(2):344-50. doi: 10.1016/j.ijrobp.2014.10.002. PMID: 25636759.
201. Eba J, Nakamura K, Mizusawa J, et al. Stereotactic body radiotherapy versus lobectomy for operable clinical stage IA lung adenocarcinoma: comparison of survival outcomes in two clinical trials with propensity score analysis (JCOG1313-A). *Jpn J Clin Oncol*. 2016 Aug;46(8):748-53. doi: 10.1093/jjco/hyw058. PMID: 27174959.
202. Lam A, Yoshida EJ, Bui K, et al. A National Cancer Database analysis of radiofrequency ablation versus stereotactic body radiotherapy in early-stage non-small cell lung cancer. *J Vasc Interv Radiol*. 2018 Jul 27doi: 10.1016/j.jvir.2018.04.029. PMID: 30061058.

203. Jeppesen SS, Hansen NCG, Schytte T, et al. Survival of localized NSCLC patients without active treatment or treated with SBRT. *Acta Oncol*. 2018 Feb;57(2):219-25. doi: 10.1080/0284186x.2017.1374558. PMID: 28885080.
204. Brooks ED, Sun B, Zhao L, et al. Stereotactic ablative radiation therapy is highly safe and effective for elderly patients with early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2017 Jul 15;98(4):900-7. doi: 10.1016/j.ijrobp.2016.12.022. PMID: 28258887.
205. Nagata Y, Hiraoka M, Shibata T, et al. Prospective trial of stereotactic body radiation therapy for both operable and inoperable T1N0M0 non-small cell lung cancer: japan clinical oncology group study JCOG0403. *Int J Radiat Oncol Biol Phys*. 2015 Dec 1;93(5):989-96. doi: 10.1016/j.ijrobp.2015.07.2278. PMID: 26581137.
206. Ubels RJ, Mokhles S, Andrinopoulou ER, et al. Quality of life during 5 years after stereotactic radiotherapy in stage I non-small cell lung cancer. *Radiat Oncol*. 2015 Apr 22;10:98. doi: 10.1186/s13014-015-0405-9. PMID: 25896787.
207. Lindberg K, Nyman J, Riesenfeld Kallskog V, et al. Long-term results of a prospective phase II trial of medically inoperable stage I NSCLC treated with SBRT - the Nordic experience. *Acta Oncol*. 2015;54(8):1096-104. doi: 10.3109/0284186x.2015.1020966. PMID: 25813471.
208. National Cancer Institute. Surveillance, epidemiology, and end results (SEER). Bethesda, MD: National Cancer Institute, Division of Cancer Control and Population Sciences, Surveillance Research Program; 2018. https://seer.cancer.gov/about/factsheets/SEER_Overview.pdf. Accessed May 14, 2019.
209. American College of Surgeons. About the National Cancer Database. Chicago, IL: American College of Surgeons; 2019. Accessed May 15, 2019.
210. Numata T, Araya J, Yoshii Y, et al. Clinical efficacy of anti-glycopeptidolipid-core IgA test for diagnosing Mycobacterium avium complex infection in lung. *Respirology*. 2015 Nov;20(8):1277-81. doi: 10.1111/resp.12640. PMID: 26338466.
211. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-83. PMID: 3558716.
212. Brunelli A, Varela G, Salati M, et al. Recalibration of the revised cardiac risk index in lung resection candidates. *Ann Thorac Surg*. 2010 Jul;90(1):199-203. doi: 10.1016/j.athoracsur.2010.03.042. PMID: 20609775.
213. Thomas DC, Blasberg JD, Arnold BN, et al. Validating the thoracic revised cardiac risk index following lung resection. *Ann Thorac Surg*. 2017 Aug;104(2):389-94. doi: 10.1016/j.athoracsur.2017.02.006. PMID: 28499655.
214. Moon MH, Moon YK, Moon SW. Segmentectomy versus lobectomy in early non-small cell lung cancer of 2 cm or less in size: a population-based study. *Respirology*. 2018 Jul;23(7):695-703. doi: 10.1111/resp.13277. PMID: 29465766.
215. Zhou H, Zhang Y, Qiu Z, et al. Nomogram to predict cause-specific mortality in patients with surgically resected stage I non-small-cell lung cancer: a competing risk analysis. *Clin Lung Cancer*. 2018 Mar;19(2):e195-e203. doi: 10.1016/j.cllc.2017.10.016. PMID: 29153966.
216. Berry MF, Canchola AJ, Gensheimer MF, et al. Factors associated with treatment of clinical stage I non-small-cell lung cancer: a population-based analysis. *Clin Lung Cancer*. 2018 Sep;19(5):e745-e58. doi: 10.1016/j.cllc.2018.05.009. PMID: 30149883.

217. Dziedzic R, Zurek W, Marjanski T, et al. Stage I non-small-cell lung cancer: long-term results of lobectomy versus sublobar resection from the Polish National Lung Cancer Registry. *Eur J Cardiothorac Surg*. 2017 Aug 1;52(2):363-9. doi: 10.1093/ejcts/ezx092. PMID: 28402455.
218. Handa Y, Tsutani Y, Ikeda T, et al. Reassessment of right middle lobe lung cancer: comparison of segments 4 and 5 tumors. *Ann Thorac Surg*. 2018 May;105(5):1543-50. doi: 10.1016/j.athoracsur.2017.12.007. PMID: 29329989.
219. Liu Y, Shen J, Liu L, et al. Impact of examined lymph node counts on survival of patients with stage IA non-small cell lung cancer undergoing sublobar resection. *J Thorac Dis*. 2018 Dec;10(12):6569-77. doi: 10.21037/jtd.2018.11.49. PMID: 30746202.
220. Lutz JA, Seguin-Givelet A, Grigoroiu M, et al. Oncological results of full thoracoscopic major pulmonary resections for clinical Stage I non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2019 Feb 1;55(2):263-70. doi: 10.1093/ejcts/ezy245. PMID: 30052990.
221. Lv X, Cao J, Dai X, et al. Survival rates after lobectomy versus sublobar resection for early-stage right middle lobe non-small cell lung cancer. *Thorac Cancer*. 2018 Aug;9(8):1026-31. doi: 10.1111/1759-7714.12782. PMID: 29927089.
222. Sekihara K, Aokage K, Oki T, et al. Long-term survival after complete resection of non-small-cell lung cancer in patients with interstitial lung disease. *Interact Cardiovasc Thorac Surg*. 2018 Apr 1;26(4):638-43. doi: 10.1093/icvts/ivx400. PMID: 29272403.
223. Jeppesen SS, Schytte T, Jensen HR, et al. Stereotactic body radiation therapy versus conventional radiation therapy in patients with early stage non-small cell lung cancer: an updated retrospective study on local failure and survival rates. *Acta Oncol*. 2013 Oct;52(7):1552-8. doi: 10.3109/0284186x.2013.813635. PMID: 23902274.
224. Inoue T, Katoh N, Onimaru R, et al. Stereotactic body radiotherapy using gated radiotherapy with real-time tumor-tracking for stage I non-small cell lung cancer. *Radiat Oncol*. 2013 Mar 21;8:69. doi: 10.1186/1748-717x-8-69. PMID: 23518013.
225. Lagerwaard FJ, Verstegen NE, Haasbeek CJ, et al. Outcomes of stereotactic ablative radiotherapy in patients with potentially operable stage I non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2012 May 1;83(1):348-53. doi: 10.1016/j.ijrobp.2011.06.2003. PMID: 22104360.
226. Onishi H, Shirato H, Nagata Y, et al. Hypofractionated stereotactic radiotherapy (HypoFXSRT) for stage I non-small cell lung cancer: updated results of 257 patients in a Japanese multi-institutional study. *J Thorac Oncol*. 2007 Jul;2(7 Suppl 3):S94-100. doi: 10.1097/JTO.0b013e318074de34. PMID: 17603311.
227. Baumann P, Nyman J, Lax I, et al. Factors important for efficacy of stereotactic body radiotherapy of medically inoperable stage I lung cancer. A retrospective analysis of patients treated in the Nordic countries. *Acta Oncol*. 2006;45(7):787-95. doi: 10.1080/02841860600904862. PMID: 16982541.
228. Uhlig J, Ludwig JM, Goldberg SB, et al. Survival rates after thermal ablation versus stereotactic radiation therapy for stage 1 non-small cell lung cancer: a national cancer database study. *Radiology*. 2018 Dec;289(3):862-70. doi: 10.1148/radiol.2018180979. PMID: 30226453.
229. Karasawa K, Hayakawa S, Machitori Y, et al. Accelerated hypofractionated radiotherapy versus stereotactic body radiotherapy for the treatment of stage I nonsmall cell lung cancer-a single institution experience with long-term follow-up. *Technol Cancer Res*

Treat. 2018 Jan 1;17:1533033818806318. doi: 10.1177/1533033818806318. PMID: 30317929.

230. Manyam BV, Videtic GMM, Verdecchia K, et al. Effect of tumor location and dosimetric predictors for chest wall toxicity in single-fraction stereotactic body radiation therapy for stage I non-small cell lung cancer. *Pract Radiat Oncol*. 2019 Mar;9(2):e187-e95. doi: 10.1016/j.prro.2018.11.011. PMID: 30529796.
231. Detillon D, Aarts MJ, De Jaeger K, et al. Video-assisted thoracic lobectomy versus stereotactic body radiotherapy for stage I non-small cell lung cancer in elderly patients: a propensity matched comparative analysis. *Eur Respir J*. 2019 Mar 28doi: 10.1183/13993003.01561-2018. PMID: 30923188.
232. Baine MJ, Sleightholm R, Neilsen BK, et al. Stereotactic body radiation therapy versus nonradiotherapeutic ablative procedures (laser/cryoablation and electrocautery) for early-stage non-small cell lung cancer. *J Natl Compr Canc Netw*. 2019 May 1;17(5):450-8. doi: 10.6004/jnccn.2018.7269. PMID: 31085762.
233. Cummings MA, Ma SJ, Hermann G, et al. Comparison of single- and five-fraction regimens of stereotactic body radiation therapy for peripheral early-stage non-small-cell lung cancer: a two-institution propensity-matched analysis. *Clin Lung Cancer*. 2018 Nov;19(6):511-7. doi: 10.1016/j.cllc.2018.07.006. PMID: 30131257.
234. Lee S, Song SY, Kim SS, et al. Feasible optimization of stereotactic ablative radiotherapy dose by tumor size for stage I non-small-cell lung cancer. *Clin Lung Cancer*. 2018 Mar;19(2):e253-e61. doi: 10.1016/j.cllc.2017.11.001. PMID: 29196082.
235. Wink KCJ, Lock S, Rossi M, et al. Contact of a tumour with the pleura is not associated with regional recurrence following stereotactic ablative radiotherapy for early stage non-small cell lung cancer. *Radiother Oncol*. 2019 Feb;131:120-6. doi: 10.1016/j.radonc.2018.11.024. PMID: 30773178.
236. Shibamoto Y, Hashizume C, Baba F, et al. Stereotactic body radiotherapy using a radiobiology-based regimen for stage I nonsmall cell lung cancer: a multicenter study. *Cancer*. 2012 Apr 15;118(8):2078-84. doi: 10.1002/cncr.26470. PMID: 22009495.
237. Shirvani SM, Jiang J, Chang JY, et al. Comparative effectiveness of 5 treatment strategies for early-stage non-small cell lung cancer in the elderly. *Int J Radiat Oncol Biol Phys*. 2012 Dec 1;84(5):1060-70. doi: 10.1016/j.ijrobp.2012.07.2354. PMID: 22975611.
238. Louie BE, Wilson JL, Kim S, et al. Comparison of video-assisted thoracoscopic surgery and robotic approaches for clinical Stage I and Stage II non-small cell lung cancer using the Society of Thoracic Surgeons Database. *Ann Thorac Surg*. 2016 Sep;102(3):917-24. doi: 10.1016/j.athoracsur.2016.03.032. PMID: 27209613.
239. Husain ZA, Kim AW, Yu JB, et al. Defining the high-risk population for mortality after resection of early stage NSCLC. *Clin Lung Cancer*. 2015 Nov;16(6):e183-7. doi: 10.1016/j.cllc.2015.04.007. PMID: 25979646.
240. Samson P, Patel A, Garrett T, et al. Effects of delayed surgical resection on short-term and long-term outcomes in clinical stage I non-small cell lung cancer. *Ann Thorac Surg*. 2015 Jun;99(6):1906-12; discussion 13. doi: 10.1016/j.athoracsur.2015.02.022. PMID: 25890663.
241. Shirvani SM, Jiang J, Chang JY, et al. Lobectomy, sublobar resection, and stereotactic ablative radiotherapy for early-stage non-small cell lung cancers in the elderly. *JAMA Surg*. 2014 Dec;149(12):1244-53. doi: 10.1001/jamasurg.2014.556. PMID: 25321323.

242. Puri V, Crabtree TD, Bell JM, et al. National cooperative group trials of "high-risk" patients with lung cancer: are they truly "high-risk"? *Ann Thorac Surg*. 2014 May;97(5):1678-83; discussion 83-5. doi: 10.1016/j.athoracsur.2013.12.028. PMID: 24534644.
243. Melvan JN, Sancheti MS, Gillespie T, et al. Nonclinical factors associated with 30-day mortality after lung cancer resection: an analysis of 215,000 patients using the National Cancer Data Base. *J Am Coll Surg*. 2015 Aug;221(2):550-63. doi: 10.1016/j.jamcollsurg.2015.03.056. PMID: 26206651.
244. Rosen JE, Hancock JG, Kim AW, et al. Predictors of mortality after surgical management of lung cancer in the National Cancer Database. *Ann Thorac Surg*. 2014 Dec;98(6):1953-60. doi: 10.1016/j.athoracsur.2014.07.007. PMID: 25443003.
245. Samson P, Crabtree T, Broderick S, et al. Quality measures in clinical stage I non-small cell lung cancer: improved performance is associated with improved survival. *Ann Thorac Surg*. 2017 Jan;103(1):303-11. doi: 10.1016/j.athoracsur.2016.07.003. PMID: 27665480.
246. Valle LF, Jagsi R, Bobiak SN, et al. Variation in definitive therapy for localized non-small cell lung cancer among national comprehensive cancer network institutions. *Int J Radiat Oncol Biol Phys*. 2016 Feb 1;94(2):360-7. doi: 10.1016/j.ijrobp.2015.10.030. PMID: 26853344.
247. Shapiro M, Mhango G, Kates M, et al. Extent of lymph node resection does not increase perioperative morbidity and mortality after surgery for stage I lung cancer in the elderly. *Eur J Surg Oncol*. 2012 Jun;38(6):516-22. doi: 10.1016/j.ejso.2011.12.018. PMID: 22244908.
248. Schuchert MJ, Awais O, Abbas G, et al. Influence of age and IB status after resection of node-negative non-small cell lung cancer. *Ann Thorac Surg*. 2012 Mar;93(3):929-35; discussion 35-6. doi: 10.1016/j.athoracsur.2011.09.047. PMID: 22364984.
249. Licht PB, Jorgensen OD, Ladegaard L, et al. A national study of nodal upstaging after thoracoscopic versus open lobectomy for clinical stage I lung cancer. *Ann Thorac Surg*. 2013 Sep;96(3):943-9; discussion 9-50. doi: 10.1016/j.athoracsur.2013.04.011. PMID: 23684159.
250. Yang CF, Sun Z, Speicher PJ, et al. Use and outcomes of minimally invasive lobectomy for stage I non-small cell lung cancer in the national cancer data base. *Ann Thorac Surg*. 2016 Mar;101(3):1037-42. doi: 10.1016/j.athoracsur.2015.11.018. PMID: 26822346.
251. Stokes WA, Bronsert MR, Meguid RA, et al. Post-treatment mortality after surgery and stereotactic body radiotherapy for early-stage non-small-cell lung cancer. *J Clin Oncol*. 2018 Mar 1;36(7):642-51. doi: 10.1200/jco.2017.75.6536. PMID: 29346041.
252. Puri V, Crabtree TD, Bell JM, et al. Treatment outcomes in stage I lung cancer: a comparison of surgery and stereotactic body radiation therapy. *J Thorac Oncol*. 2015 Dec;10(12):1776-84. doi: 10.1097/jto.0000000000000680. PMID: 26334753.
253. Brown LM, Louie BE, Jackson N, et al. Recurrence and survival after segmentectomy in patients with prior lung resection for early-stage non-small cell lung cancer. *Ann Thorac Surg*. 2016 Oct;102(4):1110-8. doi: 10.1016/j.athoracsur.2016.04.037. PMID: 27350237.
254. Bibault JE, Mirabel X, Lacornerie T, et al. Adapted prescription dose for Monte Carlo algorithm in lung SBRT: clinical outcome on 205 patients. *PLoS One*. 2015;10(7):e0133617. doi: 10.1371/journal.pone.0133617. PMID: 26207808.

255. Katoh N, Soda I, Tamamura H, et al. Clinical outcomes of stage I and IIA non-small cell lung cancer patients treated with stereotactic body radiotherapy using a real-time tumor-tracking radiotherapy system. *Radiat Oncol*. 2017 Jan 5;12(1):3. doi: 10.1186/s13014-016-0742-3. PMID: 28057036.
256. Grills IS, Hope AJ, Guckenberger M, et al. A collaborative analysis of stereotactic lung radiotherapy outcomes for early-stage non-small-cell lung cancer using daily online cone-beam computed tomography image-guided radiotherapy. *J Thorac Oncol*. 2012 Sep;7(9):1382-93. doi: 10.1097/JTO.0b013e318260e00d. PMID: 22843086.
257. Haidar YM, Rahn DA, 3rd, Nath S, et al. Comparison of outcomes following stereotactic body radiotherapy for non-small cell lung cancer in patients with and without pathological confirmation. *Ther Adv Respir Dis*. 2014 Feb;8(1):3-12. doi: 10.1177/1753465813512545. PMID: 24334338.
258. Rosen LR, Fischer-Valuck BW, Katz SR, et al. Helical image-guided stereotactic body radiotherapy (SBRT) for the treatment of early-stage lung cancer: a single-institution experience at the Willis-Knighton Cancer Center. *Tumori*. 2014 Jan-Feb;100(1):42-8. doi: 10.1700/1430.15814. PMID: 24675490.
259. Allibhai Z, Taremi M, Bezjak A, et al. The impact of tumor size on outcomes after stereotactic body radiation therapy for medically inoperable early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2013 Dec 1;87(5):1064-70. doi: 10.1016/j.ijrobp.2013.08.020. PMID: 24210082.
260. Mathieu D, Campeau MP, Bahig H, et al. Long-term quality of life in early-stage non-small cell lung cancer patients treated with robotic stereotactic ablative radiation therapy. *Pract Radiat Oncol*. 2015 Jul-Aug;5(4):e365-73. doi: 10.1016/j.prro.2014.12.002. PMID: 25680997.
261. Taremi M, Hope A, Lindsay P, et al. Predictors of radiotherapy induced bone injury (RIBI) after stereotactic lung radiotherapy. *Radiat Oncol*. 2012 Sep 17;7:159. doi: 10.1186/1748-717x-7-159. PMID: 22985910.
262. Ferrero C, Badellino S, Filippi AR, et al. Pulmonary function and quality of life after VMAT-based stereotactic ablative radiotherapy for early stage inoperable NSCLC: a prospective study. *Lung Cancer*. 2015 Sep;89(3):350-6. doi: 10.1016/j.lungcan.2015.06.019. PMID: 26164208.
263. Videtic GM, Hu C, Singh AK, et al. A randomized phase 2 study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer: NRG oncology RTOG 0915 (NCCTG N0927). *Int J Radiat Oncol Biol Phys*. 2015 Nov 15;93(4):757-64. doi: 10.1016/j.ijrobp.2015.07.2260. PMID: 26530743.
264. Taremi M, Hope A, Dahele M, et al. Stereotactic body radiotherapy for medically inoperable lung cancer: prospective, single-center study of 108 consecutive patients. *Int J Radiat Oncol Biol Phys*. 2012 Feb 1;82(2):967-73. doi: 10.1016/j.ijrobp.2010.12.039. PMID: 21377293.
265. Crabtree T, Puri V, Timmerman R, et al. Treatment of stage I lung cancer in high-risk and inoperable patients: comparison of prospective clinical trials using stereotactic body radiotherapy (RTOG 0236), sublobar resection (ACOSOG Z4032), and radiofrequency ablation (ACOSOG Z4033). *J Thorac Cardiovasc Surg*. 2013 Mar;145(3):692-9. doi: 10.1016/j.jtcvs.2012.10.038. PMID: 23174176.

266. Robinson CG, DeWees TA, El Naqa IM, et al. Patterns of failure after stereotactic body radiation therapy or lobar resection for clinical stage I non-small-cell lung cancer. *J Thorac Oncol*. 2013 Feb;8(2):192-201. doi: 10.1097/JTO.0b013e31827ce361. PMID: 23287852.
267. Nyman J, Hallqvist A, Lund JA, et al. SPACE - A randomized study of SBRT vs conventional fractionated radiotherapy in medically inoperable stage I NSCLC. *Radiother Oncol*. 2016 Oct;121(1):1-8. doi: 10.1016/j.radonc.2016.08.015. PMID: 27600155.
268. Jeon W, Ahn SJ, Kim YC, et al. Correlation of biologically effective dose and the tumor control in Stage I (<5 cm) non-small cell lung cancer with stereotactic ablative radiotherapy: a single institutional cohort study. *Jpn J Clin Oncol*. 2018 Feb 1;48(2):144-52. doi: 10.1093/jjco/hyx172. PMID: 29194510.
269. Ma SJ, Serra LM, Syed YA, et al. Comparison of single- and three-fraction schedules of stereotactic body radiation therapy for peripheral early-stage non-small-cell lung cancer. *Clin Lung Cancer*. 2018 Mar;19(2):e235-e40. doi: 10.1016/j.cllc.2017.10.010. PMID: 29153897.
270. Badellino S, Muzio JD, Schivazappa G, et al. No differences in radiological changes after 3D conformal vs VMAT-based stereotactic radiotherapy for early stage non-small cell lung cancer. *Br J Radiol*. 2017 Oct;90(1078):20170143. doi: 10.1259/bjr.20170143. PMID: 28749172.
271. Videtic GM, Stephans KL, Woody NM, et al. 30 Gy or 34 Gy? Comparing 2 single-fraction SBRT dose schedules for stage I medically inoperable non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2014 Sep 1;90(1):203-8. doi: 10.1016/j.ijrobp.2014.05.017. PMID: 25015198.
272. Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA*. 2010 Mar 17;303(11):1070-6. doi: 10.1001/jama.2010.261. PMID: 20233825.
273. Ezer N, Kale M, Sigel K, et al. Outcomes after video-assisted thoracoscopic lobectomy versus open lobectomy for early-stage lung cancer in older adults. *Ann Am Thorac Soc*. 2018 Jan;15(1):76-82. doi: 10.1513/AnnalsATS.201612-980OC. PMID: 29121474.
274. Ueda T, Suzuki K, Matsunaga T, et al. Postoperative atrial fibrillation is less frequent in pulmonary segmentectomy compared with lobectomy. *Gen Thorac Cardiovasc Surg*. 2018 Feb;66(2):95-100. doi: 10.1007/s11748-017-0858-x. PMID: 29134538.
275. Weiss E, Wijesooriya K, Dill SV, et al. Tumor and normal tissue motion in the thorax during respiration: analysis of volumetric and positional variations using 4D CT. *Int J Radiat Oncol Biol Phys*. 2007 Jan 1;67(1):296-307. doi: 10.1016/j.ijrobp.2006.09.009. PMID: 17189078.
276. National Cancer Institute. Common terminology criteria for adverse events (CTCAE). Version 4.0. U.S. Department of Health and Human Services, National Institutes of Health and the National Cancer Institute. Washington, DC: June 14 2010. https://www.eortc.be/services/doc/ctc/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf
277. RTOG Foundation. Cooperative group common toxicity criteria Philadelphia, PA: NRG Oncology Philadelphia West Research Center; 2019. Accessed May 15, 2019.

278. Factor OB, Vu CC, Schneider JG, et al. Stereotactic body radiation therapy for stage I non-small cell lung cancer: a small academic hospital experience. *Front Oncol*. 2014;4:287. doi: 10.3389/fonc.2014.00287. PMID: 25368843.
279. Stanic S, Paulus R, Timmerman RD, et al. No clinically significant changes in pulmonary function following stereotactic body radiation therapy for early- stage peripheral non-small cell lung cancer: an analysis of RTOG 0236. *Int J Radiat Oncol Biol Phys*. 2014 Apr 1;88(5):1092-9. doi: 10.1016/j.ijrobp.2013.12.050. PMID: 24661663.
280. Guckenberger M, Allgauer M, Appold S, et al. Safety and efficacy of stereotactic body radiotherapy for stage 1 non-small-cell lung cancer in routine clinical practice: a patterns-of-care and outcome analysis. *J Thorac Oncol*. 2013 Aug;8(8):1050-8. doi: 10.1097/JTO.0b013e318293dc45. PMID: 23817193.
281. Fischer-Valuck BW, Durci M, Katz SR, et al. Influence of patient characteristics on survival following treatment with helical stereotactic body radiotherapy (SBRT) in stage I non-small-cell lung cancer. *Thorac Cancer*. 2013 Feb;4(1):27-34. doi: 10.1111/j.1759-7714.2012.00137.x. PMID: 28920325.
282. Chang JY, Liu H, Balter P, et al. Clinical outcome and predictors of survival and pneumonitis after stereotactic ablative radiotherapy for stage I non-small cell lung cancer. *Radiat Oncol*. 2012 Sep 10;7:152. doi: 10.1186/1748-717x-7-152. PMID: 22963661.
283. Lagerwaard FJ, Aaronson NK, Gundy CM, et al. Patient-reported quality of life after stereotactic ablative radiotherapy for early-stage lung cancer. *J Thorac Oncol*. 2012 Jul;7(7):1148-54. doi: 10.1097/JTO.0b013e318252cfef. PMID: 22610256.
284. Westover KD, Seco J, Adams JA, et al. Proton SBRT for medically inoperable stage I NSCLC. *J Thorac Oncol*. 2012 Jun;7(6):1021-5. doi: 10.1097/JTO.0b013e31824de0bf. PMID: 22551902.
285. Matsuo Y, Shibuya K, Nakamura M, et al. Dose--volume metrics associated with radiation pneumonitis after stereotactic body radiation therapy for lung cancer. *Int J Radiat Oncol Biol Phys*. 2012 Jul 15;83(4):e545-9. doi: 10.1016/j.ijrobp.2012.01.018. PMID: 22436782.
286. Bongers EM, Haasbeek CJ, Lagerwaard FJ, et al. Incidence and risk factors for chest wall toxicity after risk-adapted stereotactic radiotherapy for early-stage lung cancer. *J Thorac Oncol*. 2011 Dec;6(12):2052-7. doi: 10.1097/JTO.0b013e3182307e74. PMID: 22052227.
287. Mutter RW, Liu F, Abreu A, et al. Dose-volume parameters predict for the development of chest wall pain after stereotactic body radiation for lung cancer. *Int J Radiat Oncol Biol Phys*. 2012 Apr 1;82(5):1783-90. doi: 10.1016/j.ijrobp.2011.03.053. PMID: 21868173.
288. Olsen JR, Robinson CG, El Naqa I, et al. Dose-response for stereotactic body radiotherapy in early-stage non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2011 Nov 15;81(4):e299-303. doi: 10.1016/j.ijrobp.2011.01.038. PMID: 21477948.
289. Palma D, Visser O, Lagerwaard FJ, et al. Impact of introducing stereotactic lung radiotherapy for elderly patients with stage I non-small-cell lung cancer: a population-based time-trend analysis. *J Clin Oncol*. 2010 Dec 10;28(35):5153-9. doi: 10.1200/jco.2010.30.0731. PMID: 21041709.
290. Barriger RB, Forquer JA, Brabham JG, et al. A dose-volume analysis of radiation pneumonitis in non-small cell lung cancer patients treated with stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2012 Jan 1;82(1):457-62. doi: 10.1016/j.ijrobp.2010.08.056. PMID: 21035956.

291. Haasbeek CJ, Lagerwaard FJ, Antonisse ME, et al. Stage I nonsmall cell lung cancer in patients aged > or =75 years: outcomes after stereotactic radiotherapy. *Cancer*. 2010 Jan 15;116(2):406-14. doi: 10.1002/cncr.24759. PMID: 19950125.
292. Lagerwaard FJ, Haasbeek CJ, Smit EF, et al. Outcomes of risk-adapted fractionated stereotactic radiotherapy for stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2008 Mar 1;70(3):685-92. doi: 10.1016/j.ijrobp.2007.10.053. PMID: 18164849.
293. Ball D, Mai GT, Vinod S, et al. Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial. *Lancet Oncol*. 2019 Apr;20(4):494-503. doi: 10.1016/S1470-2045(18)30896-9. PMID: 30770291.
294. Ye L, Xu F, Shi S, et al. A SUVmax-based propensity matched analysis of stereotactic body radiotherapy versus surgery in stage I non-small cell lung cancer: unveiling the role of 18F-FDG PET/CT in clinical decision-making. *Clin Transl Oncol*. 2018 Aug;20(8):1026-34. doi: 10.1007/s12094-017-1819-7. PMID: 29327241.
295. Ackerson BG, Tong BC, Hong JC, et al. Stereotactic body radiation therapy versus sublobar resection for stage I NSCLC. *Lung Cancer*. 2018 Nov;125:185-91. doi: 10.1016/j.lungcan.2018.09.020. PMID: 30429018.
296. Bach PB, Cramer LD, Schrag D, et al. The influence of hospital volume on survival after resection for lung cancer. *N Engl J Med*. 2001 Jul 19;345(3):181-8. doi: 10.1056/nejm200107193450306. PMID: 11463014.
297. Robbins HA, Callister M, Sasieni P, et al. Benefits and harms in the National Lung Screening Trial: expected outcomes with a modern management protocol. *Lancet Respiratory Medicine*. 2019doi: 10.1016/S2213-2600(19)30136-5.
298. Rachet B, Siemiatycki J, Abrahamowicz M, et al. A flexible modeling approach to estimating the component effects of smoking behavior on lung cancer. *J Clin Epidemiol*. 2004 Oct;57(10):1076-85. doi: 10.1016/j.jclinepi.2004.02.014. PMID: 15528059.
299. Remen T, Pintos J, Abrahamowicz M, et al. Risk of lung cancer in relation to various metrics of smoking history: a case-control study in Montreal. *BMC Cancer*. 2018 Dec 19;18(1):1275. doi: 10.1186/s12885-018-5144-5. PMID: 30567516.
300. Meza R, de Koning HJ, Kong C-Y, et al. Evaluation of the benefits and harms of lung cancer screening with with low-dose CT: a collaborative modeling study for the U.S. Preventive Services Task Force. Prepared by the Cancer Intervention and Surveillance Modeling Network (CISNET), Lung Cancer Working Group under Contract No. HHSA-290-2015-00011-I, Task Order 11. Rockville, MD: Agency for Healthcare Research and Quality; in process.
301. Lovinfosse P, Janvary ZL, Coucke P, et al. FDG PET/CT texture analysis for predicting the outcome of lung cancer treated by stereotactic body radiation therapy. *Eur J Nucl Med Mol Imaging*. 2016 Jul;43(8):1453-60. doi: 10.1007/s00259-016-3314-8. PMID: 26830299.
302. Woody NM, Stephans KL, Andrews M, et al. A histologic basis for the efficacy of SBRT to the lung. *J Thorac Oncol*. 2017 Mar;12(3):510-9. doi: 10.1016/j.jtho.2016.11.002. PMID: 28017592.
303. Horner-Rieber J, Bernhardt D, Dern J, et al. Histology of non-small cell lung cancer predicts the response to stereotactic body radiotherapy. *Radiother Oncol*. 2017 Nov;125(2):317-24. doi: 10.1016/j.radonc.2017.08.029. PMID: 28919006.

304. Shultz DB, Trakul N, Abelson JA, et al. Imaging features associated with disease progression after stereotactic ablative radiotherapy for stage I non-small-cell lung cancer. *Clin Lung Cancer*. 2014 Jul;15(4):294-301.e3. doi: 10.1016/j.cllc.2013.12.011. PMID: 24594400.
305. Atallah S, Cho BC, Allibhai Z, et al. Impact of pretreatment tumor growth rate on outcome of early-stage lung cancer treated with stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2014 Jul 1;89(3):532-8. doi: 10.1016/j.ijrobp.2014.03.003. PMID: 24929163.
306. Marwaha G, Stephans KL, Woody NM, et al. Lung stereotactic body radiation therapy: regional nodal failure is not predicted by tumor size. *J Thorac Oncol*. 2014 Nov;9(11):1693-7. doi: 10.1097/jto.0000000000000313. PMID: 25185531.
307. Hamamoto Y, Kataoka M, Yamashita M, et al. Lung-cancer related chest events detected by periodical follow-up CT after stereotactic body radiotherapy for stage I primary lung cancer: retrospective analysis of incidence of lung-cancer related chest events and outcomes of salvage treatment. *Jpn J Radiol*. 2012 Oct;30(8):671-5. doi: 10.1007/s11604-012-0107-2. PMID: 22836906.
308. Mak RH, Hermann G, Lewis JH, et al. Outcomes by tumor histology and KRAS mutation status after lung stereotactic body radiation therapy for early-stage non-small-cell lung cancer. *Clin Lung Cancer*. 2015 Jan;16(1):24-32. doi: 10.1016/j.cllc.2014.09.005. PMID: 25450872.
309. Kishi T, Matsuo Y, Ueki N, et al. Pretreatment Modified Glasgow Prognostic Score predicts clinical outcomes after stereotactic body radiation therapy for early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2015 Jul 1;92(3):619-26. doi: 10.1016/j.ijrobp.2015.02.018. PMID: 26068494.
310. Paul S, Lee PC, Mao J, et al. Long term survival with stereotactic ablative radiotherapy (SABR) versus thoracoscopic sublobar lung resection in elderly people: national population based study with propensity matched comparative analysis. *BMJ*. 2016 Jul 8;354:i3570. doi: 10.1136/bmj.i3570. PMID: 27400862.
311. Roach MC, Rehman S, DeWees TA, et al. It's never too late: smoking cessation after stereotactic body radiation therapy for non-small cell lung carcinoma improves overall survival. *Pract Radiat Oncol*. 2016 Jan-Feb;6(1):12-8. doi: 10.1016/j.prro.2015.09.005. PMID: 26598909.
312. Sun V, Kim JY, Williams AC, et al. Quality of life and symptoms following stereotactic body radiotherapy in early-stage lung cancer patients. *J Community Support Oncol*. 2014 Nov;12(11):407-14. PMID: 25789332.
313. Koshy M, Malik R, Mahmood U, et al. Stereotactic body radiotherapy and treatment at a high volume facility is associated with improved survival in patients with inoperable stage I non-small cell lung cancer. *Radiother Oncol*. 2015 Feb;114(2):148-54. doi: 10.1016/j.radonc.2014.12.004. PMID: 25586951.
314. van den Bergh KA, Essink-Bot ML, Bunge EM, et al. Impact of computed tomography screening for lung cancer on participants in a randomized controlled trial (NELSON trial). *Cancer*. 2008 Jul 15;113(2):396-404. doi: 10.1002/cncr.23590. PMID: 18484588.
315. Mazzone PJ, Silvestri GA, Patel S, et al. Screening for Lung Cancer: CHEST Guideline and Expert Panel Report. *Chest*. 2018 Jan 24doi: 10.1016/j.chest.2018.01.016. PMID: 29374513.

316. Sullivan FM, Farmer E, Mair FS, et al. Detection in blood of autoantibodies to tumour antigens as a case-finding method in lung cancer using the EarlyCDT(R)-Lung Test (ECLS): study protocol for a randomized controlled trial. *BMC Cancer*. 2017 Mar 11;17(1):187. doi: 10.1186/s12885-017-3175-y. PMID: 28284200.
317. Sagawa M, Nakayama T, Tanaka M, et al. A randomized controlled trial on the efficacy of thoracic CT screening for lung cancer in non-smokers and smokers of <30 pack-years aged 50-64 years (JECS study): research design. *Jpn J Clin Oncol*. 2012 Dec;42(12):1219-21. doi: 10.1093/jjco/hys157. PMID: 23042771.
318. Yang W, Qian F, Teng J, et al. Community-based lung cancer screening with low-dose CT in China: Results of the baseline screening. *Lung Cancer*. 2018 Mar;117:20-6. doi: 10.1016/j.lungcan.2018.01.003. PMID: 29496251.
319. Detterbeck FC, Boffa DJ, Kim AW, et al. The eighth edition lung cancer stage classification. *Chest*. 2017 Jan;151(1):193-203. doi: 10.1016/j.chest.2016.10.010. PMID: 27780786.
320. Reck M, Rabe KF. Precision diagnosis and treatment for advanced non-small-cell lung cancer. *N Engl J Med*. 2017 Aug 31;377(9):849-61. doi: 10.1056/NEJMra1703413. PMID: 28854088.
321. Morrow DA. Chest discomfort. In Harrison's principles of internal medicine. [cited 1/22/18]. New York, NY: McGraw-Hill. 2014. Available from: http://accessmedicine.mhmedical.com/content.aspx?bookid=1130&sectionid=79724231. ClinicalTrials.gov Identifier:
322. Ettinger DS, Wood DE, Aisner DL, et al. Non-small cell lung cancer, version 5.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2017 Apr;15(4):504-35. PMID: 28404761.
323. American Cancer Society Medical and Editorial Content Team. Non-small cell lung cancer survival rates, by stage. Atlanta, GA: American Cancer Society; 2017. https://www.cancer.org/cancer/non-small-cell-lung-cancer/detection-diagnosis-staging/survival-rates.html. Accessed January 22, 2018.
324. Hazelton WD, Jeon J, Meza R, et al. Chapter 8: the FHCRC lung cancer model. *Risk Anal*. 2012 Jul;32 Suppl 1:S99-S116. doi: 10.1111/j.1539-6924.2011.01681.x. PMID: 22882896.
325. Heuvelmans MA, Oudkerk M, de Jong PA, et al. The impact of radiologists' expertise on screen results decisions in a CT lung cancer screening trial. *Eur Radiol*. 2015 Mar;25(3):792-9. doi: 10.1007/s00330-014-3467-4. PMID: 25366707.
326. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: small cell lung cancer. Version 2.2017. Fort Washington, PA: National Comprehensive Cancer Network; September 15 2016. https://www.tri-kobe.org/nccn/guideline/lung/english/small.pdf
327. Chen VW, Ruiz BA, Hsieh MC, et al. Analysis of stage and clinical/prognostic factors for lung cancer from SEER registries: AJCC staging and collaborative stage data collection system. *Cancer*. 2014 Dec 1;120 Suppl 23:3781-92. doi: 10.1002/cncr.29045. PMID: 25412390.
328. Wender R, Fontham ET, Barrera E, Jr., et al. American Cancer Society lung cancer screening guidelines. *CA Cancer J Clin*. 2013 Mar-Apr;63(2):107-17. doi: 10.3322/caac.21172. PMID: 23315954.

329. Smith RA, Andrews K, Brooks D, et al. Cancer screening in the United States, 2016: a review of current American Cancer Society guidelines and current issues in cancer screening. *CA Cancer J Clin*. 2016 Mar-Apr;66(2):96-114. doi: 10.3322/caac.21336. PMID: 26797525.
330. American Lung Association. Providing guidance on lung cancer screening to patients and physicians. An update from the American Lung Association Screening Committee. American Lung Association. April 30, 2015 2015. http://www.lung.org/assets/documents/lung-cancer/lung-cancer-screening-report.pdf
331. Jaklitsch MT, Jacobson FL, Austin JH, et al. The American Association for Thoracic Surgery guidelines for lung cancer screening using low-dose computed tomography scans for lung cancer survivors and other high-risk groups. *J Thorac Cardiovasc Surg*. 2012 Jul;144(1):33-8. doi: 10.1016/j.jtcvs.2012.05.060. PMID: 22710039.
332. Oudkerk M, Devaraj A, Vliegenthart R, et al. European position statement on lung cancer screening. *Lancet Oncol*. 2017 Dec;18(12):e754-e66. doi: 10.1016/S1470-2045(17)30861-6. PMID: 29208441.
333. Wood DE, Eapen GA, Ettinger DS, et al. Lung cancer screening. *J Natl Compr Canc Netw*. 2012 Feb;10(2):240-65. PMID: 22308518.
334. Lewin G, Morissette K, Dickinson J, et al. Recommendations on screening for lung cancer. *CMAJ*. 2016 Apr 05;188(6):425-32. doi: 10.1503/cmaj.151421. PMID: 26952527.
335. Wiener RS, Gould MK, Arenberg DA, et al. 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. doi: 10.1164/rccm.201508-1671ST. PMID: 26426785.
336. Mazzone P, Powell CA, Arenberg D, et al. Components necessary for high-quality lung cancer screening: American College of Chest Physicians and American Thoracic Society Policy Statement. *Chest*. 2015 Feb;147(2):295-303. doi: 10.1378/chest.14-2500. PMID: 25356819.
337. Fintelmann FJ, Bernheim A, Digumarthy SR, et al. The 10 pillars of lung cancer screening: rationale and logistics of a lung cancer screening program. *Radiographics*. 2015 Nov-Dec;35(7):1893-908. doi: 10.1148/rg.2015150079. PMID: 26495797.
338. Ramsey SD, Malin JL, Goulart B, et al. Implementing lung cancer screening using low-dose computed tomography: recommendations from an expert panel. *J Oncol Pract*. 2015 Jan;11(1):e44-9. doi: 10.1200/JOP.2014.001528. PMID: 25491043.
339. Mulshine JL, D'Amico TA. Issues with implementing a high-quality lung cancer screening program. *CA Cancer J Clin*. 2014 Sep-Oct;64(5):352-63. doi: 10.3322/caac.21239. PMID: 24976072.
340. Carter-Harris L, Gould MK. Multilevel barriers to the successful implementation of lung cancer screening: why does it have to be so hard? *Ann Am Thorac Soc*. 2017 Aug;14(8):1261-5. doi: 10.1513/AnnalsATS.201703-204PS. PMID: 28541749.
341. Wood DE, Kazerooni EA, Baum SL, et al. Lung cancer screening, version 3.2018, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2018 Apr;16(4):412-41. doi: 10.6004/jnccn.2018.0020. PMID: 29632061.

342. Goodwin JS, Nishi S, Zhou J, et al. Use of the shared decision-making visit for lung cancer screening among Medicare enrollees. *JAMA Intern Med*. 2019 Jan 14doi: 10.1001/jamainternmed.2018.6405. PMID: 30640388.
343. Brenner AT, Malo TL, Margolis M, et al. Evaluating shared decision making for lung cancer screening. *JAMA Intern Med*. 2018 Aug 13doi: 10.1001/jamainternmed.2018.3054. PMID: 30105393.
344. Couet N, Desroches S, Robitaille H, et al. Assessments of the extent to which health-care providers involve patients in decision making: a systematic review of studies using the OPTION instrument. *Health Expect*. 2015 Aug;18(4):542-61. doi: 10.1111/hex.12054. PMID: 23451939.
345. Crothers K, Kross EK, Reisch LM, et al. Patients' attitudes regarding lung cancer screening and decision aids. A survey and focus group study. *Ann Am Thorac Soc*. 2016 Nov;13(11):1992-2001. doi: 10.1513/AnnalsATS.201604-289OC. PMID: 27652509.
346. Henderson LM, Jones LM, Marsh MW, et al. Opinions, practice patterns, and perceived barriers to lung cancer screening among attending and resident primary care physicians. *Risk Manag Healthc Policy*. 2017;10:189-95. doi: 10.2147/RMHP.S143152. PMID: 29403320.
347. Hoffman RM, Sussman AL, Getrich CM, et al. Attitudes and beliefs of primary care providers in New Mexico about lung cancer screening using low-dose computed tomography. *Prev Chronic Dis*. 2015 Jul 9;12:E108. doi: 10.5888/pcd12.150112. PMID: 26160294.
348. Simmons VN, Gray JE, Schabath MB, et al. High-risk community and primary care providers knowledge about and barriers to low-dose computed topography lung cancer screening. *Lung Cancer*. 2017 Apr;106:42-9. doi: 10.1016/j.lungcan.2017.01.012. PMID: 28285693.
349. Lewis JA, Petty WJ, Tooze JA, et al. Low-Dose CT lung cancer screening practices and attitudes among primary care providers at an academic medical center. *Cancer Epidemiol Biomarkers Prev*. 2015 Apr;24(4):664-70. doi: 10.1158/1055-9965.Epi-14-1241. PMID: 25613118.
350. Hoffmann TC, Del Mar C. Patients' expectations of the benefits and harms of treatments, screening, and tests: a systematic review. *JAMA Intern Med*. 2015 Feb;175(2):274-86. doi: 10.1001/jamainternmed.2014.6016. PMID: 25531451.
351. Hoffmann TC, Del Mar C. Clinicians' expectations of the benefits and harms of treatments, screening, and tests: a systematic review. *JAMA Intern Med*. 2017 Mar 1;177(3):407-19. doi: 10.1001/jamainternmed.2016.8254. PMID: 28097303.
352. Hoffman RM, Couper MP, Zikmund-Fisher BJ, et al. Prostate cancer screening decisions: results from the National Survey of Medical Decisions (DECISIONS study). *Arch Intern Med*. 2009 Sep 28;169(17):1611-8. doi: 10.1001/archinternmed.2009.262. PMID: 19786681.
353. Dobler CC, Midthun DE, Montori VM. Quality of shared decision making in lung cancer screening: the right process, with the right partners, at the right time and place. *Mayo Clin Proc*. 2017 Nov;92(11):1612-6. doi: 10.1016/j.mayocp.2017.08.010. PMID: 29101930.
354. Goodson JD. POINT: Should only primary care physicians provide shared decision-making services to discuss the risks/benefits of a low-dose chest CT scan for lung cancer screening? Yes. *Chest*. 2017 Jun;151(6):1213-5. doi: 10.1016/j.chest.2016.11.057. PMID: 28041890.

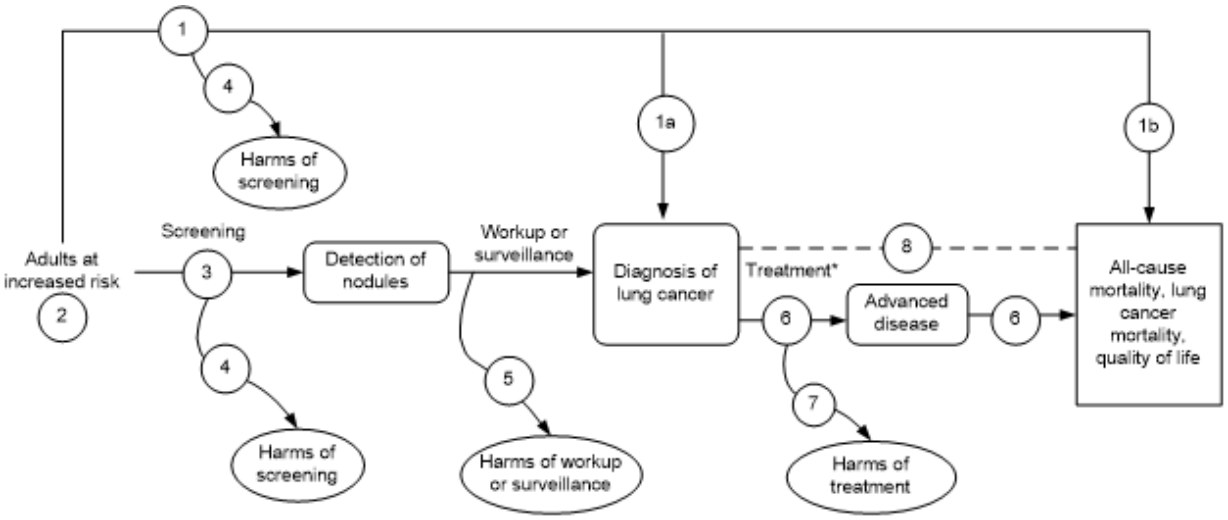
355. Dobler CC. Shared decision making rarely happens for lung cancer screening. *JAMA Intern Med*. 2019 Jan 1;179(1):122. doi: 10.1001/jamainternmed.2018.6983. PMID: 30615081.
356. Reuland DS, Malo TL, Brenner AT. Shared decision making rarely happens for lung cancer screening-reply. *JAMA Intern Med*. 2019 Jan 1;179(1):122-3. doi: 10.1001/jamainternmed.2018.6986. PMID: 30615085.
357. Dharod A, Bellinger C, Foley K, et al. The reach and feasibility of an interactive lung cancer screening decision aid delivered by patient portal. *Appl Clin Inform*. 2019 Jan;10(1):19-27. doi: 10.1055/s-0038-1676807. PMID: 30625501.
358. Mazzone PJ, Tenenbaum A, Seeley M, et al. Impact of a lung cancer screening counseling and shared decision-making visit. *Chest*. 2017 Mar;151(3):572-8. doi: 10.1016/j.chest.2016.10.027. PMID: 27815154.
359. Brenner AT, Cubillos L, Birchard K, et al. Improving the implementation of lung cancer screening guidelines at an academic primary care practice. *J Healthc Qual*. 2018 Jan/Feb;40(1):27-35. doi: 10.1097/jhq.0000000000000089. PMID: 28885238.
360. Eberth JM, Qiu R, Adams SA, et al. Lung cancer screening using low-dose CT: the current national landscape. *Lung Cancer*. 2014 Sep;85(3):379-84. doi: 10.1016/j.lungcan.2014.07.002. PMID: 25088660.
361. Eberth JM, Bozorgi P, Lebron LM, et al. Geographic availability of low-dose computed tomography for lung cancer screening in the United States, 2017. *Prev Chronic Dis*. 2018 Oct 4;15:E119. doi: 10.5888/pcd15.180241. PMID: 30289107.
362. American College of Radiology. Accredited facility search. Reston, VA: ACR Accreditation; n.d.
363. Iaccarino JM, Clark J, Bolton R, et al. A national survey of pulmonologists' views on low-dose computed tomography screening for lung cancer. *Ann Am Thorac Soc*. 2015 Nov;12(11):1667-75. doi: 10.1513/AnnalsATS.201507-467OC. PMID: 26368003.
364. Carter-Harris L, Brandzel S, Wernli KJ, et al. A qualitative study exploring why individuals opt out of lung cancer screening. *Fam Pract*. 2017 Apr 01;34(2):239-44. doi: 10.1093/fampra/cmw146. PMID: 28122849.
365. Cardarelli R, Roper KL, Cardarelli K, et al. Identifying community perspectives for a lung cancer screening awareness campaign in Appalachia Kentucky: the Terminate Lung Cancer (TLC) Study. *J Cancer Educ*. 2017 Mar;32(1):125-34. doi: 10.1007/s13187-015-0914-0. PMID: 26411308.
366. Heny J. Kaiser Family Foundation. 2017 Employer Health Benefits Survey. San Francisco, CA: Kaiser Family Foundation; 2017. Accessed May 20, 2019.
367. Aberle DR, Adams AM, Berg CD, et al. Baseline characteristics of participants in the randomized national lung screening trial. *J Natl Cancer Inst*. 2010 Dec 1;102(23):1771-9. doi: 10.1093/jnci/djq434. PMID: 21119104.
368. Curry SJ, Krist AH, Owens DK, et al. Risk assessment for cardiovascular disease with nontraditional risk factors: US Preventive Services Task Force recommendation statement. *JAMA*. 2018 Jul 17;320(3):272-80. doi: 10.1001/jama.2018.8359. PMID: 29998297.
369. Siu AL, Bibbins-Domingo K, Grossman DC, et al. Screening for chronic obstructive pulmonary disease: US Preventive Services Task Force recommendation statement. *JAMA*. 2016 Apr 5;315(13):1372-7. doi: 10.1001/jama.2016.2638. PMID: 27046365.

370. Lin JS, Bowles EJA, Williams SB, et al. Thyroid cancer: screening. Evidence Synthesis No. 151. AHRQ Publication No. 15-05221-EF-1. Rockville, MD: Quality AfHRa; May 2017.
371. LeFevre ML, U. S. Preventive Services Task Force. Screening for abdominal aortic aneurysm: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014 Aug 19;161(4):281-90. doi: 10.7326/M14-1204. PMID: 24957320.
372. Guirguis-Blake JM, Beil TL, Sun X, et al. Primary care screening for abdominal aortic aneurysm: a systematic evidence review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 109. AHRQ Publication No. 14-05202-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; January 2014.
373. Tanner NT, Kanodra NM, Gebregziabher M, et al. The association between smoking abstinence and mortality in the National Lung Screening Trial. *Am J Respir Crit Care Med*. 2016 Mar 01;193(5):534-41. doi: 10.1164/rccm.201507-1420OC. PMID: 26502000.
374. Syrek JT, Chin J, Ashby L, et al. Center for Medicare & Medicaid Services Decision memo for screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439N). Baltimore, MD: Centers for Medicare & Medicaid Services; 2015. http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274. Accessed May 20, 2019.
375. Siu AL. Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2015 Oct 20;163(8):622-34. doi: 10.7326/m15-2023. PMID: 26389730.
376. Pineiro B, Simmons VN, Palmer AM, et al. Smoking cessation interventions within the context of low-dose computed tomography lung cancer screening: a systematic review. *Lung Cancer*. 2016 Aug;98:91-8. doi: 10.1016/j.lungcan.2016.05.028. PMID: 27393513.
377. Iaccarino JM, Duran C, Slatore CG, et al. Combining smoking cessation interventions with LDCT lung cancer screening: a systematic review. *Prev Med*. 2019 Apr;121:24-32. doi: 10.1016/j.ypmed.2019.02.016. PMID: 30753860.
378. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017 Sep 21;358:j4008. doi: 10.1136/bmj.j4008. PMID: 28935701.
379. Clark MM, Cox LS, Jett JR, et al. Effectiveness of smoking cessation self-help materials in a lung cancer screening population. *Lung Cancer*. 2004 Apr;44(1):13-21. doi: 10.1016/j.lungcan.2003.10.001. PMID: 15013579.
380. van der Aalst CM, de Koning HJ, van den Bergh KA, et al. The effectiveness of a computer-tailored smoking cessation intervention for participants in lung cancer screening: a randomised controlled trial. *Lung Cancer*. 2012 May;76(2):204-10. doi: 10.1016/j.lungcan.2011.10.006. PMID: 22054915.
381. Ferketich AK, Otterson GA, King M, et al. A pilot test of a combined tobacco dependence treatment and lung cancer screening program. *Lung Cancer*. 2012 May;76(2):211-5. doi: 10.1016/j.lungcan.2011.10.011. PMID: 22088938.
382. Pozzi P, Munarini E, Bravi F, et al. A combined smoking cessation intervention within a lung cancer screening trial: a pilot observational study. *Tumori*. 2015 May-Jun;101(3):306-11. doi: 10.5301/tj.5000282. PMID: 25838249.

383. Filippo L, Principe R, Cesario A, et al. Smoking cessation intervention within the framework of a lung cancer screening program: preliminary results and clinical perspectives from the "Cosmos-II" Trial. *Lung*. 2015 Feb;193(1):147-9. doi: 10.1007/s00408-014-9661-y. PMID: 25323328.
384. Taylor KL, Hagerman CJ, Luta G, et al. Preliminary evaluation of a telephone-based smoking cessation intervention in the lung cancer screening setting: A randomized clinical trial. *Lung Cancer*. 2017 Jun;108:242-6. doi: 10.1016/j.lungcan.2017.01.020. PMID: 28216065.
385. Marshall HM, Courtney DA, Passmore LH, et al. Brief tailored smoking cessation counseling in a lung cancer screening population is feasible: a pilot randomized controlled trial. *Nicotine Tob Res*. 2016 Jul;18(7):1665-9. doi: 10.1093/ntr/ntw010. PMID: 26834052.
386. Dhanasopon AP, Salazar MC, Hoag JR, et al. Fate of pneumonectomy patients variably captured by non-small cell lung cancer staging system. *Ann Thorac Surg*. 2017 Dec;104(6):1829-36. doi: 10.1016/j.athoracsur.2017.06.073. PMID: 29074151.
387. Lee SY, Hong MJ, Jeon HS, et al. Functional intronic ERCC1 polymorphism from regulomeDB can predict survival in lung cancer after surgery. *Oncotarget*. 2015 Sep 15;6(27):24522-32. doi: 10.18632/oncotarget.4083. PMID: 26056042.
388. Miura H, Inoue T, Shiomi H, et al. Differences in rates of radiation-induced true and false rib fractures after stereotactic body radiation therapy for Stage I primary lung cancer. *J Radiat Res*. 2015 Mar;56(2):332-7. doi: 10.1093/jrr/rru107. PMID: 25504640.
389. Yousaf-Khan U, van der Aalst C, de Jong PA, et al. Final screening round of the NELSON lung cancer screening trial: the effect of a 2.5-year screening interval. *Thorax*. 2017 Jan;72(1):48-56. doi: 10.1136/thoraxjnl-2016-208655. PMID: 27364640.
390. Zhou H, Tapias LF, Gaissert HA, et al. Lymph node assessment and impact on survival in video-assisted thoracoscopic lobectomy or segmentectomy. *Ann Thorac Surg*. 2015 Sep;100(3):910-6. doi: 10.1016/j.athoracsur.2015.04.034. PMID: 26165483.
391. Brain K, Lifford KJ, Carter B, et al. Long-term psychosocial outcomes of low-dose CT screening: results of the UK Lung Cancer Screening randomised controlled trial. *Thorax*. 2016 Nov;71(11):996-1005. doi: 10.1136/thoraxjnl-2016-208283. PMID: 27471048.
392. Brain K, Carter B, Lifford KJ, et al. Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial. *Thorax*. 2017 Oct;72(10):912-8. doi: 10.1136/thoraxjnl-2016-209690. PMID: 28710339.
393. Pinsky PF, Marcus PM, Kramer BS, et al. Diagnostic procedures after a positive spiral computed tomography lung carcinoma screen. *Cancer*. 2005 Jan 1;103(1):157-63. doi: 10.1002/cncr.20746. PMID: 15529306.
394. Li K, Husing A, Sookthai D, et al. Selecting high-risk individuals for lung cancer screening: a prospective evaluation of existing risk models and eligibility criteria in the German EPIC Cohort. *Cancer Prev Res (Phila)*. 2015 Sep;8(9):777-85. doi: 10.1158/1940-6207.capr-14-0424. PMID: 26076698.
395. McKee BJ, Regis SM, McKee AB, et al. Performance of ACR Lung-RADS in a clinical CT lung screening program. *J Am Coll Radiol*. 2015 Mar;12(3):273-6. doi: 10.1016/j.jacr.2014.08.004. PMID: 25176499.
396. Colinet B, Jacot W, Bertrand D, et al. A new simplified comorbidity score as a prognostic factor in non-small-cell lung cancer patients: description and comparison with the

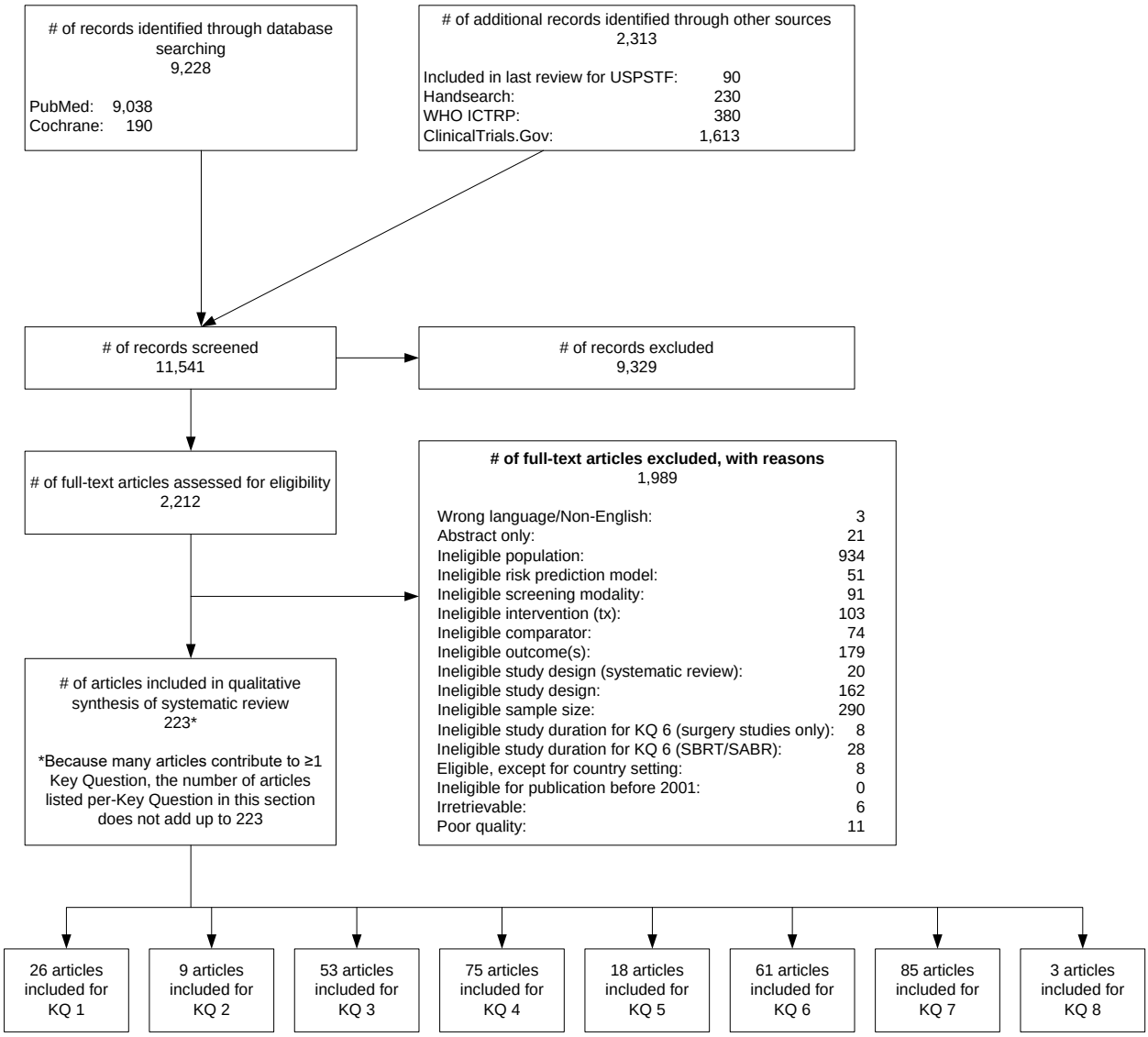
Charlson's index. *Br J Cancer*. 2005 Nov 14;93(10):1098-105. doi: 10.1038/sj.bjc.6602836. PMID: 16234816.

Figure 1. Analytic Framework



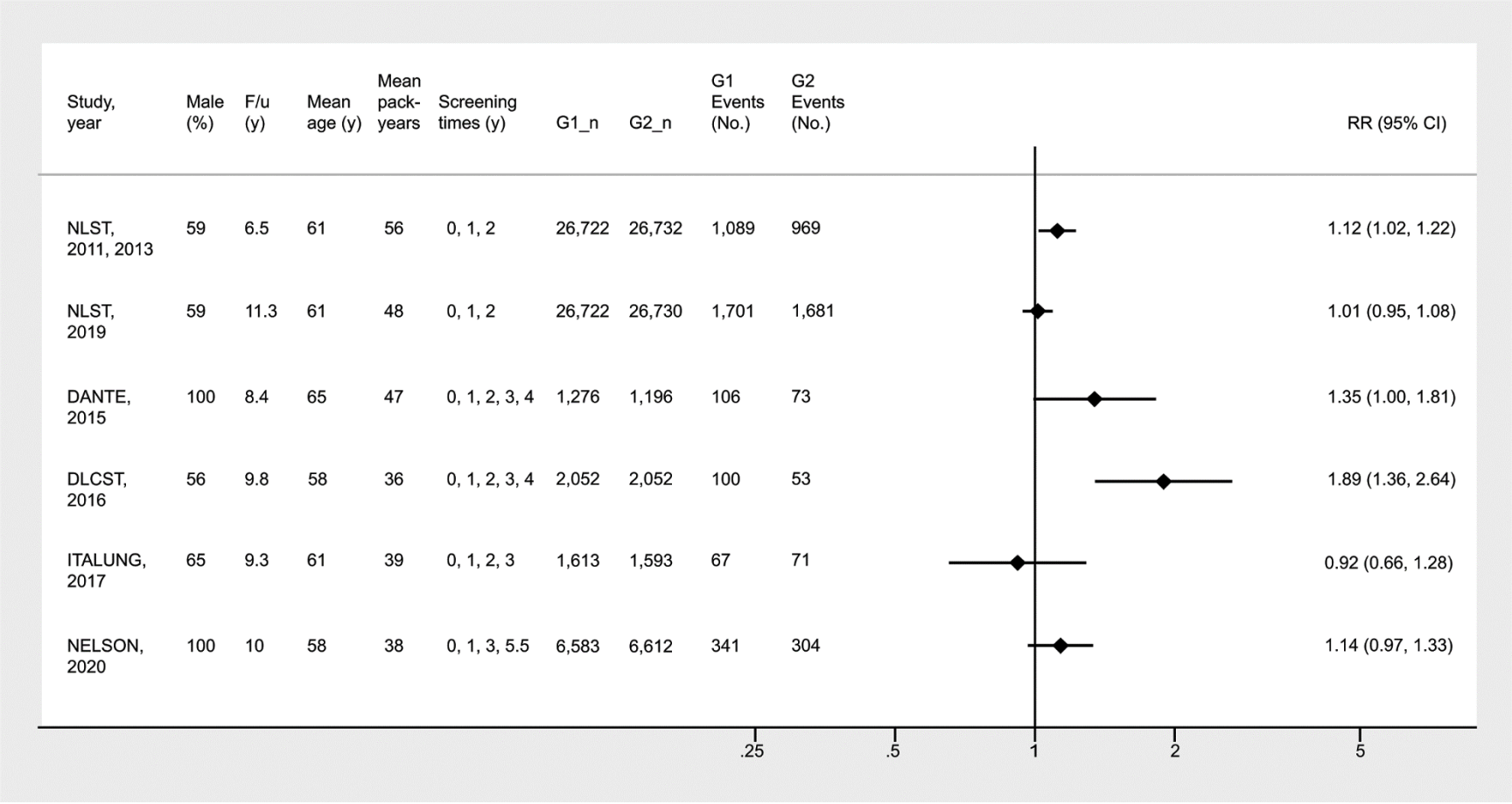
* The evaluation of evidence on treatment was limited to studies of surgical resection or stereotactic body radiotherapy for stage I NSCLC.
Abbreviations: NSCLC=non-small cell lung cancer.

Figure 2. Summary of Evidence Search and Selection



Abbreviations: KQ=key question; SBRT/SABR=SBRT=stereotactic body radiotherapy/SABR= stereotactic ablative radiation.

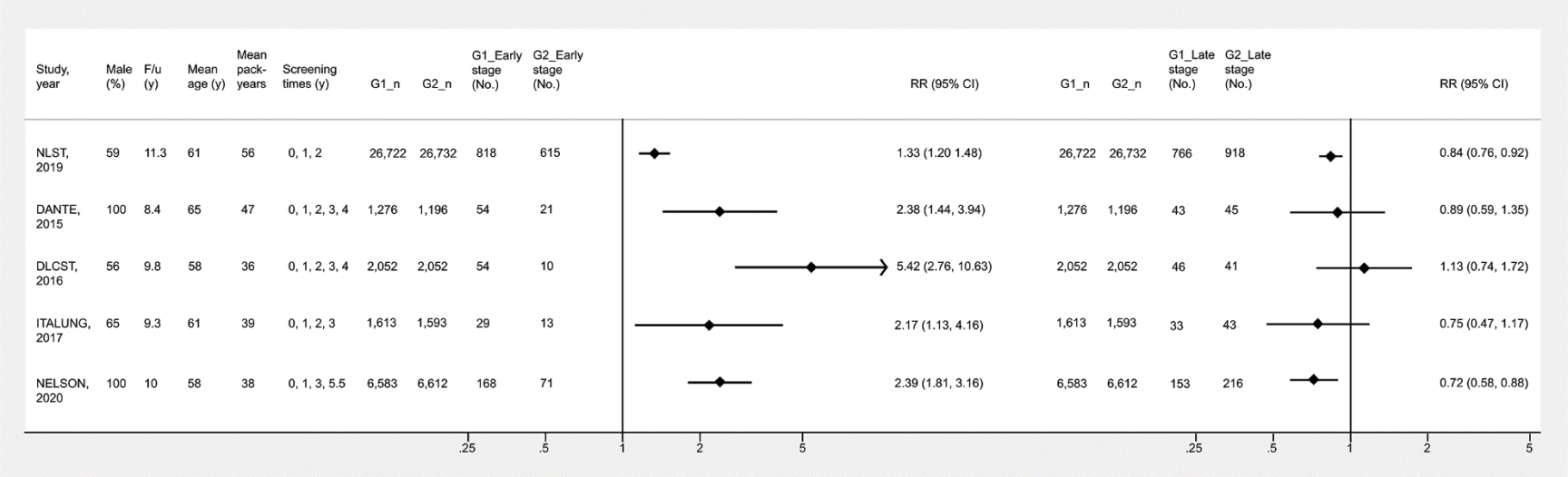
Figure 3. Trial Results for Lung Cancer Incidence (KQ 1)



Note: G1=LDCT; G2=Control; Favors Intervention indicates fewer incident lung cancers with intervention (LDCT screening); Favors Control indicates more incident lung cancers with intervention. Two rows are included in the figure for the NLST, showing the data from the 6.5-year followup and from the extended post-screening followup data at a median of 11.3 years after randomization for lung cancer incidence. The NELSON trial reported lung cancer incidence for the 13,195 males enrolled in the trial, excluding the 2,594 females that were enrolled. Therefore, the NELSON results in the figure above include only data for male participants (data were not reported for the female participants). The trial did not report total person-years of followup for lung cancer incidence, but those were able to be calculated from other data that were reported (5.58 cases per 1,000 person-years vs. 4.91 cases per 1,000 person-years at 10 years; RR, 1.14 [95% CI, 0.97, 1.33]).The Nelson trial reported median age and median pack-years instead of mean age and mean pack years. The LUSI trial was not included in the figure above because it did not reporting person-years of followup. The LUSI trial reported 85 lung cancers in the intervention group and 67 in the control group at a mean of 8.8 years follow up (p=0.16).

Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; LUSI=Lung cancer Screening Intervention; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

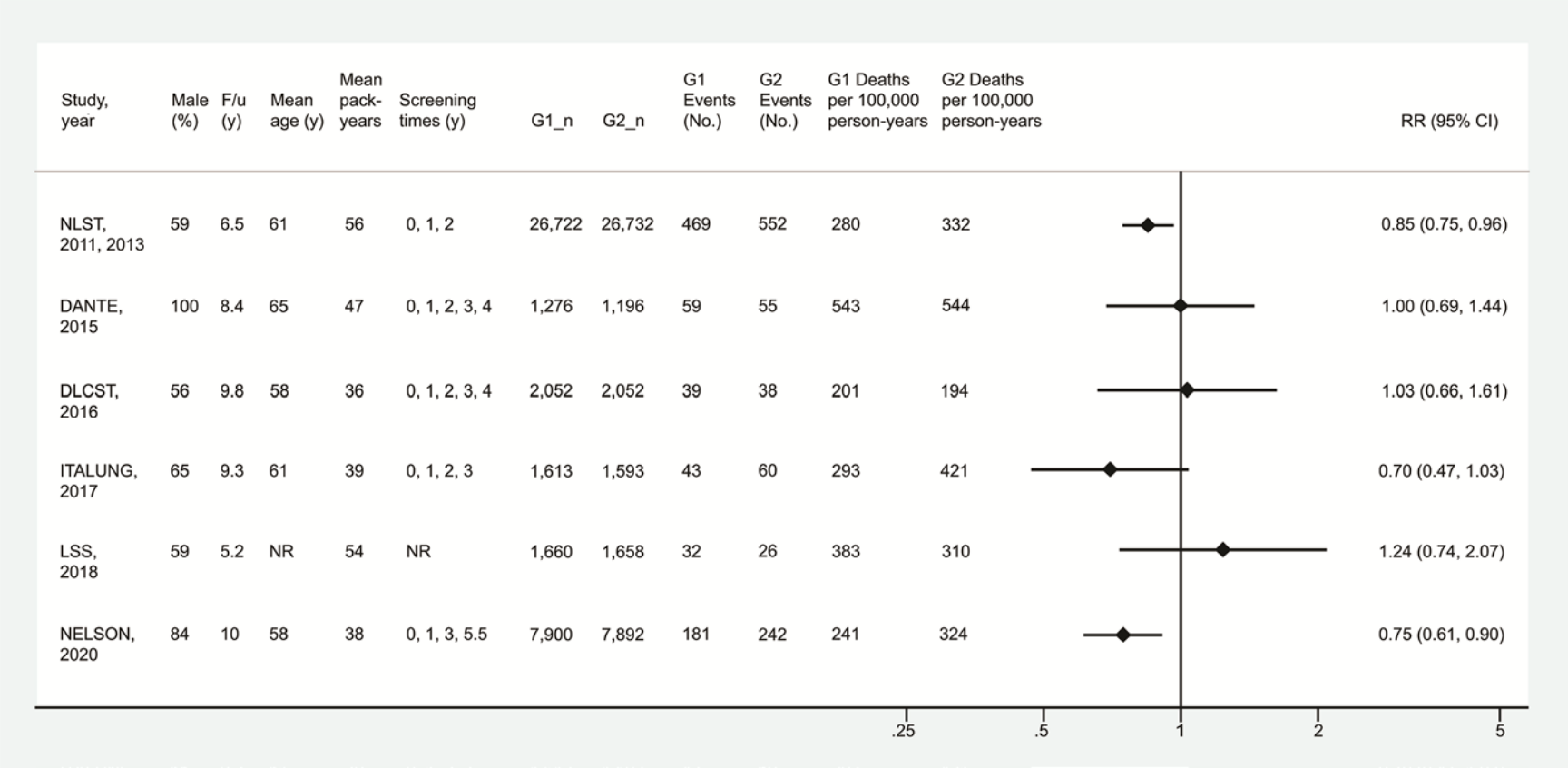
Figure 4. Trial Results for Incidence of Early (I-II) and Late (III-IV) Stage Lung Cancer (KQ 1)



Note: G1=LDCT; G2=Control; The MILD trial randomized participants to annual screening, biennial screening, or a control group. For the 10-year followup, the annual and biennial screening groups were combined. At the 10-year followup, the median duration of screening for those in the screening groups was 6.2 years.

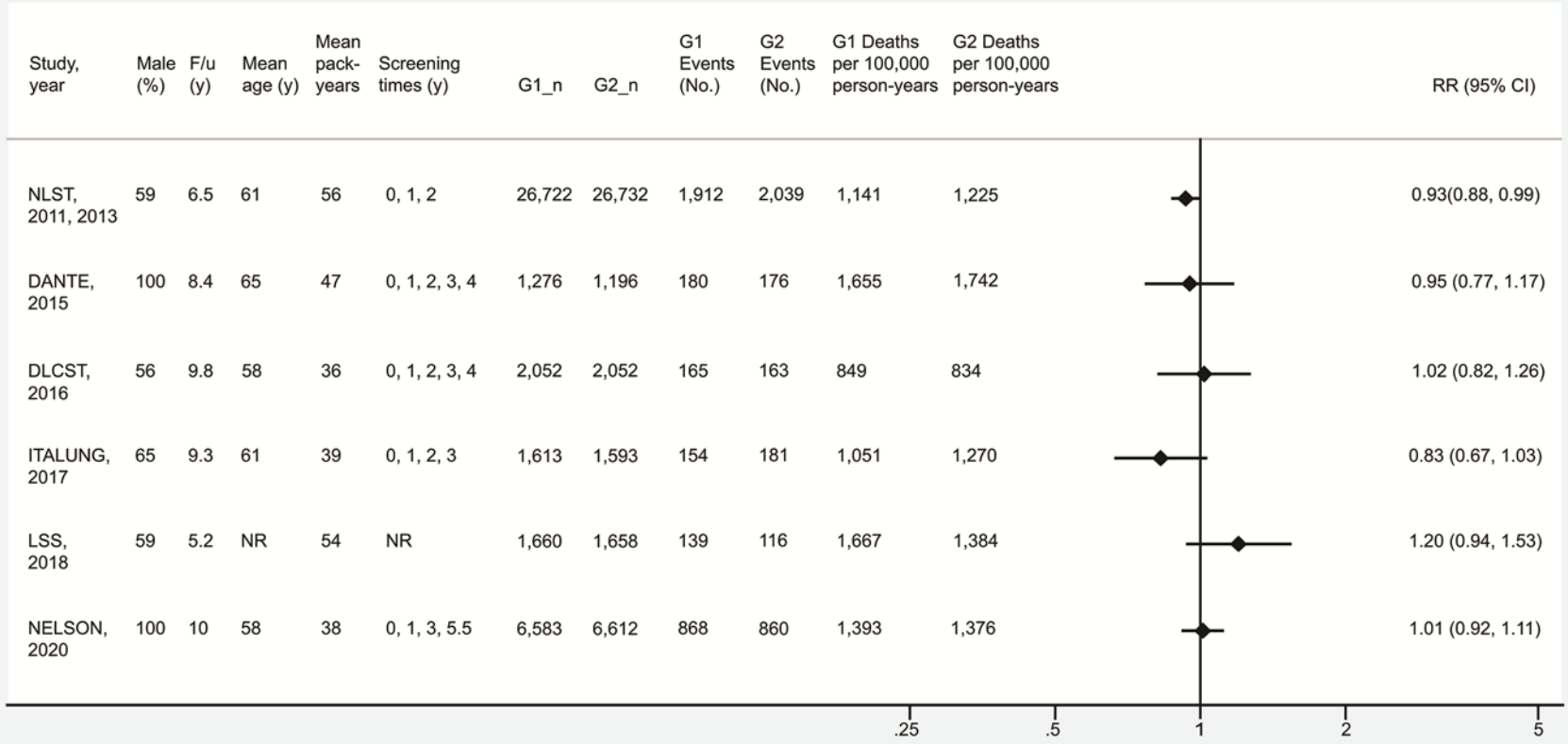
Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; MILD=Multicentric Italian Lung Detection; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

Figure 5. Trial Results for Lung Cancer Mortality (KQ 1)



Note: G1=LDCT; G2=Control. The NLST trial reported extended post-screening followup data at 12.3 years after randomization (not included in the figure above because person-years of followup were not reported): 1,147 lung cancer deaths occurred in the LDCT screening group (42.9 cases per 1,000 participants) and 1236 occurred in the CXR control group (46.2 cases per 1,000 participants) (RR, 0.92 [95% CI, 0.85, 1.00] and absolute difference between groups of 3.3 [95% CI, -0.2, 6.8] lung cancer deaths per 1,000 participants). The ITALUNG and LSS trials reported median pack per years instead of mean pack per years. The NELSON trial reported its main results for the 13,195 males enrolled in the trial (excluding the females enrolled), reporting 156 lung cancer deaths in the screening group and 206 lung cancer deaths in the control group for males at 10 years of followup (rate ratio 0.76 [95% CI, 0.61 to 0.94]). For the 2,594 females, NELSON reported 25 lung cancer deaths in the screening group and 36 in the control group at 10 years of followup (rate ratio 0.67 [95% CI, 0.38 to 1.14]). The NELSON results in the figure above combine data for all participants in the trial. The Nelson trial reported median age and median pack-years instead of mean age and mean pack-years. The LUSI trial was not included in the figure above because it did not report person-years of followup. The study reported 29 lung cancer deaths in the intervention group and 40 lung cancer deaths in the control group at a mean of 8.8 years follow up (p=0.19).
Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; LSS=Lung Screening Study; LUSI=Lung cancer Screening Intervention; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

Figure 6. Trial Results for All-Cause Mortality (KQ 1)



Note: G1=LDCT; G2=Control. The NLST trial reported extended post-screening followup data at 12.3 years after randomization (not included in the figure above because person-years of followup were not reported): 5,253 deaths occurred in the LDCT screening group (196.6 cases per 1,000 participants) and 5,366 deaths in the CXR group (200.7 cases per 1,000 participants) (RR, 0.97 [95% CI, 0.94, 1.01]). The ITALUNG and LSS trials reported median pack per years instead of mean pack per years. The NELSON trial reported all-cause mortality for its primary analysis of the 13,195 males enrolled in the trial, excluding the 2,594 females that were enrolled. Therefore, the NELSON results in the figure above include only data for male participants (data were not reported for the female participants). The Nelson trial reported median age and median pack-years instead of mean age and mean pack-years.

Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; LSS=Lung Screening Study; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

Table 1. NSCLC Staging Overview, Typical 5-Year Survival, and Treatment Approaches[28, 257-261]

Stage	Description	TNM Classifications	5-Year Survival	Treatment Approach
I	Tumor ≤4 cm with no involvement of lymph nodes or distant metastasis	T1-2a N0 M0	77-92% for Stage 1a; 68% for Stage 1b	Surgical resection, including lobectomy; SBRT (mainly for nonsurgical candidates)
II	Tumor >4 cm and ≤7 cm with no involvement of lymph nodes or distant metastasis OR tumor ≤5 cm with metastases in ipsilateral pulmonary/hilar lymph nodes and no distant metastasis	T2b-3 N0 M0 T1-2 N1 M0	53-60%	Lobectomy + adjuvant chemotherapy
III	Heterogeneous group of disease, includes tumors ≥7 cm with or without ipsilateral lymph node involvement and smaller tumors with metastasis to the ipsilateral mediastinal/subcarinal nodes, contralateral mediastinal/hilar nodes, or supraclavicular nodes	T1-4 N0-3 M0	13-36%	Combined modality approach (chemotherapy, radiation therapy, +/- surgery, and/or immunotherapy)*
IV	Presence of distant metastasis: single or multiple extra-thoracic metastasis, malignant pleural or pericardial effusion	Any T or N M1a-c	1-10%	Combined modality approach (chemotherapy, radiation therapy, targeted molecular therapy and/or immunotherapy and +/- surgery)*

*Tailored to patient disease and performance status.

Abbreviations: a=separate tumor nodule[s] in contralateral lobe, tumor with pleural or pericardial nodule(s) or malignant pleural or pericardial effusions; b=single extrapulmonary metastasis; c=multiple extrapulmonary metastases in one or more organs; M=distant metastasis; N=regional lymph nodes; NSCLC=non-small cell lung cancer; SBRT=stereotactic body radiation therapy; T=primary tumor; TNM=Tumor Node Metastasis.

Table 2. Characteristics of Included RCTs Evaluating Screening With LDCT Compared With CXR or With No Screening[a]

Study	Recruitment Years	Sample Size; Country	Mean Age (Ages Eligible)	% Male	Baseline Smoking Status	Eligibility Criteria for Pack-Years; Years Since Quitting	Screening Rounds, n	Screening Intervals, y	Total Median Followup, y	Quality
DANTE[61, 71, 72]	2001-2006	2,472; Italy	65 (60-74)	100	Current: 57% Former: 43% Mean pack-years: 47	≥20; <10 y	5	0, 1, 2, 3, 4	8.4	Fair
DLCST[65, 67]	2004-2006	4,104; Denmark	58 (50-70)	56	Current: 76% Former: 24% Mean pack-years: 36	≥20; quit after age 50 and <10 y ago	5	0, 1, 2, 3, 4	9.8	Fair
ITALUNG[62]	2004-2006	3,206; Italy	61 (55-69)	65	Current: 65% Former: 35% Median pack-years: 39	≥20 in the last 10 years or quit within the last 10 year	4	0, 1, 2, 3	9.3[†]	Fair
LSS[69, 70, 75]	2000-2001	3,318; U.S.	NR (55-74)	59	Current: 58% Former: 42% Median pack-years: 54	≥30; <10 y	2	0, 1	5.2	Fair
LUSI[59, 60, 73]	2007-2011	4,052; Germany	NR (50-69)	65	Current: 62% Former: 35% Mean pack-years: NR	≥25 y of 15 cigarettes[‡] or ≥30 y of 10 cigarettes[‡]; ≤10 y	5	0, 1, 2, 3, 4	8.8	Fair
NELSON[33, 76-79]	2003-2006	15,792; the Netherlands and Belgium	58 median (50-74)	84	Current: 55% Former: 45% Median pack-years: 38	>15 cigarettes/day for >25 years or >10 cigarettes/day for >30 years; ≤10 y	4	0, 1, 3, 5.5	10	Fair
NLST[32, 56-58, 63, 64, 66, 68, 74]	2002-2004	53,542; U.S.	61 (55-74)	59	Current: 48% Former: 52% Mean pack-years: 56	≥30; ≤15 y	3	0, 1, 2	7 (and post-trial followup to 12.3 years)	Good

[*] NLST and LSS compared screening with LDCT vs. screening with CXR. All other trials compared screening with LDCT with no screening.

[†] The ITALUNG study reported 9.3 years for lung cancer–specific mortality and 8.5 years for lung cancer incidence.

[‡] The LSS was a feasibility pilot study.

Abbreviations: CXR=chest X-ray; DANTE=Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; LDCT=low-dose computed tomography; LSS=Lung Screening Study; LUSI=The German Lung Cancer Screening Intervention Trial; n=number; NLST=National Lung Screening Trial; NR=not reported; RCT=randomized, controlled trial.

Table 3. Predictors Used in Risk Prediction Models for Identifying Adults at Higher Risk of Lung Cancer Mortality and Model Applicability

Model Name	LCDRAT[8] [4]	Kovalchik Model[56]	PLCOm2012[8] [5]	Simplified PLCOm2012[8] [3]	COPD-LUCSS[88]	Bach Model[90]	LLP Model[92]	Simplified LLP[83, 92*]	TSCE Incidence Model[93]	Knoke Model[96]	TSCE CPS Death Model[94]	TSCE NHS/HPFS Death Model[324]	HUNT Lung Cancer Model [95]
Risk Factors													
Personal													
Age	X	X	X	X	X[†]	X	X	X	X	X	X	X	X
Sex	X					X	X	X	X		X	X	
Race and/or ethnicity	X		X							X[‡]			
Body mass index	X	X	X		X[§]								X
Education (levels)	X[‖]		X[‖]										
Previous malignant tumor			X				X						
Smoking History													
Smoking status									X	X	X	X	
Cessation age										X			
Smoking duration	X		X	X		X	X[¶]	X[¶]	X	X	X	X	
Cigarettes per day	X		X	X		X			X	X	X	X	X
Pack-years	X[#]	X			X[#]								X
Quit duration	X	X[††]	X	X		X			X	X	X	X	X
Family History of Cancer													
Cases of lung cancer	X[‡‡]	X[‡‡]	X				X						
Age of onset of lung cancer							X[§§]						
Exposures and Lung Conditions													
Emphysema	X	X			X[‖‖]								
COPD			X										
Pneumonia							X						
Daily cough													X

Table 3. Predictors Used in Risk Prediction Models for Identifying Adults at Higher Risk of Lung Cancer Mortality and Model Applicability

Model Name	LCDRAT[8] [4]	Kovalchik Model[56]	PLCOm2012[8] [5]	Simplified PLCOm2012[8] [3]	COPD-LUCSS[88]	Bach Model[90]	LLP Model[92]	Simplified LLP[83, 92*]	TSCE Incidence Model[93]	Knoke Model[96]	TSCE CPS Death Model[94]	TSCE NHS/HPFS Death Model[324]	HUNT Lung Cancer Model [95]
Daily indoor exposure to smoke (hours)													X
Asbestos exposure						X	X						
Applying the Model Information													
Applicable to never smokers							X	X	X	X	X	X	
Applicable to former smokers	X	X	X	X	X	X	X	X	X	X	X	X	X
Applicable to current smokers	X	X	X	X	X	X	X	X	X	X	X	X	X
Model predicts risk of incidence	X		X	X	X	X	X	X	X				X
Model predicts survival	X¶¶	X								X	X	X	
Time horizon of prediction	5 y	5 y	6 y	6 y	NR	1 y (iterative)	5 y	5 y	1 y (iterative)	1 y (iterative)	1 y (iterative)	1 y (iterative)	6 and 16 years
Model formula printed			X	X	X	X	X	X	X	X	X	X	X
Discrimin-ation & calibration[##]													
Discrimination for lung cancer incidence (AUC) range	0.70-0.80	--	0.69-0.89	0.68-0.78	NR	0.68-0.78	0.66-0.79	0.66-0.74	0.67-0.78	0.67-0.77	0.62-0.74	0.67-0.78	0.87 (6 years)
Discrimination for lung cancer mortality (AUC) range	0.73-0.81	0.80	0.72-0.81	0.71-0.80	NR	0.71-0.80	0.67-0.77	0.68-0.79	0.68-0.79	0.68-0.78	0.63-0.77	0.68-0.79	NR
Calibration of model for lung cancer	0.94-1.06	--	0.87-0.98	1.02-1.04	NR	0.99-1.09	0.68-1.05	0.76-1.07	0.79-0.87	0.70-1.09	0.59-0.90	0.76-0.85	NR (shown as calibration plots that

Table 3. Predictors Used in Risk Prediction Models for Identifying Adults at Higher Risk of Lung Cancer Mortality and Model Applicability

Model Name	LCDRAT[8] [4]	Kovalchik Model[56]	PLCOm2012[8] [5]	Simplified PLCOm2012[8] [3]	COPD-LUCSS[88]	Bach Model[90]	LLP Model[92]	Simplified LLP[83, 92*]	TSCE Incidence Model[93]	Knoke Model[96]	TSCE CPS Death Model[94]	TSCE NHS/HPFS Death Model[324]	HUNT Lung Cancer Model [95]
incidence; range													show fairly good calibration)
Calibration of model for lung cancer mortality, range	0.94-1.31	0.97	0.95-1.01	1.02-1.19	NR	0.97-1.21	0.69-1.18	0.79-1.12	0.84-0.94	0.79-0.89	0.64-0.99	0.80-0.92	NR

* The simplified version of the LLP model uses the same parameter estimates as the original LLP model. However, when applying this model to a participant, it is assumed that only information on age and smoking history is known. Thus, the simplified model assumes that the participant had no prior diagnosis of pneumonia, no occupational exposure to asbestos, no prior diagnosis of a malignant tumor, and no family history of lung cancer.

† Age > 60

‡ Only applicable to white males ages 40 to 79 years.

§ BMI <25.

‖ 1≤12 grade; 2=high school graduate; 3=post-high school but not college; 4=some college; 5=bachelor's degree; 6=graduate school.

¶ Smoking duration levels for model: never; 1-20 years; 21-40 years; 41-60 years; >60 years.

Binary: >1 pack/day.

** Pack-years: >60.

†† Categories: 0=less than 1 year; 1=1 to 5 years; 2=more than 5 years.

‡‡ 0=No first-degree relatives with lung cancer; 1=1 first-degree relative with lung cancer; 2=2 or more first-degree relatives with lung cancer.

§§ Early onset (age <60 years); late onset (age ≥60 years).

‖‖ Radiologic emphysema.

¶¶ Model can estimate 10-year risk, but authors report 5-year estimates because the NLST only had 5.5 years of followup data.

LCDRAT: Cohorts used for external validation: PLCO-CXR and NLST-CXR. Discrimination higher in NHIS and PLCO vs. NLST cohorts. Calibration metric: Ratio of model-predicted cases to observed cases. A value of 1 indicates optimal calibration. **Kovalchik:** Cohort used for external validation: PLCO-CXR. Calibration metric: Ratio of model-predicted cases to observed cases.

PLCOm2012: Cohorts used for external validation: PLCO-CXR and control, 45 and UP study, NLST-CT and CXR, NHIS. Discrimination higher in PLCO vs. NLST cohorts. Calibration metric reported in table from ten Haaf et al: slope of calibration plot observed vs. expected. Perfect calibration if slope=1. Two studies reported calibration as the median (or mean) and 90th percentile absolute differences between observed and predicted risk probabilities, which ranged from 0.006-0.009 and 0.016-0.042, respectively.

For all other models except the HUNT model, discrimination and calibration are reported from the ten Haaf study. The range of discrimination and calibration outcomes are estimated using the NLST CT and CXR arms, and the PLCO-CXR and control arms. In general, discrimination and calibration were better in the PLCO cohorts than in the NLST cohorts. An exhaustive search and synthesis of risk model performance metrics was not in the scope of this review; thus, the numbers in this table are not a comprehensive description of discrimination and calibration reported in all studies of these models (inclusion was limited to studies that reported eligible benefits and harms outcomes and compared with USPSTF 2013 or NLST criteria).

Abbreviations: AUC=area under the curve; BMI=body mass index; COPD=chronic obstructive pulmonary disease; COPD-LUCSS=COPD-Lung Cancer Screening Score; CPS=Cancer Prevention Study; HPFS=Health Professionals Follow-Up Study; LCDRAT=Lung Cancer Death Risk Assessment Tool; LLP=Liverpool Lung Project; NHS=Nurses' Health Study; NLST=National Lung Screening Trial; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; TSCE=Two Stage Clonal Expansion Model.

Table 4. PLCOm2012 Model Estimated Benefits and Harms Over 6 Years Compared With USPSTF or NLST Criteria

Author, Year	Method for Determining Lung Cancer Incidence Risk Threshold	Risk Threshold	Cohort to Estimate Outcomes	Benefits	Harms: False-Positive Number (%)	Harms: False-Positive Rate
Tammemagi et al, 2013[85]	Fixed NLST population	1.35%	PLCO-CXR arm	Screen-prevented deaths: PLCOm2012: 81 NLST: 69 NNS: PLCOm2012: 174 NLST: 203	Model: 13,581 (96%) NLST: 13,662 (96.6%)	Model: 37.1 NLST: 37.3
Landy 2019 [89]	Fixed NLST population[32]	1.3%	NHIS 2015 data	Screen-prevented deaths: PLCOm2012: 56,528 USPSTF: 41,298 NNS: PLCOm2012: 222 USPSTF: 194	NR	NR
ten Haaf et al, 2017[83]	Fixed NLST population	1.35%	PLCO-CXR arm	NR	Model: 24904 (97.5%) NLST: 24784 (97.9%)	Model: 37.5 NLST: 37.8
ten Haaf et al, 2017[83]	Fixed NLST population	1.36%	PLCO-control arm	NR	Model: 24287 (97.7%) NLST: 24248 (97.8%)	Model: 38.3 NLST: 38.1
Weber et al, 2017[86]	Fixed NLST population	1.73%	45 and Up Study	NR	Model: 12,982 (96.9%) NLST: 12,929 (97.3%)	Model: 24.8 NLST: 24.7
Tammemagi et al, 2014[87]	NLST mortality benefit	1.51%	PLCO-CXR arm	NNS: Model: 225 USPSTF: NR	Model: 12378 (95.8%) USPSTF: 13688 (96.6%)	Model: 33.8 USPSTF: 37.3
Landy 2019 [89]	NLST mortality benefit[58]	1.51%	NHIS 2015 data	Screen-prevented deaths: PLCOm2012: 54,456 USPSTF: 41,298 NNS: PLCOm2012: 207 USPSTF: 194	NR	NR
Weber et al, 2017[86]	NLST mortality benefit	1.51%	45 and Up Study	NR	Model: 14,642 (97.1%) USPSTF: 13,800 (97.1%)	Model: 28.0 USPSTF: 23.7
Weber et al, 2017[86]	Optimal ROC classification	1.49%	45 and Up Study	NR	Model: 14,774 (97.1%) USPSTF: 13,800 (97.1%)	Model: 28.2 USPSTF: 23.7
Weber et al, 2017[86]	Conservative	2%	45 and Up Study	NR	Model: 11,168 (96.6%) USPSTF: 13,800 (97.1%)	Model: 21.3 USPSTF: 23.7
Landy 2019 [89]	Fixed USPSTF population	2.19%	NHIS 2015 data	Screen-prevented deaths: PLCOm2012: 47,401 USPSTF: 41,298 NNS: PLCOm2012: 169 USPSTF: 194	NR	NR

Abbreviations: CXR=chest X-ray; NLST=National Lung Screening Trial; NHIS=National Health Interview Survey; NNS=number needed to screen; NR=not reported; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; ROC=receiver operating characteristics; USPSTF=U.S. Preventive Services Task Force.

Table 5. Summary of Modeling Studies Evaluating Screen-Prevented Lung Cancer Deaths and NNS to Prevent One Lung Cancer Death*

Author, Year	Model	Comparator	Time Horizon, y	Risk Threshold (Selection Method)	Cohort to Estimate Outcomes (Sample Size)	Screen-Prevented Lung Cancer Deaths, Model vs. Comparator	NNS, Model vs. Comparator	FP per Prevented Deaths, Model vs. Comparator	Overdiagnosed Lung Cancers per Prevented Death, Model vs. Comparator
Tammemagi, 2013[85]	PLCOm2012 model	NLST	6	1.35% (fixed population)	PLCO-CXR arm (37,327)	81 vs. 69	174 vs. 203	167 vs. 196	1.04 vs. 1.04
Landy 2019[89]	PLCOm2012 model	USPSTF	6	1.3% (Reference Tammemagi et al 2013[32])	NHIS 2015 (12,600,000)	56,528 vs. 41,298	222 vs. 194	150 vs. 133	NR
Landy 2019[89]	PLCOm2012 model	USPSTF	6	1.51% (NLST mortality benefit-Reference Tammemagi et al 2014[58])	NHIS 2015 (11,300,000)	54,456 vs. 41,298	207 vs. 194	141 vs. 133	NR
Landy 2019[89]	PLCOm2012 model	USPSTF	6	2.19% (fixed population)	NHIS 2015 (8,000,000)	47,401 vs. 41,298	169 vs. 194	119 vs. 133	NR
Katki, 2016[84]	LCDRAT model	NLST	5	1.2% (fixed population)	NHIS 2010-2012 (9,018,130)	55,717 (95% CI, 53,033 to 58,400) vs. 46,488 (95% CI, 43,924 to 49,053)	162 (157-166) vs. 194 (187-201)	116 (113-119) vs. 133 (128-137)	0.91 vs. 0.93
Landy 2019[89]	LCDRAT model	USPSTF	5	1.2% (reference Katki, 2016[3])	NHIS 2015 (9,000,000)	53,732 vs. 41,298	168 vs. 194	119 vs. 133	NR
Landy 2019[89]	LCDRAT model	USPSTF	5	1.33% (fixed population)	NHIS 2015 (8,000,000)	51,019 vs. 41,298	156 vs. 194	112 vs. 133	NR
Katki, 2016[84]	LCDRAT model	NLST	5	0.9% (fixed effectiveness)	NHIS 2010-2012 (12,101,749)	62,382 (95% CI, 59,567 to 65,196) vs. 46,488 (95% CI, 43,924 to 49,053)	194 (188-200) vs. 194 (187-201)	134 (131-138) vs. 133 (128-137)	0.92 vs. 0.93
Kovalchik, 2013[56]	Kovalchik et al	NLST	5	0.84% (risk quintile 3-5)	NLST-CT (26,604)	77 vs. 88	208 vs. 302	78 vs. 108	NR
Kovalchik, 2013[56]	Kovalchik et al	NLST	5	1.23% (risk quintile 4-5)	NLST-CT (26,604)	64 vs. 88	166 vs. 302	64 vs. 108	NR

*Kovalchik et al applied a model to NLST, intrinsically conferring NLST benefits in lung cancer detection and mortality reduction. The other two studies assumed NLST-like benefits to calculated outcomes.

Abbreviations: CI=confidence interval; CXR=chest X-ray; FP=false positive; LCDRAT=Lung Cancer Death Risk Assessment Tool; NHIS=National Health Interview Survey; NLST=National Lung Screening Trial; NLST-CT=National Lung Screening Trial-Computerized Tomography arm; NNS=number needed to screen; NR=not reported; PLCO= Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; vs.=versus.

Table 6. Accuracy of LDCT for Lung Cancer Screening in RCTs (KQ 3)

Trial Name Author, Year	Number Analyzed	Nodule Classification Framework*	Threshold for Positive†	Screening Protocol	Sn	Sp	PPV	NPV
DANTE Infante, 2015[61]	2,450	I-ELCAP	>5-mm average diameter	5 annual screens	79.5%	75.5%	18.6%	98.1%
DLCST Pedersen, 2009[122]	4,104	DLCST	>15-mm maximum diameter or 5-15 mm with >25% volume increase on 3-month repeat	5 annual screens (4 reported)	NR	NR	9.5%	NR
ITALUNG Lopes Pegna, 2013[99]	1,406	I-ELCAP	≥5-mm average diameter solid nodule, ≥10-mm GGN average diameter, any part-solid nodule	4 annual screens‡	95.0%	26.4%	3.6%	99.4%
LSS Croswell, 2010[119]	1,610	NLST	≥3-mm maximum diameter T0, ≥4 mm maximum diameter for T1	2 annual screens	NR	NR	7.0%	NR
LUSI Becker, 2015[59]	2,028	I-ELCAP	≥5-mm average diameter	5 annual screens (4 completed)	93.5%	62%	7.2%	99.7%
MILD Sverzellati, 2016[82]	1,152	Modified NELSON	Volume >250 mm^3 or 60-250 mm^3 with >25% volume increase on 3-month repeat	5 annual screens	68.5%	99.2%	40.6%	99.7%
MILD Sverzellati, 2016[82]	1,151	Modified NELSON	Volume >250 mm^3 or 60-250 mm^3 with >25% volume increase on 3-month repeat	3 biennial screens	73.5%	99.2%	42.4%	99.8%
NELSON De Koning, 2020[76]	6,583§	NELSON	Volume >500 mm^3 or 50-500 mm^3 with VDT<400 d on 3-month repeat	4 rounds; baseline and after 1 y, 3 y, 5.5 y	59.0%	95.8%§	43.5%§	97.7%§
NLST Pinsky, 2013[101]	26,022	NLST	≥4-mm longest diameter	3 annual screens	93.1%	76.5%	3.3%	99.9%
UKLS Field, 2016[97]	1,994	Modified NELSON‖	Volume >500 mm^3 or 50-500 mm^3 with VDT<400 d on 3-month repeat	1 screen	NR	NR	36.8%	NR
Mean, range	NA	NA	NA	NA	80.3%, 59.0%-95.0%	76.4%, 26.4%-99.2%	21.3%, 3.3%-43.5%	99.2%, 97.7%-99.9%

* We categorized whether the approach to nodule classification was most similar to the approach used in NLST, NELSON, DLCST, or I-ELCAP.

† These are the abbreviated criteria for a positive screen. Studies also considered specific features of nodules, for example.

‡ Study ongoing at the time of this publication.

§ This evaluation excluded some NELSON participants because it was limited to males in the screening group (data were not presented for the 1,317 females in the screening group). The accuracy calculations in this row used NELSON's approach to classifying results, with indeterminate results that required a 3-month followup LDCT being categorized as negatives as long as the 3-month followup LDCT was negative (whereas other studies categorized the same type of thing, when any additional LDCT was required for evaluation, as a false positive).

‖ Nodules with volumes <50 mm^3 were split into two categories. Those <15 mm^3 received no further followup. Those 15-49 mm^3 received followup LDCT scan in 1 year.

Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; GGN=ground-glass nodule; I-ELCAP=International Early Lung Cancer Action Program; ITALUNG=Italian Lung Cancer Screening Trial; LDCT=low-dose computed tomography; LSS=Lung Screening Study; LUSI=The German Lung Cancer Screening Intervention Trial; MILD=Multi-centric Italian Lung Detection; NA=not applicable; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial; NR=not reported; NPV=negative predictive value; PPV=positive predictive value; RCT=randomized, controlled trial; Sn=sensitivity; Sp=specificity; UKLS= UK Lung cancer Screening; VDT=volume doubling time.

Table 7. Accuracy of LDCT for Lung Cancer Screening in Nonrandomized Studies (KQ 3)

Author, Year	Trial/Database	Country	Number Analyzed	Threshold for Positive*	Screening Protocol	Sn	Sp	PPV	NPV
Crucitti, 2015[111]	"Un respiro per la vita"	Italy	1,500	>4 mm, avg max and min	1 scan	NR	34.0%	4.6%	NR
Henschke, 2004[131]	I-ELCAP	U.S.	2,698	≥5 mm, avg max and min	2 annual scans	97.0%	90.0%	Baseline: 20.9% Annual: 11.0%	Baseline: 99.2% Annual: 100%
Henschke, 2013[107]	I-ELCAP	Multinational	21,136	≥5 mm, avg max and min ≥6 mm, avg max and min	Annual scans; data is from baseline scans	NR† NR†	NR† NR†	3.5%† 5.5%†	NR† NR†
Toyoda, 2008[126]	Osaka	Japan	18,070	"Need for further clinical exam"	2 annual scans	88.9%	92.6%	NR	NR
Tsushima, 2008[123]	Azumi & Shinshu	Japan	2,486	>3 mm	Annual scans	100.0%	96.9%	9.9%	100.0%
Tammemagi, 2017[115]	PanCan	Canada	2,537	≥1 mm	T0: Baseline T1: 1 year T4: 4 years	92.7%	NR	NR	NR
Swensen, 2005[130]	Mayo	U.S.	1,520	NCN >4 mm, avg max and min	5 annual scans	95.5%	37.9%	5.8%	99.3%
Menezes, 2010[121]	Toronto	Canada	3,552	≥5 mm, avg max and min	6 annual screenings	87.7%	99.3%	NR	NR
Veronesi, 2008[127]	COSMOS	Italy	5,201	≥5 mm	1 scan	91.0%	99.7%	NR	NR
Mean, range	NA	NA	NA	NA	NA	93.3%, 87.7% to 100%	78.6%, 34.0% to 99.7%	8.7%, 3.5% to 20.9%	99.6%, 99.2% to 100%

* These are the abbreviated criteria for a positive screen. Studies also considered specific features of nodules, for example.

† Study reported data to allow calculation of PPV (reporting total positives and true positives) but did not report data to allow calculation of Sn, Sp, or NPV. However, an investigator from the study team submitted public comments on the draft report stating the following: Sn 97.5%, Sp 84.4%, and NPV 100% for the 5-mm threshold for a positive test and Sn 97.5%, Sp 90.3%, and NPV 100% for the 6-mm threshold for a positive test. The study also reported data for higher thresholds (7 mm, 8 mm, and 9 mm) that would allow calculation of PPV.

Abbreviations: avg=average; COSMOS=Continuing Observation of Smoking Subjects; I-ELCAP=International Early Lung Cancer Action Program; LDCT=low-dose computed tomography; max=maximum; min=minimum; NA=not applicable; NCN=National Cancer Network; NPV=negative predictive value; NR=not reported; PPV=positive predictive value; Sn=sensitivity; Sp=specificity; U.S.=United States.

Table 8. LDCT Parameters, by Study Type

	kV	mAs	Slice Width (mm)	Overlap*	Multi/Single Detector	Estimated Dose/Study (mSv)
Trials						
COSMOS[124, 134]	140	30	2.5	NR	MDCT	1.0 (men), 1.4 (women)
DANTE[71]	140	40	5	Yes	Both	NR
DLCST[122]	120	40	3 and 1, 1.5 and 1	Yes	MDCT	NR
ITALUNG[125]	120-140	20-43	3	NR	Both	NR
LSS[70]	120-140	60	5	NR	NR	NR
LUSI[60]	NR	NR	1	NR	MDCT	1.6-2
MILD[80]	120	30	0.75	NR	Both	0.7
NELSON[77]	80-140	40-80	0.7	Yes	MDCT	NR
NLST[32]	120-140	40-80	1-2.5	Yes	MDCT	1.5
Cohort Studies						
Crucitti et al, 2015[111]	120	35	1	No	MDCT	2.36
Mayo Lung Project[152]	120	40	3.75	NR	MDCT	0.65
PLuSS[137]	140	40-60	2.5	No	NR	NR
Toronto[118]	120	40-60	1-1.25	Yes	MDCT	NR
Tsushima et al, 2008[123]	120	25	5	NR	MDCT	NR

***** Overlap is an approach to image reconstruction. Helical (spiral) CT allows overlapping image reconstruction at arbitrary positions without additional radiation exposure to patients, theoretically increasing ability to detect smaller nodules (compared with consecutive reconstruction).

Abbreviations: COSMOS=Continuing Observation of Smoking Subjects; DANTE=Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; LSS=Lung Screening Study; LUSI=The German Lung Cancer Screening Intervention Trial; MDCT=multidetector computed tomography; MILD=Multi-centric Italian Lung Detection; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial; NR=not reported; PLuSS=Pittsburgh Lung Screening Study.

Table 9. Number and Percentage of False-Positive Results After Screening With LDCT

Study Author, Year	Country	I-ELCAP or Lung-RADS	Screening Years	Definition of Positive Nodule by Study Authors*	False-Positive Results*	False-Positive Percentage*
Clinical Trials						
DLCST Pedersen, 2009[122] Saghir 2012[65]	Denmark	NA	Baseline	≥5 mm	T0: 162 T1: 34 T2: 39 T3: 32 T4: 35	T0: 7.90% T1: 1.7% T2: 2.0% T3: 1.6% T4: 1.9%
LSS Gohagan, 2004[70] Gohagan, 2005[69]	U.S.	NA	0, 1	Baseline: >3 mm Year 1: ≥4 mm	T0: 295 T1: 352	T0: 18.6% T1: 25.2%
LUSI Becker, 2015[59]	Germany	NA	0, 1, 2, 3, 4	≥5 mm Incidence nodules: VDT <600 of known nodule	T0: 428 T1: 77 T2: 65 T3: 95 T4: 82	T0: 21.1% T1: 4.1% T2: 3.5% T3: 5.2% T4: 5.2%
MILD Sverzellati, 2016[82]	Italy	NA	LDCT1 (annual screening): 0, T1, T2, T3, T4, T5, T6 LDCT2 (biennial screening): 0, T1, T2, T3 (T0.1, T1.1, and T2.1 indicate those converted to annual screening)	>60 mm^3 Incidence nodules: volume increase >25%	LDCT1: T0: 160 T1: 31 T2: 48 T3: 25 T4: 18 T5: 5 T6: 11 LDCT2 T0: 152 T0.1: 3 T1: 46 T1.1: 8 T2: 26 T2.1: 9 T3: 33 Total: 271	LDCT1: T0: 13.9% T1: 2.8% T2: 4.4% T3: 2.4% T4: 1.8% T5: 0.6% T6: 2.6% LDCT2 T0: 13.2% T0.1: 2.0% T1: 4.2% T1.1: 4.6% T2: 2.6% T2.1: 5.4% T3: 4.4% Total: 6.1%
NELSON van Klaveren, 2009[120] de Koning 2020[76]	Netherlands and Belgium	NA	0, 1, 3, 5.5	Volume >50 mm^3 (>9.8 mm in diameter) Incidence nodules: VDT <400 days	T0: 1,500† T1: 516† T2 (males only): 521 T3 (males only): 175	T0: 19.8%‡ T1: 7.1%‡ T2 (males only): 9.0% T3 (males only): 3.9%

Table 9. Number and Percentage of False-Positive Results After Screening With LDCT

Study Author, Year	Country	I-ELCAP or Lung-RADS	Screening Years	Definition of Positive Nodule by Study Authors*	False-Positive Results*	False-Positive Percentage*
NLST Aberle, 2011[32] Pinsky, 2014[64]	U.S.	NA	0, 1, 2	≥4 mm	T0: 6,921 T1: 6,733 T2: 3,843 <65 subgroup: T0: 4,796 T1: 4,678 T2: 2,603 ≥65 subgroup: T0: 2,125 T1: 2,058 T2: 1,232	T0: 26.3% T1: 27.2% T2: 15.9% <65 subgroup: T0: 24.8% T1: 25.7% T2: 14.6% ≥65 subgroup: T0: 30.3% T1: 31.5% T2: 19.5%
UKLS, Field, 2016[117]	U.K.	NA	Baseline	>50mm^3	494	26.90%
Cohort Studies						
NA Henschke, 2013[107]	International	I-ELCAP	Baseline	Based on size cut-off as indicated	5 mm: 3,277 6 mm: 2,040 7 mm: 1,385 8 mm: 965 9 mm: 727	5 mm: 15.5% 6 mm: 9.7% 7 mm: 6.6% 8 mm: 4.6% 9 mm: 3.4%
NLST LDCT cohort Yip, 2014[104]	U.S.	NA	Baseline	Based on size cutoff as indicated; assessed how false-positive screens would have been reduced if the NLST had used higher thresholds	5 mm: 3,848 6 mm: 2,470 7 mm: 1,621 8 mm: 1,144 9 mm: 858	5 mm: 14.4% 6 mm: 9.2% 7 mm: 6.1% 8 mm: 4.3% 9 mm: 3.2%

Table 9. Number and Percentage of False-Positive Results After Screening With LDCT

Study Author, Year	Country	I-ELCAP or Lung-RADS	Screening Years	Definition of Positive Nodule by Study Authors*	False-Positive Results*	False-Positive Percentage*
NLST LDCT cohort, if using Lung-RADS Pinsky, 2018[139]	U.S.	NA	Baseline, cumulative (includes up to 2 annual screens)	Lung-RADS	NR	Risk decile (based on Tammemagi risk prediction model, 6-year lung cancer risk): Baseline 1: 8.3% 2: 9.8% 3: 11.0% 4: 10.1% 5: 11.6% 6: 11.9% 7: 13.1% 8: 13.8% 9: 14.7% 10:17.6% Cumulative 1: 12.9% 2: 15.3% 3: 16.2% 4: 15.7% 5: 18.3% 6: 19.2% 7: 21.3% 8: 20.7% 9: 22.3% 10: 25.9%

Table 9. Number and Percentage of False-Positive Results After Screening With LDCT

Study Author, Year	Country	I-ELCAP or Lung-RADS	Screening Years	Definition of Positive Nodule by Study Authors*	False-Positive Results*	False-Positive Percentage*
VHA demonstration Kinsinger, 2017[38]	U.S.	NA	Baseline	Not reported clearly in the paper but cited Fleischner guidelines from 2013 state any nodule ≥5 mm; also recommended followup of small nodules if they were new, were growing, or had suspicious features.	All sites: 1,226 Site 1: 333 Site 2: 66 Site 3: 178 Site 4: 238 Site 5: 153 Site 6: 61 Site 7: 109 Site 8: 88	All sites: 58% of veterans screened; 28.9% of those eligible for screening Percentages below are of those eligible for screening: Site 1: 38.3% Site 2: 14.0% Site 3: 45.8% Site 4: 30.6% Site 5: 53.1% Site 6: 22.4% Site 7: 12.6% Site 8: 28.0%
NA Menezes, 2010[121]	Canada	I-ELCAP	0, 1, 2, 3, 4, 5	≥5 mm	Baseline: 556 Y1: 249 Y2: 64 Y3: 9 Y4: 5 Y5: 2	Baseline: 16.6% Y1: 9.3% Y2: 9.6% Y3: 5.2% Y4: 13.9% Y5: 28.6%
NA Henschke, 2006[128]	Japan	I-ELCAP	0, 1	≥5 mm Incidence nodules: any new nodule	Baseline: 3,781 Annual: 1,386	Baseline:12% Annual: 5.0%
NA Henschke, 2004[131]	U.S.	I-ELCAP	0, 1	≥5 mm Incidence nodules : any new nodule	I-ELCAP 1: Baseline: 130 Annual: 137 I-ELCAP 2: Baseline: 238 Annual: 117	I-ELCAP 1: Baseline: 9.6% Annual: 12.2% I-ELCAP 2: Baseline: 9.9% Annual: 5.2%
NA Swensen, 2005[130]	U.S.	NA	0, 1, 2, 3, 4	>4 mm (initially followup for any nodule was at least 6 months but later moved out to 12 months)	Baseline: All nodules: 749 >4 mm: 404 Incidence: All nodules: 773 >4 mm: 378	Baseline: All nodules: 49.3% >4 mm: 26.6% Incidence: All nodules: could not calculate >4 mm: could not calculate

Table 9. Number and Percentage of False-Positive Results After Screening With LDCT

Study Author, Year	Country	I-ELCAP or Lung-RADS	Screening Years	Definition of Positive Nodule by Study Authors*	False-Positive Results*	False-Positive Percentage*
NA Tsushima, 2008[123]	Japan	NA	Baseline	<3 mm solid	175	7.0%
PLuSS Wilson, 2008[137]	U.S.	NA	0,1	0.5-0.9 cm average diameter with spiculated border or > 1.0 cm average diameter.	741	20.30%
NA Crucitti, 2015[111]	Italy	NA	0, 1	Noncalcified nodule of any size resulted in another CT after 1 year; NCN ≥5 mm indicated further evaluation	Baseline: 500	Baseline: 33.3%

* Definition of positive for these calculations was the threshold leading to further evaluation (further CT scans, biopsy, etc.), including CT scans at intervals shorter than the next routine screening CT scan. False-positive results calculated using the number of tests leading to further evaluation (further CT scans, biopsy, etc.) and false-positive percentage calculated by dividing the number of false-positive results by the number of people screened with LDCT scan.

† Data reported here based on the systematic review's definition of positive tests. If indeterminant results are reclassified based on 3-month followup LDCT scans, then the number of false-positive results for the first two screening rounds would be 196 and 128, respectively. The protocol for reading nodules included the freedom of radiologists to manually up- or downgrade results. This led to a net decrease of 119 false-positive results in the baseline round.[325]

‡ Data reported here based on the systematic review's definition of positive tests. If indeterminant results are reclassified based on 3-month followup LDCT scans, then the false-positive percentage (percentage of all persons screened) would be 1.7 percent and 1.0 percent, respectively.

Abbreviations: DLCST=Danish Lung Cancer Screening Trial; I-ELCAP=International Early Lung Cancer Action Program; LDCT=low-dose computed tomography; LUSI=German Lung Cancer Screening Intervention Trial; MILD=Multi-centric Italian Lung Detection; NA=not applicable; NCN=National Cancer Network; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial; NLST-CT=National Lung Screening Trial-Computed Tomography; PLuSS=Pittsburgh Lung Screening Study; T=time; U.K.=United Kingdom; UKLS= UK Lung cancer Screening; U.S.=United States; VHA=Veterans Health Administration; VDT=volume doubling time.

Table 10. False-Positive Evaluations

Author, Year Country	Associated Trial Nodule Management (I-ELCAP or Lung-RADS) N Participants Screened with LDCT	Needle Biopsies and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)	Other Procedures and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)	Surgical Procedures and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)
Aberle, 2011[32] U.S.	NLST NA 26,722	66 (0.25) Most severe complication classified as major:* 0 (0) Most severe complication classified as intermediate:† 6 (0.02) Most severe complication classified as minor:‡ 1 (0.004) Death within 60 days: 0 (0)	Bronchoscopy: 227 (0.85) Most severe complication classified as major:* 2 (0.007) Most severe complication classified as intermediate:† 9 (0.034) Most severe complication classified as minor:‡ 0 (0) Death within 60 days: 4 (0.015)	Thoracotomy, thoracoscopy, or mediastinoscopy: 164 (0.61) Most severe complication classified as major:* 9 (0.034) Most severe complication classified as intermediate:† 13 (0.049) Most severe complication classified as minor:‡ 4 (0.015) Death within 60 days: 2 (0.007)
Becker, 2012[60] Germany	LUSI NA 2,029	9 (0.44)	NR	NR
Church, 2013[57] U.S.	NLST NA 26,715	Bronchoscopy, with biopsy: 108 (0.40)	Bronchoscopy, without biopsy: 42 (0.16) Other procedure: 122 (0.46)	Mediastinoscopy or mediastinotomy: 12 (0.045) Thoracoscopy: 38 (0.14) Thoracotomy: 41 (0.15)
Croswell, 2010[119] U.S.	NA NA 1,610	NR	Bronchoscopy (minimally invasive): 25 (1.55) Lung biopsy, mediastinoscopy, mediastinotomy, thoracentesis, or VATS thoracoscopy (moderately invasive): 20 (1.24)	Lung resection and thoracotomy (major surgical procedure): 8 (0.50)
Field, 2016[117] U.K.	UKLS Trial NA 1,994	7 (0.35)	EBUS: 1 (0.05)	NR
Infante, 2011[140] Italy	DANTE NA 1,276	NR	NR	Total surgical procedure: 17 (1.33) Mediastinoscopy: 3 (0.24) VATS wedge resection: 7 (0.55) Open wedge resection: 6 (0.47) Open segmentectomy:1 (0.08)

Table 10. False-Positive Evaluations

Author, Year Country	Associated Trial Nodule Management (I-ELCAP or Lung-RADS) N Participants Screened with LDCT	Needle Biopsies and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)	Other Procedures and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)	Surgical Procedures and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)
Lopes Pegna, 2013[99] Italy	ITALUNG I-ELCAP 1,406	1 (0.07)	NR	Surgical resection: 4 (0.28)
Menezes, 2010[121] Canada	NA I-ELCAP 3,352	3 (0.09)[§] Pneumothorax: 1 (0.03)	NR	NR
Pinsky, 2014[64] U.S.	NLST NA **Under 65 Cohort** Year 0: 19,306 Year 1: 18,184 Year 2: 17,798 Total: 55,288 LDCTs **65+ Cohort** Year 0: 7,003 Year 1: 6,531 Year 2: 6,304 Total: 19,838 LDCTs	NR Total complications: Year 0: 18 (0.07) Year 1: 16 (0.06) Year 2: 13 (0.05) Note: these were reported as complications for invasive procedures and NR how many were attributable to biopsies.	Invasive Procedures / Total Complications / Major Complications **Under 65** Year 0: 168 (0.87) / 10 (0.05) / 1 (0.01) Year 1: 84 (0.46) / 14 (0.08) / 2 (0.01) Year 2: 73 (0.41) / 8 (0.04) / 3 (0.02) Total: 325 (0.59) / 32 (0.06) / 6 (0.01) **65+** Year 0: 86 (1.23) / 8 (0.11) / 2 (0.03) Year 1: 44 (0.67) / 2 (0.03) / 2 (0.03) Year 2: 47 (0.75) / 5 (0.08) / 2 (0.03) Total: 177 (0.89) / 15 (0.08) / 6 (0.03) Of all LDCTs, invasive procedures after false-positive screens: 3.3% vs. 2.7% for those ≥65 vs. <65 (p=0.039).	**Under 65** Baseline: 60 (0.31) Year 1: 34 (0.19) Year 2: 25 (0.14) Total: 119 (0.22) **65+** Baseline: 29 (0.41) Year 1: 17 (0.26) Year 2: 18 (0.29) Total: 64 (0.32)
Swensen, 2005[130] U.S.	NA NA 1,520	NR	NR	13 (0.86) participants underwent 15 surgeries Surgical mortality: 0 (0)

Table 10. False-Positive Evaluations

Author, Year Country	Associated Trial Nodule Management (I-ELCAP or Lung-RADS) N Participants Screened with LDCT	Needle Biopsies and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)	Other Procedures and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)	Surgical Procedures and Complications Following a False Positive Result Among Participants Screened with LDCT N (%)
van 't Westeinde, 2012[138] Netherlands/Belgium	NELSON NA 7915	NR	Bronchoscopy: 121 (1.53)	NR
Veronesi, 2008[127] Italy	NA NA 5,201	NR	NR	Surgical biopsy: 15 (0.29)
Veronesi, 2012[135] Italy	COSMOS NA 5,203	29 (0.56)	NR	NR
Wagnetz, 2012[118] Canada	NA I-ELCAP 4,782	20 (0.42)	NR	VATS: 5 (0.10)
Walker, 2015[133] U.S.	NA Lung-RADS 1,654	NR	NR	5 (0.30) Surgery-related deaths: 0 (0)

* Major complications: Acute respiratory failure, anaphylaxis, bronchopulmonary fistula, stroke, cardiac arrest, cardiac vascular accident, congestive heart failure, tube placement, death, hemothorax, myocardial infarction, respiratory arrest, tube thoracostomy or other drainage for more than 4 days, wound dehiscence; bronchial stump leak, empyema, injury to vital organ or vessel, mechanical ventilation over 48 hours post-op, complications requiring intervention, thromboembolic complication, chylous fistula, brachial plexopathy, lung collapse, infarcted sigmoid colon.

† Intermediate complications: Blood loss requiring a transfusion, cardiac arrhythmia requiring medical attention, fever requiring antibiotics, hospitalization post procedure, referral to a pain specialist, pneumothorax requiring tube placement, rib fracture(s), vocal cord immobility/paralysis, requiring antibiotics, ST elevation, infections, cardiac ischemia, bronchitis, pneumonia, pleural effusion, sepsis, respiratory distress, mucous plug requiring bronchoscopy, steroid-induced diabetes.

ǂ Minor complications: Allergic reaction, bronchospasm, vasovagal reaction/hypotension, subcutaneous emphysema, atelectasis, pneumothorax with no chest tube, ileus, seroma, paresthesias/hyperesthesias.

Table 10. False-Positive Evaluations

[§] Four additional individuals who were not diagnosed with lung cancer (although followup was ongoing at the time of publication) were recommended to have biopsies. Of those four, two people had insufficient biopsies limited by low cellularity, one had a pneumothorax prior to a sample being obtained, and one had resolution of the nodule prior to a biopsy being obtained.

Abbreviations: COSMOS=Continuing Observation of Smoking Subjects; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; EBUS=endobronchial ultrasound; I-ELCAP=International Early Lung Cancer Action Program; ITALUNG=Italian Lung Cancer Screening Trial; LUSI=German Lung Cancer Screening Intervention Trial; N=number of participants; NA=not applicable; NLST=National Lung Screening Trial; NR=not reported; U.K.=United Kingdom; UKLS=UK Lung cancer Screening; U.S.=United States; VATS=video-assisted thoracoscopic surgery; Y=year.

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

Table Key Question and Topic	No. of Studies (k), No. of Observations (n)	Summary of Findings	Consistency and Precision	Study Quality	Limitations (Including Reporting Bias)	Overall Strength of Evidence	Applicability
KQ 1. Benefits of screening	k=7 RCTs (26 publications), 86,486 participants	The good-quality NLST (n=53,542) reported a reduction in lung cancer mortality (IRR 0.85 [95% CI, 0.75 to 0.96]) and all-cause mortality (IRR 0.93 [95% CI, 0.88 to 0.99]) with three rounds of annual LDCT compared with CXR (NNS=323 to prevent 1 lung cancer death over 6.5 years). NELSON (n=15,792) found a reduction in lung cancer mortality (IRR, 0.75 [95% CI, 0.61 to 0.90]) but not all-cause mortality (IRR, 1.01 [95% CI, 0.92 to 1.11]) with four rounds of LDCT screening using volumetric measurements with increasing intervals (baseline, 1 year, 3 years, and 5.5 years) compared with no screening (NNS=130 to prevent 1 lung cancer death over 10 years).	Consistent among trials adequately powered; precise	Good: 1 Fair: 6	All but two of the seven trials were underpowered to assess for a lung cancer mortality benefit.	High for benefit*	High-risk current and former smokers (with ≥30 pack-years [NLST] or >15 cigarettes/day for >25 years or >10 cigarettes/day for >30 years [NELSON]); ages 50-74; NLST and NELSON participants were younger, more highly educated, and less likely to be current smokers than the U.S. screening-eligible population; limited racial and ethnic diversity; US population eligible for screening faces higher risk of death from competing causes than trial participants; mainly conducted at large academic centers; NLST did not use current U.S. screening protocols such as Lung-RADS; NELSON used volumetric measurements for screening.

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

Table Key Question and Topic	No. of Studies (k), No. of Observations (n)	Summary of Findings	Consistency and Precision	Study Quality	Limitations (Including Reporting Bias)	Overall Strength of Evidence	Applicability
KQ 2. Risk prediction models	k=9; 13 risk prediction models evaluated in 9 cohorts comprising 21,922,733 participants	**Benefits:** Studies of three models (PCLOm2012, LCDRAT, and Kovalchik model) reported increased screen-preventable deaths compared with risk factor–based criteria (k=4; 21,682,066 participants from 4 cohorts). Most findings from these studies also showed improved NNS. **Harms:** Most studies did not report on actual harms of screening. Studies of all models reported similar numbers of false-positive selections for screening (i.e., the model selected people to be screened who did not have or develop lung cancer or death from lung cancer) and mixed findings for rates of false-positive selections or false-positive selections per prevented death when comparing risk prediction models to risk factor–based criteria.†	Consistent; imprecise (results highly dependent on risk threshold selected)	Good: 6 Fair: 3	No trials have compared use of a risk prediction model with risk factor-based criteria; evidence base is limited by lack of an established risk threshold; most models were evaluated by a single study in one to two cohorts.	Low for greater benefits and similar or reduced harms	High-risk current and former smokers; mainly applicable to NLST or USPSTF screen-eligible persons (ages 55-74 years or 55-80 years)
KQ 3. Accuracy of screening with LDCT	k=24 n=107,200	Sensitivity ranged from 59% to 100% (k=13, n=76,856) and was over 80% in vast majority of studies. Specificity ranged from 26.4% to 99.7% (k=13, n=75,819) and was over 75% in vast majority. PPV ranged from 3.3% to 43.5%. NPV ranged from 97.7% to 100%. Reliability among radiologists was fair to moderate (k=3).	Reasonably consistent; imprecise (except precise for NPV)	Good: 3 Fair: 21	Incomplete or unreported followup length may have led to differential measurement. Heterogeneity in screening protocols and definitions (e.g., positive tests, indeterminate tests).	Moderate	U.S. and highly developed countries; most conducted in past 10 years. Similar LDCT technologies used across studies; varying nodule classification protocols that could likely be replicated in the U.S.; few studies used nodule classification approach recommended by ACR (Lung-RADS).

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

Table Key Question and Topic	No. of Studies (k), No. of Observations (n)	Summary of Findings	Consistency and Precision	Study Quality	Limitations (Including Reporting Bias)	Overall Strength of Evidence	Applicability
KQs 4 and 5. Harms of screening, workup, or surveillance	Radiation: k=9 n=74,963 participants	**Radiation from 1 LDCT**: range 0.65 mSv to 2.3 6mSv **Cumulative radiation exposure:** 20.8 mSv to 32.5 mSv for annual screening for 25 years **Radiation-induced cancer:** 0.26 to 0.81 major cancers for every 1,000 people screened with 10 annual LDCTs[‡]	Consistent; imprecise	Good: 3 Fair: 6	Estimates of radiation-induced cancers are based on modeling.	Moderate for radiation-induced harms	Estimates were not provided for lifetime risk of radiation-induced cancers or fatal cancers from annual screening from 55 to 80 (i.e., USPSTF 2013 recommendation).
	False positives: k=27 n=115,6544 participants False-positive followup evaluations: k=14 n=56,223 participants	**False-positive rates:** range 7.9%-49.3% for baseline screening and 0.6%-28.6% for incidence screening rounds; rates generally declined with each round. NLST reported 26.3%, 27.2%, and 15.9% for baseline, year 1, and year 2, respectively; rates were lower in NELSON; the VA implementation study reported 58% of those screened (28.9% of screen-eligibles) at baseline and over 30% variation across eight sites. **Invasive procedures for false-positive results,** range of rates for every 1,000 people screened (NLST rate): 0.9 to 5.6 needle biopsies (2.5) resulting in 0.3 to 0.7 complications; 5 to 13 surgical procedures; (17 total invasive procedures, resulting in <1 major complication[§])	Consistent; imprecise	Good: 8 Fair: 19 Good: 4 Fair: 10	Heterogeneity in screening protocols, definitions of positive and false-positive results, and reporting of procedures and complication rates.	Moderate for harms due to false-positive results	Most studies did not use current nodule evaluation protocols such as Lung-RADS; an evaluation using NLST data estimated that 23.4% of all invasive procedures for false-positive results from the NLST would have been prevented by using Lung-RADS.
	Overdiagnosis: k=12 n=95,290 participants	**Overdiagnosis**: Estimates ranged from 0% to 67.2% that a screen-detected lung cancer is overdiagnosed; NLST data indicate approximately 4 cases of overdiagnosis over 6.5 years (and 3 lung cancer deaths prevented) per 1,000 people screened.[‖]	Inconsistent; imprecise	Good: 2 Fair: 10	Inadequate duration of followup and heterogeneity limit the evaluation.	Low for harms	NLST estimate is based on 3 annual screens and 6.5 years of followup; uncertain whether it would increase or decrease with ongoing screening and longer followup.

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

Table Key Question and Topic	No. of Studies (k), No. of Observations (n)	Summary of Findings	Consistency and Precision	Study Quality	Limitations (Including Reporting Bias)	Overall Strength of Evidence	Applicability
	Smoking behavior: k=7 n=29,038 participants	**LDCT vs. no screening (k=2):** Evidence on cessation an intensity does not indicate harm of false reassurance. **Positive or indeterminate results vs. normal results:** Abnormal or indeterminate results may increase cessation and continued abstinence, but normal screening test results had no influence.	Inconsistent; Imprecise	Good: 0 Fair: 7	Most RCTs of LDCT did not report on outcomes to assess for false reassurance.	Low for no harms	The two RCTs providing data for LDCT vs. no screening were conducted in Denmark (DLCST) and the Netherlands and Belgium (NELSON).
	Psychosocial harms: k=9 n=14,715 participants	**General HRQoL:** No significant differences over 6 months to 2 y of followup between LDCT and controls (k=2 RCTs, n=3,937); worse HRQoL for persons receiving true-positive results vs. other results. **Anxiety and depression:** No significant increase over 2 weeks to 2 y of followup for LDCT vs. controls (k=6 RCTs, n=12,096); increased anxiety for individuals receiving true-positive results vs. other results. **Distress:** no significant increase over approximately 2 y of followup for LDCT vs. controls (k=2 RCTs, n=5,180); temporary increase for those receiving indeterminate results vs. other results. **Other potential psychosocial consequences of screening:** each generally assessed by a single study, often without a non-LDCT comparison group, and not indicative of harm	Reasonably consistent and precise for HRQoL, anxiety and depression, and distress Consistency unknown and imprecise for other outcomes	Good: 1 Fair: 8	Relatively short followup (2 y or less); RCTs did not assess these outcomes over the duration of the trials.	Moderate for no harm over 2 y (HRQoL, anxiety, and distress) for LDCT vs. controls. Moderate for worse short-term HRQoL, anxiety, and distress for those who received true-positive or indeterminate results vs. other results	High-risk current and former smokers; studies lacked racial and ethnic diversity; most studies conducted in Europe; trials did not use current protocols such as Lung-RADS.

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

Table Key Question and Topic	No. of Studies (k), No. of Observations (n)	Summary of Findings	Consistency and Precision	Study Quality	Limitations (Including Reporting Bias)	Overall Strength of Evidence	Applicability
	Incidental findings (IFs): k=7 n=80,485	Rates of reported significant IFs ranged from 4.4 to 40.7%. Common IFs were coronary artery calcification; aortic aneurysms; emphysema; infectious and inflammatory processes; and masses, nodules, or cysts of the kidney, breast, adrenal, liver, thyroid, pancreas, spine, and lymph nodes. IFs led to consultations, additional imaging, and invasive procedures. Nonlung cancers were diagnosed in 0.39% of NLST LDCT arm participants during screening. **Incidental detection of thyroid cancer:** In NLST,¶ thyroid cancer incidence was roughly double during 3 years of active LDCT screening compared with CXR screening (HR, 2.19 [95% CI, 1.07–4.47]), but not during subsequent years (HR,1.08 [95% CI, 0.49–2.37]).	Consistent; imprecise	Fair: 7	No standard definition for which IFs were significant or actionable. Few studies on followup evaluations and distal outcomes.	Moderate for harms	Screen-eligible adults undergoing LDCT in academic or tertiary lung cancer screening centers.

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

Table Key Question and Topic	No. of Studies (k), No. of Observations (n)	Summary of Findings	Consistency and Precision	Study Quality	Limitations (Including Reporting Bias)	Overall Strength of Evidence	Applicability
KQ 6. Efficacy of surgical resection for Stage I NSCLC	k=36 uncontrolled cohort studies n=212,274	**5-year OS for surgical resection** (including lobectomy and SLR approaches), range: 33 to 86% for Stage I, 58 to 83% for Stage IA, and 42 to 79% for Stage IB. In pathologic Stage I patients in the NCDB from 2003 to 2006 the 5-year OS was 61% for surgical resection (n=54,350). Survival rates in the NCDB, SEER, and VA VINCI databases for Stage I, covering the years 2003-2015, ranged from 53% to 75% for lobectomy (n=23,707). Survival rates were generally higher for lobectomy than SLR, for smaller than larger tumors, and for patients who are female, younger, nonsmokers, or had fewer comorbidities than patients who are male, older, smokers, or sicker.	Reasonably consistent; imprecise	Good: 5 Fair: 31	Information related to deviations from intervention, missing data, and sources of survival outcomes often lacking; heterogeneity related to staging of NSCLC (clinical or pathologic) and surgical approaches (among studies and over time).	Moderate for benefit	Persons with Stage I NSCLC; some studies were more than 10 years old and may be less applicable to current approaches and outcomes (studies were from 1983 to 2018)
KQ 6. Efficacy of SBRT for Stage I NSCLC	k=27 uncontrolled cohort studies n=38,915	5-year OS (and other measures of long-term survival) varied substantially across studies (range: 20 to 80%) and by subgroups defined by clinical characteristics (e.g., operability of tumor) and patient age; survival may be higher among younger than older patients.	Inconsistent; imprecise	Good: 2 Fair: 25	Information related to deviations from intervention, missing data, and sources of survival outcomes often lacking; substantial heterogeneity related to staging and operability of tumors.	Low for benefit	Persons with operable or inoperable Stage I NSCLC

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

Table Key Question and Topic	No. of Studies (k), No. of Observations (n)	Summary of Findings	Consistency and Precision	Study Quality	Limitations (Including Reporting Bias)	Overall Strength of Evidence	Applicability
KQ 7. Harms of surgical resection	k=29 uncontrolled cohort studies n=755,427	30-day mortality rates ranged from 0 to 4% in most studies; rates of 90-day mortality were slightly higher (range: 2 to 5% in most studies). Less than one-third of patients in most studies experienced treatment-related adverse events. Adverse events reported in ≥10% of patients included pulmonary events (e.g., air leak, pleural effusion) and cardiac arrhythmias.	Reasonably consistent; reasonably precise	Good: 3 Fair: 26	Information related to deviations from intervention, missing data, and sources of survival outcomes often lacking; potential selective reporting of adverse events.	Moderate for harms	Persons having lobectomy or SLR for the treatment of Stage I NSCLC
KQ 7. Harms of stereotactic body radiation therapy	k=1 RCT (comparing dosing regimens), 1 uncontrolled clinical trial, and 58 uncontrolled cohort studies n=49,654	30- and 90-day mortality rates ranged from 0 to 3%. Adverse events were experienced by a majority of patients, but most were of mild or moderate severity. Adverse events reported in ≥10% of patients included were pulmonary events (e.g., cough, dyspnea, pneumonitis, fibrosis) or respiratory disorders (including dyspnea), chest wall pain, fatigue, and dermatologic reactions. Incidence of rib fracture ranged from 0% (n=80 patients) to 42% (n=169 patients).	Reasonably consistent; imprecise	Good: 1 Fair: 59	Information related to deviations from intervention, missing data, and sources of survival outcomes often lacking; potential selective reporting of adverse events.	Low for harms	Persons having SBRT/SABR for the treatment of operable or inoperable Stage I NSCLC
KQ 8. Change in mortality from a specified change in lung cancer incidence (and stage shift)	k=2 RCTs (NLST and NELSON) n=69,334	An absolute increase in lung cancer incidence of 0.5-0.6%, increase in Stage I lung cancers of 19-27%, decrease in Stage IV lung cancers of 14-19% were associated with 52-83 fewer lung cancer deaths and 0 (NELSON) to 84 (NLST) fewer all-cause deaths per 100,000 person-years.	Consistent; precise for lung cancer mortality but imprecise for all-cause mortality	Good: 1 Fair: 1	Reporting bias not detected.	High	3 annual rounds of screening with LDCT (compared with CXR) in NLST or 4 rounds of screening with increasing intervals as conducted in NELSON (volumetric approach); applicable to workup of lung cancers and subsequent treatments used in the NLST and NELSON; same applicability issues as listed for KQ 1.

* Strength of evidence was graded as moderate prior to final publication of NELSON because of unknown consistency (with a single good quality study that was adequately powered) but was changed to high after including NELSON in the evidence report.

Table 11. Summary of Evidence on Screening for Lung Cancer With LDCT

† The language "false positive" here refers to model performance metrics with respect to lung cancer events (diagnosis or deaths), not with respect to LDCT results.
‡ One study estimated a lifetime risk of fatal cancer of 0.11 per 1,000 subjects after the four screening rounds.[136]
§ NLST reported 11 major complications and 6 deaths within 60 days of invasive procedures among those with false-positive results (2 deaths after surgical resections and 4 after bronchoscopy).
‖ Based on converting data to per 1,000 screened from study that reported 1.38 cases of overdiagnosis in every 320 patients needed to screen to prevent one death from lung cancer.[142]
¶ This study specifically addressed the potential for overdiagnosis of thyroid cancer through incidental detection.
Abbreviations: ACR=American College of Radiology; CI=confidence interval; CPS=Cancer Prevention Study; CXR=chest X-ray; DLCST=Danish Lung Cancer Screening Trial; HR=hazard ratio; HRQoL=hazard ratio quality of life; IFs=incidental findings; IRR=incidence rate ratio; KQ=key question; LCDRAT=Lung Cancer Death Risk Assessment Tool; LCRAT=Lung Cancer Risk Assessment Tool; LDCT=low-dose computed tomography; LLP=Liverpool Lung Project; n=number; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NHS=Nurses' Health Study; NLST=National Lung Screening Trial; NNS=number needed to screen; NPV=negative predictive value; NSCLC=non-small cell lung cancer; OS=overall survival; PPV=positive predictive value; RCT=randomized, controlled trial; SABR=stereotactic ablative radiation; SBRT=stereotactic body radiotherapy; SLR=sublobar resection; TSCE=Two-Stage Clonal Expansion; USPSTF=U.S. Preventive Services Task Force; VA=Veteran's Administration.

Appendix A Table 1. Overview of Lung-RADS Classification System (Version 1.0)

Category Classification	Category Descriptor	Category	Findings	Management
Incomplete		0	Part or all of lungs cannot be evaluated Prior chest CT examination(s) being located for comparison	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed
Negative	No nodules and definitely benign nodules	1	No lung nodules Nodule(s) with specific calcifications: complete, central, popcorn, concentric rings, and fat- containing nodules	Continue annual screening with LDCT in 12 months
Benign appearance or behavior	Nodules with a very low 90% likelihood of becoming a clinically active cancer due to size or lack of growth	2	Solid nodule(s): <6 mm, new <4 mm Part solid nodule(s): <6 mm total diameter on baseline screening Nonsolid nodule(s) (GGN): <20 mm OR ≥20 mm and unchanged or slowly growing Category 3 or 4 nodules unchanged for ≥3 months	Continue annual screening with LDCT in 12 months
Probably benign	Probably benign finding(s): short-term followup suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	Solid nodule(s): ≥6 to <8 mm at baseline OR new 4 mm to <6 mm Part solid nodule(s) ≥6 mm total diameter with solid component <6 mm OR new <6 mm total diameter nonsolid nodule(s) (GGN) ≥20 mm Nonsolid nodule(s) (GGN) ≥20 mm on baseline CT or new	6-month LDCT
Suspicious	Findings for which additional diagnostic testing and/or tissue sampling is recommended	4A	Solid nodule(s): ≥8 to <15 mm at baseline OR growing <8 mm OR new 6 to <8 mm Part solid nodule(s): ≥6 mm with solid component ≥6 mm to <8 mm OR with a new or growing <4 mm solid component Endobronchial nodule	3-month LDCT; PET/CT may be used when there is a ≥8 mm solid component
		4B	Solid nodule(s) ≥15 mm OR new or growing and ≥8 mm Part solid nodule(s) with a solid component ≥8 mm OR a new or growing ≥4 mm solid component	Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥8 mm solid component.
		4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy	

Adapted from Lung-RADS™ Version 1.0 Assessment Categories Release date: April 28, 2014
Abbreviations: CT=computed tomography; GGN=ground glass nodule; LDCT=low-dose computed tomography; PET=positron emission tomography.

Appendix A Table 2. Overview of Lung-RADS Classification System (Version 1.1)

Category Classification	Category Descriptor	Category	Findings	Management
Incomplete		0	Part or all of lungs cannot be evaluated; prior chest CT examination(s) being located for comparison	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed
Negative	No nodules and definitely benign nodules	1	No lung nodules; nodule(s) with specific calcifications: complete, central, popcorn, concentric rings, and fat- containing nodules	Continue annual screening with LDCT in 12 months
Benign appearance or behavior	Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth	2	**Perifissural nodule**(s)* <10 mm (524 mm^3) **Solid nodule(s):** <6 mm (<113 mm^3), new <4 mm (<34 mm^3) **Part solid nodule(s):** <6 mm total diameter (<113 mm^3) on baseline screening **Nonsolid nodule(s) (GGN):** <30 mm (<14,137 mm^3) OR ≥30 mm (≥14,137 mm^3) and unchanged or slowly growing **Category 3 or 4 nodules unchanged for ≥3 months**	Continue annual screening with LDCT in 12 months
Probably benign	Probably benign finding(s): short-term followup suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	**Solid nodule(s):** ≥6 to <8 mm (≥113 to <268 mm^3) at baseline OR new 4 mm to <6 mm (34 to <113 mm^3) **Part solid nodule(s):** ≥6 mm total diameter (≥113 mm^3) with solid component <6 mm (<113 mm^3) OR new <6 mm total diameter (<113 mm^3) **Nonsolid nodule(s):** (GGN) ≥30 mm (≥14,137 mm^3) on baseline CT or new	6-month LDCT
Suspicious	Findings for which additional diagnostic testing is recommended	4A	**Solid nodule(s):** ≥8 to <15 mm at baseline (≥268 to <1,767 mm^3) OR growing <8 mm (<268 mm^3) OR new 6 to <8 mm (113 to <268 mm^3) **Part solid nodule(s):** ≥6 mm (≥113 mm^3) with solid component ≥6 mm to <8 mm (≥113 to <268 mm^3) OR with a new or growing <4 mm (<34 mm^3) solid component **Endobronchial nodule**	3-month LDCT; PET/CT may be used when there is a ≥8 mm (≥268 mm^3) solid component
Very suspicious	Findings for which additional diagnostic testing and/or tissue sampling is recommended	4B	**Solid nodule(s)** ≥15 mm (≥1,767 mm^3) OR new and growing and ≥8 mm (≥268 mm^3) **Part solid nodule(s)** with a solid component ≥8 mm (≥268 mm^3) OR a new or growing ≥4 mm (≥34 mm^3) solid component	Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥8 mm (≥268 mm^3) solid component. For new large nodules that develop on an annual repeat screening CT, a 1- month LDCT may be recommended to address potentially infectious or inflammatory conditions
		4X	Category 3 or 4 nodules with additional features or imaging findings that increase the suspicion of malignancy†	
Other	Clinically significant or potentially clinically significant findings (nonlung cancer)	S	Modifier: may add on to category 0-4 coding	As appropriate to the specific finding

Adapted from Lung-RADS Version 1.1 Assessment Categories Release date: 2019

Appendix A Table 2. Overview of Lung-RADS Classification System (Version 1.1)

* Solid nodules with smooth margins, an oval, lentiform or triangular shape, and maximum diameter less than 10 mm or 524 mm^3 (perifissural nodules) should be classified as category 2.
† These include, for example, spiculation, GGN that doubles in size in 1 year, and enlarged lymph nodes.

Abbreviations: CT=computed tomography; GGN=ground glass nodule; LDCT=low-dose computed tomography; NA=not applicable; PET=positron emission tomography.

Some notes on use of Lung-RADS Version 1.1:
1) Nodule mean diameter is calculated by measuring both the long and short axes to one decimal point and reporting mean nodule diameter to one decimal point.
2) Size thresholds: Apply to nodules at first detection, and that grow and reach a higher size category.
3) Growth is defined as an increase in size of >1.5 mm (>2 mm^3).
4) Exam category: Each exam should be coded 0-4 based on the nodule(s) with the highest degree of suspicion.

Appendix A Table 3. Typical Treatment Approaches of SCLC, by Stage[326]

Stage	Treatment Approach
Limited disease	Clinical stage T1-2, N0: Lobectomy + chemotherapy +/− concurrent radiation therapy Clinical stage >T1-2, N0: chemotherapy +/− concurrent or sequential radiation therapy tailored to patient performance status
Extensive disease	Chemotherapy +/− radiation therapy tailored to location and symptoms of metastatic site

Abbreviations: SCLC=small-cell lung cancer; T=tumor.

Appendix A Table 4. Stage of Detected Lung Cancers in LDCT Screening Groups for NLST and NELSON Trials

Stage	NLST (%)	NELSON (%)
Ia	40	58
Ib	10	10
IIa	3.4	5
IIb	3.7	1
IIIa	9.5	14
IIIb	11.7	3
IV	21.7	14

*For reference, the stage distribution based on data from the SEER 18 registry in 2010 is as follows: Ia (11.7%), Ib (8.5%), IIa (1.0%), IIb (3.1%), IIIa (8.5%), IIIb (14.8%), IV (45.1%), occult or unknown (7.3%).[327] Participants in the NLST were younger, better educated, and healthier than individuals of similar age and smoking eligibility in the United States. (SCLC accounted for 7 percent of CT screen-detected cancers in the NELSON trial and 13 percent in NLST).

Abbreviations: LDCT=low-dose computed tomography; NELSON=The Dutch-Belgian Randomized Lung Cancer Screening Trial; NLST=National Lung Screening Trial; SCLC=small cell lung cancer

Appendix A Table 5. Recommendations for Lung Cancer Screening With LDCT

Organization	Year	Target Population	Recommendation and Related Comments	Endorse shared decision making?
American Academy of Family Physicians[44]	2013	Persons with a high risk of lung cancer on the basis of age and smoking history	Insufficient evidence to recommend screening. Screening cannot be recommended on the basis of a single study conducted in major medical centers.	Yes
American Cancer Society[328, 329]	2013	NLST criteria. Excludes life-limiting comorbid conditions, metallic implants or devices in the chest or back, or oxygen requirement	Discussion about screening should be initiated, including benefits, limitations, harms. Recommends only if there is access to a high-volume, high-quality lung cancer screening and treatment center.	Yes
American Lung Association[330]	2015	NLST criteria	Screening with LDCT recommended. Screening should occur in institutions that are able to provide a comprehensive screening program; smoking cessation is the best method of reducing lung cancer risk among those who smoke.	Yes
American Association for Thoracic Surgery[331]	2012	Persons ages 55-79 years with ≥30 pack-year smoking history and persons ages 50-79 years with ≥20 pack-year smoking history and another risk factor for lung cancer* or lung cancer survivor	Annual screening with LDCT. Should be conducted in environments in which there are multidisciplinary teams for managing indeterminate and positive screening scans; desirable to create a program that supports smoking cessation.	Not specified
CHEST Guideline and Expert Panel Report[315]	2018	Asymptomatic persons ages 55-77 years with same smoking history criteria as NLST	Annual screening with LDCT should be offered (weak recommendation, moderate-quality evidence)	Yes
European Union[332]	2017	Lung cancer LDCT programs should use a validated risk stratification approach so that only persons deemed to be at high enough risk are screened†	Screening with LDCT. Management of screen-detected solid nodules should use semi-automatically derived volume measurements and volume-doubling time and should be quality assured. Management of lung nodules by lung cancer multidisciplinary teams. National quality assurance boards should be set up by professional bodies to ensure adherence to all minimum technical standards.	All future screenees should be provided with carefully constructed participant information on the potential benefits and harms to enable them to make an informed decision.
National Comprehensive Cancer Network[43, 333]	2012	NLST criteria and persons age 50 years or older with ≥20 pack-years smoking history and 1 additional risk factor for lung cancer‡	Screening with LDCT. Multidisciplinary screening programs will be helpful; smokers should always be encouraged to quit smoking. It is also reasonable to consider using the PLCOm2012 lung cancer risk calculator to assist in quantifying risk, considering a 1.3% threshold of lung cancer risk (over 6 years).	Patients should have a full understanding of risks and benefits.

Appendix A Table 5. Recommendations for Lung Cancer Screening With LDCT

Organization	Year	Target Population	Recommendation and Related Comments	Endorse shared decision making?
Canadian Task Force on Preventive Health Care[334]	2016	NLST criteria	Screening with LDCT every year up to 3 consecutive years (weak, low-quality evidence). Screening should only be performed in health care settings with access to expertise in early diagnosis and treatment of lung cancer.	Yes, discussion about benefits and harms, including false-positive screens, adverse effects of invasive followup testing, and overdiagnosis

* Examples of additional risk factors, as specified by the American Association for Thoracic Surgery, include COPD, environmental or occupational exposure, prior cancer or radiation therapy, and genetic predisposition or family history.
† No specific model is recommended.
‡ Examples of additional risk factors, as specified by the National Comprehensive Cancer Network, include radon exposure, occupational exposure, history of cancer, family history of lung cancer, COPD, and pulmonary fibrosis.

Abbreviations: COPD=chronic obstructive pulmonary disease; CT=computed tomography; LDCT=low-dose computed tomography; NLST=National Lung Screening Trial.

CQ 1. What Are the Barriers to Implementing Lung Cancer Screening and Surveillance in Clinical Practice in the United States (e.g., Barriers to Shared Decision Making, Systematically Eliciting and Documenting a Detailed Smoking History, Systems for Tracking Nodules and Followup, and Availability of Appropriate LDCT Protocols)?

Introduction

Since the 2013 USPSTF statement on lung cancer screening, multiple expert groups and specialty societies have published consensus-based guidance documents on screening implementation.[315, 335-339] Common among these guidance statements is an acknowledgement that implementation of lung cancer screening is a highly complex process requiring multiple, inter-connected steps. There is also a growing body of literature aimed at understanding barriers to implementation of lung cancer screening. A recent perspective article offered a high-level summary of implementation barriers using a multi-level (patient, provider, and system-level) framework (**Table 6**).[340] This contextual question section is not on a comprehensive account of the many clinical and technical aspects of screening implementation. Rather, it highlights some of the salient barriers to the appropriate and effective implementation of lung cancer screening that have arisen since the 2013 USPSTF statement. These include barriers to SDM, systematic identification of screen-eligible patients, systems for tracking nodules and followup, and availability of LDCT protocols.

Barriers to Shared Decision Making

Screening Guidelines and SDM

Lung cancer screening guidelines are virtually unanimous in asserting that informed and SDM should occur before a patient proceeds with screening.[315, 334, 335, 341] The American Cancer Society recommends that "a process of informed and SDM with a clinician related to the potential benefits, limitations, and harms associated with screening for lung cancer with low-dose computed tomography should occur before any decision is made to initiate lung cancer screening."[328] The 2013 USPSTF recommendation stated that "the decision to begin screening should be the result of a thorough discussion of the possible benefits, limitations, and known and uncertain harms."[1] In 2014, the CMS coverage decision for lung cancer screening was issued that contained several stipulations including a requirement for "a lung cancer screening counseling and shared decision-making visit." Required elements of this visit included "the use of one or more decision aids, to include benefits, harms, followup diagnostic testing, over-diagnosis, false positive rate, and total radiation exposure."[40]

SDM in Practice

Unfortunately, emerging evidence raises concerns that SDM in practice may be far from what is intended by guidelines. A recent study found that CMS-required SDM visits were evident in just 10 percent of Medicare beneficiaries who had a screening LDCT in 2016.[342] Another study analyzed transcribed recordings of discussions between community physicians (primary care physicians and pulmonologists) and patients about initiating lung cancer screening.[343] In these discussions (n=14), which were identified by searching a large database, SDM quality was universally poor and discussion of screening harms was essentially nonexistent. Average time for screening discussion was 57 seconds and was typically focused on insurance coverage. There was no evidence that decision aids were used.

Competing Demands

Systematic reviews have found that SDM is difficult to implement well in practice, regardless of clinical context.[344] Factors associated with higher quality SDM include time (duration of encounter) and decision support interventions (including decision aids). Since the USPSTF 2013 recommendation, multiple studies have identified competing demands and limited time available to conduct SDM during clinical encounters as a central barrier to implementing SDM.[37, 345-349]

Patient Perceptions of Screening

Adding to the challenge of SDM implementation is evidence that patient's "baseline" perceptions of the benefits and harms of lung cancer screening diverge from what the evidence shows. In one study of (n=50) screen-eligible patients who had not yet seen a decision aid overestimated the likelihood of benefitting from screening by orders of magnitude. Patients also had poor awareness of potential harms of screening.[42] In another study involving focus groups of screening eligible patients (n=45), participants expressed surprise that the magnitude of their lung cancer risk and benefits of screening were lower than expected.[345] These studies suggest that patient's baseline perceptions are systematically inaccurate (i.e., biased) in favor of screening. These biases are not unique to lung cancer screening, and there is robust evidence that patients, members of the public, and clinicians typically overestimate the benefits and underestimate the harms of cancer screening tests.[350-352]

Such biases pose challenges for implementing SDM about screening in practice. Primary care physicians, who routinely discuss cancer screening with patients, recognize that initiating a conversation about the availability of a lung cancer screening test will provoke immediate assumptions on the part of the patient. For meaningful SDM, a provider who initiates such a discussion about lung cancer screening must be prepared to provide balanced information that calibrates patient perceptions and expectations to reflect what is known.

Although providing screen-eligible patients individualized, quantitative risk information is (theoretically) ideal, a first order concern is implementing processes that offer patients a) a reasonable sense of the benefits and harms of screening, including approximate likelihoods for these outcomes; b) an understanding that the screening decision involves tradeoffs between these

benefits and harms; and c) a recognition that the "weights" placed on avoiding harms relative to benefits should reflect the values of the patient him/herself.

Timing and Context of SDM

Experts have expressed a range of views about whether SDM about lung cancer screening should occur in primary care, subspecialty care, and/or within centralized screening programs.[353, 354] The potential benefits of SDM in a subspecialized LDCT screening context are the increased chances that providers will be knowledgeable about lung cancer screening, have time to dedicate to the issue of screening, and use established workflows that employ decision support tools. On the other hand, potential downsides of conducting SDM in centralized screening centers is that patients are likely to assume that a referral to a lung cancer screening program is a referral for the screening procedure itself rather than to participate in process by which they will decide whether screening is right for them. Thus, by the time the patient reaches the screening center context, absent a good prior discussion, it is likely they will arrive with inaccurate perceptions of the benefits and harms and will have already decided to be screened.[353-356]

Emerging evidence lends support to the idea that the timing and context of the SDM process (i.e., primary care vs. referral setting) can influence patient decisions. One study in a primary care population of screening-eligible patients (n=50) found viewing a video decision aid improved understanding of the nature and magnitude of the harms and benefits of screening.[42] When asked to indicate their screening preferences, 50 percent preferred screening while the other 50 percent did not. In another study of screen-eligible primary care patients (n=81) who were reached through an electronic health record portal and viewed a lung cancer screening decision aid, screening preferences were again heterogeneous: 30 percent desired screening, 44 percent were "unsure," and 26 percent declined screening.[357] In contrast to these studies in primary care context, a study of patients attending a tertiary referral lung cancer screening program (n=423) who received robust patient education and decision support that included decision aid viewing, 95 percent proceeded to have a screening LDCT.[358] In sum, there is evidence that, in primary care populations, informed preferences about lung cancer screening are heterogeneous (i.e., that the decision is, in fact, "preference sensitive"). SDM conducted only after a patient reaches a lung cancer screening center may miss the "decision window" during which patients actually make the decision.

System and Personnel Barriers to Identifying Eligible Populations (Detailed Smoking Histories)

One challenge to population or system level implementation in identifying populations eligible for screening is that detailed, patient-level smoking histories, including average number of cigarettes smoked per day, start dates, and quit dates, are not readily available within the electronic health record.

Moreover, smoking behavior is dynamic, meaning that these data need to be periodically verified for accuracy. Clinical demonstration studies suggest that, even with additional resources dedicated to eliciting and documenting smoking histories, these data fields often still have incomplete or inaccurate information. In the VHA implementation project, substantial resources

were dedicated to having nurses elicit and enter these data. Despite this, among 93,033 patients who met basic age and comorbidity criteria, a total of 36,555 patients (39.3%) were missing necessary smoking history data (or the tobacco pack-years were improperly calculated) needed to systematically identify screening-eligible patients.[38] In 1-year, single-site primary care implementation project, nurses and support staff were able to elicit and document smoking histories in 53 percent of ever smokers between ages 55 and 80 years.[359]

Availability of Appropriate LDCT Protocols

Another potential implementation issue is whether radiology facilities that are capable of providing LDCT scanning are available. Early studies published soon after the 2013 USPSTF statement raised concerns about limited capacity.[360] However, the number of lung cancer screening centers is growing rapidly. In 2014, there were 203 screening centers certified by the American College of Radiology (ACR) in the United States. By 2017, that number had increased to 1,748.[361] According to the ACR website, there are 2,013 ACR-certified centers as of April 2019.[362]

Systems for Tracking Nodules and Ensuring Followup (Patient Coordination)

The availability of centers that are certified to *perform* LDCT screening and to *report* results to a national registry should be distinguished from the availability of infrastructure needed to *track and manage* individuals with screen-detected lung nodules. There is broad expert consensus that screen-detected lung nodules should be managed based on established algorithms,[315, 335-339] which call for regular and timely surveillance of screen-detected nodules. Operationalizing surveillance of lung nodules for a large, high-risk population will require robust longitudinal tracking and patient coordination systems for the large numbers of individuals with lung nodules. The VHA Lung Cancer Screening Demonstration Project (LCSDP) found this aspect of implementation to be challenging and complex, as most patients screened had findings that required followup. Specifically, 56 percent of screened patients had one or more nodules that required tracking and 41 percent had incidental findings. Implementation required substantial resources for manual abstraction of patient information from records and the creation of dedicated tracking and patient coordination systems.[38]

While there is no comprehensive accounting of patient coordination and tracking systems in the United States, surveys and interviews have found that both primary care physicians and subspecialists have concerns about whether there is sufficient personnel and tracking infrastructure needed for screening implementation.[37, 345-349, 363]

Out-of-Pocket Costs for Followup of Screen-Detected Findings

ACA insurance plans are required to cover LDCTs done for *screening*. However, patients with screen-detected nodules enter diagnostic and surveillance pathways involving evaluations, imaging, and procedures that are not considered screening and are subject to copays and deductibles. Since the 2013 USPSTF statement, multiple studies in both patients and providers

have identified the issue that the costs of followup testing after positive screening results will lead to financial harm for patients.[37, 346-349, 364, 365] Even if less aggressive nodule categorization approaches (e.g., Lung-RADS) are used, the number of patients who will enter surveillance pathways for screen-detected nodules is large. Given that high-deductible insurance plans among low and middle-income Americans, the issue of patient cost as a barrier to lung cancer screening implementation requires further study.[366]

CQ 2a. Are the Participants of Randomized, Controlled Trials of Lung Cancer Screening (e.g., NLST) That Reported a Reduction in All-Cause or Lung Cancer Mortality Representative of Screening-Eligible U.S. Adults (Based on NLST Criteria or USPSTF Recommendations)?

b. How Do the 5-Year Survival Rate and Life Expectancy of Persons Eligible for Lung Cancer Screening in the United States (Based on NLST Criteria or USPSTF Recommendations) Compare With Those of NLST Participants?

c. Are the Settings and Providers in Randomized, Controlled Trials of Lung Cancer Screening (e.g., NLST) That Reported a Reduction in All-Cause or Lung Cancer Mortality Representative of U.S. Health Care Settings and Providers?

The Discussion of this report describes the applicability of NLST and other included studies. Briefly, NLST participants were younger, more highly educated, and less likely to be current smokers than the U.S. screening-eligible population.[367] Furthermore, the NLST was mainly conducted at large academic centers, potentially limiting its applicability to community-based practice (e.g., because of challenges with implementation, level of expertise). Many of the trial centers are well-recognized for expertise in radiology as well as cancer diagnosis and treatment.[32] Community centers may be less equipped for screening programs and for treatment of lung cancers identified by screening. For example, the NLST publication noted that mortality associated with surgical resection of lung cancer was much lower in the trial than that reported for the U.S. population (1% vs. 4%).[32, 296]

A study using data from the 2012 Health and Retirement Study (HRS) (a national survey of adults 50 and older) evaluated comorbidities, life expectancy, smoking history, and other characteristics in the screening-eligible population and in NLST participants; it reported a lower 5-year survival rate and life expectancy in the screening-eligible persons compared with NLST participants (87% vs. 93%, $p<0.001$, and 18.7 years vs. 21.2 years, respectively).[25] Screening-eligible HRS respondents were older, more likely to be current smokers, and more likely to have been diagnosed with comorbidities than NLST participants. The authors concluded that the

general U.S. population eligible for lung cancer screening is probably less likely to benefit from early detection compared with the NLST participants because they face a high risk of death from competing causes, such as heart disease, diabetes, or stroke.

CQ 3. Does Screening for Lung Cancer With LDCT Have Unintended Benefits From Detecting Incidental Findings (e.g., Coronary Artery Calcium, Chronic Obstructive Pulmonary Disease, or Extrapulmonary Nodules) Leading to Interventions That Improve Health Outcomes?

Common incidental findings identified in this systematic review included coronary artery calcification, aortic aneurysms, emphysema, infections, and masses or nodules (e.g., of the thyroid or pancreas), among others. There is no trial evidence to indicate that screening with LDCT for such findings has greater unintended benefit than unintended harm. The USPSTF portfolio includes evidence reviews and recommendations covering the evidence on potential benefits and harms of screening for many of these conditions/findings in asymptomatic persons. The evidence reviews have resulted in I statements (i.e., insufficient evidence) and D recommendations (i.e., harm of screening greater than benefit). For example, the USPSTF recommendation statement on nontraditional cardiovascular risk factors concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for coronary artery calcium (CAC) in asymptomatic adults to prevent CVD events.[368] Further, USPSTF had D recommendations for screening for chronic obstructive pulmonary disease (COPD),[369] thyroid cancer,[370] and pancreatic cancer in asymptomatic adults. Regarding screening for aneurysms, USPSTF recommends one-time screening for abdominal aortic aneurysm (AAA) with ultrasonography in men ages 65 to 75 years who have ever smoked[371]; an update is in progress.[372] There is no trial evidence to indicate greater benefit than harm for using LDCT to screen for aneurysms (thoracic or abdominal).

CQ 4. What Is the Effectiveness of Smoking Cessation Intervention Among Patients Receiving LDCT Screening?

The provision of smoking cessation interventions with LDCT screening is an opportunity to improve health outcomes. In the NLST, screening with LDCT combined with smoking abstinence of 15 years provided the greatest reduction in lung cancer mortality (comparing, for example, with screening with LDCT and current smoking).[373] The Centers for Medicare & Medicaid Services also requires that smokers who undergo screening receive counseling on smoking cessation so as not to mistake screening as either a substitute for cessation or a confirmation that it is acceptable to continue smoking if the screening result is normal.[374] The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and U.S. Food and Drug Administration (FDA)–approved pharmacotherapy for cessation to adults who use tobacco.[375]

Two systematic reviews focused on this contextual question.[376, 377] Assessment of these reviews using AMSTAR-2 criteria indicates at least moderate confidence in the results.[378] Neither systematic review conducted meta-analyses because of heterogeneity of interventions and other factors. The first systematic review[376] included six studies published through July 1, 2015: three randomized, controlled trials (RCTs) (with a total of 1473 participants) and three uncontrolled studies (total 7,333 participants).[376] Two of the RCTs compared the use of written self-help materials with internet or computer-based tailored self-help materials for smoking cessation intervention among patients receiving lung cancer screening and found no statistically significant difference in abstinence rates between groups.[379, 380] The third RCT evaluated the effect of smoking cessation interventions before and after LDCT and found that smoking intervention before LDCT led to numerically higher abstinence rates at 4 months (33.3 vs. 22.2%) and 6 months (22.2% vs. 11.1%) after treatment,[381] although statistical testing was not provided for the comparison between groups (a subsequently published systematic review conducted its own statistical tests for those comparisons and reported no significant difference between groups, p=1.0[377]). Continuous abstinence rates in uncontrolled studies ranged from 19.8 percent at 1-year followup[382] to 57.1 percent at 6-months followup[383] across included studies. No rating of the risk of bias of included studies was reported. The authors reported that their findings suggest that there are benefits to implementing smoking cessation interventions in lung cancer screening programs, which may represent a teachable moment to quit smoking.[376]

The second systematic review[377]included nine studies published through May 1, 2018. It restricted eligibility to RCTs and observational studies with a comparison group, which excluded the three single-arm studies that were in the other[376] systematic review. The included five RCTs (with a total of 1,620 participants) and four observational studies (total 5,114 participants) were rated as poor to fair quality with significant potential for bias and limited generalizability.[377] Though the studies provided insufficient evidence to support a particular approach to smoking cessation interventions in the LDCT screening setting, the authors suggested that more intensive interventions (e.g., multiple counseling sessions) appear to be more effective approaches to smoking cessation. Table 7 summarizes the five RCTs included in the review. Sample sizes ranged from 18 to 1,284, with three of the studies having fewer than 100 participants. The largest study (with 1,284 participants) was part of the NELSON lung cancer screening trial.[380] Only one of the studies found a statistically significant difference in smoking cessation outcomes between groups, with an intervention of six weekly telephone counseling calls compared to a list of resources.[384] Two of the studies used two or fewer counseling sessions as the intervention, while the other two distributed tailored smoking cessation resources. Four of the comparison groups for the RCTs distributed nontailored resources; the other altered the timing of smoking cessation counseling sessions. The authors of the systematic review conducted a search of ongoing trials, finding 11 ongoing RCTs assessing smoking cessation interventions in the context of LDCT screening.[377]

In sum, limited evidence exists to establish the effectiveness of smoking cessation interventions in lung cancer screening programs. However, this is an active area of research, with numerous ongoing trials comparing intervention methods. Further research to determine components of smoking cessation interventions that can optimize outcome by testing different modalities in lung cancer screening programs and to identify strategies to effectively integrate smoking cessation interventions in lung cancer screening sites have also been suggested.

Appendix A Table 6. Summary of Multilevel Barriers to Effective Lung Cancer Screening

Patient-level barriers
• Competing needs and demands for health care • Cost • Fear (e.g., procedures, diagnosis, treatment) • Lack of awareness • Lack of interest due to stigma associated with smoking • Limited access to care due to financial or social factors • Limited information and misinformation • Logistical issues (e.g., inconvenience, time) • Mistrust of the health care system and/or health care • Nihilism
Provider-level barriers
• Competing demands for time • Evolving attitudes about the effectiveness of screening • Lack of awareness • Limited information and misinformation • Limited training in SDM • Nihilism related to treatment of lung cancer • Requirement for behavior change (adaptive challenge)
System-level barriers
• Lack of support from health system leaders • Limited resources to support screening, including equipment, personnel, and information technology resources • Competing demands for limited resources (e.g., other screening programs or preventive health interventions) • Uncertain return on investment • Complexity of implementation (requires multidisciplinary collaboration) o Conflicting upper age range recommendations for screening o Identification of screening-eligible patients (gaps in smoking status data)

Source: Carter-Harris L, Gould MK. Multilevel barriers to the successful implementation of lung cancer screening: why does it have to be so hard? *Ann Am Thorac Soc*. 2017 Aug;14(8):1261-5. doi: 10.1513/AnnalsATS.201703-204PS. PMID: 28541749.[340]

Appendix A Table 7. Summary of Randomized, Controlled Trials in the Systematic Review From 2019

Author, Year	Trial	Sample Size	Intervention	Comparison	Findings
Clark, 2004[379]	NA	171	Internet-based resources (10 links).	Written self-help materials from the NCI.	No significant difference in 12 month quit rates or change in readiness to quit. Increased number of quit attempts in intervention group (p=0.011).
Aalst, 2012[380]	NELSON	1284	Computer-generated, tailored self-help material based on input of individual smoking behaviors and history.	Standard brochure with smoking cessation information for different stages of readiness to quit.	No significant difference in point prevalence, quit attempts, or prolonged smoking abstinence at 24 months followup.
Ferketich, 2012[381]	NA	18	Smoking cessation counseling with a medical oncologist occurring before LDCT performed followed by 12-week tobacco dependence protocol.	Smoking cessation counseling with a medical oncologist occurring after LDCT performed followed by 12-week tobacco dependence protocol.	No significant difference in abstinence among those who received counseling before LDCT and those who received counseling after LDCT at 4 months and 6 months.
Marshall, 2016[385]	NA	55	Single face-to-face tailored counseling session with take-home audio education materials, printed materials, and telephone helpline referral.	Nontailored printed smoking cessation materials and telephone helpline referral.	No significant difference in quit rates at 12 months for patients receiving counseling intervention compared to the control group.
Taylor, 2017[384]	NA	92	Resources list plus 6 weekly, proactive counseling calls.	Resource list: Booklet, website, contact information for local resources, text messaging link.	Higher 7-day point prevalence cessation at 3-months in patients who received telephone counseling.

Abbreviations: LDCT=low-dose computed tomography; NA=not applicable; NCI=National Cancer Institute; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial.

Screening Searches
PubMed, 4-30-18

Search	Query	Items Found
#1	Search (“Lung Neoplasms”[MeSH] OR NSCLC[tiab] OR “lung cancer”[tiab] OR “lung cancers” [tiab] OR “lung-cancer”[tiab] OR “lung malignancy”[tiab] OR “lung malignancies”[tiab] OR “lung nodule”[tiab] OR “lung nodules” [tiab] OR “pulmonary nodule”[tiab] OR “pulmonary nodules”[tiab] OR “lung mass”[tiab] OR “lung masses”[tiab] OR (“Squamous Cell Carcinoma”[MeSH] OR Adenocarcinoma[MeSH]) and (Lung[MeSH] OR Lung Diseases[MeSH]))	209038
#2	Search (“Mass Screening”[MeSH] OR screen*[tw] OR “Early Diagnosis”[MeSH] OR “Tomography, X-Ray Computed”[Mesh] OR “CT scan”[tiab] OR “CT scans”[tiab] OR “CAT scan”[tiab] OR “CAT scans”[tiab] OR “spiral CT”[tiab] OR “spiral computed tomography”[tiab] OR “low-dose computed tomography”[tiab] OR LDCT[tiab] OR ((early[tiab] or earlier[tiab] or earliest[tiab]) AND (detect*[tiab] or diagnos*[tiab] or discover*[tiab] or find[tiab] or finding[tiab])))	1561323
#3	Search (#1 and #2)	33537
#4	Search (DANTE[tiab] OR “Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays”[All Fields] OR DLCST[tiab] OR “Danish Lung Cancer Screening Trial”[tiab] OR ITALUNG[tiab] OR “Italian Lung Cancer Screening Trial”[All Fields] OR LUSI[tiab] OR “Lung Cancer Screening Intervention”[All Fields] OR MILD[tiab] OR “Multicentric Italian Lung Detection”[All Fields] OR NELSON[tiab] OR “Dutch-Belgian Lung Cancer Screening trial”[All Fields] OR NLST[tiab] OR “National Lung Screening Trial”[All Fields])	306902
#5	Search (#1 and #4)	2661
#6	Search (#3 or #5)	35398
#7	Search (#3 or #5) Filters: Publication date from 2012/01/01 to 2018/12/31	12321
#8	Search (“Risk prediction model”[tw] OR “Risk prediction models”[tw] OR “Risk Assessment”[MeSH] OR “risk assessment”[tw] OR “risk model”[tw] OR “risk models”[tw] OR “Decision Support Techniques”[MeSH] OR “Decision Support Systems, Clinical”[Mesh] OR “clinical prediction”[tw] OR “Logistic Models”[MeSH] OR microsimulation*[tw] OR “simulation model”[tw] OR “simulation models”[tw] OR “Assessment tool”[tw] OR “Assessment tools”[tw] OR “prediction score”[tw] OR “Risk Factors”[MeSH] OR “Predictive Value of Tests”[MeSH] OR “Sensitivity and Specificity”[MeSH] OR (Predict*[tw] AND (model*[tw] OR outcome*[tw] OR risk*[tw] OR rule[tw] OR rules[tw])) OR “risk-targeted”[tw] OR “mortality risk”[tw])	2073965
#9	Search (#1 and #8)	26417
#10	Search (#1 and #8) Filters: Publication date from 2014/04/01 to 2018/12/31	6640
#11	Search (#7 or #10)	16840
#12	Search (#7 or #10) Filters: Humans	16584
#13	Search (#7 or #10) Filters: Humans; English	15409
#14	Search (#7 or #10) Filters: Humans; English; Child: birth-18 years	605
#15	Search (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt])	1642710
#16	Search (#13 NOT #14)	14804
#17	Search (#16 NOT #15)	14186
#18	Search (“systematic review”[ti] OR “meta-analysis”[pt] OR “meta-analysis”[ti] OR “systematic literature review”[ti] OR “this systematic review”[tw] OR (“systematic review”[tiab] AND review[pt]) OR meta synthesis[ti] OR “meta synthesis”[ti] OR “cochrane database syst rev”[ta])	178836
#19	Search (#17 and #18)	**485**
#20	Search (“Randomized Controlled Trial”[Publication Type] OR “Single-Blind Method”[MeSH] OR “Double-Blind Method”[MeSH] OR “Random Allocation”[MeSH] OR ((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]))	618965
#21	Search (#17 and #20)	**462**
#22	Search (“Case-Control Studies”[MeSH] OR “Cohort Studies”[MeSH] OR “Epidemiologic Studies”[MeSH] OR “Follow-Up Studies”[MeSH] OR “Evaluation Studies”[Publication Type] OR “Program Evaluation”[MeSH] OR “observational study”[tw] OR “observational studies”[tw] OR “Cohort Studies”[MeSH] OR “Comparative Study”[pt] OR “Validation Studies”[pt] OR “Prospective Studies”[MeSH] OR “cohort”[tw] OR “case control”[tw])	4054856
#23	Search (#17 and #22)	**5869**

Appendix B1. Original Search Strategies and Update Searches

Cochrane Library, 5-2-2018

ID	Cochrane Library Search	Hits
#1	[mh “Lung Neoplasms”] or NSCLC:ti,ab or “lung cancer”:ti,ab or “lung cancers”:ti,ab or “lung-cancer”:ti,ab or “lung malignancy”:ti,ab or “lung malignancies”:ti,ab or “lung nodule”:ti,ab or “lung nodules”:ti,ab or “pulmonary nodule”:ti,ab or “pulmonary nodules”:ti,ab or “lung mass”:ti,ab or “lung masses”:ti,ab or (([mh “Squamous Cell Carcinoma”] or [mh Adenocarcinoma]) and ([mh Lung] or [mh “Lung Diseases”]))	13223
#2	[mh “Mass Screening”] or screen*:kw or [mh “Early Diagnosis”] or [mh “Tomography, X-Ray Computed”] or “CT scan”:ti,ab or “CT scans”:ti,ab or “CAT scan”:ti,ab or “CAT scans”:ti,ab or “spiral CT”:ti,ab or “spiral computed tomography”:ti,ab or “low-dose computed tomography”:ti,ab or LDCT:ti,ab or ((early:ti,ab or earlier:ti,ab or earliest:ti,ab) and (detect*:ti,ab or diagnos*:ti,ab or discover*:ti,ab or find:ti,ab or finding:ti,ab))	42901
#3	#1 and #2	1293
#4	DANTE:ti,ab or “Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays” or DLCST:ti,ab or “Danish Lung Cancer Screening Trial”:ti,ab or ITALUNG:ti,ab or “Italian Lung Cancer Screening Trial” or LUSI:ti,ab or “Lung Cancer Screening Intervention” or MILD:ti,ab or “Multicentric Italian Lung Detection” or NELSON:ti,ab or “Dutch-Belgian Lung Cancer Screening trial” or NLST:ti,ab or “National Lung Screening Trial”:kw	43092
#5	#1 and #4	541
#6	#3 or #5	1615
#7	#6 Publication Year from 2012 to 2018	916
#8	“Risk prediction model”:ti,ab,kw or “Risk prediction models”:ti,ab,kw or [mh “Risk Assessment”] or “risk assessment”:ti,ab,kw or “risk model”:ti,ab,kw or “risk models”:ti,ab,kw or [mh “Decision Support Techniques”] or [mh “Decision Support Systems, Clinical”] or “clinical prediction”:ti,ab,kw or [mh “Logistic Models”] or microsimulation*:ti,ab,kw or “simulation model”:ti,ab,kw or “simulation models”:ti,ab,kw or “Assessment tool”:ti,ab,kw or “Assessment tools”:ti,ab,kw or “prediction score”:ti,ab,kw or [mh “Risk Factors”] or [mh “Predictive Value of Tests”] or [mh “Sensitivity and Specificity”] or (Predict*:ti,ab,kw and (model*:ti,ab,kw or outcome*:ti,ab,kw or risk*:ti,ab,kw or rule:ti,ab,kw or rules:ti,ab,kw)) or “risk-targeted”:ti,ab,kw or “mortality risk”:ti,ab,kw	102435
#9	#1 and #8	1595
#10	#9 Publication Year from 2014 to 2018	637
#11	#7 or #10	1385
#12	child:ti or child:ab or child:kw or children:ti or children:ab or children:kw or adolescen*:ti or adolescen*:ab or adolescen*:kw or teen:ti or teen:ab or teen:kw or teens:ti or teens:ab or teens:kw or teenage*:ti or teenage*:ab or teenage*:kw or youth:ti or youth:ab or youth:kw or youths:ti or youths:ab or youths:kw or pediatric*:ti or pediatric*:ab or pediatric*:kw or paediatric*:ti or paediatric*:ab or paediatric*:kw or boys:ti or boys:ab or boys:kw or girls:ti or girls:ti or girls:kw	191065
#13	#11 not #12	1353
#14	#13 in Cochrane Reviews (Reviews and Protocols) and Other Reviews	46
#15	“randomized controlled trial”:pt or “randomized controlled trial”:ti or “randomized controlled trial as topic”:pt or “single-blind method”:pt or “double-blind method”:pt or “random allocation”:pt	466945
#16	#13 and #15	387
#17	[mh “Case-Control Studies”] or [mh “Cohort Studies”] or [mh “Epidemiologic Studies”] or [mh “ Follow-Up Studies “] or [mh “Seroepidemiologic Studies”] or “Evaluation Studies”:pt or [mh “Program Evaluation”] or “observational study” or “observational studies” or [mh “case-control studies”] or “comparative study”:pt or “validation studies”:pt or [mh “Prospective Studies”] or “cohort” or “case control”	305186
#18	(#13 and #17) not (#14 or #16) in Methods Studies, Technology Assessments, Economic Evaluations and Cochrane Groups	4

Intervention searches
PubMed, 5-1-2018

Search	Query	Items Found
#4	Search (“Carcinoma, Non-Small-Cell Lung”[MeSH] OR “non-small-cell lung cancer”[All Fields] OR NSCLC[tiab] OR (“non small cell”[tiab] AND lung*[tiab] AND cancer*[tiab]) OR “Carcinoma, Squamous Cell”[Mesh] OR Adenocarcinoma[MeSH] OR “Carcinoma, Large Cell”[MeSH])	493740
#5	Search ((stag* AND (one or “1” or I or two or “2” or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)))	836529
#6	Search (((early or earlier or earliest) AND (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging)))	880795
#7	Search (#5 or #6)	1496819
#8	Search (#4 and #7)	106951
#9	Search (“Margins of Excision”[Mesh] OR Pneumonectomy OR Lobectomy OR (resection* and lung*[tw]))	38216
#10	Search (#8 and #9)	3942
#11	Search (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt])	1643073
#12	Search (#10 not #11)	3885
#13	Search (#10 not #11) Filters: Humans	3647
#14	Search (#10 not #11) Filters: Humans; English	2921
#15	Search (#10 not #11) Filters: Publication date from 2012/01/01 to 2018/12/31; Humans; English	1253
#16	Search (#10 not #11) Filters: Publication date from 2012/01/01 to 2018/12/31; Humans; English; Child: birth-18 years	45
#17	Search (#15 NOT #16)	1208
#18	Search (“systematic review”[ti] OR “meta-analysis”[pt] OR “meta-analysis”[ti] OR “systematic literature review”[ti] OR “this systematic review”[tw] OR (“systematic review”[tiab] AND review[pt]) OR meta synthesis[ti] OR “meta synthesis”[ti] OR “cochrane database syst rev”[ta])	178955
#19	Search (#17 and #18)	29
#20	Search (“Randomized Controlled Trial”[Publication Type] OR “Single-Blind Method”[MeSH] OR “Double-Blind Method”[MeSH] OR “Random Allocation”[MeSH] OR ((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]))	619155
#21	Search (#17 and #20)	41
#22	Search (“Case-Control Studies”[MeSH] OR “Cohort Studies”[MeSH] OR “Epidemiologic Studies”[MeSH] OR “Follow-Up Studies”[MeSH] OR “Evaluation Studies”[Publication Type] OR “Program Evaluation”[MeSH] OR “observational study”[tw] OR “observational studies”[tw] OR “Cohort Studies”[MeSH] OR “Comparative Study”[pt] OR “Validation Studies”[pt] OR “Prospective Studies”[MeSH] OR “cohort”[tw] OR “case control”[tw])	4056042
#23	Search (#17 and #22)	842

Appendix B1. Original Search Strategies and Update Searches

Cochrane Library, 5-2-2018

ID	Search	Hits
#1	[mh "Carcinoma, Non-Small-Cell Lung"] or "non-small-cell lung cancer" or NSCLC:ti,ab or ("non small cell":ti,ab and lung*:ti,ab and cancer*:ti,ab) or [mh "Carcinoma, Squamous Cell"] or [mh Adenocarcinoma] or [mh "Carcinoma, Large Cell"]	15389
#2	stag* and (one or "1" or I or two or "2" or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)	62403
#3	(early or earlier or earliest) and (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging)	51466
#4	#2 or #3	96758
#5	#1 and #4	6205
#6	([mh "Margins of Excision"] or Pneumonectomy or Lobectomy or (resection* and lung*:ti,ab,kw))	2545
#7	#5 and #6	540
#8	letter:pt or newspaper article:pt or editorial:pt or comment:pt	9229
#9	#7 not #8	539
#10	child:ti or child:ab or child:kw or children:ti or children:ab or children:kw or adolescen*:ti or adolescen*:ab or adolescen*:kw or teen:ti or teen:ab or teen:kw or teens:ti or teens:ab or teens:kw or teenage*:ti or teenage*:ab or teenage*:kw or youth:ti or youth:ab or youth:kw or youths:ti or youths:ab or youths:kw or pediatric*:ti or pediatric*:ab or pediatric*:kw or paediatric*:ti or paediatric*:ab or paediatric*:kw or boys:ti or boys:ab or boys:kw or girls:ti or girls:ti or girls:kw	190954
#11	#9 not #10	528
#12	#11 Publication Year from 2012 to 2018, in Cochrane Reviews, Other Reviews	**30**
#13	"randomized controlled trial":pt or "randomized controlled trial":ti or "randomized controlled trial as topic":pt or "single-blind method":pt or "double-blind method":pt or "random allocation":pt	466999
#14	#11 and #13 Publication Year from 2012 to 2018	**59**
#15	[mh "Case-Control Studies"] or [mh "Cohort Studies"] or [mh "Epidemiologic Studies"] or [mh " Follow-Up Studies "] or [mh "Seroepidemiologic Studies"] or "Evaluation Studies":pt or [mh "Program Evaluation"] or "observational study" or "observational studies" or [mh "case-control studies"] or "comparative study":pt or "validation studies":pt or [mh "Prospective Studies"] or "cohort" or "case control"	305126
#16	#11 and #15 Publication Year from 2012 to 2018, in Methods Studies, Technology Assessments, Economic Evaluations and Cochrane Groups	**2**

SBRT-SABR Patch Searches
PubMed, 8-10-2018

Search	Query	Items Found
#1	Search (“Carcinoma, Non-Small-Cell Lung”[MeSH] OR “non-small-cell lung cancer”[All Fields] OR NSCLC[tiab] OR (“non small cell”[tiab] AND lung*[tiab] AND cancer*[tiab]) OR “Carcinoma, Squamous Cell”[Mesh] OR Adenocarcinoma[MeSH] OR “Carcinoma, Large Cell”[MeSH])	500717
#2	Search stag* AND (one or “1” or I or two or “2” or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)	851242
#3	Search (early or earlier or earliest) AND (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging)	896718
#4	Search (#2 or #3)	1523639
#5	Search (#1 and #4)	108779
#6	Search “Radiosurgery”[Mesh] OR “stereotactic body radiotherapy” OR SBRT[tw] OR “stereotactic body RT” OR “Stereotactic RT” OR “stereotactic ablative radiotherapy” OR SABR[tw]	14808
#7	Search (#5 and #6)	1086
#8	Search letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt]	1666509
#9	Search (#7 not #8)	1050
#10	Search ((#9 AND Humans[Mesh:NOEXP]) OR (#9 NOT Animals[Mesh:NOEXP]))	1048
#11	Search ((#9 AND Humans[Mesh:NOEXP]) OR (#9 NOT Animals[Mesh:NOEXP])) Sort by: Author Filters: English	994
#12	Search ((#9 AND Humans[Mesh:NOEXP]) OR (#9 NOT Animals[Mesh:NOEXP])) Sort by: Author Filters: Publication date from 2014/01/01 to 2018/12/31; English	580
#13	Search ((((“systematic review”[ti] OR “meta-analysis”[pt] OR “meta-analysis”[ti] OR “systematic literature review”[ti] OR “this systematic review”[tw] OR (“systematic review”[tiab] AND review[pt]) OR meta synthesis[ti] OR “meta synthesis”[ti] OR “cochrane database syst rev”[ta]))))	186300
#14	Search (#12 and #13)	**22**
#15	Search “Randomized Controlled Trial”[Publication Type] OR “Single-Blind Method”[MeSH] OR “Double-Blind Method”[MeSH] OR “Random Allocation”[MeSH] OR ((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract])	629547
#16	Search (#12 and #15)	**15**
#17	Search “Case-Control Studies”[MeSH] OR “Cohort Studies”[MeSH] OR “Epidemiologic Studies”[MeSH] OR “Follow-Up Studies”[MeSH] OR “Evaluation Studies”[Publication Type] OR “Program Evaluation”[MeSH] OR “observational study”[tw] OR “observational studies”[tw] OR “Cohort Studies”[MeSH] OR “Comparative Study”[pt] OR “Validation Studies”[pt] OR “Prospective Studies”[MeSH] OR “cohort”[tw] OR “case control”[tw]	4116689
#18	Search (#12 and #17)	**282**

Cochrane Library, 8-13-2018

ID	Search	Hits
#1	[mh "Carcinoma, Non-Small-Cell Lung"] or "non-small-cell lung cancer" or NSCLC:ti,ab or ("non small cell":ti,ab and lung*:ti,ab and cancer*:ti,ab) or [mh "Carcinoma, Squamous Cell"] or [mh Adenocarcinoma] or [mh "Carcinoma, Large Cell"]	16679
#2	stag* and (one or "1" or I or two or "2" or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)	68855
#3	(early or earlier or earliest) and (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging)	52720
#4	#2 or #3	101973
#5	#1 and #4	6519
#6	[mh "Radiosurgery"] OR "stereotactic body radiotherapy" OR SBRT:ti,ab,kw OR "stereotactic body RT" OR "Stereotactic RT" OR "stereotactic ablative radiotherapy" OR SABR:ti,ab,kw	605
#7	#5 and #6	115
#8	letter:pt or newspaper article:pt or editorial:pt or comment:pt	9517
#9	#7 not #8	114
#10	child:ti or child:ab or child:kw or children:ti or children:ab or children:kw or adolescen*:ti or adolescen*:ab or adolescen*:kw or teen:ti or teen:ab or teen:kw or teens:ti or teens:ab or teens:kw or teenage*:ti or teenage*:ab or teenage*:kw or youth:ti or youth:ab or youth:kw or youths:ti or youths:ab or youths:kw or pediatric*:ti or pediatric*:ab or pediatric*:kw or paediatric*:ti or paediatric*:ab or paediatric*:kw or boys:ti or boys:ab or boys:kw or girls:ti or girls:ti or girls:kw	199855
#11	#9 and #10 with Cochrane Library publication date between Jan 2014 and Dec 2018	**3**

Gray Literature

ClinicalTrials.gov, unlimited by status (Completed/Terminated/Has Results, etc.) 5-8-18

Screening

"Other terms" search box:

(screen* OR "Early Diagnosis" OR "X-Ray Computed Tomography" OR "CT scan" OR "CT scans" OR "CAT scan" OR "CAT scans" OR "spiral CT" OR "spiral computed tomography" OR "low-dose computed tomography" OR LDCT OR ((early or earlier or earliest) AND (detect* or diagnos* or discover* or find or finding)) OR DANTE OR "Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays" OR DLCST OR "Danish Lung Cancer Screening Trial" OR ITALUNG OR "Italian Lung Cancer Screening Trial" OR LUSI OR "Lung Cancer Screening Intervention" OR "Multicentric Italian Lung Detection" OR NELSON and Trial* OR "Dutch-Belgian Lung Cancer Screening trial" OR NLST OR "National Lung Screening Trial")

Disease search box

("Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung-cancer" OR "lung malignancy" OR "lung malignancies" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR (("Squamous Cell Carcinoma" OR Adenocarcinoma) AND lung*))

Limit to Age Groups Checkboxes for Adult and Senior

Last update posted 01/01/2012–05/08/2018

For a search of:

(screen* OR "Early Diagnosis" OR "X-Ray Computed Tomography" OR "CT scan" OR "CT scans" OR "CAT scan" OR "CAT scans" OR "spiral CT" OR "spiral computed tomography" OR "low-dose computed tomography" OR LDCT OR ((early or earlier or earliest) AND (detect* or diagnos* or discover* or find or finding)) OR DANTE OR "Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays" OR DLCST OR "Danish Lung Cancer Screening Trial" OR ITALUNG OR "Italian Lung Cancer Screening Trial" OR LUSI OR "Lung Cancer Screening Intervention" OR "Multicentric Italian Lung Detection" OR NELSON and Trial* OR "Dutch-Belgian Lung Cancer Screening trial" OR NLST OR "National

Lung Screening Trial") AND ("Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung-cancer" OR "lung malignancy" OR "lung malignancies" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR (("Squamous Cell Carcinoma" OR Adenocarcinoma) AND lung*)) [DISEASE] AND INFLECT EXACT ("Adult" OR "Senior") [AGE-GROUP] AND INFLECT ("01/01/2012" : "05/08/2018") [LAST-UPDATE-POSTED]

Intervention search

For a search of:

Condition box:

"Non-Small-Cell Lung Carcinoma" OR "non-small-cell lung cancer" OR NSCLC OR "non small cell" AND lung* AND cancer* OR "Squamous Cell Carcinoma" OR Adenocarcinoma OR "Large Cell Carcinoma"

Other terms box:

(early OR earlier OR earliest) OR (stag* AND (one or 1 or I or two or 2 or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb))

Intervention box:

"Margins of Excision" OR Pneumonectomy OR Lobectomy OR (resection* and lung*) AND INFLECT EXACT ("Adult" OR "Senior") [AGE-GROUP] AND INFLECT ("01/01/2012" : "05/08/2018") [LAST-UPDATE-POSTED]

All together:

early OR (stag* AND (one or 1 or I or two or 2 or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)) | "Non-Small-Cell Lung Carcinoma" OR "non-small-cell lung cancer" OR NSCLC OR "non small cell" AND lung* AND cancer* OR "Squamous Cell Carcinoma" OR Adenocarcinoma OR "Large Cell Carcinoma" | "Margins of Excision" OR Pneumonectomy OR Lobectomy OR resection* and lung* | Adult, Senior | Last update posted from 01/01/2012 to 05/08/2018

WHO ICTRP 5-4-18

Screening search

Title box:

screen* OR "Early Diagnosis" OR "X-Ray Computed Tomography" OR "CT scan" OR "CT scans" OR "CAT scan" OR "CAT scans" OR "spiral CT" OR "spiral computed tomography" OR "low-dose computed tomography" OR LDCT OR ((early or earlier or earliest) AND (detect* or diagnos* or discover* or find or finding)) OR DANTE OR "Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays" OR DLCST OR "Danish Lung Cancer Screening Trial" OR ITALUNG OR "Italian Lung Cancer Screening Trial" OR LUSI OR "Lung Cancer Screening Intervention" OR "Multicentric Italian Lung Detection" OR (NELSON and Trial*) OR "Dutch-Belgian Lung Cancer Screening trial" OR NLST OR "National Lung Screening Trial"

Condition box:

"Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung malignancy" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR "Squamous Cell Carcinoma" OR Adenocarcinoma

Recruitment Status: ALL

Limited to trials registered between Jan 1, 2012 – May 4, 2018

Condition box:

"Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung malignancy" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR "Squamous Cell Carcinoma" OR Adenocarcinoma

Intervention search

Condition box:
"Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung malignancy" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR "Squamous Cell Carcinoma" OR Adenocarcinoma

Intervention box:
"Margins of Excision" OR Pneumonectomy OR Lobectomy OR (resection* and lung*)

Recruitment Status: ALL

Limited to trials registered between Jan 1, 2012 – May 4, 2018

Gray Literature SBRT Searches

ClinicalTrials.gov, 8-13-2018

For a search of:

Condition box:
"Non-Small-Cell Lung Carcinoma" OR "non-small-cell lung cancer" OR NSCLC OR "non small cell" AND lung* AND cancer* OR "Squamous Cell Carcinoma" OR Adenocarcinoma OR "Large Cell Carcinoma"

Other terms box:
(early OR earlier OR earliest) OR (stag* AND (one or 1 or I or two or 2 or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb))

Intervention box:
Radiosurgery OR "stereotactic body radiotherapy" OR SBRT OR "stereotactic body RT" OR "Stereotactic RT" OR "stereotactic ablative radiotherapy" OR SABR

AND INFLECT EXACT ("Adult" OR "Senior") [AGE-GROUP] AND INFLECT ("01/01/2014" : "08/13/2018") [LAST-UPDATE-POSTED]

WHO ICTRP, 8-14-2018

Condition box:
"Non-Small-Cell Lung Carcinoma" OR "non-small-cell lung cancer" OR NSCLC OR "non small cell" AND lung* AND cancer* OR "Squamous Cell Carcinoma" OR Adenocarcinoma OR "Large Cell Carcinoma"

Intervention box:
Radiosurgery OR "stereotactic body radiotherapy" OR SBRT OR "stereotactic body RT" OR "Stereotactic RT" OR "stereotactic ablative radiotherapy" OR SABR

Recruitment status: ALL

Date of registration between: 01/01/2014 and 08/14/2018

Appendix B1. Original Search Strategies and Update Searches

Update searches
SCREENING
PubMed, May 28, 2019

Search	Query	Items found
#1	Search ("Lung Neoplasms"[MeSH] OR NSCLC[tiab] OR "lung cancer"[tiab] OR "lung cancers" [tiab] OR "lung-cancer"[tiab] OR "lung malignancy"[tiab] OR "lung malignancies"[tiab] OR "lung nodule"[tiab] OR "lung nodules" [tiab] OR "pulmonary nodule"[tiab] OR "pulmonary nodules"[tiab] OR "lung mass"[tiab] OR "lung masses"[tiab] OR ("Squamous Cell Carcinoma"[MeSH] OR Adenocarcinoma[MeSH]) and (Lung[MeSH] OR Lung Diseases[MeSH])))	219968
#2	Search ("Mass Screening"[MeSH] OR screen*[tw] OR "Early Diagnosis"[MeSH] OR "Tomography, X-Ray Computed"[Mesh] OR "CT scan"[tiab] OR "CT scans"[tiab] OR "CAT scan"[tiab] OR "CAT scans"[tiab] OR "spiral CT"[tiab] OR "spiral computed tomography"[tiab] OR "low-dose computed tomography"[tiab] OR LDCT[tiab] OR ((early[tiab] or earlier[tiab] or earliest[tiab]) AND (detect*[tiab] or diagnos*[tiab] or discover*[tiab] or find[tiab] or finding[tiab])))	1677161
#3	Search (#1 and #2)	36110
#4	Search (DANTE[tiab] OR "Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays"[All Fields] OR DLCST[tiab] OR "Danish Lung Cancer Screening Trial"[tiab] OR ITALUNG[tiab] OR "Italian Lung Cancer Screening Trial"[All Fields] OR LUSI[tiab] OR "Lung Cancer Screening Intervention"[All Fields] OR MILD[tiab] OR "Multicentric Italian Lung Detection"[All Fields] OR NELSON[tiab] OR "Dutch-Belgian Lung Cancer Screening trial"[All Fields] OR NLST[tiab] OR "National Lung Screening Trial"[All Fields])	327764
#5	Search (#1 and #4)	2806
#6	Search (#3 or #5)	38027
#7	Search (#3 or #5) Filters: Publication date from 2017/04/30 to 2019/12/31	3454
#8	Search ("Risk prediction model"[tw] OR "Risk prediction models"[tw] OR "Risk Assessment"[MeSH] OR "risk assessment"[tw] OR "risk model"[tw] OR "risk models"[tw] OR "Decision Support Techniques"[MeSH] OR "Decision Support Systems, Clinical"[Mesh] OR "clinical prediction"[tw] OR "Logistic Models"[MeSH] OR microsimulation*[tw] OR "simulation model"[tw] OR "simulation models"[tw] OR "Assessment tool"[tw] OR "Assessment tools"[tw] OR "prediction score"[tw] OR "Risk Factors"[MeSH] OR "Predictive Value of Tests"[MeSH] OR "Sensitivity and Specificity"[MeSH] OR (Predict*[tw] AND (model*[tw] OR outcome*[tw] OR risk*[tw] OR rule[tw] OR rules[tw])) OR "risk-targeted"[tw] OR "mortality risk"[tw])	2231663
#9	Search (#1 and #8)	28279
#10	Search (#1 and #8) Filters: Publication date from 2017/04/30 to 2019/12/31	2628
#11	Search (#7 or #10)	5194
#12	Search (#7 or #10) NOT (animals[mh] NOT humans[mh])	5137
#13	Search (#7 or #10) NOT (animals[mh] NOT humans[mh]) Filters: English	4815
#14	Search (#7 or #10) NOT (animals[mh] NOT humans[mh]) Filters: English; Child: birth-18 years	181
#15	Search ((letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt]))	1744651
#16	Search (#13 not #14)	4634
#17	Search (#16 not #15)	4476
#18	Search ("systematic review"[ti] OR "meta-analysis"[pt] OR "meta-analysis"[ti] OR "systematic literature review"[ti] OR "this systematic review"[tw] OR ("systematic review"[tiab] AND review[pt]) OR meta synthesis[ti] OR "meta synthesis"[ti] OR "cochrane database syst rev"[ta])	208402
#19	Search (#17 and #18)	**159**
#20	Search "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH] OR ((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract])	656996
#21	Search (#17 and #20)	**118**
#22	Search ("Case-Control Studies"[MeSH] OR "Cohort Studies"[MeSH] OR "Epidemiologic Studies"[MeSH] OR "Follow-Up Studies"[MeSH] OR "Evaluation Studies"[Publication Type] OR "Program Evaluation"[MeSH] OR "observational study"[tw] OR "observational studies"[tw] OR "Cohort Studies"[MeSH] OR "Comparative Study"[pt] OR "Validation Studies"[pt] OR "Prospective Studies"[MeSH] OR "cohort"[tw] OR "case control"[tw])	4286922
#23	Search (#17 and #22)	**1908**

Appendix B1. Original Search Strategies and Update Searches

Cochrane Library, May 28, 2019

ID	Cochrane Library Search	Hits
#1	[mh "Lung Neoplasms"] or NSCLC:ti,ab or "lung cancer":ti,ab or "lung cancers":ti,ab or "lung-cancer":ti,ab or "lung malignancy":ti,ab or "lung malignancies":ti,ab or "lung nodule":ti,ab or "lung nodules":ti,ab or "pulmonary nodule":ti,ab or "pulmonary nodules":ti,ab or "lung mass":ti,ab or "lung masses":ti,ab or (([mh "Squamous Cell Carcinoma"] or [mh Adenocarcinoma]) and ([mh Lung] or [mh "Lung Diseases"]))	18607
#2	[mh "Mass Screening"] or screen*:kw or [mh "Early Diagnosis"] or [mh "Tomography, X-Ray Computed"] or "CT scan":ti,ab or "CT scans":ti,ab or "CAT scan":ti,ab or "CAT scans":ti,ab or "spiral CT":ti,ab or "spiral computed tomography":ti,ab or "low-dose computed tomography":ti,ab or LDCT:ti,ab or ((early:ti,ab or earlier:ti,ab or earliest:ti,ab) and (detect*:ti,ab or diagnos*:ti,ab or discover*:ti,ab or find:ti,ab or finding:ti,ab))	51662
#3	#1 and #2	1757
#4	DANTE:ti,ab or "Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays" or DLCST:ti,ab or "Danish Lung Cancer Screening Trial":ti,ab or ITALUNG:ti,ab or "Italian Lung Cancer Screening Trial" or LUSI:ti,ab or "Lung Cancer Screening Intervention" or MILD:ti,ab or "Multicentric Italian Lung Detection" or NELSON:ti,ab or "Dutch-Belgian Lung Cancer Screening trial" or NLST:ti,ab or "National Lung Screening Trial":kw	55900
#5	#1 and #4	643
#6	#3 or #5	2126
#7	#6 Publication Year from April 2017 to 2019	948
#8	"Risk prediction model":ti,ab,kw or "Risk prediction models":ti,ab,kw or [mh "Risk Assessment"] or "risk assessment":ti,ab,kw or "risk model":ti,ab,kw or "risk models":ti,ab,kw or [mh "Decision Support Techniques"] or [mh "Decision Support Systems, Clinical"] or "clinical prediction":ti,ab,kw or [mh "Logistic Models"] or microsimulation*:ti,ab,kw or "simulation model":ti,ab,kw or "simulation models":ti,ab,kw or "Assessment tool":ti,ab,kw or "Assessment tools":ti,ab,kw or "prediction score":ti,ab,kw or [mh "Risk Factors"] or [mh "Predictive Value of Tests"] or [mh "Sensitivity and Specificity"] or (Predict*:ti,ab,kw and (model*:ti,ab,kw or outcome*:ti,ab,kw or risk*:ti,ab,kw or rule:ti,ab,kw or rules:ti,ab,kw)) or "risk-targeted":ti,ab,kw or "mortality risk":ti,ab,kw	114475
#9	#1 and #8	1868
#10	#9 Publication Year from April 2017 to 2019	748
#11	#7 or #10	1514
#12	child:ti or child:ab or child:kw or children:ti or children:ab or children:kw or adolescen*:ti or adolescen*:ab or adolescen*:kw or teen:ti or teen:ab or teen:kw or teens:ti or teens:ab or teens:kw or teenage*:ti or teenage*:ab or teenage*:kw or youth:ti or youth:ab or youth:kw or youths:ti or youths:ab or youths:kw or pediatric*:ti or pediatric*:ab or pediatric*:kw or paediatric*:ti or paediatric*:ab or paediatric*:kw or boys:ti or boys:ab or boys:kw or girls:ti or girls:ti or girls:kw	224306
#13	#11 not #12	1487
#14	#13 in Cochrane Reviews (Reviews and Protocols)	**8**
#15	"randomized controlled trial":pt or "randomized controlled trial":ti or "randomized controlled trial as topic":pt or "single-blind method":pt or "double-blind method":pt or "random allocation":pt	512254
#16	#13 and #15	**160**
#17	[mh "Case-Control Studies"] or [mh "Cohort Studies"] or [mh "Epidemiologic Studies"] or [mh " Follow-Up Studies "] or [mh "Seroepidemiologic Studies"] or "Evaluation Studies":pt or [mh "Program Evaluation"] or "observational study" or "observational studies" or [mh "case-control studies"] or "comparative study":pt or "validation studies":pt or [mh "Prospective Studies"] or "cohort" or "case control"	314610
#18	(#13 and #17) not (#14 or #16) in other study types	**0**

INTERVENTIONS

PubMed, May 28, 2019

Search	Query	Items found
#1	Search ("Carcinoma, Non-Small-Cell Lung"[MeSH] OR "non-small-cell lung cancer"[All Fields] OR NSCLC[tiab] OR ("non small cell"[tiab] AND lung*[tiab] AND cancer*[tiab]) OR "Carcinoma, Squamous Cell"[Mesh] OR Adenocarcinoma[MeSH] OR "Carcinoma, Large Cell"[MeSH])	523587
#2	Search ((stag* AND (one or "1" or I or two or "2" or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)))	895746
#3	Search ((early or earlier or earliest) AND (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging))	941894

Appendix B1. Original Search Strategies and Update Searches

Search	Query	Items found
#4	Search (#2 or #3)	1601919
#5	Search (#1 and #4)	114508
#6	Search (“Margins of Excision”[Mesh] OR Pneumonectomy OR Lobectomy OR (resection* and lung*[tw]))	40469
#7	Search (#5 and #6)	4291
#8	Search (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt])	1744651
#9	Search (#7 not #8)	4226
#10	Search (#9 NOT (animals[mh] NOT humans[mh]))	4225
#11	Search (#9 NOT (animals[mh] NOT humans[mh])) Filters: English	3452
#12	Search (#9 NOT (animals[mh] NOT humans[mh])) Filters: Publication date from 2017/05/01 to 2019/12/31; English	536
#13	Search (#9 NOT (animals[mh] NOT humans[mh])) Filters: Publication date from 2017/05/01 to 2019/12/31; English; Child: birth-18 years	18
#14	Search (#12 not #13)	518
#15	Search ((“systematic review”[ti] OR “meta-analysis”[pt] OR “meta-analysis”[ti] OR “systematic literature review”[ti] OR “this systematic review”[tw] OR (“systematic review”[tiab] AND review[pt]) OR meta synthesis[ti] OR “meta synthesis”[ti] OR “cochrane database syst rev”[ta]))	208402
#16	Search (#14 and #15)	**15**
#17	Search (“Randomized Controlled Trial”[Publication Type] OR “Single-Blind Method”[MeSH] OR “Double-Blind Method”[MeSH] OR “Random Allocation”[MeSH] OR ((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]))	656996
#18	Search (#14 and #17)	**13**
#19	Search (“Case-Control Studies”[MeSH] OR “Cohort Studies”[MeSH] OR “Epidemiologic Studies”[MeSH] OR “Follow-Up Studies”[MeSH] OR “Evaluation Studies”[Publication Type] OR “Program Evaluation”[MeSH] OR “observational study”[tw] OR “observational studies”[tw] OR “Cohort Studies”[MeSH] OR “Comparative Study”[pt] OR “Validation Studies”[pt] OR “Prospective Studies”[MeSH] OR “cohort”[tw] OR “case control”[tw])	4286922
#20	Search (#14 and #19)	**286**

Appendix B1. Original Search Strategies and Update Searches

Cochrane Library, May 28, 2019

ID	Search	Hits
#1	[mh “Carcinoma, Non-Small-Cell Lung”] or “non-small-cell lung cancer” or NSCLC:ti,ab or (“non small cell”:ti,ab and lung*:ti,ab and cancer*:ti,ab) or [mh “Carcinoma, Squamous Cell”] or [mh Adenocarcinoma] or [mh “Carcinoma, Large Cell”]	20425
#2	stag* and (one or “1” or I or two or “2” or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)	85688
#3	(early or earlier or earliest) and (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging)	62072
#4	#2 or #3	125155
#5	#1 and #4	8538
#6	([mh “Margins of Excision”] or Pneumonectomy or Lobectomy or (resection* and lung*:ti,ab,kw))	3692
#7	#5 and #6	900
#8	letter:pt or newspaper article:pt or editorial:pt or comment:pt	14366
#9	#7 not #8	897
#10	child:ti or child:ab or child:kw or children:ti or children:ab or children:kw or adolescen*:ti or adolescen*:ab or adolescen*:kw or teen:ti or teen:ab or teen:kw or teens:ti or teens:ab or teens:kw or teenage*:ti or teenage*:ab or teenage*:kw or youth:ti or youth:ab or youth:kw or youths:ti or youths:ab or youths:kw or pediatric*:ti or pediatric*:ab or pediatric*:kw or paediatric*:ti or paediatric*:ab or paediatric*:kw or boys:ti or boys:ab or boys:kw or girls:ti or girls:ti or girls:kw	224306
#11	#9 not #10	880
#12	#11 Publication Year from 2017 to 2019, in Cochrane Reviews, Cochrane Protocols	**9**
#13	“randomized controlled trial”:pt or “randomized controlled trial”:ti or “randomized controlled trial as topic”:pt or “single-blind method”:pt or “double-blind method”:pt or “random allocation”:pt	512254
#14	#11 and #13 Publication Year from 2017 to 2019, in Trials	**30**
#15	[mh “Case-Control Studies”] or [mh “Cohort Studies”] or [mh “Epidemiologic Studies”] or [mh “ Follow-Up Studies “] or [mh “Seroepidemiologic Studies”] or “Evaluation Studies”:pt or [mh “Program Evaluation”] or “observational study” or “observational studies” or [mh “case-control studies”] or “comparative study”:pt or “validation studies”:pt or [mh “Prospective Studies”] or “cohort” or “case control”	314610
#16	#11 and #15 publication date from May 2017 to Dec 2019, in Clinical Answers and Special collections	**0**

SBRT-SABR SEARCHES

PubMed, 5-28-19

Search	Query	Items found
#1	Search ((“Carcinoma, Non-Small-Cell Lung”[MeSH] OR “non-small-cell lung cancer”[All Fields] OR NSCLC[tiab] OR (“non small cell”[tiab] AND lung*[tiab] AND cancer*[tiab]) OR “Carcinoma, Squamous Cell”[Mesh] OR Adenocarcinoma[MeSH] OR “Carcinoma, Large Cell”[MeSH]))	523587
#2	Search (stag* AND (one or “1” or I or two or “2” or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb))	895746
#3	Search ((early or earlier or earliest) AND (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging))	941894
#4	Search (#2 or #3)	1601919
#5	Search (#1 and #4)	114508
#6	Search (“Radiosurgery”[Mesh] OR “stereotactic body radiotherapy” OR SBRT[tw] OR “stereotactic body RT” OR “Stereotactic RT” OR “stereotactic ablative radiotherapy” OR SABR[tw])	15921
#7	Search ((#5 and #6))	1217
#8	Search (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt])	1744651
#9	Search (#7 not #8)	1176
#10	Search (#9 NOT (animals[mh] NOT humans[mh]))	1174
#11	Search (#9 NOT (animals[mh] NOT humans[mh])) Filters: English	1117
#12	Search (#9 NOT (animals[mh] NOT humans[mh])) Filters: Publication date from 2017/08/10 to 2019/12/31; English	253
#13	Search (((“systematic review”[ti] OR “meta-analysis”[pt] OR “meta-analysis”[ti] OR “systematic literature review”[ti] OR “this systematic review”[tw] OR (“systematic review”[tiab] AND review[pt]) OR meta synthesis[ti] OR “meta synthesis”[ti] OR “cochrane database syst rev”[ta]))	208402
#14	Search (#12 and #13)	**7**
#15	Search (“Randomized Controlled Trial”[Publication Type] OR “Single-Blind Method”[MeSH] OR “Double-Blind Method”[MeSH] OR “Random Allocation”[MeSH] OR ((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]))	656996
#16	Search (#12 and #15)	**5**
#17	Search (“Case-Control Studies”[MeSH] OR “Cohort Studies”[MeSH] OR “Epidemiologic Studies”[MeSH] OR “Follow-Up Studies”[MeSH] OR “Evaluation Studies”[Publication Type] OR “Program Evaluation”[MeSH] OR “observational study”[tw] OR “observational studies”[tw] OR “Cohort Studies”[MeSH] OR “Comparative Study”[pt] OR “Validation Studies”[pt] OR “Prospective Studies”[MeSH] OR “cohort”[tw] OR “case control”[tw])	4286922
#18	Search (#12 and #17)	**108**

Cochrane Library, 5-28-19, SABR search

ID	Search	Hits
#1	[mh "Carcinoma, Non-Small-Cell Lung"] or "non-small-cell lung cancer" or NSCLC:ti,ab or ("non small cell":ti,ab and lung*:ti,ab and cancer*:ti,ab) or [mh "Carcinoma, Squamous Cell"] or [mh Adenocarcinoma] or [mh "Carcinoma, Large Cell"]	20425
#2	stag* and (one or "1" or I or two or "2" or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb)	85688
#3	(early or earlier or earliest) and (discover* or found or find or finding or uncover* or diagnos* or detect* or stage* or staging)	62072
#4	#2 or #3	125155
#5	#1 and #4	8538
#6	[mh "Radiosurgery"] OR "stereotactic body radiotherapy" OR SBRT:ti,ab,kw OR "stereotactic body RT" OR "Stereotactic RT" OR "stereotactic ablative radiotherapy" OR SABR:ti,ab,kw	779
#7	#5 and #6	170
#8	letter:pt or newspaper article:pt or editorial:pt or comment:pt	14366
#9	#7 not #8	169
#10	child:ti or child:ab or child:kw or children:ti or children:ab or children:kw or adolescen*:ti or adolescen*:ab or adolescen*:kw or teen:ti or teen:ab or teen:kw or teens:ti or teens:ab or teens:kw or teenage*:ti or teenage*:ab or teenage*:kw or youth:ti or youth:ab or youth:kw or youths:ti or youths:ab or youths:kw or pediatric*:ti or pediatric*:ab or pediatric*:kw or paediatric*:ti or paediatric*:ab or paediatric*:kw or boys:ti or boys:ab or boys:kw or girls:ti or girls:ti or girls:kw	224306
#11	#9 not #10 with Cochrane Library publication date from Jan 2014 to Dec 2019	163
#12	#11 in in Cochrane Reviews and Cochrane Protocols	**4**
#13	"randomized controlled trial":pt or "randomized controlled trial":ti or "randomized controlled trial as topic":pt or "single-blind method":pt or "double-blind method":pt or "random allocation":pt	512254
#14	#11 and #13	**17**
#15	[mh "Case-Control Studies"] or [mh "Cohort Studies"] or [mh "Epidemiologic Studies"] or [mh " Follow-Up Studies "] or [mh "Seroepidemiologic Studies"] or "Evaluation Studies":pt or [mh "Program Evaluation"] or "observational study" or "observational studies" or [mh "case-control studies"] or "comparative study":pt or "validation studies":pt or [mh "Prospective Studies"] or "cohort" or "case control"	314610
#16	(#11 and #15) NOT (#12 or #14) in Cochrane Reviews, Cochrane Protocols, Trials, Clinical Answers and Special collections	**19**

Lung Cancer Gray Literature Updates, May 28, 2019

SCREENING

ClinicalTrials.gov, May 28, 2019

436 results

"Other terms" search box**:**

(screen* OR "Early Diagnosis" OR "X-Ray Computed Tomography" OR "CT scan" OR "CT scans" OR "CAT scan" OR "CAT scans" OR "spiral CT" OR "spiral computed tomography" OR "low-dose computed tomography" OR LDCT OR ((early or earlier or earliest) AND (detect* or diagnos* or discover* or find or finding)) OR DANTE OR "Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays" OR DLCST OR "Danish Lung Cancer Screening Trial" OR ITALUNG OR "Italian Lung Cancer Screening Trial" OR LUSI OR "Lung Cancer Screening Intervention" OR "Multicentric Italian Lung Detection" OR NELSON and Trial* OR "Dutch-Belgian Lung Cancer Screening trial" OR NLST OR "National Lung Screening Trial")

Disease search box:

("Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung-cancer" OR "lung malignancy" OR "lung malignancies" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR (("Squamous Cell Carcinoma" OR Adenocarcinoma) AND lung*))

Limit to age groups checkboxes for Adult and Older Adults

Last update posted 05/01/2018 – 05/28/2018

WHO ICTRP, May 28, 2019
51 results
Title box:
screen* OR "Early Diagnosis" OR "X-Ray Computed Tomography" OR "CT scan" OR "CT scans" OR "CAT scan" OR "CAT scans" OR "spiral CT" OR "spiral computed tomography" OR "low-dose computed tomography" OR LDCT OR ((early or earlier or earliest) AND (detect* or diagnos* or discover* or find or finding)) OR DANTE OR "Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays" OR DLCST OR "Danish Lung Cancer Screening Trial" OR ITALUNG OR "Italian Lung Cancer Screening Trial" OR LUSI OR "Lung Cancer Screening Intervention" OR "Multicentric Italian Lung Detection" OR (NELSON and Trial*) OR "Dutch-Belgian Lung Cancer Screening trial" OR NLST OR "National Lung Screening Trial"
Condition box:
"Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung malignancy" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR "Squamous Cell Carcinoma" OR Adenocarcinoma
Recruitment Status: ALL
Limited to trials registered between May 1, 2018 – May 28, 2019
INTERVENTIONS
ClinicalTrials.gov, May 28, 2019
40 results
Condition box:
"Non-Small-Cell Lung Carcinoma" OR "non-small-cell lung cancer" OR NSCLC OR "non small cell" AND lung* AND cancer* OR "Squamous Cell Carcinoma" OR Adenocarcinoma OR "Large Cell Carcinoma"
Other terms box:
(early OR earlier OR earliest) OR (stag* AND (one or 1 or I or two or 2 or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb))
Intervention box:
"Margins of Excision" OR Pneumonectomy OR Lobectomy OR (resection* and lung*)
Limit to age groups checkboxes for Adult and Older Adult
Last update posted 05/01/2018 – 05/28/2019
WHO ICTRP, May 28, 2019
26 results
Condition box:
"Lung Neoplasms" OR NSCLC OR "lung cancer" OR "lung cancers" OR "lung malignancy" OR "lung nodule" OR "lung nodules" OR "pulmonary nodule" OR "pulmonary nodules" OR "lung mass" OR "lung masses" OR "Squamous Cell Carcinoma" OR Adenocarcinoma
Intervention box:
"Margins of Excision" OR Pneumonectomy OR Lobectomy OR (resection* and lung*)
Recruitment Status: ALL
Limited to trials registered between May 1, 2018 – May 28, 2019

SBRT-SABR
ClinicalTrials.gov, May 28, 2019
55 results

Condition box
"Non-Small-Cell Lung Carcinoma" OR "non-small-cell lung cancer" OR NSCLC OR "non small cell" AND lung* AND cancer* OR "Squamous Cell Carcinoma" OR Adenocarcinoma OR "Large Cell Carcinoma"
Other terms box:
(early OR earlier OR earliest) OR (stag* AND (one or 1 or I or two or 2 or II or 1a or Ia or 1b or Ib or 1c or Ic or 2a or IIa or 2b or IIb))
Intervention box:
Radiosurgery OR "stereotactic body radiotherapy" OR SBRT OR "stereotactic body RT" OR "Stereotactic RT" OR "stereotactic ablative radiotherapy" OR SABR
Limit to age groups checkboxes for Adult and Older Adults
Last update posted 05/01/2018 – 05/28/2018
WHO ICTRP, May 28, 2019
87 results
Condition box:
"Non-Small-Cell Lung Carcinoma" OR "non-small-cell lung cancer" OR NSCLC OR "non small cell" AND lung* AND cancer* OR "Squamous Cell Carcinoma" OR Adenocarcinoma OR "Large Cell Carcinoma"
Intervention box:
Radiosurgery OR "stereotactic body radiotherapy" OR SBRT OR "stereotactic body RT" OR "Stereotactic RT" OR "stereotactic ablative radiotherapy" OR SABR
Recruitment status: ALL
Date of registration between: 05/01/2018 – 05/28/2018

Appendix B2. Eligibility Criteria

	Include	Exclude
Populations	**KQs 1–5, 8:** Asymptomatic adults (age ≥18 years) **KQs 6, 7:** Adults (age ≥18 years) with early (Stage I) non-small cell lung cancer	**KQs 1–5, 8:** Children, persons with symptoms or prior diagnosis of lung cancer **KQs 6, 7**: Children, persons with nonprimary lung cancer or other than Stage I lung cancer
Risk prediction	**KQ 2:** Externally validated models including demographic variables, clinical variables, or biomarkers intended for identifying persons at increased risk who are more likely to benefit from screening	**KQ 2:** Models including a single variable or biomarker, models not considering smoking and age (known risk factors for lung cancer)
Screening	**KQs 1, 3, 4, 8:** LDCT*	**KQs 1, 3, 4, 8:** No screening, chest X-ray, sputum cytology, and other screening modalities
Workup or surveillance	**KQ 5:** Computed tomography, biopsy, positron emission tomography, or other tests used after screening	Not applicable
Interventions	**KQs 6, 7:** Surgical resection or SBRT	**KQs 6, 7:** Chemotherapy, natural therapies, immunotherapy, or targeted molecular therapy
Comparisons	**KQs 1, 8:** Chest X-ray, no screening, or usual care **KQ 2:** 2013 USPSTF recommendations or criteria used by trials showing benefit (e.g., NLST) **KQ 3:** • There is no single gold standard for assessing accuracy • Comparison (reference standard) could be subsequent diagnosis of lung cancer within 1 year (likely resulting from repeat imaging and subsequent biopsy), biopsy, or subsequent imaging • Sensitivity and false-negative screens (false reassurance): Typically determined by considering new lung cancer presenting within 1 year of a normal screening study as false-negative screens • Specificity and false-positive screens: Initial positive LDCT result that is found to be benign with tissue diagnosis or subsequent imaging **KQs 4, 5:** Chest X-ray, no screening, usual care, or no comparison group **KQs 6, 7:** No comparison group is required; although the review did not assess comparative effectiveness of treatments, comparative effectiveness studies were eligible if they provided data for eligible populations, interventions, and outcomes and met the other eligibility criteria	**KQs 1–3, 8:** Studies without a comparison group

Appendix B2. Eligibility Criteria

	Include	Exclude
Outcomes	**KQ 1a:** Incidence of lung cancer (all stages), distribution of lung cancer types and stages **KQ 1b:** All-cause mortality, lung cancer mortality, quality of life, or functional status **KQ 2:** Estimated number of deaths from lung cancer or all-cause mortality that can be prevented by screening, estimated screening effectiveness (e.g., number needed to screen), or estimated screening harms **KQ 3:** Sensitivity, specificity, and predictive value **KQ 4:** Radiation exposure, false-positive results, overdiagnosis,† smoking cessation rates, psychosocial harms, incidental findings leading to additional tests and subsequent harms, and unnecessary treatment (e.g., surgical resection for a benign nodule) **KQ 5**: Radiation exposure, false-positive results, overdiagnosis,† smoking cessation rates, psychosocial harms, incidental findings leading to additional tests and subsequent harms, unnecessary treatment (e.g., surgical resection for a benign nodule), and harms of workup (e.g., biopsy leading to an adverse event) **KQ 6:** 5- and 10-year incidence of advanced disease and mortality (survival rates) **KQ 7:** Harms of treatment, including mortality, infection, bleeding, bronchopleural fistula, and respiratory failure **KQ 8:** All-cause and lung cancer mortality	Costs
Study designs	All KQs: Controlled trials **KQ 2:** Modeling studies are also eligible, clinical prediction tools must include multiple factors **KQ 3:** Studies evaluating accuracy are also eligible **KQs 4, 5, 7:** Prospective cohort and case-control studies are also eligible **KQ 6:** Prospective cohort studies are also eligible	All other study designs‡ **KQ 2:** Models including a single variable or biomarker, models not considering smoking and age (known risk factors for lung cancer) **KQs 1–5, 8:** Studies with a sample size less than 1,000 **KQs 6, 7:** For surgery (established standard treatment), studies with a sample size less than 500; for SBRT, no limit on sample size
Study duration	**KQs 1–5, 7, 8:** Any length of time **KQ 6:** At least 5 years of followup	**KQ 6:** Less than 5 years of followup
Settings	Published in or after 2001	
Countries	Studies conducted in countries categorized as “Very High” on the 2016 Human Development Index (as defined by the United Nations Development Programme)	Studies conducted in countries that are not categorized as “Very High” on the 2016 Human Development Index
Language	English	Languages other than English
Study quality	Good or fair quality	Poor quality (according to design-specific USPSTF criteria)

* The review focused on computed tomography but also searched for and allowed for inclusion of new trials (published since the search cutoff dates of the last review) of other screening modalities. Older studies (before 2013) of other screening modalities were not carried forward to this update.

† Defined as detection of disease that would never progress to produce symptoms or death.

‡ Systematic reviews are excluded from the evidence review. However, separate searches were conducted to identify relevant systematic reviews, and the citations of all studies included in those systematic reviews were reviewed to ensure that database searches captured all relevant primary studies.

Abbreviations: KQ=key question; LDCT=low-dose computed tomography; NLST=National Lung Screening Trial; SBRT=stereotactic body radiotherapy; USPSTF=U.S. Preventive Services Task Force.

Randomized, Controlled Trials and Cohort Studies

Criteria

- Initial assembly of comparable groups
- Randomized, controlled trials (RCTs)—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; cohort studies—consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, crossovers, adherence, and contamination)
- Important differential loss to followup or overall high loss to followup
- Measurements that are equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: Adjustment for potential confounders for cohort studies or intention-to-treat analysis for RCTs; for cluster RCTs, correction for correlation coefficient

Definition of Ratings Based on Above Criteria

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (followup ≥80%); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention is given to confounders in analysis. In addition, intention-to-treat analysis is used for RCTs.

Fair: Studies will be graded "fair" if any or all of the following problems occur without the important limitations noted in the "poor" category below: Generally comparable groups are assembled initially, but some question remains on whether some (although not major) differences occurred in followup; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention-to-treat analysis is lacking for RCTs.

Poor: Studies will be graded "poor" if any of the following major limitations exist: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. Intention-to-treat analysis is lacking for RCTs.

Sources: U.S. Preventive Services Task Force. U.S. Preventive Services Task Force, Procedure Manual, Appendix VI. Rockville, MD: U.S. Preventive Services Task Force; 2015[51]

Diagnostic Accuracy Studies

Criteria:

- Screening test relevant, available for primary care, and adequately described
- Credible reference standard, performed regardless of test results
- Reference standard interpreted independently of screening test
- Indeterminate results handled in a reasonable manner
- Spectrum of patients included in study
- Sample size
- Reliable screening test

Definition of Ratings Based on Above Criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; assesses reliability of test; has few or handles indeterminate results in a reasonable manner; includes large number (greater than 100) of broad-spectrum patients with and without disease.

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; has moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients.

Poor: Has a fatal flaw, such as uses inappropriate reference standard; improperly administers screening test; biased ascertainment of reference standard; has very small sample size or very narrow selected spectrum of patients.

Source: U.S. Preventive Services Task Force. U.S. Preventive Services Task Force, Procedure Manual, Appendix VI. Rockville, MD: U.S. Preventive Services Task Force; 2015[51]

Appendix C. Excluded Studies

X1. Non-English
X2. Abstract only
X3. Ineligible population
X4. Ineligible risk prediction model
X5. Ineligible screening modality
X6. Ineligible intervention
X7. Ineligible comparator
X8. Ineligible outcome(s)
X9. Ineligible study design
X10. Ineligible study design
X11. Ineligible sample size
X12. Ineligible duration for KQ 6 (surgery studies)
X13. Ineligible duration for KQ 6 (SBRT/SABR studies)
X14. Eligible, except for country setting
X15. Eligible, except published prior to 2001
X16. Irretrievable
X17. Poor quality

1. How big is too big for lung nodules on screening scans? *BMJ*. 2013 Feb 20;346:f1070. doi: 10.1136/bmj.f1070. PMID: 23427128. E[73]xclusion Code: X2.
2. Who to screen for lung cancer. *BMJ*. 2013 Jul 23;347:f4686. doi: 10.1136/bmj.f4686. PMID: 23882010. Exclusion Code: X10.
3. Quality of life following stereotactic ablative radiation therapy versus surgery for early-stage lung cancer: results from the rosel randomized controlled trial and a systematic review. *International journal of radiation oncology*. 2016;Conference: 58th Annual Meeting of the American Society for Radiation Oncology, ASTRO 2016. United States. 96(2 Supplement 1):S10-S1. doi: 10.1016/j.ijrobp.2016.06.039. PMID: CN-01448175. Exclusion Code: X2.
4. Abdelsattar ZM, Allen MS, Shen KR, et al. Variation in hospital adoption rates of video-assisted thoracoscopic lobectomy for lung cancer and the effect on outcomes. *Ann Thorac Surg*. 2017 Feb;103(2):454-60. doi: 10.1016/j.athoracsur.2016.08.091. PMID: 27825690. Exclusion Code: X3.
5. Abdelsattar ZM, Shen KR, Yendamuri S, et al. Outcomes after sleeve lung resections versus pneumonectomy in the United States. *Ann Thorac Surg*. 2017 Nov;104(5):1656-64. doi: 10.1016/j.athoracsur.2017.05.086. PMID: 28935348. Exclusion Code: X3.
6. Abdul Rahim M, North J, Costello S. Stereotactic ablative radiotherapy for inoperable early stage non-small cell lung cancer-Dunedin experience. *J Med Imaging Radiat Oncol*. 2013;57:120-. doi: 10.1111/1754-9485.12121. PMID: CN-01011012. Exclusion Code: X2.
7. Abdulla S, Salavati A, Saboury B, et al. Quantitative assessment of global lung inflammation following radiation therapy using FDG PET/CT: a pilot study. *Eur J Nucl Med Mol Imaging*. 2014 Feb;41(2):350-6. doi: 10.1007/s00259-013-2579-4. PMID: 24085504. Exclusion Code: X3.
8. Abe J, Okazaki T, Kikuchi N, et al. Preoperative bronchoscopic cancer confirmation does not increase risk of recurrence in stage1A non-small cell lung cancer. *Gen Thorac Cardiovasc Surg*. 2018 May;66(5):284-90. doi: 10.1007/s11748-018-0909-y. PMID: 29564776. Exclusion Code: X8.
9. Abe T, Shirai K, Saitoh J, et al. Incidence, risk factors, and dose-volume relationship of radiation-induced rib fracture after carbon ion radiotherapy for lung cancer. *Acta Oncol*. 2016;55(2):163-6. doi: 10.3109/0284186x.2015.1088169. PMID: 26399488. Exclusion Code: X6.

10. Aberle DR, Adams AM, Berg CD, et al. Baseline characteristics of participants in the randomized national lung screening trial. *J Natl Cancer Inst*. 2010 Dec 1;102(23):1771-9. doi: 10.1093/jnci/djq434. PMID: 21119104. Exclusion Code: X8.
11. Abramyuk A, Appold S, Zophel K, et al. Quantitative modifications of TNM staging, clinical staging and therapeutic intent by FDG-PET/CT in patients with non small cell lung cancer scheduled for radiotherapy--a retrospective study. *Lung Cancer*. 2012 Nov;78(2):148-52. doi: 10.1016/j.lungcan.2012.08.001. PMID: 22922126. Exclusion Code: X3.
12. Accordino MK, Wright JD, Buono D, et al. Trends in use and safety of image-guided transthoracic needle biopsies in patients with cancer. *J Oncol Pract*. 2015 May;11(3):e351-9. doi: 10.1200/jop.2014.001891. PMID: 25604594. Exclusion Code: X3.
13. Adebahr S, Collette S, Shash E, et al. LungTech, an EORTC Phase II trial of stereotactic body radiotherapy for centrally located lung tumours: a clinical perspective. *Br J Radiol*. 2015 Jul;88(1051):20150036. doi: 10.1259/bjr.20150036. PMID: 25873481. Exclusion Code: X10.
14. Advani M, Purohit G, Vyas S, et al. Comparison of Diagnostic Potential of Narrow Band Imaging Bronchoscopy Over White Light Bronchoscopy in Lung Cancer. *J Bronchology Interv Pulmonol*. 2018 Apr;25(2):132-6. doi: 10.1097/lbr.0000000000000469. PMID: 29346246. Exclusion Code: X3.
15. Agostini P, Lugg ST, Adams K, et al. Postoperative pulmonary complications and rehabilitation requirements following lobectomy: a propensity score matched study of patients undergoing video-assisted thoracoscopic surgery versus thoracotomydagger. *Interact Cardiovasc Thorac Surg*. 2017 Jun 1;24(6):931-7. doi: 10.1093/icvts/ivx002. PMID: 28329213. Exclusion Code: X3.
16. Agostini PJ, Lugg ST, Adams K, et al. Risk factors and short-term outcomes of postoperative pulmonary complications after VATS lobectomy. *J Cardiothorac Surg*. 2018 Apr 12;13(1):28. doi: 10.1186/s13019-018-0717-6. PMID: 29673386. Exclusion Code: X11.
17. Agzarian J, Hanna WC, Schneider L, et al. Postdischarge venous thromboembolic complications following pulmonary oncologic resection: An underdetected problem. *J Thorac Cardiovasc Surg*. 2016 Apr;151(4):992-9. doi: 10.1016/j.jtcvs.2015.11.038. PMID: 26707765. Exclusion Code: X3.
18. Ahmed N, Hasan S, Schumacher L, et al. Stereotactic body radiotherapy for central lung tumors: Finding the balance between safety and efficacy in the "no fly" zone. *Thorac Cancer*. 2018 Oct;9(10):1211-4. doi: 10.1111/1759-7714.12764. PMID: 30095228. Exclusion Code: X3.
19. Ahn H, Lee KW, Lee KH, et al. Effect of computed tomography window settings and reconstruction plane on 8th edition T-stage classification in patients with lung adenocarcinoma manifesting as a subsolid nodule. *Eur J Radiol*. 2018 Jan;98:130-5. doi: 10.1016/j.ejrad.2017.11.015. PMID: 29279151. Exclusion Code: X3.
20. Ahn SY, Yoon SH, Yang BR, et al. Risk of pleural recurrence after percutaneous transthoracic needle biopsy in stage I non-small-cell lung cancer. *Eur Radiol*. 2019 Jan;29(1):270-8. doi: 10.1007/s00330-018-5561-5. PMID: 29948086. Exclusion Code: X11.
21. Ai D, Xu G, Feng L, et al. Dexmedetomidine does not reduce atrial fibrillation after lung cancer surgery. *J Cardiothorac Vasc Anesth*. 2015 Apr;29(2):396-401. doi: 10.1053/j.jvca.2014.05.013. PMID: 25440618. Exclusion Code: X3.
22. Akashita S, Tachibana Y, Sakamaki K, et al. Detection of pure ground-glass nodules in the lung by low-dose multi-detector computed tomography, with use of an iterative reconstruction method: a comparison with conventional image reconstruction by the filtered back-projection method. *Jpn J Radiol*. 2015 Mar;33(3):113-21. doi: 10.1007/s11604-014-0384-z. PMID: 25552203. Exclusion Code: X3.
23. Akin H, Olcmen A, Isgorucu O, et al. Approach to patients with chylothorax complicating pulmonary resection. *Thorac Cardiovasc Surg*. 2012 Mar;60(2):135-9. doi: 10.1055/s-0030-1270990. PMID: 21557161. Exclusion Code: X3.

24. Akthar AS, Ferguson MK, Koshy M, et al. Limitations of PET/CT in the detection of occult N1 metastasis in clinical stage I(T1-2aN0) non-small cell lung cancer for staging prior to stereotactic body radiotherapy. *Technol Cancer Res Treat*. 2017 Feb;16(1):15-21. doi: 10.1177/1533034615624045. PMID: 26792491. Exclusion Code: X6.
25. Akthar AS, Koshy M, Ferguson MK, et al. Effect of endoscopic bronchial ultrasound on outcomes for stage i non-small-cell lung cancer patients receiving hypofractionated radiotherapy. *Clin Lung Cancer*. 2018 Mar;19(2):e227-e33. doi: 10.1016/j.cllc.2017.08.003. PMID: 28939097. Exclusion Code: X10.
26. Al-Alao BS, O'Callaghan DS, Gately K, et al. Surgical resection for non-small cell lung cancer: clinical features and outcomes for a consecutive series at an Irish tertiary referral centre. *Ir J Med Sci*. 2013 Jun;182(2):217-25. doi: 10.1007/s11845-012-0863-0. PMID: 23139062. Exclusion Code: X11.
27. Al-Ameri A, Malhotra P, Thygesen H, et al. Risk of malignancy in pulmonary nodules: a validation study of four prediction models. *Lung Cancer*. 2015 Jul;89(1):27-30. doi: 10.1016/j.lungcan.2015.03.018. PMID: 25864782. Exclusion Code: X4.
28. Al-Ameri M, Bergman P, Franco-Cereceda A, et al. Video-assisted thoracoscopic versus open thoracotomy lobectomy: a Swedish nationwide cohort study. *J Thorac Dis*. 2018 Jun;10(6):3499-506. doi: 10.21037/jtd.2018.05.177. PMID: 30069346. Exclusion Code: X3.
29. Albano D, Borghesi A, Bosio G, et al. Pulmonary mucosa-associated lymphoid tissue lymphoma: (18)F-FDG PET/CT and CT findings in 28 patients. *Br J Radiol*. 2017 Nov;90(1079):20170311. doi: 10.1259/bjr.20170311. PMID: 28830222. Exclusion Code: X3.
30. Albers J, Parker W, Kildea J, et al. Chest wall pain following lung stereotactic body radiation therapy using 48Gy in three fractions: A search for predictors. *Cancer Radiother*. 2019 Apr;23(2):98-103. doi: 10.1016/j.canrad.2018.07.140. PMID: 30952561. Exclusion Code: X3.
31. Alberti N, Ferretti G, Buy X, et al. Diaphragmatic hernia after lung percutaneous radiofrequency ablation: incidence and risk factors. *Cardiovasc Intervent Radiol*. 2014 Dec;37(6):1516-22. doi: 10.1007/s00270-014-0854-9. PMID: 24519640. Exclusion Code: X6.
32. Alberts L, El Sharouni SY, Hofman FN, et al. Changes in pulmonary function after stereotactic body radiotherapy and after surgery for stage I and II non-small cell lung cancer, a description of two cohorts. *Anticancer Res*. 2015 Dec;35(12):6773-9. PMID: 26637895. Exclusion Code: X3.
33. Aldrich MC, Mercaldo SF, Sandler KL, et al. Evaluation of USPSTF Lung Cancer Screening Guidelines among African American adult smokers. *JAMA Oncol*. 2019 Jun 27doi: 10.1001/jamaoncol.2019.1402. PMID: 31246249. Exclusion Code: X4.
34. Alexander ES, Machan JT, Ng T, et al. Cost and effectiveness of radiofrequency ablation versus limited surgical resection for stage I non-small-cell lung cancer in elderly patients: is less more? *J Vasc Interv Radiol*. 2013 Apr;24(4):476-82. doi: 10.1016/j.jvir.2012.12.016. PMID: 23462066. Exclusion Code: X11.
35. Alexander M, Evans SM, Stirling RG, et al. The influence of comorbidity and the simplified comorbidity score on overall survival in non-small cell lung cancer-a prospective cohort study. *J Thorac Oncol*. 2016 May;11(5):748-57. doi: 10.1016/j.jtho.2016.01.016. PMID: 26851495. Exclusion Code: X3.
36. Algan O, Confer M, Algan S, et al. Quantitative evaluation of correlation of dose and FDG-PET uptake value with clinical chest wall complications in patients with lung cancer treated with stereotactic body radiation therapy. *J Xray Sci Technol*. 2015;23(6):727-36. doi: 10.3233/xst-150523. PMID: 26756408. Exclusion Code: X3.
37. Ali N, Lifford KJ, Carter B, et al. Barriers to uptake among high-risk individuals declining participation in lung cancer screening: a mixed methods analysis of the UK Lung Cancer Screening (UKLS) trial. *BMJ Open*. 2015 Jul 14;5(7):e008254. doi: 10.1136/bmjopen-2015-008254. PMID: 26173719. Exclusion Code: X8.

38. Alite F, Balasubramanian N, Adams W, et al. Decreased Risk of Radiation Pneumonitis With Coincident Concurrent Use of Angiotensin-converting Enzyme Inhibitors in Patients Receiving Lung Stereotactic Body Radiation Therapy. *Am J Clin Oncol*. 2018 Jun;41(6):576-80. doi: 10.1097/coc.0000000000000324. PMID: 27560156. Exclusion Code: X3.
39. Al-Jaghbeer M, Marcus M, Durkin M, et al. Diagnostic yield of electromagnetic navigational bronchoscopy. *Ther Adv Respir Dis*. 2016 Aug;10(4):295-9. doi: 10.1177/1753465816637053. PMID: 26944363. Exclusion Code: X3.
40. Alshora S, McKee BJ, Regis SM, et al. Adherence to Radiology Recommendations in a Clinical CT Lung Screening Program. *J Am Coll Radiol*. 2018 Feb;15(2):282-6. doi: 10.1016/j.jacr.2017.10.014. PMID: 29289507. Exclusion Code: X8.
41. Altorki NK, Yip R, Hanaoka T, et al. Sublobar resection is equivalent to lobectomy for clinical stage 1A lung cancer in solid nodules. *J Thorac Cardiovasc Surg*. 2014 Feb;147(2):754-62; Discussion 62-4. doi: 10.1016/j.jtcvs.2013.09.065. PMID: 24280722. Exclusion Code: X11.
42. Ambrogi MC, Fanucchi O, Dini P, et al. Wedge resection and radiofrequency ablation for stage I nonsmall cell lung cancer. *Eur Respir J*. 2015 Apr;45(4):1089-97. doi: 10.1183/09031936.00188014. PMID: 25700387. Exclusion Code: X11.
43. Amini A, Yang J, Williamson R, et al. Dose constraints to prevent radiation-induced brachial plexopathy in patients treated for lung cancer. *Int J Radiat Oncol Biol Phys*. 2012 Mar 1;82(3):e391-8. doi: 10.1016/j.ijrobp.2011.06.1961. PMID: 22284035. Exclusion Code: X3.
44. Amir GJ, Lehmann HP. After detection: the improved accuracy of lung cancer assessment using radiologic computer-aided diagnosis. *Acad Radiol*. 2016 Feb;23(2):186-91. doi: 10.1016/j.acra.2015.10.014. PMID: 26616209. Exclusion Code: X9.
45. Amit G, Purdie TG, Levinshtein A, et al. Automatic learning-based beam angle selection for thoracic IMRT. *Med Phys*. 2015 Apr;42(4):1992-2005. doi: 10.1118/1.4908000. PMID: 25832090. Exclusion Code: X3.
46. Anami K, Yamashita S, Yamamoto S, et al. Contralateral mediastinal lymph node micrometastases assessed by video-assisted thoracoscopic surgery in stage I non-small cell left lung cancer. *Eur J Cardiothorac Surg*. 2013 Apr;43(4):778-82. doi: 10.1093/ejcts/ezs415. PMID: 22822105. Exclusion Code: X11.
47. Anand AK, Punnakal AU, Chaudhoory AR, et al. Stereotactic body radiation therapy (SBRT) for lung and liver tumours. *J Indian Med Assoc*. 2012 Jul;110(7):462-4. PMID: 23520671. Exclusion Code: X9.
48. Andersen MB, Harders SW, Ganeshan B, et al. CT texture analysis can help differentiate between malignant and benign lymph nodes in the mediastinum in patients suspected for lung cancer. *Acta Radiol*. 2016 Jun;57(6):669-76. doi: 10.1177/0284185115598808. PMID: 26271125. Exclusion Code: X3.
49. Andratschke N, Zimmermann F, Boehm E, et al. Stereotactic radiotherapy of histologically proven inoperable stage I non-small cell lung cancer: patterns of failure. *Radiother Oncol*. 2011 Nov;101(2):245-9. doi: 10.1016/j.radonc.2011.06.009. PMID: 21724287. Exclusion Code: X11.
50. Andriole GL. Update of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Recent Results Cancer Res*. 2014;202:53-7. doi: 10.1007/978-3-642-45195-9_6. PMID: 24531777. Exclusion Code: X3.
51. Antonoff MB, Hofstetter WL, Correa AM, et al. Clinical prediction of pathologic complete response in superior sulcus non-small cell lung cancer. *Ann Thorac Surg*. 2016 Jan;101(1):211-7. doi: 10.1016/j.athoracsur.2015.06.019. PMID: 26279367. Exclusion Code: X3.
52. Aokage K, Miyoshi T, Ishii G, et al. Clinical and Pathological Staging Validation in the Eighth Edition of the TNM Classification for Lung Cancer: Correlation between Solid Size on Thin-Section Computed Tomography and Invasive Size in Pathological Findings in the New T Classification. *J Thorac Oncol*. 2017 Sep;12(9):1403-12. doi: 10.1016/j.jtho.2017.06.003. PMID: 28627462. Exclusion Code: X3.

53. Aokage K, Okada M, Suzuki K, et al. Is cancer history really an exclusion criterion for clinical trial of lung cancer? Influence of gastrointestinal tract cancer history on the outcomes of lung cancer surgery. *Jpn J Clin Oncol*. 2017 Feb 15;47(2):145-56. doi: 10.1093/jjco/hyw157. PMID: 28173108. Exclusion Code: X11.
54. Aokage K, Yoshida J, Ishii G, et al. Identification of early t1b lung adenocarcinoma based on thin-section computed tomography findings. *J Thorac Oncol*. 2013 Oct;8(10):1289-94. doi: 10.1097/JTO.0b013e31829f6d3b. PMID: 24457240. Exclusion Code: X6.
55. Aoki M, Sato M, Hirose K, et al. Radiation-induced rib fracture after stereotactic body radiotherapy with a total dose of 54-56 Gy given in 9-7 fractions for patients with peripheral lung tumor: impact of maximum dose and fraction size. *Radiat Oncol*. 2015 Apr 22;10:99. doi: 10.1186/s13014-015-0406-8. PMID: 25897487. Exclusion Code: X3.
56. Apostolova I, Rogasch J, Buchert R, et al. Quantitative assessment of the asphericity of pretherapeutic FDG uptake as an independent predictor of outcome in NSCLC. *BMC Cancer*. 2014 Dec 1;14:896. doi: 10.1186/1471-2407-14-896. PMID: 25444154. Exclusion Code: X3.
57. Appel S, Lawrence YR, Goldstein J, et al. Stereotactic ablative body radiation for stage I lung cancer in Israel: a retrospective single-center report. *Isr Med Assoc J*. 2017 Jan;19(1):39-43. PMID: 28457113. Exclusion Code: X10.
58. Aprile V, Bertoglio P, Dini P, et al. Is left upper lobectomy always worthwhile for early stage lung cancer? A comparison between left upper lobectomy, trisegmentectomy, and lingulectomy. *J Surg Oncol*. 2018 Mar;117(4):618-24. doi: 10.1002/jso.24884. PMID: 29049856. Exclusion Code: X11.
59. Arcangeli S, Falcinelli L, Bracci S, et al. Treatment outcomes and patterns of radiologic appearance after hypofractionated image-guided radiotherapy delivered with helical tomotherapy (HHT) for lung tumours. *Br J Radiol*. 2017 Mar;90(1071):20160853. doi: 10.1259/bjr.20160853. PMID: 28256158. Exclusion Code: X6.
60. Argon A, Nart D, Veral A. The value of cytokeratin 5/6, p63 and thyroid transcription factor-1 in adenocarcinoma, squamous cell carcinoma and non-small-cell lung cancer of the lung. *Turk Patoloji Derg*. 2015;31(2):81-8. doi: 10.5146/tjpath.2015.01302. PMID: 25944390. Exclusion Code: X5.
61. Armato SG, 3rd, McNitt-Gray MF, Reeves AP, et al. The Lung Image Database Consortium (LIDC): an evaluation of radiologist variability in the identification of lung nodules on CT scans. *Acad Radiol*. 2007 Nov;14(11):1409-21. doi: 10.1016/j.acra.2007.07.008. PMID: 17964464. Exclusion Code: X3.
62. Armato SG, 3rd, Roberts RY, Kocherginsky M, et al. Assessment of radiologist performance in the detection of lung nodules: dependence on the definition of "truth". *Acad Radiol*. 2009 Jan;16(1):28-38. doi: 10.1016/j.acra.2008.05.022. PMID: 19064209. Exclusion Code: X3.
63. Armato SG, 3rd, Roberts RY, McNitt-Gray MF, et al. The Lung Image Database Consortium (LIDC): ensuring the integrity of expert-defined "truth". *Acad Radiol*. 2007 Dec;14(12):1455-63. doi: 10.1016/j.acra.2007.08.006. PMID: 18035275. Exclusion Code: X3.
64. Arrieta O, Vega-Gonzalez MT, Lopez-Macias D, et al. Randomized, open-label trial evaluating the preventive effect of tetracycline on afatinib induced-skin toxicities in non-small cell lung cancer patients. *Lung Cancer*. 2015 Jun;88(3):282-8. doi: 10.1016/j.lungcan.2015.03.019. PMID: 25882778. Exclusion Code: X3.
65. Arslan S, Yilmaz A, Bayramgurler B, et al. CT- guided transthoracic fine needle aspiration of pulmonary lesions: accuracy and complications in 294 patients. *Med Sci Monit*. 2002 Jul;8(7):Cr493-7. PMID: 12118196. Exclusion Code: X3.
66. Asakura K, Izumi Y, Yamauchi Y, et al. Incidence of pleural recurrence after computed tomography-guided needle biopsy in stage I lung cancer. *PLoS One*. 2012;7(8):e42043. doi: 10.1371/journal.pone.0042043. PMID: 22876299. Exclusion Code: X11.

67. Asakura K, Mitsuboshi S, Tsuji M, et al. Pulmonary arterial enlargement predicts cardiopulmonary complications after pulmonary resection for lung cancer: a retrospective cohort study. *J Cardiothorac Surg*. 2015 Sep 9;10:113. doi: 10.1186/s13019-015-0315-9. PMID: 26353804. Exclusion Code: X11.
68. Ashraf H, de Hoop B, Shaker SB, et al. Lung nodule volumetry: segmentation algorithms within the same software package cannot be used interchangeably. *Eur Radiol*. 2010 Aug;20(8):1878-85. doi: 10.1007/s00330-010-1749-z. PMID: 20306082. Exclusion Code: X3.
69. Asplund SA, Johnsson AA, Vikgren J, et al. Effect of radiation dose level on the detectability of pulmonary nodules in chest tomosynthesis. *Eur Radiol*. 2014 Jul;24(7):1529-36. doi: 10.1007/s00330-014-3182-1. PMID: 24792590. Exclusion Code: X3.
70. Atallah S, Cho BC, Allibhai Z, et al. Impact of pretreatment tumor growth rate on outcome of early-stage lung cancer treated with stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2014 Jul 1;89(3):532-8. doi: 10.1016/j.ijrobp.2014.03.003. PMID: 24929163. Exclusion Code: X13.
71. Attili F, Petrone G, Abdulkader I, et al. Accuracy and inter-observer agreement of the Procore 25 gauge needle for endoscopic ultrasound-guided tissue core biopsy. *Dig Liver Dis*. 2015 Nov;47(11):943-9. doi: 10.1016/j.dld.2015.07.003. PMID: 26216067. Exclusion Code: X3.
72. Avanzo M, Barbiero S, Trovo M, et al. Voxel-by-voxel correlation between radiologically radiation induced lung injury and dose after image-guided, intensity modulated radiotherapy for lung tumors. *Phys Med*. 2017 Oct;42:150-6. doi: 10.1016/j.ejmp.2017.09.127. PMID: 29173909. Exclusion Code: X3.
73. Awais O, Reidy MR, Mehta K, et al. Electromagnetic Navigation Bronchoscopy-Guided Dye Marking for Thoracoscopic Resection of Pulmonary Nodules. *Ann Thorac Surg*. 2016 Jul;102(1):223-9. doi: 10.1016/j.athoracsur.2016.02.040. PMID: 27157054. Exclusion Code: X3.
74. Awano N, Ikushima S, Izumo T, et al. Efficacy and safety of stereotactic body radiotherapy using CyberKnife in Stage I primary lung tumor. *Jpn J Clin Oncol*. 2017 Oct 1;47(10):969-75. doi: 10.1093/jjco/hyx100. PMID: 28981731. Exclusion Code: X10.
75. Axelsson R, Herlin G, Baath M, et al. Role of scintigraphy with technetium-99m depreotide in the diagnosis and management of patients with suspected lung cancer. *Acta Radiol*. 2008 Apr;49(3):295-302. doi: 10.1080/02841850701793777. PMID: 18365818. Exclusion Code: X3.
76. Bach PB, Kattan MW, Thornquist MD, et al. Variations in lung cancer risk among smokers. *J Natl Cancer Inst*. 2003 Mar 19;95(6):470-8. PMID: 12644540. Exclusion Code: X7.
77. Backhus LM, Farjah F, Liang CK, et al. Imaging surveillance and survival for surgically resected non-small-cell lung cancer. *J Surg Res*. 2016 Jan;200(1):171-6. doi: 10.1016/j.jss.2015.06.048. PMID: 26231974. Exclusion Code: X3.
78. Backhus LM, Farjah F, Zeliadt SB, et al. Predictors of imaging surveillance for surgically treated early-stage lung cancer. *Ann Thorac Surg*. 2014 Dec;98(6):1944-51; discussion 51-2. doi: 10.1016/j.athoracsur.2014.06.067. PMID: 25282167. Exclusion Code: X8.
79. Bade M, Bahr V, Brandt U, et al. Effect of smoking cessation counseling within a randomised study on early detection of lung cancer in Germany. *J Cancer Res Clin Oncol*. 2016 May;142(5):959-68. doi: 10.1007/s00432-015-2105-0. PMID: 26814889. Exclusion Code: X8.
80. Bagan P, De Dominicis F, Hernigou J, et al. Complete thoracoscopic lobectomy for cancer: comparative study of three-dimensional high-definition with two-dimensional high-definition video systems dagger. *Interact Cardiovasc Thorac Surg*. 2015 Jun;20(6):820-3. doi: 10.1093/icvts/ivv031. PMID: 25736286. Exclusion Code: X11.
81. Baglietto L, Ponzi E, Haycock P, et al. DNA methylation changes measured in pre-diagnostic peripheral blood samples are associated with smoking and lung cancer risk. *Int J Cancer*. 2017 Jan 1;140(1):50-61. doi: 10.1002/ijc.30431. PMID: 27632354. Exclusion Code: X10.

82. Bahig H, Filion E, Vu T, et al. Severe radiation pneumonitis after lung stereotactic ablative radiation therapy in patients with interstitial lung disease. *Pract Radiat Oncol*. 2016 Sep-Oct;6(5):367-74. doi: 10.1016/j.prro.2016.01.009. PMID: 27068780. Exclusion Code: X10.
83. Bahig H, Filion E, Vu T, et al. Excellent Cancer Outcomes Following Patient-adapted Robotic Lung SBRT But a Case for Caution in Idiopathic Pulmonary Fibrosis. *Technol Cancer Res Treat*. 2015 Dec;14(6):667-76. doi: 10.7785/tcrt.2012.500445. PMID: 24988054. Exclusion Code: X10.
84. Baimatova I, Smith C, Beckert L, et al. Treatment of octogenarians with lung cancer: A single centre audit of treatments and outcomes. *N Z Med J*. 2015 Aug 7;128(1419):29-34. PMID: 26365843. Exclusion Code: X3.
85. Baine MJ, Verma V, Schonewolf CA, et al. Histology significantly affects recurrence and survival following SBRT for early stage non-small cell lung cancer. *Lung Cancer*. 2018 Apr;118:20-6. doi: 10.1016/j.lungcan.2018.01.021. PMID: 29571997. Exclusion Code: X3.
86. Bak SH, Lee HY, Kim JH, et al. Quantitative CT Scanning Analysis of Pure Ground-Glass Opacity Nodules Predicts Further CT Scanning Change. *Chest*. 2016 Jan;149(1):180-91. doi: 10.1378/chest.15-0034. PMID: 26313232. Exclusion Code: X3.
87. Baker RR, Tockman MS, Marsh BR, et al. Screening for bronchogenic carcinoma: the surgical experience. *J Thorac Cardiovasc Surg*. 1979 Dec;78(6):876-82. PMID: 502570. Exclusion Code: X5.
88. Baldvinsson K, Oskarsdottir GN, Orrason AW, et al. Resection rate and operability of elderly patients with non-small cell lung cancer: Nationwide study from 1991 to 2014. *Interact Cardiovasc Thorac Surg*. 2017 May 1;24(5):733-9. doi: 10.1093/icvts/ivw415. PMID: 28329255. Exclusion Code: X3.
89. Baldwin DR, Duffy SW, Wald NJ, et al. UK Lung Screen (UKLS) nodule management protocol: modelling of a single screen randomised controlled trial of low-dose CT screening for lung cancer. *Thorax*. 2011 Apr;66(4):308-13. doi: 10.1136/thx.2010.152066. PMID: 21317179. Exclusion Code: X8.
90. Balekian AA, Tanner NT, Fisher JM, et al. Factors Associated with a Positive Baseline Screening Exam Result in the National Lung Screening Trial. *Ann Am Thorac Soc*. 2016 Sep;13(9):1568-74. doi: 10.1513/AnnalsATS.201602-091OC. PMID: 27387658. Exclusion Code: X8.
91. Baliga S, Bennion N, Richardson KM, et al. Stereotactic Body Radiation Therapy in Unbiopsied PET+ Pulmonary Tumors. *Oncology*. 2014;28(1S)PMID: CN-01010573. Exclusion Code: X2.
92. Bandoh S, Fujita J, Tojo Y, et al. Diagnostic accuracy and safety of flexible bronchoscopy with multiplanar reconstruction images and ultrafast Papanicolaou stain: evaluating solitary pulmonary nodules. *Chest*. 2003 Nov;124(5):1985-92. PMID: 14605077. Exclusion Code: X3.
93. Bang DH, Lim D, Hwang WS, et al. Lateral topography for reducing effective dose in low-dose chest CT. *AJR Am J Roentgenol*. 2013 Jun;200(6):1294-7. doi: 10.2214/ajr.12.9001. PMID: 23701067. Exclusion Code: X3.
94. Banik A, Schwarzer R, Pawlowska I, et al. Women with family cancer history are at risk for poorer physical quality of life and lower self-efficacy: a longitudinal study among men and women with non-small cell lung cancer. *Health Qual Life Outcomes*. 2017 Apr 4;15(1):62. doi: 10.1186/s12955-017-0645-5. PMID: 28376887. Exclusion Code: X8.
95. Barta JA, Henschke CI, Flores RM, et al. Lung cancer diagnosis by fine needle aspiration is associated with reduction in resection of nonmalignant lung nodules. *Ann Thorac Surg*. 2017 Jun;103(6):1795-801. doi: 10.1016/j.athoracsur.2016.11.055. PMID: 28274517. Exclusion Code: X3.
96. Baumann JL, Li M, Poulsen A, et al. Analysis of microsatellite mutations in buccal cells from a case-control study for lung cancer. *Cancer Epidemiol*. 2012 Feb;36(1):e33-9. doi: 10.1016/j.canep.2011.06.003. PMID: 22056752. Exclusion Code: X5.

97. Baumann P, Nyman J, Hoyer M, et al. Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic body radiotherapy. *J Clin Oncol*. 2009 Jul 10;27(20):3290-6. doi: 10.1200/jco.2008.21.5681. PMID: 19414667. Exclusion Code: X11.

98. Baxa J, Matouskova T, Ludvik J, et al. Single-source Dual-energy CT as a Part of (18)F-FDG PET/CT: Direct Comparison of Iodine-related and Metabolic Parameters in Non-small Cell Lung Cancer. *Anticancer Res*. 2018 Jul;38(7):4131-7. doi: 10.21873/anticanres.12704. PMID: 29970540. Exclusion Code: X3.

99. Bayanati H, R ET, Souza CA, et al. Quantitative CT texture and shape analysis: can it differentiate benign and malignant mediastinal lymph nodes in patients with primary lung cancer? *Eur Radiol*. 2015 Feb;25(2):480-7. doi: 10.1007/s00330-014-3420-6. PMID: 25216770. Exclusion Code: X3.

100. Bedetti B, Bertolaccini L, Rocco R, et al. Segmentectomy versus lobectomy for stage I non-small cell lung cancer: a systematic review and meta-analysis. *J Thorac Dis*. 2017 Jun;9(6):1615-23. doi: 10.21037/jtd.2017.05.79. PMID: 28740676. Exclusion Code: X9.

101. Belfiore G, Ronza F, Belfiore MP, et al. Patients' survival in lung malignancies treated by microwave ablation: our experience on 56 patients. *Eur J Radiol*. 2013 Jan;82(1):177-81. doi: 10.1016/j.ejrad.2012.08.024. PMID: 23099201. Exclusion Code: X6.

102. Bellezza G, Vannucci J, Bianconi F, et al. Prognostic implication of aquaporin 1 overexpression in resected lung adenocarcinoma. *Interact Cardiovasc Thorac Surg*. 2017 Dec 1;25(6):856-61. doi: 10.1093/icvts/ivx202. PMID: 29106595. Exclusion Code: X3.

103. Bellinger CR, Khan I, Chatterjee AB, et al. Bronchoscopy Safety in Patients With Chronic Obstructive Lung Disease. *J Bronchology Interv Pulmonol*. 2017 Apr;24(2):98-103. doi: 10.1097/lbr.0000000000000333. PMID: 28005831. Exclusion Code: X3.

104. Bendixen M, Jorgensen OD, Kronborg C, et al. Postoperative pain and quality of life after lobectomy via video-assisted thoracoscopic surgery or anterolateral thoracotomy for early stage lung cancer: a randomised controlled trial. *Lancet Oncol*. 2016 Jun;17(6):836-44. doi: 10.1016/s1470-2045(16)00173-x. PMID: 27160473. Exclusion Code: X11.

105. Bergamo C, Sigel K, Mhango G, et al. Inequalities in lung cancer care of elderly patients with schizophrenia: an observational cohort study. *Psychosom Med*. 2014 Apr;76(3):215-20. doi: 10.1097/psy.0000000000000050. PMID: 24677164. Exclusion Code: X3.

106. Bernatowicz K, Keall P, Mishra P, et al. Quantifying the impact of respiratory-gated 4D CT acquisition on thoracic image quality: a digital phantom study. *Med Phys*. 2015 Jan;42(1):324-34. doi: 10.1118/1.4903936. PMID: 25563272. Exclusion Code: X3.

107. Berrington de Gonzalez A, Kim KP, Berg CD. Low-dose lung computed tomography screening before age 55: estimates of the mortality reduction required to outweigh the radiation-induced cancer risk. *J Med Screen*. 2008;15(3):153-8. doi: 10.1258/jms.2008.008052. PMID: 18927099. Exclusion Code: X4.

108. Berry MF, D'Amico TA, Onaitis MW, et al. Thoracoscopic approach to lobectomy for lung cancer does not compromise oncologic efficacy. *Ann Thorac Surg*. 2014 Jul;98(1):197-202. doi: 10.1016/j.athoracsur.2014.03.018. PMID: 24820392. Exclusion Code: X10.

109. Berry MF, Onaitis MW, Tong BC, et al. Feasibility of hybrid thoracoscopic lobectomy and en-bloc chest wall resection. *Eur J Cardiothorac Surg*. 2012 Apr;41(4):888-92. doi: 10.1093/ejcts/ezr150. PMID: 22219441. Exclusion Code: X3.

110. Berry MF, Yang CJ, Hartwig MG, et al. Impact of Pulmonary Function Measurements on Long-Term Survival After Lobectomy for Stage I Non-Small Cell Lung Cancer. *Ann Thorac Surg*. 2015 Jul;100(1):271-6. doi: 10.1016/j.athoracsur.2015.02.076. PMID: 25986099. Exclusion Code: X3.

111. Berthet JP, Paradela M, Jimenez MJ, et al. Extended sleeve lobectomy: one more step toward avoiding pneumonectomy in centrally located lung cancer. *Ann Thorac Surg*. 2013 Dec;96(6):1988-97. doi: 10.1016/j.athoracsur.2013.07.011. PMID: 24035301. Exclusion Code: X3.
112. Bertolaccini L, Davoli F, Pardolesi A, et al. Conversion due to vascular injury during video-assisted thoracic surgery lobectomy: A multicentre retrospective analysis from the Italian video-assisted thoracic surgery group registry. *Eur J Surg Oncol*. 2019 May;45(5):857-62. doi: 10.1016/j.ejso.2018.12.023. PMID: 30661924. Exclusion Code: X10.
113. Bhandari RP, Stanford JD, Packianathan S, et al. Stereotactic Body Radiation Therapy for Stage I Non-Small Cell Lung Cancer: A Retrospective, Single-Center Study of 55 Patients. *Oncology*. 2016;91(4):194-204. doi: 10.1159/000447540. PMID: 27427761. Exclusion Code: X10.
114. Bhatt AD, El-Ghamry MN, Dunlap NE, et al. Tumor volume change with stereotactic body radiotherapy (SBRT) for early-stage lung cancer: evaluating the potential for adaptive SBRT. *Am J Clin Oncol*. 2015 Feb;38(1):41-6. doi: 10.1097/COC.0b013e318287bd7f. PMID: 24513663. Exclusion Code: X8.
115. Bhatt KM, Tandon YK, Graham R, et al. Electromagnetic Navigational Bronchoscopy versus CT-guided Percutaneous Sampling of Peripheral Indeterminate Pulmonary Nodules: A Cohort Study. *Radiology*. 2018 Mar;286(3):1052-61. doi: 10.1148/radiol.2017170893. PMID: 29156147. Exclusion Code: X3.
116. Biederer J, Ohno Y, Hatabu H, et al. Screening for lung cancer: Does MRI have a role? *Eur J Radiol*. 2017 Jan;86:353-60. doi: 10.1016/j.ejrad.2016.09.016. PMID: 27665148. Exclusion Code: X9.
117. Bilgin Buyukkarabacak Y, Taslak Sengul A, Meydan BC, et al. The risk of tumor cell dissemination in mediastinoscopy: a cytological study. *Turk J Med Sci*. 2015;45(4):872-6. PMID: 26422860. Exclusion Code: X3.
118. Bille A, Ahmad U, Woo KM, et al. Detection of Recurrence Patterns After Wedge Resection for Early Stage Lung Cancer: Rationale for Radiologic Follow-Up. *Ann Thorac Surg*. 2016 Oct;102(4):1067-73. doi: 10.1016/j.athoracsur.2016.04.056. PMID: 27345095. Exclusion Code: X11.
119. Bille A, Okiror L, Skanjeti A, et al. Evaluation of integrated positron emission tomography and computed tomography accuracy in detecting lymph node metastasis in patients with adenocarcinoma vs squamous cell carcinoma. *Eur J Cardiothorac Surg*. 2013 Mar;43(3):574-9. doi: 10.1093/ejcts/ezs366. PMID: 22689182. Exclusion Code: X10.
120. Bille A, Pelosi E, Skanjeti A, et al. Preoperative intrathoracic lymph node staging in patients with non-small-cell lung cancer: accuracy of integrated positron emission tomography and computed tomography. *Eur J Cardiothorac Surg*. 2009 Sep;36(3):440-5. doi: 10.1016/j.ejcts.2009.04.003. PMID: 19464906. Exclusion Code: X3.
121. Bille A, Woo KM, Ahmad U, et al. Incidence of occult pN2 disease following resection and mediastinal lymph node dissection in clinical stage I lung cancer patients. *Eur J Cardiothorac Surg*. 2017 Apr 1;51(4):674-9. doi: 10.1093/ejcts/ezw400. PMID: 28200091. Exclusion Code: X3.
122. Billmeier SE, Ayanian JZ, He Y, et al. Predictors of nursing home admission, severe functional impairment, or death one year after surgery for non-small cell lung cancer. *Ann Surg*. 2013 Mar;257(3):555-63. doi: 10.1097/SLA.0b013e31828353af. PMID: 23386241. Exclusion Code: X3.
123. Binkley MS, King MT, Shrager JB, et al. Pulmonary function after lung tumor stereotactic ablative radiotherapy depends on regional ventilation within irradiated lung. *Radiother Oncol*. 2017 May;123(2):270-5. doi: 10.1016/j.radonc.2017.03.021. PMID: 28460826. Exclusion Code: X10.
124. Binkley MS, Shrager JB, Chaudhuri A, et al. Time course and predictive factors for lung volume reduction following stereotactic ablative radiotherapy (SABR) of lung tumors. *Radiat Oncol*. 2016 Mar 15;11:40. doi: 10.1186/s13014-016-0616-8. PMID: 26975700. Exclusion Code: X10.

125. Bishawi M, Kim B, Moore WH, et al. Pulmonary function testing after stereotactic body radiotherapy to the lung. *Int J Radiat Oncol Biol Phys*. 2012 Jan 1;82(1):e107-10. doi: 10.1016/j.ijrobp.2011.01.037. PMID: 21470798. Exclusion Code: X8.
126. Biswas T, Walker P, Podder T, et al. Effect of race and insurance on the outcome of stage I non-small cell lung cancer. *Anticancer Res*. 2015 Jul;35(7):4243-9. PMID: 26124385. Exclusion Code: X12.
127. Black WC. Overdiagnosis: An underrecognized cause of confusion and harm in cancer screening. *J Natl Cancer Inst*. 2000 Aug 16;92(16):1280-2. PMID: 10944539. Exclusion Code: X10.
128. Black WC, Gareen IF, Soneji SS, et al. Cost-effectiveness of CT screening in the National Lung Screening Trial. *N Engl J Med*. 2014 Nov 06;371(19):1793-802. doi: 10.1056/NEJMoa1312547. PMID: 25372087. Exclusion Code: X8.
129. Blanchon T, Brechot JM, Grenier PA, et al. Baseline results of the Depiscan study: a French randomized pilot trial of lung cancer screening comparing low dose CT scan (LDCT) and chest X-ray (CXR). *Lung Cancer*. 2007 Oct;58(1):50-8. doi: 10.1016/j.lungcan.2007.05.009. PMID: 17624475. Exclusion Code: X11.
130. Bogoni L, Ko JP, Alpert J, et al. Impact of a computer-aided detection (CAD) system integrated into a picture archiving and communication system (PACS) on reader sensitivity and efficiency for the detection of lung nodules in thoracic CT exams. *J Digit Imaging*. 2012 Dec;25(6):771-81. doi: 10.1007/s10278-012-9496-0. PMID: 22710985. Exclusion Code: X11.
131. Bogot NR, Kazerooni EA, Kelly AM, et al. Interobserver and intraobserver variability in the assessment of pulmonary nodule size on CT using film and computer display methods. *Acad Radiol*. 2005 Aug;12(8):948-56. doi: 10.1016/j.acra.2005.04.009. PMID: 16087090. Exclusion Code: X3.
132. Boiselle PM, White CS, Ravenel JG. Computed tomographic screening for lung cancer: current practice patterns at leading academic medical centers. *JAMA Intern Med*. 2014 Feb 1;174(2):286-7. doi: 10.1001/jamainternmed.2013.12693. PMID: 24322527. Exclusion Code: X10.
133. Bollen EC, Goei R, van 't Hof-Grootenboer BE, et al. Interobserver variability and accuracy of computed tomographic assessment of nodal status in lung cancer. *Ann Thorac Surg*. 1994 Jul;58(1):158-62. PMID: 8037515. Exclusion Code: X3.
134. Booth K, Hanna GG, McGonigle N, et al. The mediastinal staging accuracy of 18F-Fluorodeoxyglycose positron emission tomography/computed tomography in non-small cell lung cancer with variable time intervals to surgery. *Ulster Med J*. 2013 May;82(2):75-81. PMID: 24082283. Exclusion Code: X3.
135. Borghesi A, Farina D, Michelini S, et al. Pulmonary adenocarcinomas presenting as ground-glass opacities on multidetector CT: three-dimensional computer-assisted analysis of growth pattern and doubling time. *Diagn Interv Radiol*. 2016 Nov-Dec;22(6):525-33. doi: 10.5152/dir.2016.16110. PMID: 27682741. Exclusion Code: X8.
136. Borst GR, Ishikawa M, Nijkamp J, et al. Radiation pneumonitis in patients treated for malignant pulmonary lesions with hypofractionated radiation therapy. *Radiother Oncol*. 2009 Jun;91(3):307-13. doi: 10.1016/j.radonc.2009.02.003. PMID: 19321217. Exclusion Code: X3.
137. Bosinceanu M, Sandu C, Ionescu LR, et al. Clinical-epidemiological study on the incidence of postoperative complications after pulmonary resection for lung cancer. *Rev Med Chir Soc Med Nat Iasi*. 2014 Oct-Dec;118(4):1040-6. PMID: 25581967. Exclusion Code: X3.
138. Botling J, Edlund K, Lohr M, et al. Biomarker discovery in non-small cell lung cancer: integrating gene expression profiling, meta-analysis, and tissue microarray validation. *Clin Cancer Res*. 2013 Jan 1;19(1):194-204. doi: 10.1158/1078-0432.ccr-12-1139. PMID: 23032747. Exclusion Code: X3.
139. Bott MJ, Patel AP, Crabtree TD, et al. Pathologic Upstaging in Patients Undergoing Resection for Stage I Non-Small Cell Lung Cancer: Are There Modifiable Predictors? *Ann Thorac Surg*. 2015 Dec;100(6):2048-53. doi: 10.1016/j.athoracsur.2015.05.100. PMID: 26277562. Exclusion Code: X8.

140. Bousamra M, 2nd, Schumer E, Li M, et al. Quantitative analysis of exhaled carbonyl compounds distinguishes benign from malignant pulmonary disease. *J Thorac Cardiovasc Surg*. 2014 Sep;148(3):1074-80; discussion 80-1. doi: 10.1016/j.jtcvs.2014.06.006. PMID: 25129599. Exclusion Code: X3.
141. Bousema JE, Dijkgraaf MGW, Papen-Botterhuis NE, et al. MEDIASTinal staging of non-small cell lung cancer by endobronchial and endoscopic ultrasonography with or without additional surgical mediastinoscopy (MEDIASTrial): study protocol of a multicenter randomised controlled trial. *BMC Surg*. 2018 May 18;18(1):27. doi: 10.1186/s12893-018-0359-6. PMID: 29776444. Exclusion Code: X3.
142. Braak SJ, Herder GJ, van Heesewijk JP, et al. Pulmonary masses: initial results of cone-beam CT guidance with needle planning software for percutaneous lung biopsy. *Cardiovasc Intervent Radiol*. 2012 Dec;35(6):1414-21. doi: 10.1007/s00270-011-0302-z. PMID: 22146973. Exclusion Code: X3.
143. Bradley JD, El Naqa I, Drzymala RE, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung cancer: the pattern of failure is distant. *Int J Radiat Oncol Biol Phys*. 2010 Jul 15;77(4):1146-50. doi: 10.1016/j.ijrobp.2009.06.017. PMID: 19800181. Exclusion Code: X11.
144. Brain K, Carter B, Lifford KJ, et al. Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial. *Thorax*. 2017 Oct;72(10):912-8. doi: 10.1136/thoraxjnl-2016-209690. PMID: 28710339. Exclusion Code: X17.
145. Brain K, Lifford KJ, Carter B, et al. Long-term psychosocial outcomes of low-dose CT screening: results of the UK Lung Cancer Screening randomised controlled trial. *Thorax*. 2016 Nov;71(11):996-1005. doi: 10.1136/thoraxjnl-2016-208283. PMID: 27471048. Exclusion Code: X17.
146. Bral S, Gevaert T, Linthout N, et al. Prospective, risk-adapted strategy of stereotactic body radiotherapy for early-stage non-small-cell lung cancer: results of a Phase II trial. *Int J Radiat Oncol Biol Phys*. 2011 Aug 1;80(5):1343-9. doi: 10.1016/j.ijrobp.2010.04.056. PMID: 20708849. Exclusion Code: X11.
147. Braun FM, Holzner V, Meinel FG, et al. Improved assessment of mediastinal and pulmonary pathologies in combined staging CT examinations using a fast-speed acquisition dual-source CT protocol. *Eur Radiol*. 2017 Dec;27(12):4931-40. doi: 10.1007/s00330-017-4888-7. PMID: 28677055. Exclusion Code: X3.
148. Brenner A, James S, Malo TL, et al. Analysis of patient-provider conversations to assess quality of shared decision making about lung cancer screening. SciAbstracts: Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill; 2018. Exclusion Code: X5.
149. Brenner DJ. Radiation risks potentially associated with low-dose CT screening of adult smokers for lung cancer. *Radiology*. 2004 May;231(2):440-5. doi: 10.1148/radiol.2312030880. PMID: 15128988. Exclusion Code: X4.
150. Brochu B, Beigelman-Aubry C, Goldmard J, et al. Computer-aided detection of lung nodules on thin collimation MDCT: impact on radiologists' performance. *J Radiol*. 2007;88(4):573-8. PMID: CN-00588342. Exclusion Code: X7.
151. Brocken P, van der Heijden HF, Dekhuijzen PN, et al. High performance of F-fluorodeoxyglucose positron emission tomography and contrast-enhanced CT in a rapid outpatient diagnostic program for patients with suspected lung cancer. *Respiration*. 2014;87(1):32-7. doi: 10.1159/000347096. PMID: 23595051. Exclusion Code: X11.
152. Brodersen J, Dirksen A, Pedersen JH. Screening for lung cancer with low-dose computed tomography. *Ann Intern Med*. 2014 Feb 04;160(3):212. doi: 10.7326/l14-5003-2. PMID: 24658700. Exclusion Code: X9.
153. Broekhuizen H, Groothuis-Oudshoorn CGM, Vliegenthart R, et al. Assessing Lung Cancer Screening Programs under Uncertainty in a Heterogeneous Population. *Value Health*. 2018 Nov;21(11):1269-77. doi: 10.1016/j.jval.2018.01.021. PMID: 30442273. Exclusion Code: X3.
154. Broodman I, VanDuijn MM, Stingl C, et al. Survivin Autoantibodies Are Not Elevated in Lung Cancer When Assayed Controlling for Specificity and Smoking Status. *Cancer Immunol Res*. 2016 Feb;4(2):165-72. doi: 10.1158/2326-6066.cir-14-0176. PMID: 26659304. Exclusion Code: X4.

155. Brooks ED, Sun B, Feng L. Association of Long-term Outcomes and Survival With Multidisciplinary Salvage Treatment for Local and Regional Recurrence After Stereotactic Ablative Radiotherapy for Early-Stage Lung Cancer. *JAMA Network Open*. 2018;1(4):e181390. doi: doi:10.1001/jamanetworkopen.2018.1390. Exclusion Code: X3.
156. Brown LM, Cooke DT, Jett JR, et al. Extent of Resection and Lymph Node Assessment for Clinical Stage T1aN0M0 Typical Carcinoid Tumors. *Ann Thorac Surg*. 2018 Jan;105(1):207-13. doi: 10.1016/j.athoracsur.2017.07.049. PMID: 29132704. Exclusion Code: X3.
157. Brunelli A, Dinesh P, Woodcock-Shaw J, et al. Ninety-Day Mortality After Video-Assisted Thoracoscopic Lobectomy: Incidence and Risk Factors. *Ann Thorac Surg*. 2017 Sep;104(3):1020-6. doi: 10.1016/j.athoracsur.2017.02.083. PMID: 28577845. Exclusion Code: X3.
158. Brunelli A, Pompili C, Salati M, et al. Preoperative maximum oxygen consumption is associated with prognosis after pulmonary resection in stage I non-small cell lung cancer. *Ann Thorac Surg*. 2014 Jul;98(1):238-42. doi: 10.1016/j.athoracsur.2014.04.029. PMID: 24874414. Exclusion Code: X11.
159. Brunelli A, Salati M, Rocco G, et al. European risk models for morbidity (EuroLung1) and mortality (EuroLung2) to predict outcome following anatomic lung resections: an analysis from the European Society of Thoracic Surgeons database. *Eur J Cardiothorac Surg*. 2017 Mar 1;51(3):490-7. doi: 10.1093/ejcts/ezw319. PMID: 27744321. Exclusion Code: X3.
160. Bryant AK, Mundt R, Sandhu APS, et al. Stereotactic body radiation therapy versus surgery for early non-small-cell lung cancer in the veterans affairs system. *International journal of radiation oncology biology physics*. 2017;99(2):S7-. doi: 10.1016/j.ijrobp.2017.06.1661. PMID: CN-01422912. Exclusion Code: X2.
161. Bugge A, Lund MB, Brunborg C, et al. Survival After Surgical Resection for Lung Cancer in Patients With Chronic Obstructive Pulmonary Disease. *Ann Thorac Surg*. 2016 Jun;101(6):2125-31. doi: 10.1016/j.athoracsur.2015.12.057. PMID: 27016839. Exclusion Code: X3.
162. Bugge AS, Lund MB, Valberg M, et al. Cause-specific death after surgical resection for early-stage non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2018 Jan 1;53(1):221-7. doi: 10.1093/ejcts/ezx274. PMID: 28950311. Exclusion Code: X10.
163. Bui NC, Lee YY, Suh M, et al. Beliefs and Intentions to Undergo Lung Cancer Screening among Korean Males. *Cancer Res Treat*. 2018 Oct;50(4):1096-105. doi: 10.4143/crt.2017.393. PMID: 29141395. Exclusion Code: X6.
164. Burt BM, Kosinski AS, Shrager JB, et al. Thoracoscopic lobectomy is associated with acceptable morbidity and mortality in patients with predicted postoperative forced expiratory volume in 1 second or diffusing capacity for carbon monoxide less than 40% of normal. *J Thorac Cardiovasc Surg*. 2014 Jul;148(1):19-28, dicussion -9.e1. doi: 10.1016/j.jtcvs.2014.03.007. PMID: 24766848. Exclusion Code: X3.
165. Butof R, Simon M, Lock S, et al. PORTAF - postoperative radiotherapy of non-small cell lung cancer: accelerated versus conventional fractionation - study protocol for a randomized controlled trial. *Trials*. 2017;18(1)doi: 10.1186/s13063-017-2346-0. PMID: CN-01441318. Exclusion Code: X6.
166. Calcagni ML, Taralli S, Cardillo G, et al. Diagnostic performance of (18)F-Fluorodeoxyglucose in 162 small pulmonary nodules incidentally detected in subjects without a history of malignancy. *Ann Thorac Surg*. 2016 Apr;101(4):1303-9. doi: 10.1016/j.athoracsur.2015.10.072. PMID: 26822348. Exclusion Code: X3.
167. Calderon-Santiago M, Priego-Capote F, Turck N, et al. Human sweat metabolomics for lung cancer screening. *Anal Bioanal Chem*. 2015 Jul;407(18):5381-92. doi: 10.1007/s00216-015-8700-8. PMID: 25935675. Exclusion Code: X5.
168. Call S, Obiols C, Rami-Porta R, et al. Video-Assisted Mediastinoscopic Lymphadenectomy for Staging Non-Small Cell Lung Cancer. *Ann Thorac Surg*. 2016 Apr;101(4):1326-33. doi: 10.1016/j.athoracsur.2015.10.073. PMID: 26806169. Exclusion Code: X3.

169. Callahan J, Kron T, Schneider ME, et al. A prospective investigation into the clinical impact of 4D-PET/CT in the characterisation of solitary pulmonary nodules. *Cancer Imaging*. 2014 Jun 5;14:24. doi: 10.1186/1470-7330-14-24. PMID: 25608679. Exclusion Code: X8.
170. Callahan J, Kron T, Siva S, et al. Geographic miss of lung tumours due to respiratory motion: a comparison of 3D vs 4D PET/CT defined target volumes. *Radiat Oncol*. 2014 Dec 16;9:291. doi: 10.1186/s13014-014-0291-6. PMID: 25511904. Exclusion Code: X3.
171. Cannon DM, Mehta MP, Adkison JB, et al. Dose-limiting toxicity after hypofractionated dose-escalated radiotherapy in non-small-cell lung cancer. *J Clin Oncol*. 2013 Dec 1;31(34):4343-8. doi: 10.1200/jco.2013.51.5353. PMID: 24145340. Exclusion Code: X6.
172. Cannon NA, Meyer J, Iyengar P, et al. Neutrophil-lymphocyte and platelet-lymphocyte ratios as prognostic factors after stereotactic radiation therapy for early-stage non-small-cell lung cancer. *J Thorac Oncol*. 2015 Feb;10(2):280-5. doi: 10.1097/jto.0000000000000399. PMID: 25299234. Exclusion Code: X10.
173. Cao C, Wang D, Chung C, et al. A systematic review and meta-analysis of stereotactic body radiation therapy versus surgery for patients with non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2019 Jan;157(1):362-73.e8. doi: 10.1016/j.jtcvs.2018.08.075. PMID: 30482524. Exclusion Code: X3.
174. Capalbo E, Peli M, Lovisatti M, et al. Trans-thoracic biopsy of lung lesions: FNAB or CNB? Our experience and review of the literature. *Radiol Med*. 2014 Aug;119(8):572-94. doi: 10.1007/s11547-013-0360-1. PMID: 24297594. Exclusion Code: X11.
175. Capasso R, Nizzoli R, Tiseo M, et al. Extra-pleuric coaxial system for CT-guided percutaneous fine-needle aspiration biopsy (FNAB) of small (</=20 mm) lung nodules: a novel technique using multiplanar reconstruction (MPR) images. *Med Oncol*. 2017 Feb;34(2):17. doi: 10.1007/s12032-016-0871-4. PMID: 28035579. Exclusion Code: X3.
176. Carlsson A, Nair VS, Luttgen MS, et al. Circulating tumor microemboli diagnostics for patients with non-small-cell lung cancer. *J Thorac Oncol*. 2014 Aug;9(8):1111-9. doi: 10.1097/jto.0000000000000235. PMID: 25157764. Exclusion Code: X3.
177. Caronia FP, Fiorelli A, Ruffini E, et al. A comparative analysis of Pancoast tumour resection performed via video-assisted thoracic surgery versus standard open approaches. *Interact Cardiovasc Thorac Surg*. 2014 Sep;19(3):426-35. doi: 10.1093/icvts/ivu115. PMID: 25052071. Exclusion Code: X3.
178. Carozzi FM, Bisanzi S, Carrozzi L, et al. Multimodal lung cancer screening using the ITALUNG biomarker panel and low dose computed tomography. Results of the ITALUNG biomarker study. *Int J Cancer*. 2017 Jul 01;141(1):94-101. doi: 10.1002/ijc.30727. PMID: 28387927. Exclusion Code: X7.
179. Carrafiello G, Mangini M, Fontana F, et al. Microwave ablation of lung tumours: single-centre preliminary experience. *Radiol Med*. 2014 Jan;119(1):75-82. doi: 10.1007/s11547-013-0301-z. PMID: 24234180. Exclusion Code: X6.
180. Carrillo SA, Daniel VC, Hall N, et al. Fusion positron emission/computed tomography underestimates the presence of hilar nodal metastases in patients with resected non-small cell lung cancer. *Ann Thorac Surg*. 2012 May;93(5):1621-4. doi: 10.1016/j.athoracsur.2012.01.006. PMID: 22429676. Exclusion Code: X3.
181. Carter G, Barrett A, Kaye J, et al. A comprehensive review of nongenetic prognostic and predictive factors influencing the heterogeneity of outcomes in advanced non-small-cell lung cancer (Provisional abstract). *Database of Abstracts of Reviews of Effects*. 2014(2):437-49. PMID: DARE-12014067536. Exclusion Code: X3.
182. Cassidy A, Myles JP, van Tongeren M, et al. The LLP risk model: an individual risk prediction model for lung cancer. *Br J Cancer*. 2008 Jan 29;98(2):270-6. doi: 10.1038/sj.bjc.6604158. PMID: 18087271. Exclusion Code: X7.

183. Cassidy RJ, Patel PR, Zhang X, et al. Stereotactic Body Radiotherapy for Early-stage Non-small-cell Lung Cancer in Patients 80 Years and Older: A Multi-center Analysis. *Clin Lung Cancer*. 2017 Sep;18(5):551-8.e6. doi: 10.1016/j.cllc.2017.03.006. PMID: 28373068. Exclusion Code: X3.

184. Casutt A, Bouchaab H, Beigelman-Aubry C, et al. Stereotactic body radiotherapy with helical TomoTherapy for medically inoperable early stage primary and second-primary non-small-cell lung neoplasm: 1-year outcome and toxicity analysis. *Br J Radiol*. 2015 May;88(1049):20140687. doi: 10.1259/bjr.20140687. PMID: 25735428. Exclusion Code: X3.

185. Casutt A, Prella M, Beigelman-Aubry C, et al. Fluoroscopic-Guided Radial Endobronchial Ultrasound Without Guide Sheath For Peripheral Pulmonary Lesions: A Safe And Efficient Combination. *Arch Bronconeumol*. 2015 Jul;51(7):338-43. doi: 10.1016/j.arbres.2014.09.017. PMID: 25769444. Exclusion Code: X3.

186. Cataldo JK. High-risk older smokers' perceptions, attitudes, and beliefs about lung cancer screening. *Cancer Med*. 2016 Apr;5(4):753-9. doi: 10.1002/cam4.617. PMID: 26822940. Exclusion Code: X8.

187. Cattoni M, Vallieres E, Brown LM, et al. External Validation of a Prognostic Model of Survival for Resected Typical Bronchial Carcinoids. *Ann Thorac Surg*. 2017 Oct;104(4):1215-20. doi: 10.1016/j.athoracsur.2017.05.019. PMID: 28821334. Exclusion Code: X3.

188. Cavic M, Spasic J, Krivokuca A, et al. TP53 and DNA-repair gene polymorphisms genotyping as a low-cost lung adenocarcinoma screening tool. *J Clin Pathol*. 2019 Jan;72(1):75-80. doi: 10.1136/jclinpath-2018-205553. PMID: 30467244. Exclusion Code: X3.

189. Cazzoli R, Buttitta F, Di Nicola M, et al. microRNAs derived from circulating exosomes as noninvasive biomarkers for screening and diagnosing lung cancer. *J Thorac Oncol*. 2013 Sep;8(9):1156-62. doi: 10.1097/JTO.0b013e318299ac32. PMID: 23945385. Exclusion Code: X5.

190. Cengiz A, Aydin F, Sipahi M, et al. The role of F-18 FDG PET/CT in differentiating benign from malignant pulmonary masses and accompanying lymph nodes. *Tuberk Toraks*. 2018 Jun;66(2):130-5. doi: 10.5578/tt.10809. PMID: 30246656. Exclusion Code: X3.

191. Centers for Medicare & Medicaid Services. Proposed decision memo for screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439N). Baltimore, MD: U.S. Centers for Medicare & Medicaid Services; 2014. https://www.cms.gov/medicare-coverage-database/details/nca-proposed-decision-memo.aspx?NCAId=274 Accessed Nov 20, 2017. Exclusion Code: X10.

192. Ceppi M, Munnia A, Cellai F, et al. Linking the generation of DNA adducts to lung cancer. *Toxicology*. 2017 Sep 1;390:160-6. doi: 10.1016/j.tox.2017.09.011. PMID: 28928033. Exclusion Code: X3.

193. Cerfolio RJ, Ojha B, Bryant AS, et al. The accuracy of integrated PET-CT compared with dedicated PET alone for the staging of patients with nonsmall cell lung cancer. *Ann Thorac Surg*. 2004 Sep;78(3):1017-23; discussion -23. doi: 10.1016/j.athoracsur.2004.02.067. PMID: 15337041. Exclusion Code: X3.

194. Cerfolio RJ, Watson C, Minnich DJ, et al. One Hundred Planned Robotic Segmentectomies: Early Results, Technical Details, and Preferred Port Placement. *Ann Thorac Surg*. 2016 Mar;101(3):1089-95; Discussion 95-6. doi: 10.1016/j.athoracsur.2015.08.092. PMID: 26846343. Exclusion Code: X3.

195. Cerra-Franco A, Liu S, Azar M, et al. Predictors of Nodal and Metastatic Failure in Early Stage Non-small-cell Lung Cancer After Stereotactic Body Radiation Therapy. *Clin Lung Cancer*. 2019 May;20(3):186-93.e3. doi: 10.1016/j.cllc.2018.12.016. PMID: 30711394. Exclusion Code: X13.

196. Cha N, Lv M, Zhao YJ, et al. Diagnostic utility of VEGF mRNA and SP1 mRNA expression in bronchial cells of patients with lung cancer. *Respirology*. 2014 May;19(4):544-8. doi: 10.1111/resp.12272. PMID: 24661424. Exclusion Code: X3.

197. Chabowski M, Szymanska-Chabowska A, Skotarczak J, et al. The role of mediastinoscopy in the diagnosis of thoracic disease: one-year single center experience. *Adv Exp Med Biol*. 2015;852:1-4. doi: 10.1007/5584_2014_101. PMID: 25416070. Exclusion Code: X11.
198. Chambers SK, Baade P, Youl P, et al. Psychological distress and quality of life in lung cancer: the role of health-related stigma, illness appraisals and social constraints. *Psychooncology*. 2015 Nov;24(11):1569-77. doi: 10.1002/pon.3829. PMID: 25920906. Exclusion Code: X6.
199. Chan A, Devanand A, Low SY, et al. Radial endobronchial ultrasound in diagnosing peripheral lung lesions in a high tuberculosis setting. *BMC Pulm Med*. 2015 Aug 19;15:90. doi: 10.1186/s12890-015-0089-9. PMID: 26285821. Exclusion Code: X3.
200. Chan EG, Landreneau JR, Schuchert MJ, et al. Preoperative (3-dimensional) computed tomography lung reconstruction before anatomic segmentectomy or lobectomy for stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2015 Sep;150(3):523-8. doi: 10.1016/j.jtcvs.2015.06.051. PMID: 26319461. Exclusion Code: X6.
201. Chandarana H, Heacock L, Rakheja R, et al. Pulmonary nodules in patients with primary malignancy: comparison of hybrid PET/MR and PET/CT imaging. *Radiology*. 2013 Sep;268(3):874-81. doi: 10.1148/radiol.13130620. PMID: 23737537. Exclusion Code: X3.
202. Chandler PD, Song Y, Lin J, et al. Lipid biomarkers and long-term risk of cancer in the Women's Health Study. *Am J Clin Nutr*. 2016 Jun;103(6):1397-407. doi: 10.3945/ajcn.115.124321. PMID: 27099252. Exclusion Code: X3.
203. Chang B, Hwang JH, Choi YH, et al. Natural history of pure ground-glass opacity lung nodules detected by low-dose CT scan. *Chest*. 2013 Jan;143(1):172-8. doi: 10.1378/chest.11-2501. PMID: 22797081. Exclusion Code: X3.
204. Chang DH, Hiss S, Mueller D, et al. Radiation Dose Reduction in Computed Tomography-Guided Lung Interventions using an Iterative Reconstruction Technique. *Rofo*. 2015 Oct;187(10):906-14. doi: 10.1055/s-0035-1553125. PMID: 26085175. Exclusion Code: X5.
205. Chang JM, Kam KH, Yen YT, et al. From biportal to uniportal video-assisted thoracoscopic anatomical lung resection: A single-institute experience. *Medicine (Baltimore)*. 2016 Oct;95(40):e5097. doi: 10.1097/md.0000000000005097. PMID: 27749589. Exclusion Code: X3.
206. Chang JY, Komaki R, Wen HY, et al. Toxicity and patterns of failure of adaptive/ablative proton therapy for early-stage, medically inoperable non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2011 Aug 1;80(5):1350-7. doi: 10.1016/j.ijrobp.2010.04.049. PMID: 21251767. Exclusion Code: X6.
207. Chang JY, Li QQ, Xu QY, et al. Stereotactic ablative radiation therapy for centrally located early stage or isolated parenchymal recurrences of non-small cell lung cancer: how to fly in a "no fly zone". *Int J Radiat Oncol Biol Phys*. 2014 Apr 1;88(5):1120-8. doi: 10.1016/j.ijrobp.2014.01.022. PMID: 24661665. Exclusion Code: X3.
208. Chang JY, Senan S, Paul MA, et al. Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials. *Lancet Oncol*. 2015 Jun;16(6):630-7. doi: 10.1016/s1470-2045(15)70168-3. PMID: 25981812. Exclusion Code: X9.
209. Chang JY, Zhang W, Komaki R, et al. Long-term outcome of phase I/II prospective study of dose-escalated proton therapy for early-stage non-small cell lung cancer. *Radiother Oncol*. 2017 Feb;122(2):274-80. doi: 10.1016/j.radonc.2016.10.022. PMID: 28139305. Exclusion Code: X6.
210. Chang WP, Lin CC. Changes in the sleep-wake rhythm, sleep quality, mood, and quality of life of patients receiving treatment for lung cancer: A longitudinal study. *Chronobiol Int*. 2017;34(4):451-61. doi: 10.1080/07420528.2017.1293678. PMID: 28282238. Exclusion Code: X3.
211. Chang YY, Chen CK, Yeh YC, et al. Diagnostic feasibility and safety of CT-guided core biopsy for lung nodules less than or equal to 8 mm: A single-institution experience. *Eur Radiol*. 2018 Feb;28(2):796-806. doi: 10.1007/s00330-017-5027-1. PMID: 28884222. Exclusion Code: X3.

212. Charvat H, Sasazuki S, Shimazu T, et al. Development of a risk prediction model for lung cancer: The Japan Public Health Center-based Prospective Study. *Cancer Sci*. 2018 Mar;109(3):854-62. doi: 10.1111/cas.13509. PMID: 29345859. Exclusion Code: X7.
213. Chellapandian D, Lehrnbecher T, Phillips B, et al. Bronchoalveolar lavage and lung biopsy in patients with cancer and hematopoietic stem-cell transplantation recipients: a systematic review and meta-analysis. *J Clin Oncol*. 2015 Feb 10;33(5):501-9. doi: 10.1200/jco.2014.58.0480. PMID: 25559816. Exclusion Code: X3.
214. Chen C, Mu CY, Su MQ, et al. Endobronchial Ultrasound-guided Transbronchial Needle Aspiration Increases the Yield of Transbronchial Lung Biopsy for the Evaluation of Peribronchial Lesions. *Chin Med J (Engl)*. 2017 5th Jan 2017;130(1):11-4. doi: 10.4103/0366-6999.196567. PMID: 28051017. Exclusion Code: X3.
215. Chen C, Zhu WD, Zhang XH, et al. Value of Ki-67 and computed tomography in the assessment of peripheral lung adenocarcinoma. *Br J Biomed Sci*. 2016;73(1):32-7. doi: 10.1080/09674845.2016.1146434. PMID: 27182675. Exclusion Code: X8.
216. Chen CY, Chen CH, Shen TC, et al. Lung cancer screening with low-dose computed tomography: Experiences from a tertiary hospital in Taiwan. *J Formos Med Assoc*. 2016 Mar;115(3):163-70. doi: 10.1016/j.jfma.2015.11.007. PMID: 26714425. Exclusion Code: X7.
217. Chen FF, Zhang D, Wang YL, et al. Video-assisted thoracoscopic surgery lobectomy versus open lobectomy in patients with clinical stage non-small cell lung cancer: a meta-analysis. *Eur J Surg Oncol*. 2013 Sep;39(9):957-63. doi: 10.1016/j.ejso.2013.06.016. PMID: 23845704. Exclusion Code: X9.
218. Chen HH, Chiu NT, Su WC, et al. Prognostic value of whole-body total lesion glycolysis at pretreatment FDG PET/CT in non-small cell lung cancer. *Radiology*. 2012 Aug;264(2):559-66. doi: 10.1148/radiol.12111148. PMID: 22692034. Exclusion Code: X3.
219. Chen K, Chen H, Yang F, et al. Validation of the Eighth Edition of the TNM Staging System for Lung Cancer in 2043 Surgically Treated Patients With Non-small-cell Lung Cancer. *Clin Lung Cancer*. 2017 Nov;18(6):e457-e66. doi: 10.1016/j.cllc.2017.04.001. PMID: 28539214. Exclusion Code: X3.
220. Chen S, Li X, Chen M, et al. Limited diagnostic value of Dual-Time-Point (18)F-FDG PET/CT imaging for classifying solitary pulmonary nodules in granuloma-endemic regions both at visual and quantitative analyses. *Eur J Radiol*. 2016 Oct;85(10):1744-9. doi: 10.1016/j.ejrad.2016.07.016. PMID: 27666611. Exclusion Code: X3.
221. Chen T, Luo J, Gu H, et al. Impact of Solid Minor Histologic Subtype in Postsurgical Prognosis of Stage I Lung Adenocarcinoma. *Ann Thorac Surg*. 2018 Jan;105(1):302-8. doi: 10.1016/j.athoracsur.2017.08.018. PMID: 29162222. Exclusion Code: X10.
222. Chen X, Gorlov IP, Ying J, et al. Initial medical attention on patients with early-stage non-small cell lung cancer. *PLoS One*. 2012;7(3):e32644. doi: 10.1371/journal.pone.0032644. PMID: 22412901. Exclusion Code: X3.
223. Chen X, Wu J, Zhang F, et al. Prognostic Significance of Pre-Operative Monocyte-to-Lymphocyte Ratio in Lung Cancer Patients Undergoing Radical Surgery. *Lab Med*. 2018 Mar 21;49(2):e29-e39. doi: 10.1093/labmed/lmx069. PMID: 29361036. Exclusion Code: X3.
224. Chen XR, Dong JN, Zhang F, et al. Efficacy and safety of image-guidance radiotherapy by helical tomotherapy in patients with lung cancer. *Medicine (Baltimore)*. 2018 Jan;97(1):e9243. doi: 10.1097/md.0000000000009243. PMID: 29505510. Exclusion Code: X14.
225. Chen Y, Li J, Zhang Y, et al. Early versus late prophylactic cranial irradiation in patients with extensive small cell lung cancer. *Strahlenther Onkol*. 2018 Oct;194(10):876-85. doi: 10.1007/s00066-018-1307-1. PMID: 29774395. Exclusion Code: X3.
226. Chen Z, Xu Z, Sun S, et al. TGF-beta1, IL-6, and TNF-alpha in bronchoalveolar lavage fluid: useful markers for lung cancer? *Sci Rep*. 2014 Jul 7;4:5595. doi: 10.1038/srep05595. PMID: 24999009. Exclusion Code: X11.

227. Cheng M, Liu L, Yang HS, et al. Circulating tumor cells are associated with bone metastasis of lung cancer. *Asian Pac J Cancer Prev*. 2014;15(15):6369-74. PMID: 25124627. Exclusion Code: X3.
228. Cheng YD, Duan CJ, Dong S, et al. Clinical controlled comparison between lobectomy and segmental resection for patients over 70 years of age with clinical stage I non-small cell lung cancer. *Eur J Surg Oncol*. 2012 Dec;38(12):1149-55. doi: 10.1016/j.ejso.2012.08.001. PMID: 22901959. Exclusion Code: X11.
229. Chesterfield-Thomas G, Goldsmith I. Impact of preoperative pulmonary rehabilitation on the Thoracoscore of patients undergoing lung resection. *Interact Cardiovasc Thorac Surg*. 2016 Nov;23(5):729-32. doi: 10.1093/icvts/ivw238. PMID: 27430554. Exclusion Code: X3.
230. Cheung P, Faria S, Ahmed S, et al. Phase II study of accelerated hypofractionated three-dimensional conformal radiotherapy for stage T1-3 N0 M0 non-small cell lung cancer: NCIC CTG BR.25. *J Natl Cancer Inst*. 2014 Aug;106(8)doi: 10.1093/jnci/dju164. PMID: 25074417. Exclusion Code: X6.
231. Chi A, Wen S, Liao Z, et al. What would be the most appropriate alpha/beta ratio in the setting of stereotactic body radiation therapy for early stage non-small cell lung cancer. *Biomed Res Int*. 2013;2013:391021. doi: 10.1155/2013/391021. PMID: 24350266. Exclusion Code: X10.
232. Chi CT. A multicenter randomized controlled trial on video-assisted thoracoscopic surgery and axillary thoracotomy for resection of early-stage non-small cell lung cancer. *Http://www.who.int/trialsearch/trial2.aspx?Trialid=chictr-trc-10000750*. 2010PMID: CN-01833643. Exclusion Code: X16.
233. Chiang A, Thibault I, Warner A, et al. A comparison between accelerated hypofractionation and stereotactic ablative radiotherapy (SABR) for early-stage non-small cell lung cancer (NSCLC): Results of a propensity score-matched analysis. *Radiother Oncol*. 2016 Mar;118(3):478-84. doi: 10.1016/j.radonc.2015.12.026. PMID: 26795773. Exclusion Code: X3.
234. Chiappetta M, Rosella F, Dall'armi V, et al. CT-guided fine-needle ago-biopsy of pulmonary nodules: predictive factors for diagnosis and pneumothorax occurrence. *Radiol Med*. 2016 Aug;121(8):635-43. doi: 10.1007/s11547-016-0639-0. PMID: 27132130. Exclusion Code: X3.
235. Chiles C, Duan F, Gladish GW, et al. Association of Coronary Artery Calcification and Mortality in the National Lung Screening Trial: A Comparison of Three Scoring Methods. *Radiology*. 2015 Jul;276(1):82-90. doi: 10.1148/radiol.15142062. PMID: 25759972. Exclusion Code: X5.
236. Chlebowski RT, Wakelee H, Pettinger M, et al. Estrogen Plus Progestin and Lung Cancer: Follow-up of the Women's Health Initiative Randomized Trial. *Clin Lung Cancer*. 2016 Jan;17(1):10-7.e1. doi: 10.1016/j.cllc.2015.09.004. PMID: 26577506. Exclusion Code: X6.
237. Cho H, Lee HY, Kim J, et al. Pure ground glass nodular adenocarcinomas: Are preoperative positron emission tomography/computed tomography and brain magnetic resonance imaging useful or necessary? *J Thorac Cardiovasc Surg*. 2015 Sep;150(3):514-20. doi: 10.1016/j.jtcvs.2015.06.024. PMID: 26189165. Exclusion Code: X3.
238. Cho HJ, Yun HJ, Yang HC, et al. Prognostic significance of nuclear factor of activated T-cells 5 expression in non-small cell lung cancer patients who underwent surgical resection. *J Surg Res*. 2018 Jun;226:40-7. doi: 10.1016/j.jss.2017.12.036. PMID: 29661287. Exclusion Code: X3.
239. Cho J, Kim ES, Kim SJ, et al. Long-Term Follow-up of Small Pulmonary Ground-Glass Nodules Stable for 3 Years: Implications of the Proper Follow-up Period and Risk Factors for Subsequent Growth. *J Thorac Oncol*. 2016 Sep;11(9):1453-9. doi: 10.1016/j.jtho.2016.05.026. PMID: 27287413. Exclusion Code: X3.
240. Cho J, Ko SJ, Kim SJ, et al. Surgical resection of nodular ground-glass opacities without percutaneous needle aspiration or biopsy. *BMC Cancer*. 2014 Nov 18;14:838. doi: 10.1186/1471-2407-14-838. PMID: 25406492. Exclusion Code: X3.

241. Cho JH, Choi YS, Kim J, et al. Long-term outcomes of wedge resection for pulmonary ground-glass opacity nodules. *Ann Thorac Surg*. 2015 Jan;99(1):218-22. doi: 10.1016/j.athoracsur.2014.07.068. PMID: 25440277. Exclusion Code: X11.
242. Choe J, Lee SM, Do KH, et al. Prognostic value of radiomic analysis of iodine overlay maps from dual-energy computed tomography in patients with resectable lung cancer. *Eur Radiol*. 2019 Feb;29(2):915-23. doi: 10.1007/s00330-018-5639-0. PMID: 30054795. Exclusion Code: X11.
243. Choi JW, Park CM, Goo JM, et al. C-arm cone-beam CT-guided percutaneous transthoracic needle biopsy of small (</= 20 mm) lung nodules: diagnostic accuracy and complications in 161 patients. *AJR Am J Roentgenol*. 2012 Sep;199(3):W322-30. doi: 10.2214/ajr.11.7576. PMID: 22915422. Exclusion Code: X3.
244. Choi MJ, Kim Y, Hong YS, et al. Transthoracic needle biopsy using a C-arm cone-beam CT system: diagnostic accuracy and safety. *Br J Radiol*. 2012 Jun;85(1014):e182-7. doi: 10.1259/bjr/95413532. PMID: 21791505. Exclusion Code: X10.
245. Choi SH, Chae EJ, Shin SY, et al. Comparisons of clinical outcomes in patients with and without a preoperative tissue diagnosis in the persistent malignant-looking, ground-glass-opacity nodules. *Medicine (Baltimore)*. 2016 Aug;95(34):e4359. doi: 10.1097/md.0000000000004359. PMID: 27559945. Exclusion Code: X3.
246. Choi SM, Heo EY, Lee J, et al. Characteristics of benign solitary pulmonary nodules confirmed by diagnostic video-assisted thoracoscopic surgery. *Clin Respir J*. 2016 Mar;10(2):181-8. doi: 10.1111/crj.12200. PMID: 25103572. Exclusion Code: X3.
247. Choi YR, An JY, Kim MK, et al. The diagnostic efficacy and safety of endobronchial ultrasound-guided transbronchial needle aspiration as an initial diagnostic tool. *Korean J Intern Med*. 2013 Nov;28(6):660-7. doi: 10.3904/kjim.2013.28.6.660. PMID: 24307841. Exclusion Code: X3.
248. Choi YY, Lee SY, Lee WK, et al. RACK1 is a candidate gene associated with the prognosis of patients with early stage non-small cell lung cancer. *Oncotarget*. 2015 Feb 28;6(6):4451-66. doi: 10.18632/oncotarget.2865. PMID: 25686824. Exclusion Code: X6.
249. Chopra A, Ford A, De Noronha R, et al. Incidental findings on positron emission tomography/CT scans performed in the investigation of lung cancer. *Br J Radiol*. 2012 Jul;85(1015):e229-37. doi: 10.1259/bjr/60606623. PMID: 22745208. Exclusion Code: X3.
250. Chou HP, Chen CK, Shen SH, et al. Percutaneous cryoablation for inoperable malignant lung tumors: midterm results. *Cryobiology*. 2015 Feb;70(1):60-5. doi: 10.1016/j.cryobiol.2014.12.004. PMID: 25541142. Exclusion Code: X6.
251. Christe A, Ebner L, Steiger P, et al. Impact of image quality, radiologists, lung segments, and Gunnar eyewear on detectability of lung nodules in chest CT. *Acta Radiol*. 2013 Jul;54(6):646-51. doi: 10.1177/0284185113483677. PMID: 23612429. Exclusion Code: X3.
252. Christe A, Leidolt L, Huber A, et al. Lung cancer screening with CT: evaluation of radiologists and different computer assisted detection software (CAD) as first and second readers for lung nodule detection at different dose levels. *Eur J Radiol*. 2013 Dec;82(12):e873-8. doi: 10.1016/j.ejrad.2013.08.026. PMID: 24074648. Exclusion Code: X3.
253. Christensen TD, Vad H, Pedersen S, et al. Coagulation profile in open and video-assisted thoracoscopic lobectomies: a cohort study. *Interact Cardiovasc Thorac Surg*. 2018 Mar 1;26(3):382-8. doi: 10.1093/icvts/ivx328. PMID: 29049684. Exclusion Code: X3.
254. Christian C, Erica S, Morandi U. The prognostic impact of tumor size in resected stage I non-small cell lung cancer: evidence for a two thresholds tumor diameters classification. *Lung Cancer*. 2006 Nov;54(2):185-91. doi: 10.1016/j.lungcan.2006.08.003. PMID: 16996167. Exclusion Code: X10.

255. Chua KLM, Sin I, Fong KW, et al. Stereotactic body radiotherapy for early stage lung cancer-historical developments and future strategies. *Chin Clin Oncol*. 2017 Sep;6(Suppl 2):S20. doi: 10.21037/cco.2017.08.02. PMID: 28917258. Exclusion Code: X10.
256. Chubachi S, Takahashi S, Tsutsumi A, et al. Radiologic features of precancerous areas of the lungs in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2017;12:1613-24. doi: 10.2147/copd.s132709. PMID: 28615934. Exclusion Code: X3.
257. Chung K, Mets OM, Gerke PK, et al. Brock malignancy risk calculator for pulmonary nodules: validation outside a lung cancer screening population. *Thorax*. 2018 Sep;73(9):857-63. doi: 10.1136/thoraxjnl-2017-211372. PMID: 29777062. Exclusion Code: X3.
258. Cieszanowski A, Lisowska A, Dabrowska M, et al. MR Imaging of Pulmonary Nodules: Detection Rate and Accuracy of Size Estimation in Comparison to Computed Tomography. *PLoS One*. 2016;11(6):e0156272. doi: 10.1371/journal.pone.0156272. PMID: 27258047. Exclusion Code: X3.
259. Citak N, Buyukkale S, Kok A, et al. Does video-assisted mediastinoscopy offer lower false-negative rates for subcarinal lymph nodes compared with standard cervical mediastinoscopy? *Thorac Cardiovasc Surg*. 2014 Oct;62(7):624-30. doi: 10.1055/s-0033-1358656. PMID: 24297632. Exclusion Code: X3.
260. Clausen E, Wittman C, Gingo M, et al. Chest computed tomography findings in HIV-infected individuals in the era of antiretroviral therapy. *PLoS One*. 2014;9(11):e112237. doi: 10.1371/journal.pone.0112237. PMID: 25409510. Exclusion Code: X8.
261. Cole AM, Pflugeisen B, Schwartz MR, et al. Cross sectional study to assess the accuracy of electronic health record data to identify patients in need of lung cancer screening. *BMC Res Notes*. 2018 Jan 10;11(1):14. doi: 10.1186/s13104-018-3124-0. PMID: 29321038. Exclusion Code: X5.
262. Coley SM, Crapanzano JP, Saqi A. FNA, core biopsy, or both for the diagnosis of lung carcinoma: Obtaining sufficient tissue for a specific diagnosis and molecular testing. *Cancer Cytopathol*. 2015 May;123(5):318-26. doi: 10.1002/cncy.21527. PMID: 25711901. Exclusion Code: X3.
263. Cornwell LD, Bakaeen FG, Lan CK, et al. Endobronchial ultrasonography-guided transbronchial needle aspiration biopsy for preoperative nodal staging of lung cancer in a veteran population. *JAMA Surg*. 2013 Nov;148(11):1024-9. doi: 10.1001/jamasurg.2013.3776. PMID: 24048268. Exclusion Code: X3.
264. Cornwell LD, Echeverria AE, Samuelian J, et al. Video-assisted thoracoscopic lobectomy is associated with greater recurrence-free survival than stereotactic body radiotherapy for clinical stage I lung cancer. *J Thorac Cardiovasc Surg*. 2018 Jan;155(1):395-402. doi: 10.1016/j.jtcvs.2017.07.065. PMID: 28888379. Exclusion Code: X10.
265. Coroller TP, Mak RH, Lewis JH, et al. Low incidence of chest wall pain with a risk-adapted lung stereotactic body radiation therapy approach using three or five fractions based on chest wall dosimetry. *PLoS One*. 2014;9(4):e94859. doi: 10.1371/journal.pone.0094859. PMID: 24728448. Exclusion Code: X3.
266. Corradetti MN, Haas AR, Rengan R. Central-airway necrosis after stereotactic body-radiation therapy. *N Engl J Med*. 2012 Jun 14;366(24):2327-9. doi: 10.1056/NEJMc1203770. PMID: 22694017. Exclusion Code: X10.
267. Corradi M, Poli D, Banda I, et al. Exhaled breath analysis in suspected cases of non-small-cell lung cancer: a cross-sectional study. *J Breath Res*. 2015 Jan 29;9(2):027101. doi: 10.1088/1752-7155/9/2/027101. PMID: 25634546. Exclusion Code: X7.
268. Corso CD, Park HS, Kim AW, et al. Racial disparities in the use of SBRT for treating early-stage lung cancer. *Lung Cancer*. 2015 Aug;89(2):133-8. doi: 10.1016/j.lungcan.2015.05.002. PMID: 26051446. Exclusion Code: X8.

269. Corso CD, Park HS, Moreno AC, et al. Stage I Lung SBRT Clinical Practice Patterns. *Am J Clin Oncol*. 2017 Aug;40(4):358-61. doi: 10.1097/coc.0000000000000162. PMID: 25503436. Exclusion Code: X8.
270. Coverley D, Higgins G, West D, et al. A quantitative immunoassay for lung cancer biomarker CIZ1b in patient plasma. *Clin Biochem*. 2017 Apr;50(6):336-43. doi: 10.1016/j.clinbiochem.2016.11.015. PMID: 27867087. Exclusion Code: X3.
271. Crabtree TD, Denlinger CE, Meyers BF, et al. Stereotactic body radiation therapy versus surgical resection for stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2010 Aug;140(2):377-86. doi: 10.1016/j.jtcvs.2009.12.054. PMID: 20400121. Exclusion Code: X11.
272. Crabtree TD, Puri V, Chen SB, et al. Does the method of radiologic surveillance affect survival after resection of stage I non-small cell lung cancer? *J Thorac Cardiovasc Surg*. 2015 Jan;149(1):45-52, 3.e1-3. doi: 10.1016/j.jtcvs.2014.07.095. PMID: 25218540. Exclusion Code: X12.
273. Crabtree TD, Puri V, Robinson C, et al. Analysis of first recurrence and survival in patients with stage I non-small cell lung cancer treated with surgical resection or stereotactic radiation therapy. *J Thorac Cardiovasc Surg*. 2014 Apr;147(4):1183-91; discussion 91-2. doi: 10.1016/j.jtcvs.2013.11.057. PMID: 24507980. Exclusion Code: X10.
274. Criss SD, Sheehan DF, Palazzo L, et al. Population impact of lung cancer screening in the United States: Projections from a microsimulation model. *PLoS Med*. 2018 Feb;15(2):e1002506. doi: 10.1371/journal.pmed.1002506. PMID: 29415013. Exclusion Code: X3.
275. Cronin KA, Gail MH, Zou Z, et al. Validation of a model of lung cancer risk prediction among smokers. *J Natl Cancer Inst*. 2006 May 03;98(9):637-40. doi: 10.1093/jnci/djj163. PMID: 16670389. Exclusion Code: X7.
276. Cruz C, Afonso M, Oliveiros B, et al. Recurrence and Risk Factors for Relapse in Patients with Non-Small Cell Lung Cancer Treated by Surgery with Curative Intent. *Oncology*. 2017;92(6):347-52. doi: 10.1159/000458533. PMID: 28278499. Exclusion Code: X11.
277. Currow DC, You H, Aranda S, et al. What factors are predictive of surgical resection and survival from localised non-small cell lung cancer? *Med J Aust*. 2014 Oct 20;201(8):475-80. PMID: 25332036. Exclusion Code: X11.
278. Cusumano G, Fournel L, Strano S, et al. Surgical Resection for Pulmonary Carcinoid: Long-Term Results of Multicentric Study-The Importance of Pathological N Status, More Than We Thought. *Lung*. 2017 Dec;195(6):789-98. doi: 10.1007/s00408-017-0056-8. PMID: 29022070. Exclusion Code: X3.
279. Cykert S, Walker PR, Edwards LJ, et al. Weighing projections of physical decline in lung cancer surgery decisions. *Am J Med Sci*. 2015 Jan;349(1):61-6. doi: 10.1097/maj.0000000000000354. PMID: 25285513. Exclusion Code: X3.
280. Dabrowska M, Krenke R, Korczynski P, et al. Diagnostic accuracy of contrast-enhanced computed tomography and positron emission tomography with 18-FDG in identifying malignant solitary pulmonary nodules. *Medicine (Baltimore)*. 2015 Apr;94(15):e666. doi: 10.1097/md.0000000000000666. PMID: 25881842. Exclusion Code: X3.
281. Dabrowska M, Przybylo Z, Zukowska M, et al. Should we be concerned about the doses of ionizing radiation related to diagnostic and follow-up imaging in patients with solitary pulmonary nodules? *Radiat Prot Dosimetry*. 2018 Jan 1;178(2):201-7. doi: 10.1093/rpd/ncx099. PMID: 28981871. Exclusion Code: X3.
282. Dai C, Shen J, Ren Y, et al. Choice of Surgical Procedure for Patients With Non-Small-Cell Lung Cancer </= 1 cm or > 1 to 2 cm Among Lobectomy, Segmentectomy, and Wedge Resection: A Population-Based Study. *J Clin Oncol*. 2016 Sep 10;34(26):3175-82. doi: 10.1200/jco.2015.64.6729. PMID: 27382092. Exclusion Code: X8.
283. Dai H, Liu J, Liang L, et al. Increased lung cancer risk in patients with interstitial lung disease and elevated CEA and CA125 serum tumour markers. *Respirology*. 2014 Jul;19(5):707-13. doi: 10.1111/resp.12317. PMID: 24903079. Exclusion Code: X3.

284. Dai J, Liu M, Swensen SJ, et al. Regional Emphysema Score Predicting Overall Survival, Quality of Life, and Pulmonary Function Recovery in Early-Stage Lung Cancer Patients. *J Thorac Oncol*. 2017 May;12(5):824-32. doi: 10.1016/j.jtho.2017.01.016. PMID: 28126539. Exclusion Code: X10.
285. Dai L, Tsay JC, Li J, et al. Autoantibodies against tumor-associated antigens in the early detection of lung cancer. *Lung Cancer*. 2016 Sep;99:172-9. doi: 10.1016/j.lungcan.2016.07.018. PMID: 27565936. Exclusion Code: X3.
286. Dale CR, Madtes DK, Fan VS, et al. Navigational bronchoscopy with biopsy versus computed tomography-guided biopsy for the diagnosis of a solitary pulmonary nodule: a cost-consequences analysis. *J Bronchology Interv Pulmonol*. 2012 Oct;19(4):294-303. doi: 10.1097/LBR.0b013e318272157d. PMID: 23207529. Exclusion Code: X10.
287. Dalwadi SM, Szeja SS, Bernicker EH, et al. Practice Patterns and Outcomes in Elderly Stage I Non-Small-cell Lung Cancer: A 2004 to 2012 SEER Analysis. *Clin Lung Cancer*. 2018 Mar;19(2):e269-e76. doi: 10.1016/j.cllc.2017.11.004. PMID: 29208356. Exclusion Code: X13.
288. Dama E, Melocchi V, Dezi F, et al. An Aggressive Subtype of Stage I Lung Adenocarcinoma with Molecular and Prognostic Characteristics Typical of Advanced Lung Cancers. *Clin Cancer Res*. 2017 Jan 1;23(1):62-72. doi: 10.1158/1078-0432.ccr-15-3005. PMID: 27358486. Exclusion Code: X6.
289. D'Amelio AM, Jr., Cassidy A, Asomaning K, et al. Comparison of discriminatory power and accuracy of three lung cancer risk models. *Br J Cancer*. 2010 Jul 27;103(3):423-9. doi: 10.1038/sj.bjc.6605759. PMID: 20588271. Exclusion Code: X7.
290. Dandachi N, Tiran V, Lindenmann J, et al. Frequency and clinical impact of preoperative circulating tumor cells in resectable non-metastatic lung adenocarcinomas. *Lung Cancer*. 2017 Nov;113:152-7. doi: 10.1016/j.lungcan.2017.10.003. PMID: 29110843. Exclusion Code: X8.
291. D'Andrilli A, Maurizi G, Andreetti C, et al. Sleeve Lobectomy Versus Standard Lobectomy for Lung Cancer: Functional and Oncologic Evaluation. *Ann Thorac Surg*. 2016 May;101(5):1936-42. doi: 10.1016/j.athoracsur.2015.11.057. PMID: 26912305. Exclusion Code: X3.
292. D'Andrilli A, Natoli G, Scarpino S, et al. Stage I non-small cell lung cancer: the presence of the lymphocyte-specific protein tyrosin kinase in the tumour infiltrate is associated with a better long-term prognosis. *Interact Cardiovasc Thorac Surg*. 2012 Jul;15(1):148-51. doi: 10.1093/icvts/ivr128. PMID: 22457183. Exclusion Code: X11.
293. Dang H, Siewerdsen JH, Stayman JW. Prospective regularization design in prior-image-based reconstruction. *Phys Med Biol*. 2015 Dec 21;60(24):9515-36. doi: 10.1088/0031-9155/60/24/9515. PMID: 26606653. Exclusion Code: X5.
294. David EA, Cooke DT, Chen Y, et al. Surgery in high-volume hospitals not commission on cancer accreditation leads to increased cancer-specific survival for early-stage lung cancer. *Am J Surg*. 2015 Oct;210(4):643-7. doi: 10.1016/j.amjsurg.2015.05.002. PMID: 26193801. Exclusion Code: X8.
295. Davis JN, Medbery C, Sharma S, et al. Stereotactic body radiotherapy for centrally located early-stage non-small cell lung cancer or lung metastases from the RSSearch((R)) patient registry. *Radiat Oncol*. 2015 May 15;10:113. doi: 10.1186/s13014-015-0417-5. PMID: 25975848. Exclusion Code: X3.
296. Davis JN, Medbery C, 3rd, Sharma S, et al. Stereotactic body radiotherapy for early-stage non-small cell lung cancer: clinical outcomes from a National Patient Registry. *J Radiat Oncol*. 2015;4(1):55-63. doi: 10.1007/s13566-014-0177-0. PMID: 25774243. Exclusion Code: X13.
297. Dawe DE, Pond GR, Ellis PM. Assessment of Referral and Chemotherapy Treatment Patterns for Elderly Patients With Non-small-Cell Lung Cancer. *Clin Lung Cancer*. 2016 Nov;17(6):563-72.e2. doi: 10.1016/j.cllc.2016.05.012. PMID: 27374398. Exclusion Code: X8.

298. de Baere T, Tselikas L, Catena V, et al. Percutaneous thermal ablation of primary lung cancer. *Diagn Interv Imaging*. 2016 Oct;97(10):1019-24. doi: 10.1016/j.diii.2016.08.016. PMID: 27692673. Exclusion Code: X6.

299. de Dios NR, Sanz X, Foro P, et al. Accelerated hypofractionated radiation therapy (AHRT) for non-small-cell lung cancer: can we leave standard fractionation? *Clin Transl Oncol*. 2017 Apr;19(4):440-7. doi: 10.1007/s12094-016-1544-7. PMID: 27553602. Exclusion Code: X6.

300. de Hoop B, van Ginneken B, Gietema H, et al. Pulmonary perifissural nodules on CT scans: rapid growth is not a predictor of malignancy. *Radiology*. 2012 Nov;265(2):611-6. doi: 10.1148/radiol.12112351. PMID: 22929331. Exclusion Code: X8.

301. de Koning HJ, Meza R, Plevritis SK, et al. Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2014 Mar 04;160(5):311-20. doi: 10.7326/m13-2316. PMID: 24379002. Exclusion Code: X4.

302. De Roza MA, Quah KH, Tay CK, et al. Diagnosis of Peripheral Lung Lesions via Conventional Flexible Bronchoscopy with Multiplanar CT Planning. *Pulm Med*. 2016;2016:5048961. doi: 10.1155/2016/5048961. PMID: 27957340. Exclusion Code: X3.

303. De Ruysscher D, Sharifi H, Defraene G, et al. Quantification of radiation-induced lung damage with CT scans: the possible benefit for radiogenomics. *Acta Oncol*. 2013 Oct;52(7):1405-10. doi: 10.3109/0284186x.2013.813074. PMID: 23957564. Exclusion Code: X3.

304. De Wever W, Bruyeer E, Demaerel P, et al. Staging of lung cancer. Do we need a diagnostic CT of the brain after an integrated PET/CT for the detection of brain metastases? *Jbr-btr*. 2010 Mar-Apr;93(2):71-6. PMID: 20524514. Exclusion Code: X3.

305. Debieuvre D, Fraboulet G, Duvert B, et al. Impact of distance from surgery department on the outcome of patients followed for non-small-cell lung cancer in the respiratory department of nonacademic hospitals: Results of the KBP-2010-study. *Bull Cancer*. 2017 Oct;104(10):840-9. doi: 10.1016/j.bulcan.2017.07.008. PMID: 28965729. Exclusion Code: X3.

306. Decaluwe H, Moons J, Fieuws S, et al. Is central lung tumour location really predictive for occult mediastinal nodal disease in (suspected) non-small-cell lung cancer staged cN0 on 18F-fluorodeoxyglucose positron emission tomography-computed tomography? *Eur J Cardiothorac Surg*. 2018 Jul 1;54(1):134-40. doi: 10.1093/ejcts/ezy018. PMID: 29447330. Exclusion Code: X6.

307. Decaluwe H, Petersen RH, Hansen H, et al. Major intraoperative complications during video-assisted thoracoscopic anatomical lung resections: an intention-to-treat analysis. *Eur J Cardiothorac Surg*. 2015 Oct;48(4):588-98; discussion 99. doi: 10.1093/ejcts/ezv287. PMID: 26385060. Exclusion Code: X3.

308. Decaluwe H, Stanzi A, Dooms C, et al. Central tumour location should be considered when comparing N1 upstaging between thoracoscopic and open surgery for clinical stage I non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2016 Jul;50(1):110-7. doi: 10.1093/ejcts/ezv489. PMID: 26819286. Exclusion Code: X8.

309. Deepak JA, Ng X, Feliciano J, et al. Pulmonologist involvement, stage-specific treatment, and survival in adults with non-small cell lung cancer and chronic obstructive pulmonary disease. *Ann Am Thorac Soc*. 2015 May;12(5):742-51. doi: 10.1513/AnnalsATS.201406-230OC. PMID: 25760983. Exclusion Code: X6.

310. Dell'Amore A, Monteverde M, Martucci N, et al. Early and long-term results of pulmonary resection for non-small-cell lung cancer in patients over 75 years of age: a multi-institutional study. *Interact Cardiovasc Thorac Surg*. 2013 Mar;16(3):250-6. doi: 10.1093/icvts/ivs473. PMID: 23178392. Exclusion Code: X3.

311. Dembitzer FR, Flores RM, Parides MK, et al. Impact of histologic subtyping on outcome in lobar vs sublobar resections for lung cancer: a pilot study. *Chest*. 2014 Jul;146(1):175-81. doi: 10.1378/chest.13-2506. PMID: 24556743. Exclusion Code: X11.
312. Demir Y, Polack BD, Karaman C, et al. The diagnostic role of dual-phase (18)F-FDG PET/CT in the characterization of solitary pulmonary nodules. *Nucl Med Commun*. 2014 Mar;35(3):260-7. doi: 10.1097/mnm.0000000000000049. PMID: 24468852. Exclusion Code: X3.
313. Deng B, Cassivi SD, de Andrade M, et al. Clinical outcomes and changes in lung function after segmentectomy versus lobectomy for lung cancer cases. *J Thorac Cardiovasc Surg*. 2014 Oct;148(4):1186-92.e3. doi: 10.1016/j.jtcvs.2014.03.019. PMID: 24746994. Exclusion Code: X11.
314. Deng C, Cao X, Wu D, et al. Small lung lesions invisible under fluoroscopy are located accurately by three-dimensional localization technique on chest wall surface and performed bronchoscopy procedures to increase diagnostic yields. *BMC Pulm Med*. 2016 Nov 29;16(1):166. doi: 10.1186/s12890-016-0328-8. PMID: 27894283. Exclusion Code: X11.
315. Deng CJ, Dai FQ, Qian K, et al. Clinical updates of approaches for biopsy of pulmonary lesions based on systematic review. *BMC Pulm Med*. 2018 Sep 3;18(1):146. doi: 10.1186/s12890-018-0713-6. PMID: 30176840. Exclusion Code: X3.
316. Denholm R, Schuz J, Straif K, et al. Is previous respiratory disease a risk factor for lung cancer? *Am J Respir Crit Care Med*. 2014 Sep 1;190(5):549-59. doi: 10.1164/rccm.201402-0338OC. PMID: 25054566. Exclusion Code: X3.
317. Deppen SA, Blume JD, Aldrich MC, et al. Predicting lung cancer prior to surgical resection in patients with lung nodules. *J Thorac Oncol*. 2014 Oct;9(10):1477-84. doi: 10.1097/jto.0000000000000287. PMID: 25170644. Exclusion Code: X3.
318. Desseroit MC, Visvikis D, Tixier F, et al. Development of a nomogram combining clinical staging with (18)F-FDG PET/CT image features in non-small-cell lung cancer stage I-III. *Eur J Nucl Med Mol Imaging*. 2016 Jul;43(8):1477-85. doi: 10.1007/s00259-016-3325-5. PMID: 26896298. Exclusion Code: X3.
319. Detillon D, Veen EJ. Postoperative Outcome After Pulmonary Surgery for Non-Small Cell Lung Cancer in Elderly Patients. *Ann Thorac Surg*. 2018 Jan;105(1):287-93. doi: 10.1016/j.athoracsur.2017.07.032. PMID: 29132701. Exclusion Code: X3.
320. de-Torres JP, Marin JM, Casanova C, et al. Identification of COPD Patients at High Risk for Lung Cancer Mortality Using the COPD-LUCSS-DLCO. *Chest*. 2016 Apr;149(4):936-42. doi: 10.1378/chest.15-1868. PMID: 26513409. Exclusion Code: X4.
321. DeWees TA, Nikitas J, Rehman S, et al. Defining Optimal Comorbidity Measures for Patients With Early-Stage Non-small cell lung cancer Treated With Stereotactic Body Radiation Therapy. *Pract Radiat Oncol*. 2019 Jan;9(1):e83-e9. doi: 10.1016/j.prro.2018.09.001. PMID: 30244094. Exclusion Code: X13.
322. Dhanasopon AP, Salazar MC, Hoag JR, et al. Fate of pneumonectomy patients variably captured by non-small cell lung cancer staging system. *Ann Thorac Surg*. 2017 Dec;104(6):1829-36. doi: 10.1016/j.athoracsur.2017.06.073. PMID: 29074151. Exclusion Code: X17.
323. Diao K, Chen YH, Catalano PJ, et al. Radiation toxicity in patients with collagen vascular disease and intrathoracic malignancy treated with modern radiation techniques. *Radiother Oncol*. 2017 Nov;125(2):301-9. doi: 10.1016/j.radonc.2017.10.002. PMID: 29102264. Exclusion Code: X3.
324. Diaz-Lagares A, Mendez-Gonzalez J, Hervas D, et al. A Novel Epigenetic Signature for Early Diagnosis in Lung Cancer. *Clin Cancer Res*. 2016 Jul 1;22(13):3361-71. doi: 10.1158/1078-0432.ccr-15-2346. PMID: 26842235. Exclusion Code: X5.
325. Dickey M, Roa W, Drodge S, et al. A planning comparison of 3-dimensional conformal multiple static field, conformal arc, and volumetric modulated arc therapy for the delivery of stereotactic body radiotherapy for early stage lung cancer. *Med Dosim*. 2015 Winter;40(4):347-51. doi: 10.1016/j.meddos.2015.04.006. PMID: 26027510. Exclusion Code: X8.

326. Digumarthy SR, Kovacina B, Otrakji A, et al. Percutaneous CT guided lung biopsy in patients with pulmonary hypertension: Assessment of complications. *Eur J Radiol*. 2016 Feb;85(2):466-71. doi: 10.1016/j.ejrad.2015.12.007. PMID: 26781153. Exclusion Code: X3.
327. Ding M, Zollinger W, Ebeling R, et al. Using max standardized uptake value from positron emission tomography to assess tumor responses after lung stereotactic body radiotherapy for different prescriptions. *J Appl Clin Med Phys*. 2018 Nov;19(6):226-33. doi: 10.1002/acm2.12453. PMID: 30216639. Exclusion Code: X3.
328. Diot Q, Kavanagh B, Schefter T, et al. Regional normal lung tissue density changes in patients treated with stereotactic body radiation therapy for lung tumors. *Int J Radiat Oncol Biol Phys*. 2012 Nov 15;84(4):1024-30. doi: 10.1016/j.ijrobp.2011.11.080. PMID: 22583607. Exclusion Code: X3.
329. Doll C, Duncker-Rohr V, Rucker G, et al. Influence of experience and qualification on PET-based target volume delineation. When there is no expert--ask your colleague. *Strahlenther Onkol*. 2014 Jun;190(6):555-62. doi: 10.1007/s00066-014-0644-y. PMID: 24615189. Exclusion Code: X3.
330. Dominioni L, Poli A, Mantovani W, et al. Assessment of lung cancer mortality reduction after chest X-ray screening in smokers: a population-based cohort study in Varese, Italy. *Lung Cancer*. 2013 Apr;80(1):50-4. doi: 10.1016/j.lungcan.2012.12.014. PMID: 23294502. Exclusion Code: X5.
331. Dominioni L, Rotolo N, Mantovani W, et al. A population-based cohort study of chest x-ray screening in smokers: lung cancer detection findings and follow-up. *BMC Cancer*. 2012 Jan 17;12:18. doi: 10.1186/1471-2407-12-18. PMID: 22251777. Exclusion Code: X5.
332. Dominioni L, Rotolo N, Poli A, et al. Cost of a population-based programme of chest x-ray screening for lung cancer. *Monaldi Arch Chest Dis*. 2013 Jun;79(2):67-72. doi: 10.4081/monaldi.2013.94. PMID: 24354094. Exclusion Code: X5.
333. Donahue JM, Morse CR, Wigle DA, et al. Oncologic efficacy of anatomic segmentectomy in stage IA lung cancer patients with T1a tumors. *Ann Thorac Surg*. 2012 Feb;93(2):381-7; discussion 7-8. doi: 10.1016/j.athoracsur.2011.10.079. PMID: 22209375. Exclusion Code: X11.
334. Dong S, Roberts SA, Chen S, et al. Survival after lobectomy versus sub-lobar resection in elderly with stage I NSCLC: a meta-analysis. *BMC Surg*. 2019 Apr 15;19(1):38. doi: 10.1186/s12893-019-0500-1. PMID: 30987622. Exclusion Code: X10.
335. Doseeva V, Colpitts T, Gao G, et al. Performance of a multiplexed dual analyte immunoassay for the early detection of non-small cell lung cancer. *J Transl Med*. 2015 Feb 12;13:55. doi: 10.1186/s12967-015-0419-y. PMID: 25880432. Exclusion Code: X5.
336. Dowling P, Clarke C, Hennessy K, et al. Analysis of acute-phase proteins, AHSG, C3, CLI, HP and SAA, reveals distinctive expression patterns associated with breast, colorectal and lung cancer. *Int J Cancer*. 2012 Aug 15;131(4):911-23. doi: 10.1002/ijc.26462. PMID: 21953030. Exclusion Code: X5.
337. Doyen J, Poudenx M, Gal J, et al. Stereotactic ablative radiotherapy after concomitant chemoradiotherapy in non-small cell lung cancer: A TITE-CRM phase 1 trial. *Radiother Oncol*. 2018 May;127(2):239-45. doi: 10.1016/j.radonc.2018.03.024. PMID: 29650404. Exclusion Code: X3.
338. Dreyer J, Bremer M, Henkenberens C. Comorbidity indexing for prediction of the clinical outcome after stereotactic body radiation therapy in non-small cell lung cancer. *Radiat Oncol*. 2018 Nov 3;13(1):213. doi: 10.1186/s13014-018-1156-1. PMID: 30390700. Exclusion Code: X3.
339. Du Q, Li E, Liu Y, et al. CTAPIII/CXCL7: a novel biomarker for early diagnosis of lung cancer. *Cancer Med*. 2018 Feb;7(2):325-35. doi: 10.1002/cam4.1292. PMID: 29356357. Exclusion Code: X3.
340. Duann CW, Hung JJ, Hsu PK, et al. Surgical outcomes in lung cancer presenting as ground-glass opacities of 3 cm or less: a review of 5 years' experience. *J Chin Med Assoc*. 2013 Dec;76(12):693-7. doi: 10.1016/j.jcma.2013.08.005. PMID: 24099986. Exclusion Code: X3.

341. Duffy SW, Field JK, Allgood PC, et al. Translation of research results to simple estimates of the likely effect of a lung cancer screening programme in the United Kingdom. *Br J Cancer*. 2014 Apr 2;110(7):1834-40. doi: 10.1038/bjc.2014.63. PMID: 24525696. Exclusion Code: X7.
342. Duijm M, Tekatli H, Oomen-de Hoop E, et al. Esophagus toxicity after stereotactic and hypofractionated radiotherapy for central lung tumors: Normal tissue complication probability modeling. *Radiother Oncol*. 2018 May;127(2):233-8. doi: 10.1016/j.radonc.2018.02.004. PMID: 29478763. Exclusion Code: X3.
343. Duncker-Rohr V, Nestle U, Momm F, et al. Stereotactic ablative radiotherapy for small lung tumors with a moderate dose. Favorable results and low toxicity. *Strahlenther Onkol*. 2013 Jan;189(1):33-40. doi: 10.1007/s00066-012-0224-y. PMID: 23179248. Exclusion Code: X10.
344. Dunlap NE, Yang W, McIntosh A, et al. Computed tomography-based anatomic assessment overestimates local tumor recurrence in patients with mass-like consolidation after stereotactic body radiotherapy for early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2012 Dec 1;84(5):1071-7. doi: 10.1016/j.ijrobp.2012.01.088. PMID: 22898383. Exclusion Code: X3.
345. Dupont G, Flory L, Morel J, et al. Postoperative lymphopenia: An independent risk factor for postoperative pneumonia after lung cancer surgery, results of a case-control study. *PLoS One*. 2018;13(10):e0205237. doi: 10.1371/journal.pone.0205237. PMID: 30321194. Exclusion Code: X3.
346. Ebara K, Takashima S, Jiang B, et al. Pleural invasion by peripheral lung cancer: prediction with three-dimensional CT. *Acad Radiol*. 2015 Mar;22(3):310-9. doi: 10.1016/j.acra.2014.10.002. PMID: 25542401. Exclusion Code: X3.
347. Echavarria MF, Cheng AM, Velez-Cubian FO, et al. Comparison of pulmonary function tests and perioperative outcomes after robotic-assisted pulmonary lobectomy vs segmentectomy. *Am J Surg*. 2016 Dec;212(6):1175-82. doi: 10.1016/j.amjsurg.2016.09.017. PMID: 27823756. Exclusion Code: X11.
348. Eguchi T, Bains S, Lee MC, et al. Impact of Increasing Age on Cause-Specific Mortality and Morbidity in Patients With Stage I Non-Small-Cell Lung Cancer: A Competing Risks Analysis. *J Clin Oncol*. 2017 Jan 20;35(3):281-90. doi: 10.1200/jco.2016.69.0834. PMID: 28095268. Exclusion Code: X3.
349. Elsayad K, Kriz J, Reinartz G, et al. Cone-beam CT-guided radiotherapy in the management of lung cancer: Diagnostic and therapeutic value. *Strahlenther Onkol*. 2016 Feb;192(2):83-91. doi: 10.1007/s00066-015-0927-y. PMID: 26630946. Exclusion Code: X3.
350. Elsayad K, Samhouri L, Scobioala S, et al. Is tumor volume reduction during radiotherapy prognostic relevant in patients with stage III non-small cell lung cancer? *J Cancer Res Clin Oncol*. 2018 Jun;144(6):1165-71. doi: 10.1007/s00432-018-2640-6. PMID: 29623466. Exclusion Code: X3.
351. Enache I, Noel G, Jeung MY, et al. Impact of 3D conformal radiotherapy on lung function of patients with lung cancer: a prospective study. *Respiration*. 2013;86(2):100-8. doi: 10.1159/000342371. PMID: 23154264. Exclusion Code: X3.
352. Endo C, Sakurada A, Notsuda H, et al. Results of long-term follow-up of patients with completely resected non-small cell lung cancer. *Ann Thorac Surg*. 2012 Apr;93(4):1061-8. doi: 10.1016/j.athoracsur.2012.01.004. PMID: 22386090. Exclusion Code: X11.
353. Eo JS, Kim HK, Kim S, et al. Gallium-68 neomannosylated human serum albumin-based PET/CT lymphoscintigraphy for sentinel lymph node mapping in non-small cell lung cancer. *Ann Surg Oncol*. 2015 Feb;22(2):636-41. doi: 10.1245/s10434-014-3986-x. PMID: 25155392. Exclusion Code: X8.
354. Eom JS, Mok JH, Kim I, et al. Radial probe endobronchial ultrasound using a guide sheath for peripheral lung lesions in beginners. *BMC Pulm Med*. 2018 Aug 13;18(1):137. doi: 10.1186/s12890-018-0704-7. PMID: 30103727. Exclusion Code: X3.

355. Erasmus JJ, Gladish GW, Broemeling L, et al. Interobserver and intraobserver variability in measurement of non-small-cell carcinoma lung lesions: implications for assessment of tumor response. *J Clin Oncol*. 2003 Jul 1;21(13):2574-82. doi: 10.1200/jco.2003.01.144. PMID: 12829678. Exclusion Code: X3.

356. Eriguchi T, Takeda A, Sanuki N, et al. Stereotactic body radiotherapy for operable early-stage non-small cell lung cancer. *Lung Cancer*. 2017 Jul;109:62-7. doi: 10.1016/j.lungcan.2017.04.022. PMID: 28577952. Exclusion Code: X10.

357. Erkmen CP, Mitchell M, Randhawa S, et al. An Enhanced Shared Decision Making Model to Address Willingness and Ability to Undergo Lung Cancer Screening and Follow-Up Treatment in Minority Underserved Populations. *J Community Health*. 2018 Feb;43(1):27-32. doi: 10.1007/s10900-017-0383-y. PMID: 28612174. Exclusion Code: X8.

358. Erol Y, Cakan A, Ergonul AG, et al. Psychiatric assessments in patients operated on due to lung cancer. *Asian Cardiovasc Thorac Ann*. 2017 Sep-Oct;25(7-8):518-21. doi: 10.1177/0218492317724044. PMID: 28776419. Exclusion Code: X3.

359. Etzel CJ, Kachroo S, Liu M, et al. Development and validation of a lung cancer risk prediction model for African-Americans. *Cancer Prev Res (Phila)*. 2008 Sep;1(4):255-65. doi: 10.1158/1940-6207.CAPR-08-0082. PMID: 19138969. Exclusion Code: X7.

360. Evangelista L, Cuocolo A, Pace L, et al. Performance of FDG-PET/CT in solitary pulmonary nodule based on pre-test likelihood of malignancy: results from the ITALIAN retrospective multicenter trial. *Eur J Nucl Med Mol Imaging*. 2018 Oct;45(11):1898-907. doi: 10.1007/s00259-018-4016-1. PMID: 29736699. Exclusion Code: X3.

361. Everitt S, Ball D, Hicks RJ, et al. Prospective Study of Serial Imaging Comparing Fluorodeoxyglucose Positron Emission Tomography (PET) and Fluorothymidine PET During Radical Chemoradiation for Non-Small Cell Lung Cancer: Reduction of Detectable Proliferation Associated With Worse Survival. *Int J Radiat Oncol Biol Phys*. 2017 Nov 15;99(4):947-55. doi: 10.1016/j.ijrobp.2017.07.035. PMID: 29063854. Exclusion Code: X3.

362. Everitt S, Schneider-Kolsky M, Yuen K, et al. Dose escalation of radical radiation therapy in non-small-cell lung cancer using positron emission tomography/computed tomography-defined target volumes: are class solutions obsolete? *J Med Imaging Radiat Oncol*. 2008 Apr;52(2):168-77. doi: 10.1111/j.1440-1673.2008.01937.x. PMID: 18373810. Exclusion Code: X3.

363. Evison M, Crosbie PA, Martin J, et al. EBUS-TBNA in elderly patients with lung cancer: safety and performance outcomes. *J Thorac Oncol*. 2014 Mar;9(3):370-6. doi: 10.1097/jto.0000000000000085. PMID: 24518088. Exclusion Code: X3.

364. Evison M, Edwards T, Balata H, et al. Prevalence of nodal metastases in lymph node stations 8 & 9 in a large UK lung cancer surgical centre without routine pre-operative EUS nodal staging. *Lung Cancer*. 2018 Jan;115:127-30. doi: 10.1016/j.lungcan.2017.11.023. PMID: 29290254. Exclusion Code: X3.

365. Evison M, Morris J, Martin J, et al. Nodal staging in lung cancer: a risk stratification model for lymph nodes classified as negative by EBUS-TBNA. *J Thorac Oncol*. 2015 Jan;10(1):126-33. doi: 10.1097/jto.0000000000000348. PMID: 25371076. Exclusion Code: X3.

366. Ezer N, Veluswamy RR, Mhango G, et al. Outcomes after Stereotactic Body Radiotherapy versus Limited Resection in Older Patients with Early-Stage Lung Cancer. *J Thorac Oncol*. 2015 Aug;10(8):1201-6. doi: 10.1097/jto.0000000000000600. PMID: 26200275. Exclusion Code: X3.

367. Fagundes CP, Shi Q, Vaporciyan AA, et al. Symptom recovery after thoracic surgery: Measuring patient-reported outcomes with the MD Anderson Symptom Inventory. *J Thorac Cardiovasc Surg*. 2015 Sep;150(3):613-9.e2. doi: 10.1016/j.jtcvs.2015.05.057. PMID: 26088408. Exclusion Code: X11.
368. Fakiris AJ, McGarry RC, Yiannoutsos CT, et al. Stereotactic body radiation therapy for early-stage non-small-cell lung carcinoma: four-year results of a prospective phase II study. *Int J Radiat Oncol Biol Phys*. 2009 Nov 1;75(3):677-82. doi: 10.1016/j.ijrobp.2008.11.042. PMID: 19251380. Exclusion Code: X11.
369. Fan L, Liu SY, Li QC, et al. Multidetector CT features of pulmonary focal ground-glass opacity: differences between benign and malignant. *Br J Radiol*. 2012 Jul;85(1015):897-904. doi: 10.1259/bjr/33150223. PMID: 22128130. Exclusion Code: X3.
370. Fan XL, Liu YX, Tian H. Video-assisted thoracoscopic surgery for treatment of early-stage non-small cell lung cancer. *Asian Pac J Cancer Prev*. 2013;14(5):2871-7. PMID: 23803046. Exclusion Code: X3.
371. Fang HY, Chen CY, Wang YC, et al. Consistently lower narcotics consumption after video-assisted thoracoscopic surgery for early stage non-small cell lung cancer when compared to open surgery: a one-year follow-up study. *Eur J Cardiothorac Surg*. 2013 Apr;43(4):783-6. doi: 10.1093/ejcts/ezs370. PMID: 22864790. Exclusion Code: X11.
372. Fang Z, He J, Fang W, et al. Long-term Outcomes of Thoracoscopic Anatomic Resections and Systematic Lymphadenectomy for Elderly High-risk Patients with Stage IB Non-small-cell Lung Cancer. *Heart Lung Circ*. 2016 Apr;25(4):392-7. doi: 10.1016/j.hlc.2015.08.022. PMID: 26546096. Exclusion Code: X11.
373. Fanidi A, Muller DC, Yuan JM, et al. Circulating Folate, Vitamin B6, and Methionine in Relation to Lung Cancer Risk in the Lung Cancer Cohort Consortium (LC3). *J Natl Cancer Inst*. 2018 Jan 1;110(1)doi: 10.1093/jnci/djx119. PMID: 28922778. Exclusion Code: X4.
374. Faris NR, Smeltzer MP, Lu F, et al. Evolution in the Surgical Care of Patients With Non-Small Cell Lung Cancer in the Mid-South Quality of Surgical Resection Cohort. *Semin Thorac Cardiovasc Surg*. 2017 Spring;29(1):91-101. doi: 10.1053/j.semtcvs.2016.10.001. PMID: 28684006. Exclusion Code: X8.
375. Farjah F, Backhus L, Cheng A, et al. Failure to rescue and pulmonary resection for lung cancer. *J Thorac Cardiovasc Surg*. 2015 May;149(5):1365-71; discussion 71-3.e3. doi: 10.1016/j.jtcvs.2015.01.063. PMID: 25791948. Exclusion Code: X3.
376. Farjah F, Wood DE, Zadworny ME, et al. Resected Lung Cancer Patients Who Would and Would Not Have Met Screening Criteria. *Ann Thorac Surg*. 2016 Jan;101(1):274-9. doi: 10.1016/j.athoracsur.2015.06.010. PMID: 26298169. Exclusion Code: X3.
377. Farr KP, Kallehauge JF, Moller DS, et al. Inclusion of functional information from perfusion SPECT improves predictive value of dose-volume parameters in lung toxicity outcome after radiotherapy for non-small cell lung cancer: A prospective study. *Radiother Oncol*. 2015 Oct;117(1):9-16. doi: 10.1016/j.radonc.2015.08.005. PMID: 26303012. Exclusion Code: X3.
378. Fassina A, Corradin M, Zardo D, et al. Role and accuracy of rapid on-site evaluation of CT-guided fine needle aspiration cytology of lung nodules. *Cytopathology*. 2011 Oct;22(5):306-12. doi: 10.1111/j.1365-2303.2010.00802.x. PMID: 20738359. Exclusion Code: X3.
379. Feczko A, McKeown E, Wilson JL, et al. Assessing Survival and Grading the Severity of Complications in Octogenarians Undergoing Pulmonary Lobectomy. *Can Respir J*. 2017;2017:6294895. doi: 10.1155/2017/6294895. PMID: 28270738. Exclusion Code: X11.
380. Federman DG, Kravetz JD, Lerz KA, et al. Implementation of an electronic clinical reminder to improve rates of lung cancer screening. *Am J Med*. 2014 Sep;127(9):813-6. doi: 10.1016/j.amjmed.2014.04.010. PMID: 24769298. Exclusion Code: X8.

381. Feng M, Yang X, Ma Q, et al. Retrospective analysis for the false positive diagnosis of PET-CT scan in lung cancer patients. *Medicine (Baltimore)*. 2017 Oct;96(42):e7415. doi: 10.1097/md.0000000000007415. PMID: 29049175. Exclusion Code: X3.
382. Feng M, Zhao J, Wang L, et al. Upregulated Expression of Serum Exosomal microRNAs as Diagnostic Biomarkers of Lung Adenocarcinoma. *Ann Clin Lab Sci*. 2018 Nov;48(6):712-8. PMID: 30610040. Exclusion Code: X3.
383. Ferguson JS, Van Wert R, Choi Y, et al. Impact of a bronchial genomic classifier on clinical decision making in patients undergoing diagnostic evaluation for lung cancer. *BMC Pulm Med*. 2016 May 17;16(1):66. doi: 10.1186/s12890-016-0217-1. PMID: 27184093. Exclusion Code: X3.
384. Ferguson MK, Watson S, Johnson E, et al. Predicted postoperative lung function is associated with all-cause long-term mortality after major lung resection for cancer. *Eur J Cardiothorac Surg*. 2014 Apr;45(4):660-4. doi: 10.1093/ejcts/ezt462. PMID: 24052607. Exclusion Code: X3.
385. Fernandes P, Lareiro S, Vouga L, et al. Uniportal Video-Assisted Thorascoscopic Surgery - The New Paradigm in the Surgical Treatment of Lung Cancer. *Rev Port Cir Cardiotorac Vasc*. 2017 Jul-Dec;24(3-4):127. PMID: 29701369. Exclusion Code: X2.
386. Fernandez FG, Kosinski AS, Burfeind W, et al. The Society of Thoracic Surgeons Lung Cancer Resection Risk Model: Higher Quality Data and Superior Outcomes. *Ann Thorac Surg*. 2016 Aug;102(2):370-7. doi: 10.1016/j.athoracsur.2016.02.098. PMID: 27209606. Exclusion Code: X3.
387. Fernandez-Bussy S, Labarca G, Canals S, et al. Diagnostic yield of endobronchial ultrasound-guided transbronchial needle aspiration for mediastinal staging in lung cancer. *J Bras Pneumol*. 2015 May-Jun;41(3):219-24. doi: 10.1590/s1806-37132015000004466. PMID: 26176519. Exclusion Code: X3.
388. Fernando H, Timmerman R. American College of Surgeons Oncology Group Z4099/Radiation Therapy Oncology Group 1021: a randomized study of sublobar resection compared with stereotactic body radiotherapy for high-risk stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2012;144(3):S35-8. doi: 10.1016/j.jtcvs.2012.06.003. PMID: CN-00968594. Exclusion Code: X10.
389. Fernando HC, Landreneau RJ, Mandrekar SJ, et al. Analysis of longitudinal quality-of-life data in high-risk operable patients with lung cancer: results from the ACOSOG Z4032 (Alliance) multicenter randomized trial. *J Thorac Cardiovasc Surg*. 2015 Mar;149(3):718-25; discussion 25-6. doi: 10.1016/j.jtcvs.2014.11.003. PMID: 25500100. Exclusion Code: X11.
390. Fielding DI, Chia C, Nguyen P, et al. Prospective randomised trial of endobronchial ultrasound-guide sheath versus computed tomography-guided percutaneous core biopsies for peripheral lung lesions. *Intern Med J*. 2012 Aug;42(8):894-900. doi: 10.1111/j.1445-5994.2011.02707.x. PMID: 22212110. Exclusion Code: X11.
391. Filaire M, Tardy MM, Richard R, et al. Prophylactic tracheotomy and lung cancer resection in patient with low predictive pulmonary function: a randomized clinical trials. *Chin Clin Oncol*. 2015 Dec;4(4):40. doi: 10.3978/j.issn.2304-3865.2015.11.05. PMID: 26730752. Exclusion Code: X3.
392. Filippo L, Principe R, Cesario A, et al. Smoking cessation intervention within the framework of a lung cancer screening program: preliminary results and clinical perspectives from the "Cosmos-II" Trial. *Lung*. 2015 Feb;193(1):147-9. doi: 10.1007/s00408-014-9661-y. PMID: 25323328. Exclusion Code: X6.
393. Finley RJ, Mayo JR, Grant K, et al. Preoperative computed tomography-guided microcoil localization of small peripheral pulmonary nodules: a prospective randomized controlled trial. *J Thorac Cardiovasc Surg*. 2015 Jan;149(1):26-31. doi: 10.1016/j.jtcvs.2014.08.055. PMID: 25293355. Exclusion Code: X6.

394. Fintelmann FJ, Troschel FM, Mario J, et al. Thoracic Skeletal Muscle Is Associated With Adverse Outcomes After Lobectomy for Lung Cancer. *Ann Thorac Surg*. 2018 May;105(5):1507-15. doi: 10.1016/j.athoracsur.2018.01.013. PMID: 29408306. Exclusion Code: X3.
395. Fiorelli A, Caronia FP, Daddi N, et al. Sublobar resection versus lobectomy for stage I non-small cell lung cancer: an appropriate choice in elderly patients? *Surg Today*. 2016 Dec;46(12):1370-82. doi: 10.1007/s00595-016-1314-8. PMID: 27085869. Exclusion Code: X11.
396. Fiorelli A, Vicidomini G, Mazzella A, et al. The influence of body mass index and weight loss on outcome of elderly patients undergoing lung cancer resection. *Thorac Cardiovasc Surg*. 2014 Oct;62(7):578-87. doi: 10.1055/s-0034-1373733. PMID: 24959934. Exclusion Code: X3.
397. Fiorelli A, Vicidomini G, Milione R, et al. The effects of lung resection on physiological motor activity of the oesophagus. *Eur J Cardiothorac Surg*. 2013 Aug;44(2):250-6;discussion 7. doi: 10.1093/ejcts/ezs711. PMID: 23355690. Exclusion Code: X3.
398. Fischer-Valuck BW, Boggs H, Katz S, et al. Comparison of stereotactic body radiation therapy for biopsy-proven versus radiographically diagnosed early-stage non-small lung cancer: a single-institution experience. *Tumori*. 2015 May-Jun;101(3):287-93. doi: 10.5301/tj.5000279. PMID: 25908031. Exclusion Code: X3.
399. Fitzgerald NR, Flanagan WM, Evans WK, et al. Eligibility for low-dose computerized tomography screening among asbestos-exposed individuals. *Scand J Work Environ Health*. 2015 Jul;41(4):407-12. doi: 10.5271/sjweh.3496. PMID: 25837734. Exclusion Code: X8.
400. Flanagan WM, Evans WK, Fitzgerald NR, et al. Performance of the cancer risk management model lung cancer screening module. *Health Rep*. 2015 May;26(5):11-8. PMID: 25993046. Exclusion Code: X7.
401. Fleming C, Rimner A, Cohen GN, et al. High- and low-dose-rate intraoperative radiotherapy for thoracic malignancies resected with close or positive margins. *Brachytherapy*. 2016 Mar-Apr;15(2):208-15. doi: 10.1016/j.brachy.2015.11.007. PMID: 26825857. Exclusion Code: X3.
402. Fletcher JW, Kymes SM, Gould M, et al. A comparison of the diagnostic accuracy of 18F-FDG PET and CT in the characterization of solitary pulmonary nodules. *J Nucl Med*. 2008 Feb;49(2):179-85. doi: 10.2967/jnumed.107.044990. PMID: 18199626. Exclusion Code: X3.
403. Flores J, Moreno-Koehler A, Finkelman M, et al. Chest X-ray (CXR) screening improves outcomes in Lung Cancer (LC) in the Prostate, Lung, Colon, and Ovary (PLCO) Randomized Controlled Trial (RCT). *Chest*. 2015;148(4 MEETING ABSTRACT) (no pagination)doi: 10.1378/chest.2247102. PMID: CN-01129112. Exclusion Code: X5.
404. Flores R, Bauer T, Aye R, et al. Balancing curability and unnecessary surgery in the context of computed tomography screening for lung cancer. *J Thorac Cardiovasc Surg*. 2014 May;147(5):1619-26. doi: 10.1016/j.jtcvs.2013.11.001. PMID: 24332102. Exclusion Code: X11.
405. Flores R, Taioli E, Yankelevitz DF, et al. Initiative for Early Lung Cancer Research on Treatment: Development of Study Design and Pilot Implementation. *J Thorac Oncol*. 2018 Jul;13(7):946-57. doi: 10.1016/j.jtho.2018.03.009. PMID: 29578108. Exclusion Code: X11.
406. Flores RM, Nicastri D, Bauer T, et al. Computed tomography screening for lung cancer: mediastinal lymph node resection in stage IA nonsmall cell lung cancer manifesting as subsolid and solid Nodules. *Ann Surg*. 2017 May;265(5):1025-33. doi: 10.1097/sla.0000000000001802. PMID: 27232256. Exclusion Code: X8.
407. Fontaine-Delaruelle C, Souquet PJ, Gamondes D, et al. Negative predictive value of transthoracic core-needle biopsy: a multicenter study. *Chest*. 2015 Aug;148(2):472-80. doi: 10.1378/chest.14-1907. PMID: 25569025. Exclusion Code: X3.
408. Foster CC, Rusthoven CG, Sher DJ, et al. Adjuvant chemotherapy following stereotactic body radiotherapy for early stage non-small-cell lung cancer is associated with lower overall: A National Cancer Database Analysis. *Lung Cancer*. 2019 Apr;130:162-8. doi: 10.1016/j.lungcan.2019.02.023. PMID: 30885339. Exclusion Code: X3.

409. Fox M, Van Berkel V, Bousamra M, 2nd, et al. Surgical management of pulmonary carcinoid tumors: sublobar resection versus lobectomy. *Am J Surg*. 2013 Feb;205(2):200-8. doi: 10.1016/j.amjsurg.2012.05.008. PMID: 23063095. Exclusion Code: X3.
410. Foy M, Spitz MR, Kimmel M, et al. A smoking-based carcinogenesis model for lung cancer risk prediction. *Int J Cancer*. 2011 Oct 15;129(8):1907-13. doi: 10.1002/ijc.25834. PMID: 21140453. Exclusion Code: X7.
411. Fraioli F, Catalano C, Almberger M, et al. Evaluation of effectiveness of a computer system (CAD) in the identification of lung nodules with low-dose MSCT: scanning technique and preliminary results. *Radiol Med*. 2005 Jan-Feb;109(1-2):40-8. PMID: 15729185. Exclusion Code: X3.
412. Fraioli F, Screaton NJ, Janes SM, et al. Non-small-cell lung cancer resectability: diagnostic value of PET/MR. *Eur J Nucl Med Mol Imaging*. 2015 Jan;42(1):49-55. doi: 10.1007/s00259-014-2873-9. PMID: 25120040. Exclusion Code: X6.
413. Franco I, Chen YH, Chipidza F, et al. Use of frailty to predict survival in elderly patients with early stage non-small-cell lung cancer treated with stereotactic body radiation therapy. *J Geriatr Oncol*. 2018 Mar;9(2):130-7. doi: 10.1016/j.jgo.2017.09.002. PMID: 28941581. Exclusion Code: X3.
414. Franke KJ, Hein M, Domanski U, et al. Transbronchial catheter aspiration and transbronchial needle aspiration in the diagnostic workup of peripheral lung lesions. *Lung*. 2015 Oct;193(5):767-72. doi: 10.1007/s00408-015-9763-1. PMID: 26156311. Exclusion Code: X11.
415. Freeman RK, Dilts JR, Ascioti AJ, et al. A comparison of quality and cost indicators by surgical specialty for lobectomy of the lung. *J Thorac Cardiovasc Surg*. 2013 Jan;145(1):68-73; discussion -4. doi: 10.1016/j.jtcvs.2012.09.012. PMID: 23058669. Exclusion Code: X8.
416. Frood R, Prestwich R, Tsoumpas C, et al. Effectiveness of Respiratory-gated Positron Emission Tomography/Computed Tomography for Radiotherapy Planning in Patients with Lung Carcinoma - A Systematic Review. *Clin Oncol (R Coll Radiol)*. 2018 Apr;30(4):225-32. doi: 10.1016/j.clon.2018.01.005. PMID: 29397271. Exclusion Code: X3.
417. Fu M, Travier N, Martin-Sanchez JC, et al. Identifying high-risk individuals for lung cancer screening: Going beyond NLST criteria. *PLoS One*. 2018;13(4):e0195441. doi: 10.1371/journal.pone.0195441. PMID: 29621354. Exclusion Code: X8.
418. Fu SS, Rothman AJ, Vock DM, et al. Program for lung cancer screening and tobacco cessation: Study protocol of a sequential, multiple assignment, randomized trial. *Contemp Clin Trials*. 2017 Sep;60:86-95. doi: 10.1016/j.cct.2017.07.002. PMID: 28687349. Exclusion Code: X8.
419. Fu YF, Gao YG, Zhang M, et al. Computed tomography-guided simultaneous coil localization as a bridge to one-stage surgery for multiple lung nodules: a retrospective study. *J Cardiothorac Surg*. 2019 Feb 26;14(1):43. doi: 10.1186/s13019-019-0870-6. PMID: 30808426. Exclusion Code: X3.
420. Fuchs FS, Zirlik S, Hildner K, et al. Confocal laser endomicroscopy for diagnosing lung cancer in vivo. *Eur Respir J*. 2013 Jun;41(6):1401-8. doi: 10.1183/09031936.00062512. PMID: 22997220. Exclusion Code: X3.
421. Fujii O, Demizu Y, Hashimoto N, et al. Particle therapy for clinically diagnosed stage I lung cancer: comparison with pathologically proven non-small cell lung cancer. *Acta Oncol*. 2015 Mar;54(3):315-21. doi: 10.3109/0284186x.2014.974828. PMID: 25383445. Exclusion Code: X6.
422. Fukui M, Suzuki K, Matsunaga T, et al. Outcomes of lung cancer resection for patients with combined pulmonary fibrosis and emphysema. *Surg Today*. 2016 Mar;46(3):341-7. doi: 10.1007/s00595-015-1234-z. PMID: 26276308. Exclusion Code: X11.
423. Fukui M, Takamochi K, Matsunaga T, et al. Risk of the preoperative underestimation of tumour size of lung cancer in patients with idiopathic interstitial pneumonias. *Eur J Cardiothorac Surg*. 2016 Sep;50(3):428-32. doi: 10.1093/ejcts/ezw065. PMID: 26987880. Exclusion Code: X8.

424. Fukui T, Kato K, Okasaka T, et al. Predictors for hilar/intrapulmonary lymph node metastasis in discrete type of clinical N1 non-small cell lung cancer. *Gen Thorac Cardiovasc Surg*. 2017 Nov;65(11):640-5. doi: 10.1007/s11748-017-0827-4. PMID: 28866794. Exclusion Code: X3.

425. Fukushima T, Tateishi K, Hanaoka M, et al. Clinical outcomes in patients with small cell lung cancer in a single institute: Comparative analysis of radiographic screening with symptom-prompted patients. *Lung Cancer*. 2015 Apr;88(1):48-51. doi: 10.1016/j.lungcan.2015.01.025. PMID: 25703893. Exclusion Code: X3.

426. Fukushima T, Tateishi K, Yamamoto H, et al. Clinical characteristics and outcomes of patients with small cell lung cancer detected by CT screening. *Med Oncol*. 2013;30(3):623. doi: 10.1007/s12032-013-0623-7. PMID: 23740004. Exclusion Code: X3.

427. Fuso L, Varone F, Magnini D, et al. Role of ultrasound-guided transbronchial biopsy in the diagnosis of peripheral pulmonary lesions. *Lung Cancer*. 2013 Jul;81(1):60-4. doi: 10.1016/j.lungcan.2013.04.004. PMID: 23639784. Exclusion Code: X8.

428. Fuso L, Varone F, Magnini D, et al. Influence of the learning effect on the diagnostic yield of endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. *J Bronchology Interv Pulmonol*. 2017 Jul;24(3):193-9. doi: 10.1097/lbr.0000000000000372. PMID: 28696965. Exclusion Code: X3.

429. Gadaleta CD, Solbiati L, Mattioli V, et al. Unresectable lung malignancy: combination therapy with segmental pulmonary arterial chemoembolization with drug-eluting microspheres and radiofrequency ablation in 17 patients. *Radiology*. 2013 May;267(2):627-37. doi: 10.1148/radiol.12120198. PMID: 23249572. Exclusion Code: X3.

430. Galetta D, Solli P, Borri A, et al. Bilobectomy for lung cancer: analysis of indications, postoperative results, and long-term outcomes. *Ann Thorac Surg*. 2012 Jan;93(1):251-7; discussion 7-8. doi: 10.1016/j.athoracsur.2011.08.086. PMID: 22112798. Exclusion Code: X3.

431. Gallagher SP, Abolhoda A, Kirkpatrick VE, et al. Learning Curve of Robotic Lobectomy for Early-Stage Non-Small Cell Lung Cancer by a Thoracic Surgeon Adept in Open Lobectomy. *Innovations (Phila)*. 2018 Sep/Oct;13(5):321-7. doi: 10.1097/imi.0000000000000552. PMID: 30407925. Exclusion Code: X3.

432. Gallardo-Estrella L, Pompe E, de Jong PA, et al. Normalized emphysema scores on low dose CT: Validation as an imaging biomarker for mortality. *PLoS One*. 2017;12(12):e0188902. doi: 10.1371/journal.pone.0188902. PMID: 29227997. Exclusion Code: X3.

433. Ganti AK, Shostrom V, Alorabi M, et al. Early stage non-small-cell lung cancer in octogenarian and older patients: A SEER Database analysis. *Clin Lung Cancer*. 2016 Jul;17(4):285-91. doi: 10.1016/j.cllc.2015.11.014. PMID: 26725852. Exclusion Code: X12.

434. Ganti AK, Williams CD, Gajra A, et al. Effect of age on the efficacy of adjuvant chemotherapy for resected non-small cell lung cancer. *Cancer*. 2015 Aug 1;121(15):2578-85. doi: 10.1002/cncr.29360. PMID: 25873330. Exclusion Code: X6.

435. Gao S, Wu H, Li W, et al. A pilot study imaging integrin alphavbeta3 with RGD PET/CT in suspected lung cancer patients. *Eur J Nucl Med Mol Imaging*. 2015 Dec;42(13):2029-37. doi: 10.1007/s00259-015-3119-1. PMID: 26153145. Exclusion Code: X3.

436. Gao SJ, Kim AW, Puchalski JT, et al. Indications for invasive mediastinal staging in patients with early non-small cell lung cancer staged with PET-CT. *Lung Cancer*. 2017 Jul;109:36-41. doi: 10.1016/j.lungcan.2017.04.018. PMID: 28577947. Exclusion Code: X11.

437. Garcia-Garrigos E, Arenas-Jimenez JJ, Sanchez-Paya J. Best Protocol for Combined Contrast-Enhanced Thoracic and Abdominal CT for Lung Cancer: A Single-Institution Randomized Crossover Clinical Trial. *AJR Am J Roentgenol*. 2018 Jun;210(6):1226-34. doi: 10.2214/ajr.17.19185. PMID: 29570376. Exclusion Code: X3.

438. Garcia-Ortega A, Briones-Gomez A, Fabregat S, et al. Benefit of Chest Ultrasonography in the Diagnosis of Peripheral Thoracic Lesions in an Interventional Pulmonology Unit. *Arch Bronconeumol*. 2016 May;52(5):244-9. doi: 10.1016/j.arbres.2015.07.012. PMID: 26411258. Exclusion Code: X3.

439. Garcia-Velloso MJ, Bastarrika G, de-Torres JP, et al. Assessment of indeterminate pulmonary nodules detected in lung cancer screening: Diagnostic accuracy of FDG PET/CT. *Lung Cancer*. 2016 Jul;97:81-6. doi: 10.1016/j.lungcan.2016.04.025. PMID: 27237032. Exclusion Code: X5.

440. Gareen IF, Sicks JD, Jain AA, et al. Identifying and collecting pertinent medical records for centralized abstraction in a multi-center randomized clinical trial: the model used by the American College of Radiology arm of the National Lung Screening Trial. *Contemp Clin Trials*. 2013 Jan;34(1):36-44. doi: 10.1016/j.cct.2012.09.002. PMID: 22982342. Exclusion Code: X8.

441. Garg K, Keith RL, Byers T, et al. Randomized controlled trial with low-dose spiral CT for lung cancer screening: feasibility study and preliminary results. *Radiology*. 2002 Nov;225(2):506-10. doi: 10.1148/radiol.2252011851. PMID: 12409588. Exclusion Code: X8.

442. Gariani J, Martin SP, Hachulla AL, et al. Noninvasive pulmonary nodule characterization using transcutaneous bioconductance: Preliminary results of an observational study. *Medicine (Baltimore)*. 2018 Aug;97(34):e11924. doi: 10.1097/md.0000000000011924. PMID: 30142805. Exclusion Code: X3.

443. Garrido P, Vinolas N, Isla D, et al. Lung cancer in Spanish women: The WORLD07 project. *Eur J Cancer Care (Engl)*. 2019 Jan;28(1):e12941. doi: 10.1111/ecc.12941. PMID: 30277293. Exclusion Code: X3.

444. Ge H, Cai J, Kelsey CR, et al. Quantification and minimization of uncertainties of internal target volume for stereotactic body radiation therapy of lung cancer. *Int J Radiat Oncol Biol Phys*. 2013 Feb 1;85(2):438-43. doi: 10.1016/j.ijrobp.2012.04.032. PMID: 22687196. Exclusion Code: X8.

445. Ge X, Gao F, Li M, et al. Diagnostic value of solid component for lung adenocarcinoma shown as ground-glass nodule on computed tomography. *Zhonghua yi xue za zhi*. 2014;94(13):1010-3. PMID: CN-01116479. Exclusion Code: X1.

446. Gelbman BD, Cham MD, Kim W, et al. Radiographic and clinical characterization of false negative results from CT-guided needle biopsies of lung nodules. *J Thorac Oncol*. 2012 May;7(5):815-20. doi: 10.1097/JTO.0b013e31824abd9c. PMID: 22729035. Exclusion Code: X3.

447. Genestreti G, Bongiovanni A, Burgio MA, et al. 111In-Pentetreotide (OctreoScan) scintigraphy in the staging of small-cell lung cancer: its accuracy and prognostic significance. *Nucl Med Commun*. 2015 Feb;36(2):135-42. doi: 10.1097/mnm.0000000000000221. PMID: 25321157. Exclusion Code: X3.

448. Georgiou HD, Taverner J, Irving LB, et al. Safety and efficacy of radial EBUS for the investigation of peripheral pulmonary lesions in patients with advanced COPD. *J Bronchology Interv Pulmonol*. 2016 Jul;23(3):192-8. doi: 10.1097/lbr.0000000000000288. PMID: 27454473. Exclusion Code: X11.

449. Geraci T, Baratta V, Young J, et al. Lobectomy for lung cancer at Veterans Administration Medical Center versus academic medical center. *Ann Thorac Surg*. 2017 Jun;103(6):1715-22. doi: 10.1016/j.athoracsur.2016.12.040. PMID: 28347532. Exclusion Code: X11.

450. Geraldson CT, Stephenson JE, Lagrew JP, et al. Use of positron emission tomography in initial staging of nonsmall cell lung carcinoma: a regional teaching hospital experience. *Am Surg*. 2012 Mar;78(3):305-8. PMID: 22524768. Exclusion Code: X8.

451. Gerber DE, Hamann HA, Santini NO, et al. Patient navigation for lung cancer screening in an urban safety-net system: Protocol for a pragmatic randomized clinical trial. *Contemp Clin Trials*. 2017 Sep;60:78-85. doi: 10.1016/j.cct.2017.07.003. PMID: 28689056. Exclusion Code: X8.

452. Ghaly G, Kamel M, Nasar A, et al. Video-assisted thoracoscopic surgery is a safe and effective alternative to thoracotomy for anatomical segmentectomy in patients with clinical stage I non-small cell lung cancer. *Ann Thorac Surg*. 2016 Feb;101(2):465-72; discussion 72. doi: 10.1016/j.athoracsur.2015.06.112. PMID: 26391692. Exclusion Code: X11.
453. Ghaly G, Rahouma M, Kamel MK, et al. Clinical predictors of nodal metastases in peripherally clinical T1a N0 non-small cell lung cancer. *Ann Thorac Surg*. 2017 Oct;104(4):1153-8. doi: 10.1016/j.athoracsur.2017.02.074. PMID: 28551047. Exclusion Code: X11.
454. Gianella P, Soccal PM, Plojoux J, et al. Utility of Rapid On-Site Cytologic Evaluation during Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration in Malignant and Nonmalignant Disease. *Acta Cytol*. 2018;62(5-6):380-5. doi: 10.1159/000493334. PMID: 30244239. Exclusion Code: X3.
455. Gibson G, Kumar AR, Steinke K, et al. Risk stratification in the investigation of pulmonary nodules in a high-risk cohort: positron emission tomography/computed tomography outperforms clinical risk prediction algorithms. *Intern Med J*. 2017 Dec;47(12):1385-92. doi: 10.1111/imj.13576. PMID: 28782248. Exclusion Code: X3.
456. Gierada DS, Pilgram TK, Ford M, et al. Lung cancer: interobserver agreement on interpretation of pulmonary findings at low-dose CT screening. *Radiology*. 2008 Jan;246(1):265-72. doi: 10.1148/radiol.2461062097. PMID: 18024436. Exclusion Code: X11.
457. Gierada DS, Politte DG, Zheng J, et al. Quantitative computed tomography classification of lung nodules: initial comparison of 2- and 3-dimensional analysis. *J Comput Assist Tomogr*. 2016 Jul-Aug;40(4):589-95. doi: 10.1097/rct.0000000000000394. PMID: 27096403. Exclusion Code: X3.
458. Gietema HA, Wang Y, Xu D, et al. Pulmonary nodules detected at lung cancer screening: interobserver variability of semiautomated volume measurements. *Radiology*. 2006 Oct;241(1):251-7. doi: 10.1148/radiol.2411050860. PMID: 16908677. Exclusion Code: X3.
459. Gilbert S, Maghera S, Seely AJ, et al. Identifying patients at higher risk of prolonged air leak after lung resection. *Ann Thorac Surg*. 2016 Nov;102(5):1674-9. doi: 10.1016/j.athoracsur.2016.05.035. PMID: 27457828. Exclusion Code: X3.
460. Gill RR, Zheng Y, Barlow JS, et al. Image-guided video assisted thoracoscopic surgery (iVATS) - phase I-II clinical trial. *J Surg Oncol*. 2015 Jul;112(1):18-25. doi: 10.1002/jso.23941. PMID: 26031893. Exclusion Code: X11.
461. Girard P, Caliandro R, Seguin-Givelet A, et al. Sensitivity of cytology specimens from bronchial aspirate or washing during bronchoscopy in the diagnosis of lung malignancies: an update. *Clin Lung Cancer*. 2017 Sep;18(5):512-8. doi: 10.1016/j.cllc.2016.11.009. PMID: 28007409. Exclusion Code: X8.
462. Giti R, Hosseinzadeh M. Efficacy of Bronchial Washing and Brushing Cytology in the Diagnosis of Non-Neoplastic Lung Diseases. *Acta Med Iran*. 2017 Oct;55(10):636-41. PMID: 29228529. Exclusion Code: X3.
463. Glick D, Lyen S, Kandel S, et al. Impact of Pretreatment Interstitial Lung Disease on Radiation Pneumonitis and Survival in Patients Treated With Lung Stereotactic Body Radiation Therapy (SBRT). *Clin Lung Cancer*. 2018 Mar;19(2):e219-e26. doi: 10.1016/j.cllc.2017.06.021. PMID: 29066051. Exclusion Code: X3.
464. Go T, Misaki N, Matsuura N, et al. Role of surgery in multi-modality treatment for carcinomatous pleuritis in patients with non-small cell lung cancer. *Surg Today*. 2015 Feb;45(2):197-202. doi: 10.1007/s00595-014-0987-0. PMID: 25034395. Exclusion Code: X3.
465. Gobara H, Arai Y, Kobayashi T, et al. Percutaneous radiofrequency ablation for patients with malignant lung tumors: a phase II prospective multicenter study (JIVROSG-0702). *Jpn J Radiol*. 2016 Aug;34(8):556-63. doi: 10.1007/s11604-016-0557-z. PMID: 27260478. Exclusion Code: X6.
466. Gohagan JK, Broski K, Gren LH, et al. Managing multi-center recruitment in the PLCO Cancer Screening Trial. *Rev Recent Clin Trials*. 2015;10(3):187-93. PMID: 26435288. Exclusion Code: X11.

467. Goldwasser DL. Estimation of the tumor size at cure threshold among aggressive non-small cell lung cancers (NSCLCs): evidence from the surveillance, epidemiology, and end results (SEER) program and the national lung screening trial (NLST). *Int J Cancer*. 2017 Mar 15;140(6):1280-92. doi: 10.1002/ijc.30548. PMID: 27925181. Exclusion Code: X10.
468. Goldwasser DL, Kimmel M. Small median tumor diameter at cure threshold (<20 mm) among aggressive non-small cell lung cancers in male smokers predicts both chest X-ray and CT screening outcomes in a novel simulation framework. *Int J Cancer*. 2013 Jan 1;132(1):189-97. doi: 10.1002/ijc.27599. PMID: 22510979. Exclusion Code: X7.
469. Gomez DR, Gillin M, Liao Z, et al. Phase 1 study of dose escalation in hypofractionated proton beam therapy for non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2013 Jul 15;86(4):665-70. doi: 10.1016/j.ijrobp.2013.03.035. PMID: 23688815. Exclusion Code: X6.
470. Gomez-Caro A, Boada M, Cabanas M, et al. False-negative rate after positron emission tomography/computer tomography scan for mediastinal staging in cI stage non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2012 Jul;42(1):93-100; discussion doi: 10.1093/ejcts/ezr272. PMID: 22290911. Exclusion Code: X11.
471. Gong J, Liu JY, Jiang YJ, et al. Fusion of quantitative imaging features and serum biomarkers to improve performance of computer-aided diagnosis scheme for lung cancer: A preliminary study. *Med Phys*. 2018 Dec;45(12):5472-81. doi: 10.1002/mp.13237. PMID: 30317652. Exclusion Code: X3.
472. Gong J, Liu JY, Sun XW, et al. Computer-aided diagnosis of lung cancer: the effect of training data sets on classification accuracy of lung nodules. *Phys Med Biol*. 2018 Feb 5;63(3):035036. doi: 10.1088/1361-6560/aaa610. PMID: 29311420. Exclusion Code: X3.
473. Gonzalez J, de-Torres JP. Lung cancer and emphysema. *Arch Bronconeumol*. 2017 Feb;53(2):47-8. doi: 10.1016/j.arbres.2016.07.010. PMID: 27566892. Exclusion Code: X2.
474. Gonzalez-Perez V, Arana E, Barrios M, et al. Differentiation of benign and malignant lung lesions: dual-energy computed tomography findings. *Eur J Radiol*. 2016 Oct;85(10):1765-72. doi: 10.1016/j.ejrad.2016.07.019. PMID: 27666614. Exclusion Code: X3.
475. Gonzalez-Rivas D, Kuo YC, Wu CY, et al. Predictive factors of postoperative complications in single-port video-assisted thoracoscopic anatomical resection: Two center experience. *Medicine (Baltimore)*. 2018 Oct;97(40):e12664. doi: 10.1097/md.0000000000012664. PMID: 30290649. Exclusion Code: X3.
476. Gossot D, Lutz JA, Grigoroiu M, et al. Unplanned procedures during thoracoscopic segmentectomies. *Ann Thorac Surg*. 2017 Nov;104(5):1710-7. doi: 10.1016/j.athoracsur.2017.05.081. PMID: 28969898. Exclusion Code: X11.
477. Grassberger C, Daartz J, Dowdell S, et al. Quantification of proton dose calculation accuracy in the lung. *Int J Radiat Oncol Biol Phys*. 2014 Jun 1;89(2):424-30. doi: 10.1016/j.ijrobp.2014.02.023. PMID: 24726289. Exclusion Code: X3.
478. Grasso RF, Cazzato RL, Luppi G, et al. Percutaneous lung biopsies: performance of an optical CT-based navigation system with a low-dose protocol. *Eur Radiol*. 2013 Nov;23(11):3071-6. doi: 10.1007/s00330-013-2932-9. PMID: 23783784. Exclusion Code: X3.
479. Gray SW, Landrum MB, Lamont EB, et al. Improved outcomes associated with higher surgery rates for older patients with early stage nonsmall cell lung cancer. *Cancer*. 2012 Mar 1;118(5):1404-11. doi: 10.1002/cncr.26363. PMID: 21800285. Exclusion Code: X12.
480. Green A, Hauge J, Iachina M, et al. The mortality after surgery in primary lung cancer: results from the Danish Lung Cancer Registry. *Eur J Cardiothorac Surg*. 2016 Feb;49(2):589-94. doi: 10.1093/ejcts/ezv107. PMID: 25825264. Exclusion Code: X3.
481. Greenberg AK, Lu F, Goldberg JD, et al. CT scan screening for lung cancer: risk factors for nodules and malignancy in a high-risk urban cohort. *PLoS One*. 2012;7(7):e39403. doi: 10.1371/journal.pone.0039403. PMID: 22768300. Exclusion Code: X7.

482. Greillier L, Cortot AB, Viguier J, et al. Perception of Lung Cancer Risk: Impact of Smoking Status and Nicotine Dependence. *Curr Oncol Rep*. 2018 Mar 5;20(Suppl 1):18. doi: 10.1007/s11912-017-0650-1. PMID: 29508085. Exclusion Code: X3.
483. Grills IS, Mangona VS, Welsh R, et al. Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer. *J Clin Oncol*. 2010 Feb 20;28(6):928-35. doi: 10.1200/jco.2009.25.0928. PMID: 20065181. Exclusion Code: X11.
484. Grinberg M, Djureinovic D, Brunnstrom HR, et al. Reaching the limits of prognostication in non-small cell lung cancer: an optimized biomarker panel fails to outperform clinical parameters. *Mod Pathol*. 2017 Jul;30(7):964-77. doi: 10.1038/modpathol.2017.14. PMID: 28281552. Exclusion Code: X3.
485. Grivaux M, Debieuvre D, Herman D, et al. Early mortality in lung cancer: French prospective multicentre observational study. *BMC Pulm Med*. 2016 Apr 2;16:45. doi: 10.1186/s12890-016-0205-5. PMID: 27039176. Exclusion Code: X3.
486. Grose D, Morrison DS, Devereux G, et al. The impact of comorbidity upon determinants of outcome in patients with lung cancer. *Lung Cancer*. 2015 Feb;87(2):186-92. doi: 10.1016/j.lungcan.2014.11.012. PMID: 25498829. Exclusion Code: X11.
487. Gross DJ, Chang EH, Rosen PL, et al. Outcomes in video-assisted thoracoscopic surgery lobectomies: challenging preconceived notions. *J Surg Res*. 2018 Nov;231:161-6. doi: 10.1016/j.jss.2018.05.040. PMID: 30278924. Exclusion Code: X3.
488. Grossi F, Belvedere O, Fasola G, et al. Tumor measurements on computed tomographic images of non-small cell lung cancer were similar among cancer professionals from different specialties. *J Clin Epidemiol*. 2004 Aug;57(8):804-8. doi: 10.1016/j.jclinepi.2003.12.020. PMID: 15485732. Exclusion Code: X3.
489. Grosso M, Priotto R, Ghirardo D, et al. Comparison of digital tomosynthesis and computed tomography for lung nodule detection in SOS screening program. *Radiol Med*. 2017 Aug;122(8):568-74. doi: 10.1007/s11547-017-0765-3. PMID: 28429205. Exclusion Code: X3.
490. Grove O, Berglund AE, Schabath MB, et al. Quantitative computed tomographic descriptors associate tumor shape complexity and intratumor heterogeneity with prognosis in lung adenocarcinoma. *PLoS One*. 2015;10(3):e0118261. doi: 10.1371/journal.pone.0118261. PMID: 25739030. Exclusion Code: X11.
491. Gu B, Burt BM, Merritt RE, et al. A dominant adenocarcinoma with multifocal ground glass lesions does not behave as advanced disease. *Ann Thorac Surg*. 2013 Aug;96(2):411-8. doi: 10.1016/j.athoracsur.2013.04.048. PMID: 23806231. Exclusion Code: X11.
492. Gu C, Pan X, Chen Y, et al. Short-term and mid-term survival in bronchial sleeve resection by robotic system versus thoracotomy for centrally located lung cancer. *Eur J Cardiothorac Surg*. 2018 Mar 1;53(3):648-55. doi: 10.1093/ejcts/ezx355. PMID: 29029111. Exclusion Code: X10.
493. Gu C, Wang R, Pan X, et al. Sublobar resection versus lobectomy in patients aged </=35 years with stage IA non-small cell lung cancer: a SEER database analysis. *J Cancer Res Clin Oncol*. 2017 Nov;143(11):2375-82. doi: 10.1007/s00432-017-2499-y. PMID: 28819775. Exclusion Code: X11.
494. Gu F, Cheung LC, Freedman ND, et al. Potential Impact of Including Time to First Cigarette in Risk Models for Selecting Ever-Smokers for Lung Cancer Screening. *J Thorac Oncol*. 2017 Nov;12(11):1646-53. doi: 10.1016/j.jtho.2017.08.001. PMID: 28818607. Exclusion Code: X4.
495. Gu F, Wacholder S, Kovalchik S, et al. Time to smoke first morning cigarette and lung cancer in a case-control study. *J Natl Cancer Inst*. 2014 Jun;106(6):dju118. doi: 10.1093/jnci/dju118. PMID: 24948709. Exclusion Code: X4.
496. Guckenberger M, Klement RJ, Kestin LL, et al. Lack of a dose-effect relationship for pulmonary function changes after stereotactic body radiation therapy for early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2013 Mar 15;85(4):1074-81. doi: 10.1016/j.ijrobp.2012.09.016. PMID: 23154077. Exclusion Code: X8.

497. Guerra L, De Ponti E, Elisei F, et al. Respiratory gated PET/CT in a European multicentre retrospective study: added diagnostic value in detection and characterization of lung lesions. *Eur J Nucl Med Mol Imaging*. 2012 Sep;39(9):1381-90. doi: 10.1007/s00259-012-2148-2. PMID: 22588628. Exclusion Code: X3.
498. Guichet PL, Liu BY, Desai B, et al. Preliminary Results of Lung Cancer Screening in a Socioeconomically Disadvantaged Population. *AJR Am J Roentgenol*. 2018 Mar;210(3):489-96. doi: 10.2214/ajr.17.18853. PMID: 29166147. Exclusion Code: X10.
499. Gulati CM, Schreiner AM, Libby DM, et al. Outcomes of unresected ground-glass nodules with cytology suspicious for adenocarcinoma. *J Thorac Oncol*. 2014 May;9(5):685-91. doi: 10.1097/jto.0000000000000143. PMID: 24722156. Exclusion Code: X3.
500. Guldbrandt LM. The effect of direct referral for fast CT scan in early lung cancer detection in general practice. A clinical, cluster-randomised trial. *Dan Med J*. 2015 Mar;62(3)PMID: 25748876. Exclusion Code: X6.
501. Guldbrandt LM, Fenger-Gron M, Rasmussen TR, et al. The effect of direct access to CT scan in early lung cancer detection: an unblinded, cluster-randomised trial. *BMC Cancer*. 2015 Nov 25;15:934. doi: 10.1186/s12885-015-1941-2. PMID: 26608727. Exclusion Code: X6.
502. Guldbrandt LM, Rasmussen TR, Rasmussen F, et al. Implementing direct access to low-dose computed tomography in general practice--method, adaption and outcome. *PLoS One*. 2014;9(11):e112162. doi: 10.1371/journal.pone.0112162. PMID: 25383780. Exclusion Code: X8.
503. Gumireddy K, Li A, Chang DH, et al. AKAP4 is a circulating biomarker for non-small cell lung cancer. *Oncotarget*. 2015 Jul 10;6(19):17637-47. doi: 10.18632/oncotarget.3946. PMID: 26160834. Exclusion Code: X5.
504. Gungor G, Demir M, Aydin G, et al. Improvement of conformal arc plans by using deformable margin delineation method for stereotactic lung radiotherapy. *J Appl Clin Med Phys*. 2018 Jan;19(1):184-93. doi: 10.1002/acm2.12237. PMID: 29218841. Exclusion Code: X3.
505. Gunluoglu MZ, Kocaturk CI, Demir A, et al. Bronchial Stump Recurrence after Complete Resection of Lung Cancer: Effect of the Distance between the Tumor and Bronchial Resection Margin. *Thorac Cardiovasc Surg*. 2018 Mar;66(2):156-63. doi: 10.1055/s-0036-1592192. PMID: 27628445. Exclusion Code: X3.
506. Guo H, Liu S, Guo J, et al. Rapid on-site evaluation during endobronchial ultrasound-guided transbronchial needle aspiration for the diagnosis of hilar and mediastinal lymphadenopathy in patients with lung cancer. *Cancer Lett*. 2016 Feb 28;371(2):182-6. doi: 10.1016/j.canlet.2015.11.038. PMID: 26656954. Exclusion Code: X3.
507. Guo NL, Wan YW. Pathway-based identification of a smoking associated 6-gene signature predictive of lung cancer risk and survival. *Artif Intell Med*. 2012 Jun;55(2):97-105. doi: 10.1016/j.artmed.2012.01.001. PMID: 22326768. Exclusion Code: X3.
508. Guo X, Li D, Wu Y, et al. Genetic variants in genes of tricarboxylic acid cycle key enzymes are associated with prognosis of patients with non-small cell lung cancer. *Lung Cancer*. 2015 Feb;87(2):162-8. doi: 10.1016/j.lungcan.2014.12.005. PMID: 25576295. Exclusion Code: X3.
509. Gupta A, Saar T, Martens O, et al. Automatic detection of multisize pulmonary nodules in CT images: Large-scale validation of the false-positive reduction step. *Med Phys*. 2018 Mar;45(3):1135-49. doi: 10.1002/mp.12746. PMID: 29359462. Exclusion Code: X3.
510. Guralnik L, Rozenberg R, Frenkel A, et al. Metabolic PET/CT-guided lung lesion biopsies: impact on diagnostic accuracy and rate of sampling error. *J Nucl Med*. 2015 Apr;56(4):518-22. doi: 10.2967/jnumed.113.131466. PMID: 25698780. Exclusion Code: X3.
511. Gursoy S, Yazgan S, Ucvet A, et al. Postpneumonectomy bronchopleural fistula in non-small cell lung cancer patients: incidence, survival, mortality, and treatment analysis. *Surg Today*. 2018 Jul;48(7):695-702. doi: 10.1007/s00595-018-1648-5. PMID: 29516277. Exclusion Code: X3.

512. Gust L, Toullec A, Benoit C, et al. Pulmonary Endogenous Fluorescence Allows the Distinction of Primary Lung Cancer from the Perilesional Lung Parenchyma. *PLoS One*. 2015;10(8):e0134559. doi: 10.1371/journal.pone.0134559. PMID: 26244637. Exclusion Code: X3.

513. Guyatt GH, Lefcoe M, Walter S, et al. Interobserver variation in the computed tomographic evaluation of mediastinal lymph node size in patients with potentially resectable lung cancer. Canadian Lung Oncology Group. *Chest*. 1995 Jan;107(1):116-9. PMID: 7813261. Exclusion Code: X3.

514. Gwozdz P, Pasieka-Lis M, Kolodziej K, et al. Prognosis of Patients With Stages I and II Non-Small Cell Lung Cancer With Nodal Micrometastases. *Ann Thorac Surg*. 2018 May;105(5):1551-7. doi: 10.1016/j.athoracsur.2017.12.006. PMID: 29305849. Exclusion Code: X11.

515. Ha D, Choi H, Zell K, et al. Association of impaired heart rate recovery with cardiopulmonary complications after lung cancer resection surgery. *J Thorac Cardiovasc Surg*. 2015 Apr;149(4):1168-73.e3. doi: 10.1016/j.jtcvs.2014.11.037. PMID: 25583106. Exclusion Code: X3.

516. Haas K, Brillante C, Sharp L, et al. Lung cancer screening: assessment of health literacy and readability of online educational resources. *BMC Public Health*. 2018 Dec 7;18(1):1356. doi: 10.1186/s12889-018-6278-8. PMID: 30526544. Exclusion Code: X3.

517. Haasbeek CJ, Lagerwaard FJ, Slotman BJ, et al. Outcomes of stereotactic ablative radiotherapy for centrally located early-stage lung cancer. *J Thorac Oncol*. 2011 Dec;6(12):2036-43. doi: 10.1097/JTO.0b013e31822e71d8. PMID: 21892102. Exclusion Code: X11.

518. Halac M, Ozhan M, Yilmaz Aksoy S, et al. The role of FDG-PET/CT in detecting unsuspected and unknown distant metastasis in the initial staging of NSCLC. *Turk J Med Sci*. 2014;44(6):1029-40. PMID: 25552157. Exclusion Code: X8.

519. Halpenny DF, Cunningham JD, Long NM, et al. Patients with a previous history of malignancy undergoing lung cancer screening: clinical characteristics and radiologic findings. *J Thorac Oncol*. 2016 Sep;11(9):1447-52. doi: 10.1016/j.jtho.2016.05.006. PMID: 27223458. Exclusion Code: X7.

520. Hamada K, Irie M, Fujino Y, et al. Prognostic value of preoperative exercise capacity in patients undergoing thoracoscopic lobectomy for non-small cell lung cancer. *Lung Cancer*. 2019 Feb;128:47-52. doi: 10.1016/j.lungcan.2018.12.013. PMID: 30642452. Exclusion Code: X3.

521. Hamaji M, Chen F, Matsuo Y, et al. Video-assisted thoracoscopic lobectomy versus stereotactic radiotherapy for stage I lung cancer. *Ann Thorac Surg*. 2015 Apr;99(4):1122-9. doi: 10.1016/j.athoracsur.2014.11.009. PMID: 25661580. Exclusion Code: X10.

522. Hamamoto Y, Kataoka M, Yamashita M, et al. Lung-cancer related chest events detected by periodical follow-up CT after stereotactic body radiotherapy for stage I primary lung cancer: retrospective analysis of incidence of lung-cancer related chest events and outcomes of salvage treatment. *Jpn J Radiol*. 2012 Oct;30(8):671-5. doi: 10.1007/s11604-012-0107-2. PMID: 22836906. Exclusion Code: X13.

523. Hamanaka R, Yokose T, Sakuma Y, et al. Prognostic impact of vascular invasion and standardization of its evaluation in stage I non-small cell lung cancer. *Diagn Pathol*. 2015 Apr 2;10:17. doi: 10.1186/s13000-015-0249-5. PMID: 25884820. Exclusion Code: X11.

524. Hamatake D, Yoshida Y, Miyahara S, et al. Surgical outcomes of lung cancer measuring less than 1 cm in diameter. *Interact Cardiovasc Thorac Surg*. 2012 Nov;15(5):854-8. doi: 10.1093/icvts/ivs337. PMID: 22904166. Exclusion Code: X12.

525. Han C, Schultheiss TE, Wong JYC. Estimation of radiation-induced secondary cancer risks for early-stage non-small cell lung cancer patients after stereotactic body radiation therapy. *Pract Radiat Oncol*. 2017 May - Jun;7(3):e185-e94. doi: 10.1016/j.prro.2016.10.009. PMID: 28089479. Exclusion Code: X16.

526. Han DH, Goo JM, Chong S, et al. Are lung imaging reporting and data system categories clear to radiologists? A survey of the Korean Society of Thoracic Radiology members on ten difficult-to-classify scenarios. *Korean J Radiol*. 2017 Mar-Apr;18(2):402-7. doi: 10.3348/kjr.2017.18.2.402. PMID: 28246521. Exclusion Code: X3.
527. Han KN, Kim HK, Lee HJ, et al. Single-port video-assisted thoracoscopic pulmonary segmentectomy: a report on 30 casesdagger. *Eur J Cardiothorac Surg*. 2016 Jan;49 Suppl 1:i42-7. doi: 10.1093/ejcts/ezv406. PMID: 26612717. Exclusion Code: X3.
528. Han SS, Erdogan SA, Toumazis I, et al. Evaluating the impact of varied compliance to lung cancer screening recommendations using a microsimulation model. *Cancer Causes Control*. 2017 Sep;28(9):947-58. doi: 10.1007/s10552-017-0907-x. PMID: 28702814. Exclusion Code: X4.
529. Han SS, ten Haaf K, Hazelton WD, et al. The impact of overdiagnosis on the selection of efficient lung cancer screening strategies. *Int J Cancer*. 2017 Jun 1;140(11):2436-43. doi: 10.1002/ijc.30602. PMID: 28073150. Exclusion Code: X4.
530. Han X, Yang X, Ye X, et al. Computed tomography-guided percutaneous microwave ablation of patients 75 years of age and older with early-stage nonsmall cell lung cancer. *Indian J Cancer*. 2015 Dec;52 Suppl 2:e56-60. doi: 10.4103/0019-509x.172514. PMID: 26728675. Exclusion Code: X6.
531. Hanas JS, Peyton MD, Lerner MR, et al. Distinguishing patients with stage I lung cancer versus control individuals using serum mass profiling. *Cancer Invest*. 2014 May;32(4):136-43. doi: 10.3109/07357907.2014.883528. PMID: 24579933. Exclusion Code: X7.
532. Hanauer M, Perentes JY, Krueger T, et al. Pre-operative localization of solitary pulmonary nodules with computed tomography-guided hook wire: report of 181 patients. *J Cardiothorac Surg*. 2016 Jan 16;11:5. doi: 10.1186/s13019-016-0404-4. PMID: 26772183. Exclusion Code: X3.
533. Hancock JG, Rosen JE, Antonicelli A, et al. Impact of adjuvant treatment for microscopic residual disease after non-small cell lung cancer surgery. *Ann Thorac Surg*. 2015 Feb;99(2):406-13. doi: 10.1016/j.athoracsur.2014.09.033. PMID: 25528723. Exclusion Code: X6.
534. Hanna WC, de Valence M, Atenafu EG, et al. Is video-assisted lobectomy for non-small-cell lung cancer oncologically equivalent to open lobectomy? *Eur J Cardiothorac Surg*. 2013 Jun;43(6):1121-5. doi: 10.1093/ejcts/ezs623. PMID: 23299237. Exclusion Code: X3.
535. Harder EM, Chen ZJ, Park HS, et al. Dose-volume predictors of esophagitis after thoracic stereotactic body radiation therapy. *Am J Clin Oncol*. 2017 Oct;40(5):477-82. doi: 10.1097/coc.0000000000000195. PMID: 26017483. Exclusion Code: X3.
536. Harder EM, Park HS, Chen ZJ, et al. Pulmonary dose-volume predictors of radiation pneumonitis following stereotactic body radiation therapy. *Pract Radiat Oncol*. 2016 Nov - Dec;6(6):e353-e9. doi: 10.1016/j.prro.2016.01.015. PMID: 27156424. Exclusion Code: X3.
537. Harders SW, Madsen HH, Hjorthaug K, et al. Characterization of pulmonary lesions in patients with suspected lung cancer: computed tomography versus [(1)(8)F] fluorodeoxyglucose-positron emission tomography/computed tomography. *Cancer Imaging*. 2012 Oct 16;12:437-46. doi: 10.1102/1470-7330.2012.0035. PMID: 23092816. Exclusion Code: X3.
538. Harders SW, Madsen HH, Hjorthaug K, et al. Mediastinal staging in non-small-cell lung carcinoma: computed tomography versus F-18-fluorodeoxyglucose positron-emission tomography and computed tomography. *Cancer Imaging*. 2014 Jun 3;14:23. doi: 10.1186/1470-7330-14-23. PMID: 25608616. Exclusion Code: X3.
539. Harders SW, Madsen HH, Hjorthaug K, et al. Limited value of (9)(9)mTc depreotide single photon emission CT compared with CT for the evaluation of pulmonary lesions. *Br J Radiol*. 2012 Jul;85(1015):e307-13. doi: 10.1259/bjr/10438644. PMID: 22745210. Exclusion Code: X11.

540. Harkenrider MM, Bertke MH, Dunlap NE. Stereotactic body radiation therapy for unbiopsied early-stage lung cancer: a multi-institutional analysis. *Am J Clin Oncol*. 2014 Aug;37(4):337-42. doi: 10.1097/COC.0b013e318277d822. PMID: 23660597. Exclusion Code: X10.

541. Hart K, Tofthagen C, Wang HL. Development and evaluation of a lung cancer screening decision aid. *Clin J Oncol Nurs*. 2016 Oct 1;20(5):557-9. doi: 10.1188/16.cjon.557-559. PMID: 27668377. Exclusion Code: X10.

542. Haruki T, Miwa K, Araki K, et al. Distribution and prevalence of locoregional recurrence after video-assisted thoracoscopic surgery for primary lung cancer. *Thorac Cardiovasc Surg*. 2016 Sep;64(6):526-32. doi: 10.1055/s-0035-1550231. PMID: 26258471. Exclusion Code: X3.

543. Harzheim D, Sterman D, Shah PL, et al. Bronchoscopic transparenchymal nodule access: feasibility and safety in an endoscopic unit. *Respiration*. 2016;91(4):302-6. doi: 10.1159/000445032. PMID: 27007334. Exclusion Code: X3.

544. Hasan S, Colonias A, Mickus T, et al. Image-based management of empiric lung stereotactic body radiotherapy (SBRT) without biopsy: Predictors from a 10-year single institution experience. *Thorac Cancer*. 2018 Jun;9(6):699-706. doi: 10.1111/1759-7714.12635. PMID: 29697204. Exclusion Code: X13.

545. Hasegawa T, Kuroda H, Sato Y, et al. The Utility of Indigo Carmine and Lipiodol Mixture for Preoperative Pulmonary Nodule Localization before Video-Assisted Thoracic Surgery. *J Vasc Interv Radiol*. 2019 Mar;30(3):446-52. doi: 10.1016/j.jvir.2018.08.024. PMID: 30819492. Exclusion Code: X11.

546. Hashimoto K, Daddi N, Giuliani M, et al. The role of endobronchial ultrasound-guided transbronchial needle aspiration in stereotactic body radiation therapy for non-small cell lung cancer. *Lung Cancer*. 2018 Sep;123:1-6. doi: 10.1016/j.lungcan.2018.06.011. PMID: 30089578. Exclusion Code: X3.

547. Hashimoto N, Iwano S, Kawaguchi K, et al. Impact of thin-section computed tomography-determined combined pulmonary fibrosis and emphysema on outcomes among patients with resected lung cancer. *Ann Thorac Surg*. 2016 Aug;102(2):440-7. doi: 10.1016/j.athoracsur.2016.03.014. PMID: 27157056. Exclusion Code: X11.

548. Hata A, Sekine Y, Kota O, et al. Impact of combined pulmonary fibrosis and emphysema on surgical complications and long-term survival in patients undergoing surgery for non-small-cell lung cancer. *Int J Chron Obstruct Pulmon Dis*. 2016;11:1261-8. doi: 10.2147/copd.s94119. PMID: 27354784. Exclusion Code: X3.

549. Hata M, Tokuuye K, Kagei K, et al. Hypofractionated high-dose proton beam therapy for stage I non-small-cell lung cancer: preliminary results of a phase I/II clinical study. *Int J Radiat Oncol Biol Phys*. 2007 Jul 1;68(3):786-93. doi: 10.1016/j.ijrobp.2006.12.063. PMID: 17379439. Exclusion Code: X6.

550. Hattori A, Matsunaga T, Hayashi T, et al. Prognostic impact of the findings on thin-section computed tomography in patients with subcentimeter non-small cell lung cancer. *J Thorac Oncol*. 2017 Jun;12(6):954-62. doi: 10.1016/j.jtho.2017.02.015. PMID: 28257958. Exclusion Code: X11.

551. Hattori A, Matsunaga T, Takamochi K, et al. Neither maximum tumor size nor solid component size is prognostic in part-solid lung cancer: impact of tumor size should be applied exclusively to solid lung cancer. *Ann Thorac Surg*. 2016 Aug;102(2):407-15. doi: 10.1016/j.athoracsur.2016.02.074. PMID: 27177840. Exclusion Code: X3.

552. Hattori A, Matsunaga T, Takamochi K, et al. Oncological characteristics of radiological invasive adenocarcinoma with additional ground-glass nodules on initial thin-section computed tomography: comparison with solitary invasive adenocarcinoma. *J Thorac Oncol*. 2016 May;11(5):729-36. doi: 10.1016/j.jtho.2016.01.008. PMID: 26802286. Exclusion Code: X10.

553. Hattori A, Matsunaga T, Takamochi K, et al. The oncological outcomes of segmentectomy in clinical-T1b lung adenocarcinoma with a solid-dominant appearance on thin-section computed tomography. *Surg Today*. 2016 Aug;46(8):914-21. doi: 10.1007/s00595-015-1256-6. PMID: 26471507. Exclusion Code: X11.

554. Hattori A, Matsunaga T, Takamochi K, et al. Importance of ground glass opacity component in clinical stage IA radiologic invasive lung cancer. *Ann Thorac Surg*. 2017 Jul;104(1):313-20. doi: 10.1016/j.athoracsur.2017.01.076. PMID: 28433219. Exclusion Code: X3.

555. Hattori A, Matsunaga T, Takamochi K, et al. Locoregional recurrence after segmentectomy for clinical-T1aN0M0 radiologically solid non-small-cell lung carcinoma. *Eur J Cardiothorac Surg*. 2017 Mar 1;51(3):518-25. doi: 10.1093/ejcts/ezw336. PMID: 28082475. Exclusion Code: X11.

556. Hattori A, Matsunaga T, Takamochi K, et al. Surgical resection for clinical-Stage I radiological pure-solid lung cancer that met the current high risk criteria. *Jpn J Clin Oncol*. 2017 Jul 1;47(7):630-8. doi: 10.1093/jjco/hyx054. PMID: 28419333. Exclusion Code: X10.

557. Hattori A, Suzuki K, Matsunaga T, et al. What is the appropriate operative strategy for radiologically solid tumours in subcentimetre lung cancer patients?dagger. *Eur J Cardiothorac Surg*. 2015 Feb;47(2):244-9. doi: 10.1093/ejcts/ezu250. PMID: 24972722. Exclusion Code: X11.

558. Hattori A, Suzuki K, Takamochi K, et al. Is bilateral pulmonary lobectomy feasible in patients with bilateral lung cancers? *Thorac Cardiovasc Surg*. 2015 Oct;63(7):589-96. doi: 10.1055/s-0034-1383816. PMID: 25025891. Exclusion Code: X3.

559. Hattori A, Takamochi K, Kitamura Y, et al. Risk factor analysis of cerebral infarction and clinicopathological characteristics of left upper pulmonary vein stump thrombus after lobectomy. *Gen Thorac Cardiovasc Surg*. 2019 Feb;67(2):247-53. doi: 10.1007/s11748-018-1017-8. PMID: 30251002. Exclusion Code: X3.

560. Hattori A, Takamochi K, Matsunaga T, et al. Oncological outcomes of sublobar resection for clinical-stage IA high-risk non-small cell lung cancer patients with a radiologically solid appearance on computed tomography. *Gen Thorac Cardiovasc Surg*. 2016 Jan;64(1):18-24. doi: 10.1007/s11748-015-0598-8. PMID: 26486132. Exclusion Code: X11.

561. Hattori K, Matsuda T, Takagi Y, et al. Preoperative six-minute walk distance is associated with pneumonia after lung resection. *Interact Cardiovasc Thorac Surg*. 2018 Feb 1;26(2):277-83. doi: 10.1093/icvts/ivx310. PMID: 29049742. Exclusion Code: X3.

562. Hawkins PG, Boonstra PS, Hobson ST, et al. Radiation-induced lung toxicity in non-small-cell lung cancer: Understanding the interactions of clinical factors and cytokines with the dose-toxicity relationship. *Radiother Oncol*. 2017 Oct;125(1):66-72. doi: 10.1016/j.radonc.2017.09.005. PMID: 28947099. Exclusion Code: X3.

563. Hayashi S, Tanaka H, Kajiura Y, et al. Stereotactic body radiotherapy for very elderly patients (age, greater than or equal to 85 years) with stage I non-small cell lung cancer. *Radiat Oncol*. 2014 Jun 16;9:138. doi: 10.1186/1748-717x-9-138. PMID: 24935216. Exclusion Code: X10.

564. Hayes JT, David EA, Qi L, et al. Risk of pneumonitis after stereotactic body radiation therapy in patients with previous anatomic lung resection. *Clin Lung Cancer*. 2015 Sep;16(5):379-84. doi: 10.1016/j.cllc.2015.01.006. PMID: 25737143. Exclusion Code: X3.

565. Hazelton WD, Goodman G, Rom WN, et al. Longitudinal multistage model for lung cancer incidence, mortality, and CT detected indolent and aggressive cancers. *Math Biosci*. 2012 Nov;240(1):20-34. doi: 10.1016/j.mbs.2012.05.008. PMID: 22705252. Exclusion Code: X7.

566. Hazelton WD, Jeon J, Meza R, et al. Chapter 8: the FHCRC lung cancer model. *Risk Anal*. 2012 Jul;32 Suppl 1:S99-S116. doi: 10.1111/j.1539-6924.2011.01681.x. PMID: 22882896. Exclusion Code: X4.

567. He F, Chen LM, Xiong WM, et al. A case-control study of the association between self-reported occupational and recreational physical activity and lung cancer. *Medicine (Baltimore)*. 2017 Sep;96(36):e7923. doi: 10.1097/md.0000000000007923. PMID: 28885346. Exclusion Code: X3.
568. Healey TT, March BT, Baird G, et al. Microwave ablation for lung neoplasms: a retrospective analysis of long-term results. *J Vasc Interv Radiol*. 2017 Feb;28(2):206-11. doi: 10.1016/j.jvir.2016.10.030. PMID: 27993505. Exclusion Code: X6.
569. Heidinger BH, Anderson KR, Moriarty EM, et al. Size measurement and T-staging of lung adenocarcinomas manifesting as solid nodules </=30 mm on CT: radiology-pathology correlation. *Acad Radiol*. 2017 Jul;24(7):851-9. doi: 10.1016/j.acra.2017.01.009. PMID: 28256438. Exclusion Code: X3.
570. Heidinger BH, Nemec U, Anderson KR, et al. "Rounding" the Size of Pulmonary Nodules: Impact of Rounding Methods on Nodule Management, as Defined by the 2017 Fleischner Society Guidelines. *Acad Radiol*. 2017 Nov;24(11):1422-7. doi: 10.1016/j.acra.2017.05.013. PMID: 28666724. Exclusion Code: X3.
571. Heineman DJ, Ten Berge MG, Daniels JM, et al. Clinical staging of stage i non-small cell lung cancer in the Netherlands-need for improvement in an era with expanding nonsurgical treatment options: data from the Dutch Lung Surgery Audit. *Ann Thorac Surg*. 2016 Nov;102(5):1615-21. doi: 10.1016/j.athoracsur.2016.07.054. PMID: 27665481. Exclusion Code: X8.
572. Hennon MW, Dexter EU, Huang M, et al. Does thoracoscopic surgery decrease the morbidity of combined lung and chest wall resection? *Ann Thorac Surg*. 2015 Jun;99(6):1929-34; discussion 34-5. doi: 10.1016/j.athoracsur.2015.02.038. PMID: 25916876. Exclusion Code: X3.
573. Hennon MW, Kumar A, Devisetty H, et al. Minimally Invasive Approaches Do Not Compromise Outcomes for Pneumonectomy: A Comparison Using the National Cancer Database. *J Thorac Oncol*. 2019 Jan;14(1):107-14. doi: 10.1016/j.jtho.2018.09.024. PMID: 30292851. Exclusion Code: X3.
574. Henschke CI, Boffetta P, Yankelevitz DF, et al. Computed tomography screening: the international early lung cancer action program experience. *Thorac Surg Clin*. 2015 May;25(2):129-43. doi: 10.1016/j.thorsurg.2014.12.001. PMID: 25901557. Exclusion Code: X10.
575. Henschke CI, Salvatore M, Cham M, et al. Baseline and annual repeat rounds of screening: implications for optimal regimens of screening. *Eur Radiol*. 2018 Mar;28(3):1085-94. doi: 10.1007/s00330-017-5029-z. PMID: 28983713. Exclusion Code: X10.
576. Herbrik M, Treffert J, Geiger B, et al. Diagnostic accuracy of virtual 18F-FDG PET/CT bronchoscopy for the detection of lymph node metastases in non-small cell lung cancer patients. *J Nucl Med*. 2011 Oct;52(10):1520-5. doi: 10.2967/jnumed.111.092593. PMID: 21908390. Exclusion Code: X3.
577. Herde RF, Kokeny KE, Reddy CB, et al. Primary pulmonary carcinoid tumor: a long-term single institution experience. *Am J Clin Oncol*. 2018 Jan;41(1):24-9. doi: 10.1097/coc.0000000000000221. PMID: 26270444. Exclusion Code: X3.
578. Hernandez-Arenas LA, Lin L, Yang Y, et al. Initial experience in uniportal subxiphoid video-assisted thoracoscopic surgery for major lung resections. *Eur J Cardiothorac Surg*. 2016 Dec;50(6):1060-6. doi: 10.1093/ejcts/ezw189. PMID: 27401700. Exclusion Code: X11.
579. Herth FJ, Eberhardt R, Sterman D, et al. Bronchoscopic transparenchymal nodule access (BTPNA): first in human trial of a novel procedure for sampling solitary pulmonary nodules. *Thorax*. 2015 Apr;70(4):326-32. doi: 10.1136/thoraxjnl-2014-206211. PMID: 25746631. Exclusion Code: X5.
580. Heuvelmans MA, Walter JE, Peters RB, et al. Relationship between nodule count and lung cancer probability in baseline CT lung cancer screening: The NELSON study. *Lung Cancer*. 2017 Nov;113:45-50. doi: 10.1016/j.lungcan.2017.08.023. PMID: 29110848. Exclusion Code: X7.

581. Heuvelmans MA, Walter JE, Vliegenthart R, et al. Disagreement of diameter and volume measurements for pulmonary nodule size estimation in CT lung cancer screening. *Thorax*. 2018;73(8):779-81. doi: 10.1136/thoraxjnl-2017-210770. PMID: CN-01704274. Exclusion Code: X7.
582. Heye T, Ley S, Heussel CP, et al. Detection and size of pulmonary lesions: how accurate is MRI? A prospective comparison of CT and MRI. *Acta Radiol*. 2012 Mar 1;53(2):153-60. doi: 10.1258/ar.2011.110445. PMID: 22287146. Exclusion Code: X3.
583. Heye T, Sommer G, Miedinger D, et al. Ultrafast 3D balanced steady-state free precession MRI of the lung: assessment of anatomic details in comparison to low-dose CT. *J Magn Reson Imaging*. 2015 Sep;42(3):602-9. doi: 10.1002/jmri.24836. PMID: 25545835. Exclusion Code: X11.
584. Higgins KA, O'Connell K, Liu Y, et al. National Cancer Database analysis of proton versus photon radiation therapy in non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2017 Jan 1;97(1):128-37. doi: 10.1016/j.ijrobp.2016.10.001. PMID: 27979443. Exclusion Code: X6.
585. Higuchi M, Yaginuma H, Yonechi A, et al. Long-term outcomes after video-assisted thoracic surgery (VATS) lobectomy versus lobectomy via open thoracotomy for clinical stage IA non-small cell lung cancer. *J Cardiothorac Surg*. 2014 May 17;9:88. doi: 10.1186/1749-8090-9-88. PMID: 24886655. Exclusion Code: X11.
586. Hino H, Karasaki T, Yoshida Y, et al. Risk factors for postoperative complications and long-term survival in lung cancer patients older than 80 years. *Eur J Cardiothorac Surg*. 2018 May 1;53(5):980-6. doi: 10.1093/ejcts/ezx437. PMID: 29272371. Exclusion Code: X3.
587. Hino H, Murakawa T, Ichinose J, et al. Results of lung cancer surgery for octogenarians. *Ann Thorac Cardiovasc Surg*. 2015;21(3):209-16. doi: 10.5761/atcs.oa.14-00160. PMID: 25740447. Exclusion Code: X11.
588. Hirai K, Takeuchi S, Usuda J. Single-incision thoracoscopic surgery and conventional video-assisted thoracoscopic surgery: a retrospective comparative study of perioperative clinical outcomesdagger. *Eur J Cardiothorac Surg*. 2016 Jan;49 Suppl 1:i37-41. doi: 10.1093/ejcts/ezv320. PMID: 26417062. Exclusion Code: X11.
589. Hiraishi Y, Izumo T, Sasada S, et al. Factors affecting bacterial culture positivity in specimens from bronchoscopy in patients with suspected lung cancer. *Respir Investig*. 2018 Nov;56(6):457-63. doi: 10.1016/j.resinv.2018.07.006. PMID: 30392535. Exclusion Code: X3.
590. Hishida T, Miyaoka E, Yokoi K, et al. Lobe-specific nodal dissection for clinical stage I and II NSCLC: Japanese multi-institutional retrospective study using a propensity score analysis. *J Thorac Oncol*. 2016 Sep;11(9):1529-37. doi: 10.1016/j.jtho.2016.05.014. PMID: 27249959. Exclusion Code: X3.
591. Hjorthaug K, Hojbjerg JA, Knap MM, et al. Accuracy of 18F-FDG PET-CT in triaging lung cancer patients with suspected brain metastases for MRI. *Nucl Med Commun*. 2015 Nov;36(11):1084-90. doi: 10.1097/mnm.0000000000000371. PMID: 26302460. Exclusion Code: X3.
592. Hofman MS, Smeeton NC, Rankin SC, et al. Observer variation in FDG PET-CT for staging of non-small-cell lung carcinoma. *Eur J Nucl Med Mol Imaging*. 2009 Feb;36(2):194-9. doi: 10.1007/s00259-008-0946-3. PMID: 18828012. Exclusion Code: X3.
593. Hoggart C, Brennan P, Tjonneland A, et al. A risk model for lung cancer incidence. *Cancer Prev Res (Phila)*. 2012 Jun;5(6):834-46. doi: 10.1158/1940-6207.capr-11-0237. PMID: 22496387. Exclusion Code: X7.
594. Holbek BL, Hansen HJ, Kehlet H, et al. Thoracoscopic pulmonary wedge resection without post-operative chest drain: an observational study. *Gen Thorac Cardiovasc Surg*. 2016 Oct;64(10):612-7. doi: 10.1007/s11748-016-0692-6. PMID: 27510705. Exclusion Code: X11.

595. Honda T, Kondo T, Murakami S, et al. Radiographic and pathological analysis of small lung adenocarcinoma using the new IASLC classification. *Clin Radiol*. 2013 Jan;68(1):e21-6. doi: 10.1016/j.crad.2012.09.002. PMID: 23146553. Exclusion Code: X3.
596. Hong S, Park EC, Kim TH, et al. Effect of pre existing respiratory conditions on survival of lung cancer patients: A nationwide population-based cohort study. *Asia Pac J Clin Oncol*. 2018 Apr;14(2):e71-e80. doi: 10.1111/ajco.12697. PMID: 28762660. Exclusion Code: X3.
597. Hong TH, Cho JH, Shin S, et al. Extended sleeve lobectomy for centrally located non-small-cell lung cancer: a 20-year single-centre experience. *Eur J Cardiothorac Surg*. 2018 Jul 1;54(1):142-8. doi: 10.1093/ejcts/ezy011. PMID: 29408983. Exclusion Code: X3.
598. Hoppe BS, Huh S, Flampouri S, et al. Double-scattered proton-based stereotactic body radiotherapy for stage I lung cancer: a dosimetric comparison with photon-based stereotactic body radiotherapy. *Radiother Oncol*. 2010 Dec;97(3):425-30. doi: 10.1016/j.radonc.2010.09.006. PMID: 20934768. Exclusion Code: X8.
599. Hoppe BS, Laser B, Kowalski AV, et al. Acute skin toxicity following stereotactic body radiation therapy for stage I non-small-cell lung cancer: who's at risk? *Int J Radiat Oncol Biol Phys*. 2008 Dec 1;72(5):1283-6. doi: 10.1016/j.ijrobp.2008.08.036. PMID: 19028267. Exclusion Code: X11.
600. Horeweg N, van der Aalst CM, Thunnissen E, et al. Characteristics of lung cancers detected by computer tomography screening in the randomized NELSON trial. *Am J Respir Crit Care Med*. 2013 Apr 15;187(8):848-54. doi: 10.1164/rccm.201209-1651OC. PMID: 23348977. Exclusion Code: X7.
601. Horeweg N, van Rosmalen J, Heuvelmans MA, et al. Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening. *Lancet Oncol*. 2014 Nov;15(12):1332-41. doi: 10.1016/s1470-2045(14)70389-4. PMID: 25282285. Exclusion Code: X7.
602. Horne ZD, Clump DA, Vargo JA, et al. Pretreatment SUVmax predicts progression-free survival in early-stage non-small cell lung cancer treated with stereotactic body radiation therapy. *Radiat Oncol*. 2014 Jan 30;9:41. doi: 10.1186/1748-717x-9-41. PMID: 24479954. Exclusion Code: X10.
603. Horne ZD, Richman AH, Dohopolski MJ, et al. Stereotactic body radiation therapy for isolated hilar and mediastinal non-small cell lung cancers. *Lung Cancer*. 2018 Jan;115:1-4. doi: 10.1016/j.lungcan.2017.10.014. PMID: 29290248. Exclusion Code: X3.
604. Horner-Rieber J, Bernhardt D, Dern J, et al. Histology of non-small cell lung cancer predicts the response to stereotactic body radiotherapy. *Radiother Oncol*. 2017 Nov;125(2):317-24. doi: 10.1016/j.radonc.2017.08.029. PMID: 28919006. Exclusion Code: X13.
605. Hosny A, Parmar C, Coroller TP, et al. Deep learning for lung cancer prognostication: A retrospective multi-cohort radiomics study. *PLoS Med*. 2018 Nov;15(11):e1002711. doi: 10.1371/journal.pmed.1002711. PMID: 30500819. Exclusion Code: X3.
606. Hostetter JM, Morrison JJ, Morris M, et al. Personalizing lung cancer risk prediction and imaging follow-up recommendations using the National Lung Screening Trial dataset. *J Am Med Inform Assoc*. 2017 Nov 1;24(6):1046-51. doi: 10.1093/jamia/ocx012. PMID: 28340104. Exclusion Code: X8.
607. Hou S, Lin X, Wang S, et al. Combination of positron emission tomography/computed tomography and chest thin-layer high-resolution computed tomography for evaluation of pulmonary nodules: Correlation with imaging features, maximum standardized uptake value, and pathology. *Medicine (Baltimore)*. 2018 Aug;97(31):e11640. doi: 10.1097/md.0000000000011640. PMID: 30075545. Exclusion Code: X3.
608. Hou YL, Chen H, Ge MJ, et al. Quantification of serum HBXAP DNA in lung cancer patients by quantitative fluorescent polymerase chain reaction. *Mol Biol Rep*. 2013 Jun;40(6):4091-6. doi: 10.1007/s11033-013-2488-4. PMID: 23456648. Exclusion Code: X3.

609. Howard DH, Richards TB, Bach PB, et al. Comorbidities, smoking status, and life expectancy among individuals eligible for lung cancer screening. *Cancer*. 2015 Dec 15;121(24):4341-7. doi: 10.1002/cncr.29677. PMID: 26372542. Exclusion Code: X5.
610. Hoyer M, Roed H, Hansen AT, et al. Prospective study on stereotactic radiotherapy of limited-stage non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2006;44(4):S128-35. doi: https://doi.org/10.1016/j.ijrobp.2006.01.012. Exclusion Code: X11.
611. Hoyer N, Wille MMW, Thomsen LH, et al. Interstitial lung abnormalities are associated with increased mortality in smokers. *Respir Med*. 2018 Mar;136:77-82. doi: 10.1016/j.rmed.2018.02.001. PMID: 29501250. Exclusion Code: X7.
612. Hrbacek J, Lang S, Graydon SN, et al. Dosimetric comparison of flattened and unflattened beams for stereotactic ablative radiotherapy of stage I non-small cell lung cancer. *Med Phys*. 2014 Mar;41(3):031709. doi: 10.1118/1.4866231. PMID: 24593713. Exclusion Code: X8.
613. Hristov B, Eguchi T, Bains S, et al. Minimally Invasive Lobectomy Is Associated With Lower Noncancer-specific Mortality in Elderly Patients: A Propensity Score Matched Competing Risks Analysis. *Ann Surg*. 2018 Apr 18doi: 10.1097/sla.0000000000002772. PMID: 29672399. Exclusion Code: X3.
614. Hristova R, Pompili C, Begum S, et al. An aggregate score to predict the risk of large pleural effusion after pulmonary lobectomy. *Eur J Cardiothorac Surg*. 2015 Jul;48(1):72-6. doi: 10.1093/ejcts/ezu413. PMID: 25352659. Exclusion Code: X4.
615. Hsieh TC, Huang WW, Lai CL, et al. Diagnostic value of tumor markers in lung adenocarcinoma-associated cytologically negative pleural effusions. *Cancer Cytopathol*. 2013 Sep;121(9):483-8. doi: 10.1002/cncy.21283. PMID: 23408492. Exclusion Code: X3.
616. Hsu HH, Ko KH, Chou YC, et al. SUVmax and tumor size predict surgical outcome of synchronous multiple primary lung cancers. *Medicine (Baltimore)*. 2016 Feb;95(6):e2351. doi: 10.1097/md.0000000000002351. PMID: 26871768. Exclusion Code: X11.
617. Hsu HH, Shen CH, Tsai WC, et al. Localization of nonpalpable pulmonary nodules using CT-guided needle puncture. *World J Surg Oncol*. 2015 Aug 15;13:248. doi: 10.1186/s12957-015-0664-9. PMID: 26271476. Exclusion Code: X11.
618. Hsu LS, Chen CW, Chang CH, et al. Influences of cardiac motion on computed tomography-guided biopsy of lung nodules located near the heart. *Medicine (Baltimore)*. 2017 Nov;96(46):e8558. doi: 10.1097/md.0000000000008558. PMID: 29145264. Exclusion Code: X3.
619. Hsu PK, Lin WC, Chang YC, et al. Multiinstitutional analysis of single-port video-assisted thoracoscopic anatomical resection for primary lung cancer. *Ann Thorac Surg*. 2015 May;99(5):1739-44. doi: 10.1016/j.athoracsur.2015.01.041. PMID: 25827674. Exclusion Code: X11.
620. Hu Z, Whitney D, Anderson JR, et al. Analytical performance of a bronchial genomic classifier. *BMC Cancer*. 2016 Feb 26;16:161. doi: 10.1186/s12885-016-2153-0. PMID: 26920854. Exclusion Code: X3.
621. Huang BT, Lin Z, Lin PX, et al. Monitor unit optimization in stereotactic body radiotherapy for small peripheral non-small cell lung cancer patients. *Sci Rep*. 2015 Dec 18;5:18453. doi: 10.1038/srep18453. PMID: 26679747. Exclusion Code: X8.
622. Huang BT, Lu JY, Lin PX, et al. Radiobiological modeling analysis of the optimal fraction scheme in patients with peripheral non-small cell lung cancer undergoing stereotactic body radiotherapy. *Sci Rep*. 2015 Dec 11;5:18010. doi: 10.1038/srep18010. PMID: 26657569. Exclusion Code: X3.
623. Huang BY, Zhou JJ, Yu ZQ, et al. Long-term observation of CT-guided radiofrequency ablation of lung neoplasm in 476 consecutive patients by a thoracic surgical service: a single-institutional experience. *Acad Radiol*. 2017 Dec;24(12):1517-25. doi: 10.1016/j.acra.2017.06.018. PMID: 28888381. Exclusion Code: X6.
624. Huang K, Senthi S, Palma DA, et al. High-risk CT features for detection of local recurrence after stereotactic ablative radiotherapy for lung cancer. *Radiother Oncol*. 2013 Oct;109(1):51-7. doi: 10.1016/j.radonc.2013.06.047. PMID: 23953413. Exclusion Code: X8.

625. Huang L, Wang L, Zhu W, et al. Area--a consistent method to evaluate pulmonary tumor size on multidetector CT imaging: an intraobserver and interobserver agreement study. *Clin Imaging*. 2013 Nov-Dec;37(6):1006-10. doi: 10.1016/j.clinimag.2013.06.011. PMID: 23993800. Exclusion Code: X3.

626. Huang P, Park S, Yan R, et al. Added value of computer-aided CT image features for early lung cancer diagnosis with small pulmonary nodules: a matched case-control study. *Radiology*. 2018 Jan;286(1):286-95. doi: 10.1148/radiol.2017162725. PMID: 28872442. Exclusion Code: X10.

627. Huang TW, Lin KH, Huang HK, et al. The role of the ground-glass opacity ratio in resected lung adenocarcinoma. *Eur J Cardiothorac Surg*. 2018 Aug 1;54(2):229-34. doi: 10.1093/ejcts/ezy040. PMID: 29471517. Exclusion Code: X3.

628. Huang Y, Hu Q, Deng Z, et al. MicroRNAs in body fluids as biomarkers for non-small cell lung cancer: a systematic review. *Technol Cancer Res Treat*. 2014 Jun;13(3):277-87. doi: 10.7785/tcrt.2012.500377. PMID: 24066954. Exclusion Code: X5.

629. Huang Y, Zhao Z, Wang T, et al. A Comparison between Prethoracoscopy Localization of Small Pulmonary Nodules by Means of Medical Adhesive versus Hookwire. *J Vasc Interv Radiol*. 2018 Nov;29(11):1547-52. doi: 10.1016/j.jvir.2018.05.013. PMID: 30293726. Exclusion Code: X3.

630. Huang YS, Chen JL, Hsu FM, et al. Response assessment of stereotactic body radiation therapy using dynamic contrast-enhanced integrated MR-PET in non-small cell lung cancer patients. *J Magn Reson Imaging*. 2018 Jan;47(1):191-9. doi: 10.1002/jmri.25758. PMID: 28480541. Exclusion Code: X8.

631. Hubers AJ, van der Drift MA, Prinsen CF, et al. Methylation analysis in spontaneous sputum for lung cancer diagnosis. *Lung Cancer*. 2014 May;84(2):127-33. doi: 10.1016/j.lungcan.2014.01.019. PMID: 24598366. Exclusion Code: X3.

632. Huellner MW, de Galiza Barbosa F, Husmann L, et al. TNM staging of non-small cell lung cancer: comparison of PET/MR and PET/CT. *J Nucl Med*. 2016 Jan;57(1):21-6. doi: 10.2967/jnumed.115.162040. PMID: 26471696. Exclusion Code: X3.

633. Hueto Perez De Heredia J, Cebollero Rivas P, Cascante Rodrigo JA, et al. Evaluation of the use of a rapid diagnostic consultation of lung cancer. Delay time of diagnosis and therapy. *Arch Bronconeumol*. 2012 Aug;48(8):267-73. doi: 10.1016/j.arbres.2012.03.009. PMID: 22575811. Exclusion Code: X3.

634. Hulbert A, Hooker CM, Keruly JC, et al. Prospective CT screening for lung cancer in a high-risk population: HIV-positive smokers. *J Thorac Oncol*. 2014 Jun;9(6):752-9. doi: 10.1097/jto.0000000000000161. PMID: 24828660. Exclusion Code: X7.

635. Hulbert A, Jusue-Torres I, Stark A, et al. Early detection of lung cancer using DNA promoter hypermethylation in plasma and sputum. *Clin Cancer Res*. 2017 Apr 15;23(8):1998-2005. doi: 10.1158/1078-0432.ccr-16-1371. PMID: 27729459. Exclusion Code: X7.

636. Hung JJ, Jeng WJ, Hsu WH, et al. Predictors of death, local recurrence, and distant metastasis in completely resected pathological stage-I non-small-cell lung cancer. *J Thorac Oncol*. 2012 Jul;7(7):1115-23. doi: 10.1097/JTO.0b013e31824cbad8. PMID: 22592210. Exclusion Code: X10.

637. Hung JJ, Jeng WJ, Hsu WH, et al. Time trends of overall survival and survival after recurrence in completely resected stage I non-small cell lung cancer. *J Thorac Oncol*. 2012 Feb;7(2):397-405. doi: 10.1097/JTO.0b013e31823b564a. PMID: 22173701. Exclusion Code: X14.

638. Hung MH, Cheng YJ, Chan KC, et al. Nonintubated uniportal thoracoscopic surgery for peripheral lung nodules. *Ann Thorac Surg*. 2014 Dec;98(6):1998-2003. doi: 10.1016/j.athoracsur.2014.07.036. PMID: 25443006. Exclusion Code: X3.

639. Hung MS, Chen IC, Lee CP, et al. Incidence and risk factors of depression after diagnosis of lung cancer: A nationwide population-based study. *Medicine (Baltimore)*. 2017 May;96(19):e6864. doi: 10.1097/md.0000000000006864. PMID: 28489782. Exclusion Code: X8.

640. Hung SK, Chen YC, Chiou WY, et al. Irradiation enhanced risks of hospitalised pneumonopathy in lung cancer patients: a population-based surgical cohort study. *BMJ Open*. 2017 Sep 27;7(9):e015022. doi: 10.1136/bmjopen-2016-015022. PMID: 28963281. Exclusion Code: X3.

641. Hung SK, Lee MS, Chiou WY, et al. High incidence of ischemic stroke occurrence in irradiated lung cancer patients: a population-based surgical cohort study. *PLoS One*. 2014;9(4):e94377. doi: 10.1371/journal.pone.0094377. PMID: 24709837. Exclusion Code: X3.

642. Huo J, Hong YR, Bian J, et al. Low rates of patient-reported physician-patient discussion about lung cancer screening among current smokers: data from Health Information National Trends Survey. *Cancer Epidemiol Biomarkers Prev*. 2019 May;28(5):963-73. doi: 10.1158/1055-9965.EPI-18-0629. PMID: 31023697. Exclusion Code: X8.

643. Huo J, Xu Y, Sheu T, et al. Complication rates and downstream medical costs associated with invasive diagnostic procedures for lung abnormalities in the community setting. *JAMA Intern Med*. 2019 Jan 14doi: 10.1001/jamainternmed.2018.6277. PMID: 30640382. Exclusion Code: X3.

644. Hwang EJ, Kim H, Park CM, et al. Cone beam computed tomography virtual navigation-guided transthoracic biopsy of small (</= 1 cm) pulmonary nodules: impact of nodule visibility during real-time fluoroscopy. *Br J Radiol*. 2018 Jul;91(1087):20170805. doi: 10.1259/bjr.20170805. PMID: 29595322. Exclusion Code: X3.

645. Hwang EJ, Park CM, Ryu Y, et al. Pulmonary adenocarcinomas appearing as part-solid ground-glass nodules: is measuring solid component size a better prognostic indicator? *Eur Radiol*. 2015 Feb;25(2):558-67. doi: 10.1007/s00330-014-3441-1. PMID: 25274618. Exclusion Code: X8.

646. Hwang J, Chung MJ, Bae Y, et al. Computer-aided detection of lung nodules: influence of the image reconstruction kernel for computer-aided detection performance. *J Comput Assist Tomogr*. 2010 Jan;34(1):31-4. doi: 10.1097/RCT.0b013e3181b5c630. PMID: 20118719. Exclusion Code: X5.

647. Hwang Y, Kang CH, Kim HS, et al. Comparison of thoracoscopic segmentectomy and thoracoscopic lobectomy on the patients with non-small cell lung cancer: a propensity score matching study. *Eur J Cardiothorac Surg*. 2015 Aug;48(2):273-8. doi: 10.1093/ejcts/ezu422. PMID: 25406426. Exclusion Code: X11.

648. Hyun K, Park IK, Song JW, et al. Electromagnetic navigation bronchoscopic dye marking for localization of small subsolid nodules: Retrospective observational study. *Medicine (Baltimore)*. 2019 Mar;98(11):e14831. doi: 10.1097/md.0000000000014831. PMID: 30882669. Exclusion Code: X3.

649. Hyun SH, Choi JY, Kim K, et al. Volume-based parameters of (18)F-fluorodeoxyglucose positron emission tomography/computed tomography improve outcome prediction in early-stage non-small cell lung cancer after surgical resection. *Ann Surg*. 2013 Feb;257(2):364-70. doi: 10.1097/SLA.0b013e318262a6ec. PMID: 22968069. Exclusion Code: X3.

650. Icard P, Heyndrickx M, Guetti L, et al. Morbidity, mortality and survival after 110 consecutive bilobectomies over 12 years. *Interact Cardiovasc Thorac Surg*. 2013 Feb;16(2):179-85. doi: 10.1093/icvts/ivs419. PMID: 23117235. Exclusion Code: X3.

651. Ichiki Y, Nagashima A, Chikaishi Y, et al. Pneumonectomy for non-small cell lung cancer. *Surg Today*. 2012 Sep;42(9):830-4. doi: 10.1007/s00595-012-0174-0. PMID: 22484985. Exclusion Code: X3.

652. Ichinose J, Kohno T, Fujimori S, et al. Invasiveness and malignant potential of pulmonary lesions presenting as pure ground-glass opacities. *Ann Thorac Cardiovasc Surg*. 2014;20(5):347-52. PMID: 24088912. Exclusion Code: X3.

653. Iguchi T, Hiraki T, Gobara H, et al. Percutaneous radiofrequency ablation of lung cancer presenting as ground-glass opacity. *Cardiovasc Intervent Radiol*. 2015 Apr;38(2):409-15. doi: 10.1007/s00270-014-0926-x. PMID: 24938905. Exclusion Code: X6.

654. Iguchi T, Hiraki T, Ishii H, et al. Transosseous route for CT fluoroscopy-guided radiofrequency ablation of lung tumors. *J Vasc Interv Radiol*. 2015 Nov;26(11):1694-8. doi: 10.1016/j.jvir.2015.08.012. PMID: 26432461. Exclusion Code: X6.

655. Ihara H, Gobara H, Hiraki T, et al. Radiofrequency ablation of lung tumors using a multitined expandable electrode: impact of the electrode array diameter on local tumor progression. *J Vasc Interv Radiol*. 2016 Jan;27(1):87-95. doi: 10.1016/j.jvir.2015.07.025. PMID: 26321016. Exclusion Code: X3.

656. Iizuka Y, Matsuo Y, Umeoka S, et al. Prediction of clinical outcome after stereotactic body radiotherapy for non-small cell lung cancer using diffusion-weighted MRI and (18)F-FDG PET. *Eur J Radiol*. 2014 Nov;83(11):2087-92. doi: 10.1016/j.ejrad.2014.07.018. PMID: 25174774. Exclusion Code: X12.

657. Imai K, Minamiya Y, Saito H, et al. Accuracy of helical computed tomography for the identification of lymph node metastasis in resectable non-small cell lung cancer. *Surg Today*. 2008;38(12):1083-90. doi: 10.1007/s00595-008-3801-z. PMID: 19039633. Exclusion Code: X3.

658. Infante M, Sestini S, Galeone C, et al. Lung cancer screening with low-dose spiral computed tomography: evidence from a pooled analysis of two Italian randomized trials. *Eur J Cancer Prev*. 2017 Jul;26(4):324-9. doi: 10.1097/cej.0000000000000264. PMID: 27222939. Exclusion Code: X10.

659. Inoue M, Okumura M, Sawabata N, et al. Clinicopathological characteristics and surgical results of lung cancer patients aged up to 50 years: the Japanese Lung Cancer Registry Study 2004. *Lung Cancer*. 2014 Feb;83(2):246-51. doi: 10.1016/j.lungcan.2013.11.007. PMID: 24296124. Exclusion Code: X3.

660. Inoue T, Shiomi H, Oh RJ. Stereotactic body radiotherapy for Stage I lung cancer with chronic obstructive pulmonary disease: special reference to survival and radiation-induced pneumonitis. *J Radiat Res*. 2015 Jul;56(4):727-34. doi: 10.1093/jrr/rrv019. PMID: 25887042. Exclusion Code: X10.

661. Iqbal SI, Molgaard C, Williamson C, et al. Purposeful creation of a pneumothorax and chest tube placement to facilitate CT-guided coil localization of lung nodules before video-assisted thoracoscopic surgical wedge resection. *J Vasc Interv Radiol*. 2014 Jul;25(7):1133-8. doi: 10.1016/j.jvir.2014.03.010. PMID: 24788210. Exclusion Code: X3.

662. Irie M, Nakanishi R, Yasuda M, et al. Risk factors for short-term outcomes after thoracoscopic lobectomy for lung cancer. *Eur Respir J*. 2016 Aug;48(2):495-503. doi: 10.1183/13993003.01939-2015. PMID: 27174883. Exclusion Code: X11.

663. Isaka M, Kojima H, Takahashi S, et al. Risk factors for local recurrence after lobectomy and lymph node dissection in patients with non-small cell lung cancer: Implications for adjuvant therapy. *Lung Cancer*. 2018 Jan;115:28-33. doi: 10.1016/j.lungcan.2017.11.014. PMID: 29290258. Exclusion Code: X3.

664. Isaka T, Takahashi K, Maehara T, et al. Intraoperative core needle biopsy under complete video-assisted thoracic surgery for indeterminate tumor of lung. *Surg Endosc*. 2015 Dec;29(12):3579-87. doi: 10.1007/s00464-015-4112-2. PMID: 25740637. Exclusion Code: X3.

665. Ishida M, Shimazaki T, Suzuki M, et al. Case series of lung abscesses following flexible bronchoscopy. *Respir Investig*. 2015 May;53(3):129-32. doi: 10.1016/j.resinv.2015.01.004. PMID: 25951100. Exclusion Code: X3.

666. Ishijima M, Nakayama H, Itonaga T, et al. Patients with severe emphysema have a low risk of radiation pneumonitis following stereotactic body radiotherapy. *Br J Radiol*. 2015 Feb;88(1046):20140596. doi: 10.1259/bjr.20140596. PMID: 25490255. Exclusion Code: X10.

667. Ishikawa Y, Nakayama H, Ito H, et al. Surgical treatment for synchronous primary lung adenocarcinomas. *Ann Thorac Surg*. 2014 Dec;98(6):1983-8. doi: 10.1016/j.athoracsur.2014.07.006. PMID: 25443005. Exclusion Code: X11.

668. Iskender I, Kadioglu SZ, Cosgun T, et al. False-positivity of mediastinal lymph nodes has negative effect on survival in potentially resectable non-small cell lung cancer. *Eur J Cardiothorac Surg*. 2012 Apr;41(4):874-9. doi: 10.1093/ejcts/ezr054. PMID: 22423060. Exclusion Code: X11.

669. Iskender I, Kadioglu SZ, Kosar A, et al. Is there any maximum standardized uptake value variation among positron emission tomography scanners for mediastinal staging in non-small cell lung cancer? *Interact Cardiovasc Thorac Surg*. 2011 Jun;12(6):965-9. doi: 10.1510/icvts.2010.258103. PMID: 21441257. Exclusion Code: X3.

670. Iskender I, Kapicibasi HO, Kadioglu SZ, et al. Comparison of integrated positron emission tomography/computed tomography and mediastinoscopy in mediastinal staging of non-small cell lung cancer: analysis of 212 patients. *Acta Chir Belg*. 2012 May-Jun;112(3):219-25. PMID: 22808763. Exclusion Code: X3.

671. Ito H, Nakayama H, Murakami S, et al. Does the histologic predominance of pathological stage IA lung adenocarcinoma influence the extent of resection? *Gen Thorac Cardiovasc Surg*. 2017 Sep;65(9):512-8. doi: 10.1007/s11748-017-0790-0. PMID: 28593420. Exclusion Code: X10.

672. Ito H, Nakayama H, Yamada K, et al. Outcomes of lobectomy in 'active' octogenarians with clinical stage I non-small-cell lung cancer. *Ann Thorac Cardiovasc Surg*. 2015;21(1):24-30. doi: 10.5761/atcs.oa.13-00353. PMID: 24747546. Exclusion Code: X11.

673. Ito H, Nakayama H, Yokose T, et al. Prophylaxis for acute exacerbation of interstitial pneumonia after lung resection. *Asian Cardiovasc Thorac Ann*. 2014 Oct;22(8):948-54. doi: 10.1177/0218492314526187. PMID: 24585320. Exclusion Code: X3.

674. Ito M, Miyata Y, Kushitani K, et al. Prediction for prognosis of resected pT1a-1bN0M0 adenocarcinoma based on tumor size and histological status: relationship of TNM and IASLC/ATS/ERS classifications. *Lung Cancer*. 2014 Aug;85(2):270-5. doi: 10.1016/j.lungcan.2014.05.014. PMID: 24976332. Exclusion Code: X3.

675. Ito R, Iwano S, Shimamoto H, et al. A comparative analysis of dual-phase dual-energy CT and FDG-PET/CT for the prediction of histopathological invasiveness of non-small cell lung cancer. *Eur J Radiol*. 2017 Oct;95:186-91. doi: 10.1016/j.ejrad.2017.08.010. PMID: 28987666. Exclusion Code: X8.

676. Iwano S, Ito S, Tsuchiya K, et al. What causes false-negative PET findings for solid-type lung cancer? *Lung Cancer*. 2013 Feb;79(2):132-6. doi: 10.1016/j.lungcan.2012.10.018. PMID: 23177277. Exclusion Code: X3.

677. Iwano S, Kitano M, Matsuo K, et al. Pulmonary lobar volumetry using novel volumetric computer-aided diagnosis and computed tomography. *Interact Cardiovasc Thorac Surg*. 2013 Jul;17(1):59-65. doi: 10.1093/icvts/ivt122. PMID: 23526418. Exclusion Code: X3.

678. Iwata H, Shirahashi K, Mizuno Y, et al. Feasibility of segmental resection in non-small-cell lung cancer with ground-glass opacity. *Eur J Cardiothorac Surg*. 2014 Sep;46(3):375-9; discussion 9. doi: 10.1093/ejcts/ezu021. PMID: 24562008. Exclusion Code: X3.

679. Iwata H, Shirahashi K, Yamamoto H, et al. Propensity score-matching analysis of hybrid video-assisted thoracoscopic surgery and thoracoscopic lobectomy for clinical stage I lung cancerdagger. *Eur J Cardiothorac Surg*. 2016 Apr;49(4):1063-7. doi: 10.1093/ejcts/ezv296. PMID: 26324682. Exclusion Code: X11.

680. Iyen-Omofoman B, Tata LJ, Baldwin DR, et al. Using socio-demographic and early clinical features in general practice to identify people with lung cancer earlier. *Thorax*. 2013 May;68(5):451-9. doi: 10.1136/thoraxjnl-2012-202348. PMID: 23321602. Exclusion Code: X3.

681. Izar B, Zhou H, Heist RS, et al. The prognostic impact of KRAS, its codon and amino acid specific mutations, on survival in resected stage I lung adenocarcinoma. *J Thorac Oncol*. 2014 Sep;9(9):1363-9. doi: 10.1097/jto.0000000000000266. PMID: 25122432. Exclusion Code: X11.

682. Izumo T, Sasada S, Chavez C, et al. Radial endobronchial ultrasound images for ground-glass opacity pulmonary lesions. *Eur Respir J*. 2015 Jun;45(6):1661-8. doi: 10.1183/09031936.00167914. PMID: 25573408. Exclusion Code: X3.

683. Jacobs CD, Jafari ME. Early results of lung cancer screening and radiation dose assessment by low-dose CT at a community hospital. *Clin Lung Cancer*. 2017 Sep;18(5):e327-e31. doi: 10.1016/j.cllc.2017.01.011. PMID: 28237242. Exclusion Code: X11.

684. Jacomelli M, Demarzo SE, Cardoso PF, et al. Radial-probe EBUS for the diagnosis of peripheral pulmonary lesions. *J Bras Pneumol*. 2016 Jul-Aug;42(4):248-53. doi: 10.1590/s1806-37562015000000079. PMID: 27832231. Exclusion Code: X3.

685. Jaconi M, Pagni F, Vacirca F, et al. C-arm cone-beam CT-guided transthoracic lung core needle biopsy as a standard diagnostic tool: an observational study. *Medicine (Baltimore)*. 2015 Mar;94(12):e698. doi: 10.1097/md.0000000000000698. PMID: 25816042. Exclusion Code: X3.

686. Jain S, Poon I, Soliman H, et al. Lung stereotactic body radiation therapy (SBRT) delivered over 4 or 11 days: a comparison of acute toxicity and quality of life. *Radiother Oncol*. 2013;108(2):320-5. doi: 10.1016/j.radonc.2013.06.045. PMID: CN-00913978. Exclusion Code: X3.

687. Jairam PM, de Jong PA, Mali WP, et al. Impact of cardiovascular calcifications on the detrimental effect of continued smoking on cardiovascular risk in male lung cancer screening participants. *PLoS One*. 2013;8(6):e66484. doi: 10.1371/journal.pone.0066484. PMID: 23840486. Exclusion Code: X8.

688. Janet-Vendroux A, Loi M, Bobbio A, et al. Which is the role of pneumonectomy in the era of parenchymal-sparing procedures? Early/long-term survival and functional results of a single-center experience. *Lung*. 2015 Dec;193(6):965-73. doi: 10.1007/s00408-015-9810-y. PMID: 26411589. Exclusion Code: X3.

689. Jang BS, Kim HJ, Kim BH, et al. Clinical outcomes of stereotactic ablative radiotherapy in patients with pulmonary metastasis. *Jpn J Clin Oncol*. 2017 Jan;47(1):61-6. doi: 10.1093/jjco/hyw147. PMID: 28122893. Exclusion Code: X3.

690. Jang H, Kim S, Wu D. Bayesian lead time estimation for the Johns Hopkins Lung Project data. *J Epidemiol Glob Health*. 2013 Sep;3(3):157-63. doi: 10.1016/j.jegh.2013.05.001. PMID: 23932058. Exclusion Code: X4.

691. Jansen RJ, Alexander BH, Hayes RB, et al. A mathematical model of case-ascertainment bias: Applied to case-control studies nested within a randomized screening trial. *PLoS One*. 2018;13(3):e0194608. doi: 10.1371/journal.pone.0194608. PMID: 29554151. Exclusion Code: X7.

692. Janssen S, Kaesmann L, Rudat V, et al. Stereotactic body radiotherapy (SBRT) with lower doses for selected patients with stage I non-small-cell lung cancer (NSCLC). *Lung*. 2016 Apr;194(2):291-4. doi: 10.1007/s00408-016-9849-4. PMID: 26842723. Exclusion Code: X10.

693. Jawitz OK, Wang Z, Boffa DJ, et al. The differential impact of preoperative comorbidity on perioperative outcomes following thoracoscopic and open lobectomies. *Eur J Cardiothorac Surg*. 2017 Jan;51(1):169-74. doi: 10.1093/ejcts/ezw239. PMID: 27458143. Exclusion Code: X3.

694. Jean RA, DeLuzio MR, Kraev AI, et al. Analyzing risk factors for morbidity and mortality after lung resection for lung cancer using the NSQIP Database. *J Am Coll Surg*. 2016 Jun;222(6):992-1000.e1. doi: 10.1016/j.jamcollsurg.2016.02.020. PMID: 27118714. Exclusion Code: X3.

695. Jenkins N, Irusen EM, Koegelenberg CF. Pulmonary scar carcinoma in South Africa. *S Afr Med J*. 2017 Mar 29;107(4):320-2. doi: 10.7196/SAMJ.2017.v107i4.12158. PMID: 28395683. Exclusion Code: X3.

696. Jensen GL, Tang C, Hess KR, et al. Patterns of metastatic progression after definitive radiation therapy for early-stage and locally advanced non-small cell lung cancer. *Clin Exp Metastasis*. 2017 Jun;34(5):315-22. doi: 10.1007/s10585-017-9850-1. PMID: 28744603. Exclusion Code: X3.

697. Jensen KW, Hsia DW, Seijo LM, et al. Multicenter experience with electromagnetic navigation bronchoscopy for the diagnosis of pulmonary nodules. *J Bronchology Interv Pulmonol*. 2012 Jul;19(3):195-9. doi: 10.1097/LBR.0b013e3182616ece. PMID: 23207460. Exclusion Code: X4.

698. Jeon HW, Kim YD, Kim KS, et al. Sublobar resection versus lobectomy in solid-type, clinical stage IA, non-small cell lung cancer. *World J Surg Oncol*. 2014 Jul 16;12:215. doi: 10.1186/1477-7819-12-215. PMID: 25027055. Exclusion Code: X11.

699. Jeon HW, Moon MH, Kim KS, et al. Extent of removal for mediastinal nodal stations for patients with clinical stage I non-small cell lung cancer: effect on outcome. *Thorac Cardiovasc Surg*. 2014 Oct;62(7):599-604. doi: 10.1055/s-0033-1360478. PMID: 24420680. Exclusion Code: X8.

700. Jeong SY, Lee KS, Shin KM, et al. Efficacy of PET/CT in the characterization of solid or partly solid solitary pulmonary nodules. *Lung Cancer*. 2008 Aug;61(2):186-94. doi: 10.1016/j.lungcan.2007.12.021. PMID: 18280613. Exclusion Code: X3.

701. Jett JR, Peek LJ, Fredericks L, et al. Audit of the autoantibody test, EarlyCDT(R)-lung, in 1600 patients: an evaluation of its performance in routine clinical practice. *Lung Cancer*. 2014 Jan;83(1):51-5. doi: 10.1016/j.lungcan.2013.10.008. PMID: 24268382. Exclusion Code: X5.

702. Jeyabalan A, Medford AR. Endobronchial ultrasound-guided transbronchial needle aspiration: patient satisfaction under light conscious sedation. *Respiration*. 2014;88(3):244-50. doi: 10.1159/000363063. PMID: 25170748. Exclusion Code: X3.

703. Jeyabalan A, Shelley-Fraser G, Medford AR. Impact of needle gauge on characterization of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) histology samples. *Respirology*. 2014 Jul;19(5):735-9. doi: 10.1111/resp.12293. PMID: 24697875. Exclusion Code: X3.

704. Jhun BW, Park HY, Jeon K, et al. Nodal stations and diagnostic performances of endobronchial ultrasound-guided transbronchial needle aspiration in patients with non-small cell lung cancer. *J Korean Med Sci*. 2012 Jan;27(1):46-51. doi: 10.3346/jkms.2012.27.1.46. PMID: 22219613. Exclusion Code: X3.

705. Jian ZH, Huang JY, Ko PC, et al. Impact of coexisting pulmonary diseases on survival of patients with lung adenocarcinoma: a STROBE-compliant article. *Medicine (Baltimore)*. 2015 Jan;94(4):e443. doi: 10.1097/md.0000000000000443. PMID: 25634179. Exclusion Code: X3.

706. Jiang W, Pang X, Xi J, et al. Clinical outcome of subcentimeter non-small cell lung cancer after surgical resection: single institution experience of 105 patients. *J Surg Oncol*. 2014 Sep;110(3):233-8. doi: 10.1002/jso.23647. PMID: 24888753. Exclusion Code: X3.

707. Jiang ZF, Wang M, Xu JL. Thymidine kinase 1 combined with CEA, CYFRA21-1 and NSE improved its diagnostic value for lung cancer. *Life Sci*. 2018 Feb 1;194:1-6. doi: 10.1016/j.lfs.2017.12.020. PMID: 29247745. Exclusion Code: X4.

708. Jiao D, Yuan H, Zhang Q, et al. Flat detector C-arm CT-guided transthoracic needle biopsy of small (</=2.0 cm) pulmonary nodules: diagnostic accuracy and complication in 100 patients. *Radiol Med*. 2016 Apr;121(4):268-78. doi: 10.1007/s11547-015-0604-3. PMID: 26646263. Exclusion Code: X3.

709. Jiao W, Zhao Y, Wang M, et al. A retrospective study of diaphragmatic motion, pulmonary function, and quality-of-life following video-assisted thoracoscopic lobectomy in patients with nonsmall cell lung cancer. *Indian J Cancer*. 2015 Feb;51 Suppl 2:e45-8. doi: 10.4103/0019-509x.151991. PMID: 25712843. Exclusion Code: X3.

710. Jimenez AR, Weiss AS, Campagna AC. Use of pulmonary function test demographic data to identify high-risk patients for lung cancer screening. *Monaldi Arch Chest Dis*. 2018 Feb 19;88(1):891. doi: 10.4081/monaldi.2018.891. PMID: 29557572. Exclusion Code: X5.

711. Jobst BJ, Weinheimer O, Trauth M, et al. Effect of smoking cessation on quantitative computed tomography in smokers at risk in a lung cancer screening population. *Eur Radiol*. 2018 Feb;28(2):807-15. doi: 10.1007/s00330-017-5030-6. PMID: 28884215. Exclusion Code: X8.

712. Jonnalagadda S, Bergamo C, Lin JJ, et al. Beliefs and attitudes about lung cancer screening among smokers. *Lung Cancer*. 2012 Sep;77(3):526-31. doi: 10.1016/j.lungcan.2012.05.095. PMID: 22681870. Exclusion Code: X8.

713. Joseph AM, Rothman AJ, Almirall D, et al. Lung Cancer Screening and Smoking Cessation Clinical Trials. SCALE (Smoking Cessation within the Context of Lung Cancer Screening) Collaboration. *Am J Respir Crit Care Med*. 2018 Jan 15;197(2):172-82. doi: 10.1164/rccm.201705-0909CI. PMID: 28977754. Exclusion Code: X10.

714. Joseph S, Harrington R, Walter D, et al. Plasma osteopontin velocity differentiates lung cancers from controls in a CT screening population. *Cancer Biomark*. 2012;12(4):177-84. doi: 10.3233/cbm-130306. PMID: 23568008. Exclusion Code: X4.

715. Jouglar E, Isnardi V, Goulon D, et al. Patterns of locoregional failure in locally advanced non-small cell lung cancer treated with definitive conformal radiotherapy: Results from the Gating 2006 trial. *Radiother Oncol*. 2018 Feb;126(2):291-9. doi: 10.1016/j.radonc.2017.11.002. PMID: 29203290. Exclusion Code: X3.
716. Jung JJ, Cho JH, Hong TH, et al. Intensive care unit (ICU) readmission after major lung resection: Prevalence, patterns, and mortality. *Thorac Cancer*. 2017 Jan;8(1):33-9. doi: 10.1111/1759-7714.12406. PMID: 27925393. Exclusion Code: X3.
717. Jung JY, Lee JM, Kim MS, et al. Comparison of fatigue, depression, and anxiety as factors affecting posttreatment health-related quality of life in lung cancer survivors. *Psychooncology*. 2018 Feb;27(2):465-70. doi: 10.1002/pon.4513. PMID: 28755492. Exclusion Code: X3.
718. Jung MY, Chong A, Seon HJ, et al. Indeterminate pleural metastasis on contrast-enhanced chest CT in non-small cell lung cancer: improved differential diagnosis with (18)F-FDG PET/CT. *Ann Nucl Med*. 2012 May;26(4):327-36. doi: 10.1007/s12149-012-0575-6. PMID: 22350956. Exclusion Code: X3.
719. Jurgens V, Ess S, Cerny T, et al. A Bayesian generalized age-period-cohort power model for cancer projections. *Stat Med*. 2014 Nov 20;33(26):4627-36. doi: 10.1002/sim.6248. PMID: 24996118. Exclusion Code: X4.
720. Kabolizadeh P, Kalash R, Huq MS, et al. Dosimetric definitions of total lung volumes in calculating parameters predictive for radiation-induced pneumonitis. *Am J Clin Oncol*. 2015 Aug;38(4):401-4. doi: 10.1097/COC.0b013e3182a2588f. PMID: 24064747. Exclusion Code: X3.
721. Kadaria D, Archie DS, SultanAli I, et al. Dual time point positron emission tomography/computed tomography scan in evaluation of intrathoracic lesions in an area endemic for histoplasmosis and with high prevalence of sarcoidosis. *Am J Med Sci*. 2013 Nov;346(5):358-62. doi: 10.1097/MAJ.0b013e31827b9b6d. PMID: 23276900. Exclusion Code: X3.
722. Kadeer X, Wang L, Zhang L, et al. Modified hook-wire placement technique for localizing multiple pulmonary nodules. *J Surg Oncol*. 2018 Dec;118(7):1188-93. doi: 10.1002/jso.25261. PMID: 30332509. Exclusion Code: X11.
723. Kadota K, Sima CS, Arcila ME, et al. KRAS mutation is a significant prognostic factor in early-stage lung adenocarcinoma. *Am J Surg Pathol*. 2016 Dec;40(12):1579-90. doi: 10.1097/pas.0000000000000744. PMID: 27740967. Exclusion Code: X3.
724. Kadoya N, Obata Y, Kato T, et al. Dose-volume comparison of proton radiotherapy and stereotactic body radiotherapy for non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2011 Mar 15;79(4):1225-31. doi: 10.1016/j.ijrobp.2010.05.016. PMID: 20732759. Exclusion Code: X6.
725. Kakar M, Mencattini A, Salmeri M. Extracting fuzzy classification rules from texture segmented HRCT lung images. *J Digit Imaging*. 2013 Apr;26(2):227-38. doi: 10.1007/s10278-012-9514-2. PMID: 22890442. Exclusion Code: X3.
726. Kakinuma R, Ashizawa K, Kobayashi T, et al. Comparison of sensitivity of lung nodule detection between radiologists and technologists on low-dose CT lung cancer screening images. *Br J Radiol*. 2012 Sep;85(1017):e603-8. doi: 10.1259/bjr/75768386. PMID: 22919013. Exclusion Code: X11.
727. Kakinuma R, Noguchi M, Ashizawa K, et al. Natural history of pulmonary subsolid nodules: a prospective multicenter study. *J Thorac Oncol*. 2016 Jul;11(7):1012-28. doi: 10.1016/j.jtho.2016.04.006. PMID: 27089851. Exclusion Code: X3.
728. Kalathiya RJ, Davenport D, Saha SP. Long-term survival after pneumonectomy for non-small-cell lung cancer. *Asian Cardiovasc Thorac Ann*. 2013 Oct;21(5):574-81. doi: 10.1177/0218492312467025. PMID: 24570560. Exclusion Code: X3.
729. Kamiya S, Iwano S, Umakoshi H, et al. Computer-aided Volumetry of Part-Solid Lung Cancers by Using CT: Solid Component Size Predicts Prognosis. *Radiology*. 2018 Jun;287(3):1030-40. doi: 10.1148/radiol.2018172319. PMID: 29533722. Exclusion Code: X3.
730. Kanakis MA, Misthos PA, Tsimpinos MD, et al. Benign emptying of the post-pneumonectomy space: recognizing this rare complication retrospectively. *Interact Cardiovasc Thorac Surg*. 2015 Nov;21(5):685-7. doi: 10.1093/icvts/ivv207. PMID: 26242316. Exclusion Code: X3.

731. Kanarek NF, Hooker CM, Mathieu L, et al. Survival after community diagnosis of early-stage non-small cell lung cancer. *Am J Med*. 2014 May;127(5):443-9. doi: 10.1016/j.amjmed.2013.12.023. PMID: 24486286. Exclusion Code: X3.

732. Kanemoto A, Matsumoto Y, Sugita T. Timing and characteristics of radiation pneumonitis after stereotactic body radiotherapy for peripherally located stage I lung cancer. *Int J Clin Oncol*. 2015 Aug;20(4):680-5. doi: 10.1007/s10147-014-0766-3. PMID: 25373854. Exclusion Code: X10.

733. Kang H, Hwangbo B, Lee G, et al. EBUS-centred versus EUS-centred mediastinal staging in lung cancer: a randomised controlled trial. *Thorax*. 2014;69(3):261-8. doi: 10.1136/thoraxjnl-2013-203881. PMID: CN-00982562. Exclusion Code: X7.

734. Kann BH, Miccio JA, Stahl JM, et al. Stereotactic body radiotherapy with adjuvant systemic therapy for early-stage non-small cell lung carcinoma: A multi-institutional analysis. *Radiother Oncol*. 2019 Mar;132:188-96. doi: 10.1016/j.radonc.2018.10.017. PMID: 30391106. Exclusion Code: X8.

735. Kann BH, Verma V, Stahl JM, et al. Multi-institutional analysis of stereotactic body radiation therapy for operable early-stage non-small cell lung carcinoma. *Radiother Oncol*. 2019 May;134:44-9. doi: 10.1016/j.radonc.2019.01.027. PMID: 31005223. Exclusion Code: X13.

736. Kanzaki M, Kikkawa T, Shimizu T, et al. Presurgical planning using a three-dimensional pulmonary model of the actual anatomy of patient with primary lung cancer. *Thorac Cardiovasc Surg*. 2013 Mar;61(2):144-50. doi: 10.1055/s-0032-1328923. PMID: 23344773. Exclusion Code: X11.

737. Kanzaki M, Maeda H, Wachi N, et al. Complete video-assisted thoracoscopic multi-subsegmentectomy based on patients' specific virtual 3-D pulmonary models. *Asian J Endosc Surg*. 2013 May;6(2):110-5. doi: 10.1111/ases.12015. PMID: 23323687. Exclusion Code: X11.

738. Kapadia NS, Valle LF, George JA, et al. Patterns of treatment and outcomes for definitive therapy of early stage non-small cell lung cancer. *Ann Thorac Surg*. 2017 Dec;104(6):1881-8. doi: 10.1016/j.athoracsur.2017.06.065. PMID: 29106887. Exclusion Code: X8.

739. Karki K, Saraiya S, Hugo GD, et al. Variabilities of magnetic resonance imaging-, computed tomography-, and positron emission tomography-computed tomography-based tumor and lymph node delineations for lung cancer radiation therapy planning. *Int J Radiat Oncol Biol Phys*. 2017 Sep 1;99(1):80-9. doi: 10.1016/j.ijrobp.2017.05.002. PMID: 28816167. Exclusion Code: X3.

740. Karp I, Sylvestre MP, Abrahamowicz M, et al. Bridging the etiologic and prognostic outlooks in individualized assessment of absolute risk of an illness: application in lung cancer. *Eur J Epidemiol*. 2016 Nov;31(11):1091-9. doi: 10.1007/s10654-016-0180-4. PMID: 27401439. Exclusion Code: X4.

741. Kashiwabara K, Semba H, Fujii S, et al. Preoperative percutaneous transthoracic needle biopsy increased the risk of pleural recurrence in pathological stage I lung cancer patients with sub-pleural pure solid nodules. *Cancer Invest*. 2016 Sep 13;34(8):373-7. doi: 10.1080/07357907.2016.1212061. PMID: 27532604. Exclusion Code: X11.

742. Kastelijn EA, El Sharouni SY, Hofman FN, et al. Clinical outcomes in early-stage NSCLC treated with stereotactic body radiotherapy versus surgical resection. *Anticancer Res*. 2015 Oct;35(10):5607-14. PMID: 26408733. Exclusion Code: X3.

743. Kates M, Swanson S, Wisnivesky JP. Survival following lobectomy and limited resection for the treatment of stage I non-small cell lung cancer<=1 cm in size: a review of SEER data. *Chest*. 2011 Mar;139(3):491-6. doi: 10.1378/chest.09-2547. PMID: 20576736. Exclusion Code: X10.

744. Katki HA, Kovalchik SA, Petito LC, et al. Implications of Nine Risk Prediction Models for Selecting Ever-Smokers for Computed Tomography Lung Cancer Screening. *Ann Intern Med*. 2018doi: doi: 10.7326/M17-2701. Exclusion Code: X8.

745. Kato T, Ishikawa K, Aragaki M, et al. Optimal predictive value of preoperative serum carcinoembryonic antigen for surgical outcomes in stage I non-small cell lung cancer: differences according to histology and smoking status. *J Surg Oncol*. 2013 May;107(6):619-24. doi: 10.1002/jso.23293. PMID: 23192365. Exclusion Code: X11.

746. Kaur MN, Xie F, Shiwcharan A, et al. Robotic Versus Video-Assisted Thoracoscopic Lung Resection During Early Program Development. *Ann Thorac Surg*. 2018 Apr;105(4):1050-7. doi: 10.1016/j.athoracsur.2017.11.013. PMID: 29502935. Exclusion Code: X3.

747. Kavanagh J, Liu G, Menezes R, et al. Importance of Long-term Low-Dose CT Follow-up after Negative Findings at Previous Lung Cancer Screening. *Radiology*. 2018 Oct;289(1):218-24. doi: 10.1148/radiol.2018180053. PMID: 29989522. Exclusion Code: X11.

748. Kavurmaci O, Akcam TI, Ergonul AG, et al. Is the Risk of Postoperative Atrial Fibrillation Predictable in Patients Undergoing Surgery Due to Primary Lung Cancer? *Heart Lung Circ*. 2018 Jul;27(7):835-41. doi: 10.1016/j.hlc.2017.06.729. PMID: 28800934. Exclusion Code: X3.

749. Kawaguchi T, Sawabata N, Miura S, et al. Prognostic impact of underlying lung disease in pulmonary wedge resection for lung cancer. *Int J Clin Oncol*. 2019 Apr;24(4):366-74. doi: 10.1007/s10147-018-1367-3. PMID: 30443810. Exclusion Code: X11.

750. Kaya A, Can AB. A weighted rule based method for predicting malignancy of pulmonary nodules by nodule characteristics. *J Biomed Inform*. 2015 Aug;56:69-79. doi: 10.1016/j.jbi.2015.05.011. PMID: 26008877. Exclusion Code: X4.

751. Kayawake H, Chen-Yoshikawa TF, Oda H, et al. Complications of endobronchial ultrasound-guided transbronchial needle aspiration. *Ann Thorac Surg*. 2017 Nov;104(5):e363-e5. doi: 10.1016/j.athoracsur.2017.06.015. PMID: 29054229. Exclusion Code: X3.

752. Kearney P, Hunsucker SW, Li XJ, et al. An integrated risk predictor for pulmonary nodules. *PLoS One*. 2017;12(5):e0177635. doi: 10.1371/journal.pone.0177635. PMID: 28545097. Exclusion Code: X3.

753. Kelada OJ, Decker RH, Nath SK, et al. High Single Doses of Radiation May Induce Elevated Levels of Hypoxia in Early-Stage Non-Small Cell Lung Cancer Tumors. *Int J Radiat Oncol Biol Phys*. 2018 Sep 1;102(1):174-83. doi: 10.1016/j.ijrobp.2018.05.032. PMID: 30102194. Exclusion Code: X3.

754. Kelley KD, Benninghoff DL, Stein JS, et al. Medically inoperable peripheral lung cancer treated with stereotactic body radiation therapy. *Radiat Oncol*. 2015 May 28;10:120. doi: 10.1186/s13014-015-0423-7. PMID: 26018408. Exclusion Code: X3.

755. Kelly RF, Tran T, Holmstrom A, et al. Accuracy and cost-effectiveness of [18F]-2-fluoro-deoxy-D-glucose-positron emission tomography scan in potentially resectable non-small cell lung cancer. *Chest*. 2004 Apr;125(4):1413-23. PMID: 15078754. Exclusion Code: X3.

756. Kelsey CR, Higgins KA, Peterson BL, et al. Local recurrence after surgery for non-small cell lung cancer: a recursive partitioning analysis of multi-institutional data. *J Thorac Cardiovasc Surg*. 2013 Oct;146(4):768-73.e1. doi: 10.1016/j.jtcvs.2013.05.041. PMID: 23856204. Exclusion Code: X3.

757. Kennedy S, Baerlocher MO. Screening for lung cancer. *CMAJ*. 2014 May 13;186(8):E296. doi: 10.1503/cmaj.131385. PMID: 24638027. Exclusion Code: X9.

758. Kennedy SA, Milovanovic L, Dao D, et al. Risk factors for pneumothorax complicating radiofrequency ablation for lung malignancy: a systematic review and meta-analysis. *J Vasc Interv Radiol*. 2014 Nov;25(11):1671-81.e1. doi: 10.1016/j.jvir.2014.07.025. PMID: 25442131. Exclusion Code: X6.

759. Kent M, Landreneau R, Mandrekar S, et al. Segmentectomy versus wedge resection for non-small cell lung cancer in high-risk operable patients. *Ann Thorac Surg*. 2013 Nov;96(5):1747-54; discussion 54-5. doi: 10.1016/j.athoracsur.2013.05.104. PMID: 23998400. Exclusion Code: X11.

760. Kent MS, Mandrekar SJ, Landreneau R, et al. Impact of sublobar resection on pulmonary function: long-term results from American College of Surgeons Oncology Group Z4032 (Alliance). *Ann Thorac Surg*. 2016 Jul;102(1):230-8. doi: 10.1016/j.athoracsur.2016.01.069. PMID: 27101728. Exclusion Code: X11.

761. Kent MS, Mandrekar SJ, Landreneau R, et al. A nomogram to predict recurrence and survival of high-risk patients undergoing sublobar resection for lung cancer: an analysis of a multicenter prospective study (ACOSOG Z4032). *Ann Thorac Surg*. 2016 Jul;102(1):239-46. doi: 10.1016/j.athoracsur.2016.01.063. PMID: 27101729. Exclusion Code: X10.

762. Kestin L, Grills I, Guckenberger M, et al. Dose-response relationship with clinical outcome for lung stereotactic body radiotherapy (SBRT) delivered via online image guidance. *Radiother Oncol*. 2014 Mar;110(3):499-504. doi: 10.1016/j.radonc.2014.02.002. PMID: 24630539. Exclusion Code: X13.

763. Khairy M, Duong DK, Shariff-Marco S, et al. An Analysis of Lung Cancer Screening Beliefs and Practice Patterns for Community Providers Compared to Academic Providers. *Cancer Control*. 2018 Jan-Dec;25(1):1073274818806900. doi: 10.1177/1073274818806900. PMID: 30375235. Exclusion Code: X3.

764. Khakwani A, Rich AL, Powell HA, et al. Lung cancer survival in England: trends in non-small-cell lung cancer survival over the duration of the National Lung Cancer Audit. *Br J Cancer*. 2013 Oct 15;109(8):2058-65. doi: 10.1038/bjc.2013.572. PMID: 24052044. Exclusion Code: X5.

765. Khan I, Morris S. A non-linear beta-binomial regression model for mapping EORTC QLQ- C30 to the EQ-5D-3L in lung cancer patients: a comparison with existing approaches. *Health Qual Life Outcomes*. 2014 Nov 12;12:163. doi: 10.1186/s12955-014-0163-7. PMID: 25388439. Exclusion Code: X10.

766. Khan KA, Kennedy MP, Moore E, et al. Radiological characteristics, histological features and clinical outcomes of lung cancer patients with coexistent idiopathic pulmonary fibrosis. *Lung*. 2015 Feb;193(1):71-7. doi: 10.1007/s00408-014-9664-8. PMID: 25381634. Exclusion Code: X3.

767. Khandhar SJ, Bowling MR, Flandes J, et al. Electromagnetic navigation bronchoscopy to access lung lesions in 1,000 subjects: first results of the prospective, multicenter NAVIGATE study. *BMC Pulm Med*. 2017 Apr 11;17(1):59. doi: 10.1186/s12890-017-0403-9. PMID: 28399830. Exclusion Code: X8.

768. Khawaja RD, Singh S, Lira D, et al. Role of compressive sensing technique in dose reduction for chest computed tomography: a prospective blinded clinical study. *J Comput Assist Tomogr*. 2014 Sep-Oct;38(5):760-7. doi: 10.1097/rct.0000000000000098. PMID: 24834892. Exclusion Code: X11.

769. Khawaja RD, Singh S, Madan R, et al. Ultra low-dose chest CT using filtered back projection: comparison of 80-, 100- and 120 kVp protocols in a prospective randomized study. *Eur J Radiol*. 2014 Oct;83(10):1934-44. doi: 10.1016/j.ejrad.2014.06.024. PMID: 25063211. Exclusion Code: X11.

770. Khorochkov E, Garvin GJ, Potoczny S, et al. Injection of Saline Into the Biopsy Tract and Rapid Patient Rollover Decreases Pneumothorax Size Following Computed Tomography-Guided Transthoracic Needle Biopsy. *Can Assoc Radiol J*. 2018 Nov;69(4):489-92. doi: 10.1016/j.carj.2018.08.002. PMID: 30309700. Exclusion Code: X11.

771. Kiankhooy A, Taylor MD, LaPar DJ, et al. Predictors of early recurrence for node-negative t1 to t2b non-small cell lung cancer. *Ann Thorac Surg*. 2014 Oct;98(4):1175-83. doi: 10.1016/j.athoracsur.2014.05.061. PMID: 25134863. Exclusion Code: X12.

772. Kim AW, Detterbeck FC, Boffa DJ, et al. Characteristics associated with the use of nonanatomic resections among Medicare patients undergoing resections of early-stage lung cancer. *Ann Thorac Surg*. 2012 Sep;94(3):895-901. doi: 10.1016/j.athoracsur.2012.04.091. PMID: 22835558. Exclusion Code: X11.

773. Kim C, Lee SM, Choe J, et al. Volume doubling time of lung cancer detected in idiopathic interstitial pneumonia: comparison with that in chronic obstructive pulmonary disease. *Eur Radiol*. 2018 Apr;28(4):1402-9. doi: 10.1007/s00330-017-5091-6. PMID: 29038933. Exclusion Code: X8.

774. Kim CH, Lee YC, Hung RJ, et al. Secondhand tobacco smoke exposure and lung adenocarcinoma in situ/minimally invasive adenocarcinoma (AIS/MIA). *Cancer Epidemiol Biomarkers Prev*. 2015 Dec;24(12):1902-6. doi: 10.1158/1055-9965.epi-15-0436. PMID: 26503035. Exclusion Code: X3.

775. Kim D, Ferraris VA, Davenport D, et al. Outcomes of lobar and sublobar resections for non-small-cell lung cancer: a single-center experience. *South Med J*. 2015 Apr;108(4):230-4. doi: 10.14423/smj.0000000000000272. PMID: 25871994. Exclusion Code: X11.
776. Kim D, Kim HK, Choi YS, et al. Central lung cancer management: impact of bronchial resection margin length. *Thorac Cardiovasc Surg*. 2015 Oct;63(7):583-8. doi: 10.1055/s-0034-1383813. PMID: 25032722. Exclusion Code: X3.
777. Kim DH, Jung JH, Son SH, et al. Quantification of intratumoral metabolic macroheterogeneity on 18F-FDG PET/CT and its prognostic significance in pathologic N0 squamous cell lung carcinoma. *Clin Nucl Med*. 2016 Feb;41(2):e70-5. doi: 10.1097/rlu.0000000000000930. PMID: 26284762. Exclusion Code: X6.
778. Kim DH, Son SH, Kim CY, et al. Prediction for recurrence using F-18 FDG PET/CT in pathologic N0 lung adenocarcinoma after curative surgery. *Ann Surg Oncol*. 2014 Feb;21(2):589-96. doi: 10.1245/s10434-013-3270-5. PMID: 24046125. Exclusion Code: X3.
779. Kim ES, Kim YT, Kang CH, et al. Prevalence of and risk factors for postoperative pulmonary complications after lung cancer surgery in patients with early-stage COPD. *Int J Chron Obstruct Pulmon Dis*. 2016;11:1317-26. doi: 10.2147/copd.s105206. PMID: 27366059. Exclusion Code: X11.
780. Kim H, Lussier YA, Noh OK, et al. Prognostic implication of pulmonary function at the beginning of postoperative radiotherapy in non-small cell lung cancer. *Radiother Oncol*. 2014 Dec;113(3):374-8. doi: 10.1016/j.radonc.2014.11.007. PMID: 25441612. Exclusion Code: X6.
781. Kim H, Park CM, Jeon S, et al. Validation of prediction models for risk stratification of incidentally detected pulmonary subsolid nodules: a retrospective cohort study in a Korean tertiary medical centre. *BMJ Open*. 2018 May 24;8(5):e019996. doi: 10.1136/bmjopen-2017-019996. PMID: 29794091. Exclusion Code: X4.
782. Kim H, Park CM, Lee M, et al. Impact of reconstruction algorithms on CT radiomic features of pulmonary tumors: analysis of intra- and inter-reader variability and inter-reconstruction algorithm variability. *PLoS One*. 2016;11(10):e0164924. doi: 10.1371/journal.pone.0164924. PMID: 27741289. Exclusion Code: X8.
783. Kim H, Park CM, Woo S, et al. Pure and part-solid pulmonary ground-glass nodules: measurement variability of volume and mass in nodules with a solid portion less than or equal to 5 mm. *Radiology*. 2013 Nov;269(2):585-93. doi: 10.1148/radiol.13121849. PMID: 23864104. Exclusion Code: X3.
784. Kim H, Park CM, Yoon SH, et al. Open Bronchus Sign on CT: A Risk Factor for Hemoptysis after Percutaneous Transthoracic Biopsy. *Korean J Radiol*. 2018 Sep-Oct;19(5):880-7. doi: 10.3348/kjr.2018.19.5.880. PMID: 30174477. Exclusion Code: X3.
785. Kim HJ, Cha SI, Kim CH, et al. Risk factors of postoperative acute lung injury following lobectomy for nonsmall cell lung cancer. *Medicine (Baltimore)*. 2019 Mar;98(13):e15078. doi: 10.1097/md.0000000000015078. PMID: 30921242. Exclusion Code: X3.
786. Kim HY, Jung KW, Lim KY, et al. Lung Cancer Screening with Low-Dose CT in Female Never Smokers: Retrospective Cohort Study with Long-term National Data Follow-up. *Cancer Res Treat*. 2018 Jul;50(3):748-56. doi: 10.4143/crt.2017.312. PMID: 28724283. Exclusion Code: X10.
787. Kim HY, Naidich DP, Lim KY, et al. Transient pulmonary eosinophilia incidentally found on low-dose computed tomography: findings in 40 individuals. *J Comput Assist Tomogr*. 2008 Jan-Feb;32(1):101-7. doi: 10.1097/RCT.0b013e31806535e5. PMID: 18303297. Exclusion Code: X3.
788. Kim IH, Lee IH, Lee JE, et al. Prognostic impact of multiple clinicopathologic risk factors and c-MET overexpression in patients who have undergone resection of stage IB non-small-cell lung cancer. *Clin Lung Cancer*. 2016 Sep;17(5):e31-e43. doi: 10.1016/j.cllc.2016.01.005. PMID: 26992846. Exclusion Code: X11.

789. Kim JI, Park CM, Kim H, et al. Non-specific benign pathological results on transthoracic core-needle biopsy: how to differentiate false-negatives? *Eur Radiol*. 2017 Sep;27(9):3888-95. doi: 10.1007/s00330-017-4766-3. PMID: 28188426. Exclusion Code: X3.

790. Kim K, Kim SJ, Kim IJ, et al. Prognostic value of volumetric parameters measured by F-18 FDG PET/CT in surgically resected non-small-cell lung cancer. *Nucl Med Commun*. 2012 Jun;33(6):613-20. doi: 10.1097/MNM.0b013e328351d4f5. PMID: 22407127. Exclusion Code: X3.

791. Kim KW, Kim HK, Kim J, et al. Outcomes of curative-intent surgery and adjuvant treatment for pulmonary large cell neuroendocrine carcinoma. *World J Surg*. 2017 Jul;41(7):1820-7. doi: 10.1007/s00268-017-3908-8. PMID: 28204910. Exclusion Code: X3.

792. Kim MP, Correa AM, Hofstetter W, et al. Limitations of 18F-2-deoxy-D-glucose positron emission tomography in N1 detection in patients with pathologic stage II-N1 and implications for management. *Ann Thorac Surg*. 2015 Feb;99(2):414-20. doi: 10.1016/j.athoracsur.2014.09.023. PMID: 25497068. Exclusion Code: X3.

793. Kim SH, Kim HK, Choi YS, et al. Pleural recurrence and long-term survival after thoracotomy and thoracoscopic lobectomy. *Ann Thorac Surg*. 2013 Nov;96(5):1769-75. doi: 10.1016/j.athoracsur.2013.05.037. PMID: 23968762. Exclusion Code: X11.

794. Kim SK, Allen-Auerbach M, Goldin J, et al. Accuracy of PET/CT in characterization of solitary pulmonary lesions. *J Nucl Med*. 2007 Feb;48(2):214-20. PMID: 17268017. Exclusion Code: X3.

795. Kim SK, Manzerova J, Christos P, et al. Impact of radiation therapy in surgically resected limited-stage small cell lung carcinoma. *Lung*. 2017 Jun;195(3):341-6. doi: 10.1007/s00408-017-9992-6. PMID: 28353115. Exclusion Code: X11.

796. Kim SR, Han HJ, Park SJ, et al. Comparison between surgery and radiofrequency ablation for stage I non-small cell lung cancer. *Eur J Radiol*. 2012 Feb;81(2):395-9. doi: 10.1016/j.ejrad.2010.12.091. PMID: 21310562. Exclusion Code: X6.

797. Kim SS, Song SY, Kwak J, et al. Clinical prognostic factors and grading system for rib fracture following stereotactic body radiation therapy (SBRT) in patients with peripheral lung tumors. *Lung Cancer*. 2013 Feb;79(2):161-6. doi: 10.1016/j.lungcan.2012.10.011. PMID: 23182662. Exclusion Code: X3.

798. Kim TJ, Lee JH, Lee CT, et al. Diagnostic accuracy of CT-guided core biopsy of ground-glass opacity pulmonary lesions. *AJR Am J Roentgenol*. 2008 Jan;190(1):234-9. doi: 10.2214/ajr.07.2441. PMID: 18094317. Exclusion Code: X3.

799. Kim Y, Kim YK, Lee BE, et al. Ultra-low-dose CT of the thorax using iterative reconstruction: evaluation of image quality and radiation dose reduction. *AJR Am J Roentgenol*. 2015 Jun;204(6):1197-202. doi: 10.2214/ajr.14.13629. PMID: 26001228. Exclusion Code: X3.

800. Kim YJ, Kim SS, Song SY, et al. Feasibility of stereotactic radiotherapy for lung lesions and conventional radiotherapy for nodal areas in primary lung malignancies. *Radiat Oncol*. 2018 Jul 11;13(1):127. doi: 10.1186/s13014-018-1071-5. PMID: 29996863. Exclusion Code: X3.

801. Kimura D, Fukuda I, Tsushima T, et al. Management of acute ischemic stroke after pulmonary resection: incidence and efficacy of endovascular thrombus aspiration. *Gen Thorac Cardiovasc Surg*. 2019 Mar;67(3):306-11. doi: 10.1007/s11748-018-1024-9. PMID: 30367330. Exclusion Code: X11.

802. Kimura T, Matsuura K, Murakami Y, et al. CT appearance of radiation injury of the lung and clinical symptoms after stereotactic body radiation therapy (SBRT) for lung cancers: are patients with pulmonary emphysema also candidates for SBRT for lung cancers? *Int J Radiat Oncol Biol Phys*. 2006 Oct 1;66(2):483-91. doi: 10.1016/j.ijrobp.2006.05.008. PMID: 16904838. Exclusion Code: X3.

803. Kimura T, Togami T, Takashima H, et al. Radiation pneumonitis in patients with lung and mediastinal tumours: a retrospective study of risk factors focused on pulmonary emphysema. *Br J Radiol*. 2012 Feb;85(1010):135-41. doi: 10.1259/bjr/32629867. PMID: 21385918. Exclusion Code: X3.

804. Kinoshita F, Toyokawa G, Matsubara T, et al. Prognosis of Early-stage Part-solid and Pure-solid Lung Adenocarcinomas. *Anticancer Res*. 2019 May;39(5):2665-70. doi: 10.21873/anticanres.13391. PMID: 31092466. Exclusion Code: X11.

805. Kiranantawat N, Srisala N, Sungsiri J, et al. Transthoracic imaging-guided biopsy of lung lesions: evaluation of benign non-specific pathologic diagnoses. *J Med Assoc Thai*. 2015 May;98(5):501-7. PMID: 26058280. Exclusion Code: X11.

806. Kirchner J, Sawicki LM, Nensa F, et al. Prospective comparison of (18)F-FDG PET/MRI and (18)F-FDG PET/CT for thoracic staging of non-small cell lung cancer. *Eur J Nucl Med Mol Imaging*. 2019 Feb;46(2):437-45. doi: 10.1007/s00259-018-4109-x. PMID: 30074073. Exclusion Code: X8.

807. Kirienko M, Cozzi L, Rossi A, et al. Ability of FDG PET and CT radiomics features to differentiate between primary and metastatic lung lesions. *Eur J Nucl Med Mol Imaging*. 2018 Sep;45(10):1649-60. doi: 10.1007/s00259-018-3987-2. PMID: 29623375. Exclusion Code: X3.

808. Kirmani BH, Rintoul RC, Win T, et al. Stage migration: results of lymph node dissection in the era of modern imaging and invasive staging for lung cancer. *Eur J Cardiothorac Surg*. 2013 Jan;43(1):104-9; discussion 9-10. doi: 10.1093/ejcts/ezs184. PMID: 22529185. Exclusion Code: X8.

809. Kishi T, Matsuo Y, Ueki N, et al. Pretreatment Modified Glasgow Prognostic Score predicts clinical outcomes after stereotactic body radiation therapy for early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2015 Jul 1;92(3):619-26. doi: 10.1016/j.ijrobp.2015.02.018. PMID: 26068494. Exclusion Code: X13.

810. Kiss N, Isenring E, Gough K, et al. The prevalence of weight loss during (chemo)radiotherapy treatment for lung cancer and associated patient- and treatment-related factors. *Clin Nutr*. 2014 Dec;33(6):1074-80. doi: 10.1016/j.clnu.2013.11.013. PMID: 24325888. Exclusion Code: X3.

811. Kiss N, Krishnasamy M, Everitt S, et al. Dosimetric factors associated with weight loss during (chemo)radiotherapy treatment for lung cancer. *Eur J Clin Nutr*. 2014 Dec;68(12):1309-14. doi: 10.1038/ejcn.2014.166. PMID: 25117989. Exclusion Code: X6.

812. Kitamura Y, Suzuki K, Teramukai S, et al. Feasibility of pulmonary resection for lung cancer in patients with coronary artery disease or atrial fibrillation. *Ann Thorac Surg*. 2017 Feb;103(2):432-40. doi: 10.1016/j.athoracsur.2016.08.077. PMID: 27793400. Exclusion Code: X10.

813. Klabatsa A, Chicklore S, Barrington SF, et al. The association of 18F-FDG PET/CT parameters with survival in malignant pleural mesothelioma. *Eur J Nucl Med Mol Imaging*. 2014 Feb;41(2):276-82. doi: 10.1007/s00259-013-2561-1. PMID: 24057459. Exclusion Code: X3.

814. Kleedehn M, Kim DH, Lee FT, et al. Preoperative pulmonary nodule localization: a comparison of methylene blue and hookwire techniques. *AJR Am J Roentgenol*. 2016 Dec;207(6):1334-9. doi: 10.2214/ajr.16.16272. PMID: 27657546. Exclusion Code: X3.

815. Klement RJ, Allgauer M, Appold S, et al. Support vector machine-based prediction of local tumor control after stereotactic body radiation therapy for early-stage non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2014 Mar 1;88(3):732-8. doi: 10.1016/j.ijrobp.2013.11.216. PMID: 24411630. Exclusion Code: X8.

816. Klinkenberg TJ, Dinjens L, Wolf RFE, et al. CT-guided percutaneous hookwire localization increases the efficacy and safety of VATS for pulmonary nodules. *J Surg Oncol*. 2017 Jun;115(7):898-904. doi: 10.1002/jso.24589. PMID: 28230245. Exclusion Code: X3.

817. Kluthke RA, Kickuth R, Bansmann PM, et al. The additional value of the lateral chest radiograph for the detection of small pulmonary nodules-a ROC analysis. *Br J Radiol*. 2016 Nov;89(1067):20160394. doi: 10.1259/bjr.20160394. PMID: 27605206. Exclusion Code: X5.

818. Kneuertz PJ, Singer E, D'Souza DM, et al. Postoperative complications decrease the cost-effectiveness of robotic-assisted lobectomy. *Surgery*. 2019 Feb;165(2):455-60. doi: 10.1016/j.surg.2018.08.024. PMID: 30268372. Exclusion Code: X11.

819. Ko JP, Suh J, Ibidapo O, et al. Lung adenocarcinoma: correlation of quantitative CT findings with pathologic findings. *Radiology*. 2016 Sep;280(3):931-9. doi: 10.1148/radiol.2016142975. PMID: 27097236. Exclusion Code: X3.
820. Kobayashi H, Ohkubo M, Narita A, et al. A method for evaluating the performance of computer-aided detection of pulmonary nodules in lung cancer CT screening: detection limit for nodule size and density. *Br J Radiol*. 2017 Feb;90(1070):20160313. doi: 10.1259/bjr.20160313. PMID: 27897029. Exclusion Code: X5.
821. Kobayashi M, Matsumoto T, Ryuge S, et al. CAXII Is a sero-diagnostic marker for lung cancer. *PLoS One*. 2012;7(3):e33952. doi: 10.1371/journal.pone.0033952. PMID: 22439015. Exclusion Code: X4.
822. Kobayashi Y, Fukui T, Ito S, et al. How long should small lung lesions of ground-glass opacity be followed? *J Thorac Oncol*. 2013 Mar;8(3):309-14. doi: 10.1097/JTO.0b013e31827e2435. PMID: 23399958. Exclusion Code: X3.
823. Kocher F, Fiegl M, Mian M, et al. Cardiovascular comorbidities and events in NSCLC: often underestimated but worth considering. *Clin Lung Cancer*. 2015 Jul;16(4):305-12. doi: 10.1016/j.cllc.2014.12.007. PMID: 25659438. Exclusion Code: X3.
824. Kocher F, Lunger F, Seeber A, et al. Incidental diagnosis of asymptomatic non-small-cell lung cancer: a registry-based analysis. *Clin Lung Cancer*. 2016 Jan;17(1):62-7.e1. doi: 10.1016/j.cllc.2015.08.006. PMID: 26420370. Exclusion Code: X5.
825. Kodama H, Yamakado K, Hasegawa T, et al. Radiofrequency ablation using a multiple-electrode switching system for lung tumors with 2.0-5.0-cm maximum diameter: phase II clinical study. *Radiology*. 2015 Dec;277(3):895-902. doi: 10.1148/radiol.2015141153. PMID: 26053308. Exclusion Code: X3.
826. Kodama H, Yamakado K, Hasegawa T, et al. Radiofrequency ablation for ground-glass opacity-dominant lung adenocarcinoma. *J Vasc Interv Radiol*. 2014 Mar;25(3):333-9. doi: 10.1016/j.jvir.2013.11.035. PMID: 24581457. Exclusion Code: X3.
827. Kodama K, Higashiyama M, Okami J, et al. Oncologic outcomes of segmentectomy versus lobectomy for clinical T1a N0 M0 non-small cell lung cancer. *Ann Thorac Surg*. 2016 Feb;101(2):504-11. doi: 10.1016/j.athoracsur.2015.08.063. PMID: 26542438. Exclusion Code: X11.
828. Koenigkam-Santos M, Optazaite E, Sommer G, et al. Contrast-enhanced magnetic resonance imaging of pulmonary lesions: description of a technique aiming clinical practice. *Eur J Radiol*. 2015 Jan;84(1):185-92. doi: 10.1016/j.ejrad.2014.10.007. PMID: 25455411. Exclusion Code: X3.
829. Kohman LJ, Gu L, Altorki N, et al. Biopsy first: Lessons learned from Cancer and Leukemia Group B (CALGB) 140503. *J Thorac Cardiovasc Surg*. 2017 Jun;153(6):1592-7. doi: 10.1016/j.jtcvs.2016.12.045. PMID: 28274562. Exclusion Code: X11.
830. Kohutek ZA, Wu AJ, Zhang Z, et al. FDG-PET maximum standardized uptake value is prognostic for recurrence and survival after stereotactic body radiotherapy for non-small cell lung cancer. *Lung Cancer*. 2015 Aug;89(2):115-20. doi: 10.1016/j.lungcan.2015.05.019. PMID: 26078260. Exclusion Code: X10.
831. Koike T, Kitahara A, Sato S, et al. Lobectomy versus segmentectomy in radiologically pure solid small-sized non-small cell lung cancer. *Ann Thorac Surg*. 2016 Apr;101(4):1354-60. doi: 10.1016/j.athoracsur.2015.10.048. PMID: 26794890. Exclusion Code: X11.
832. Koike T, Koike T, Yamato Y, et al. Prognostic predictors in non-small cell lung cancer patients undergoing intentional segmentectomy. *Ann Thorac Surg*. 2012 Jun;93(6):1788-94. doi: 10.1016/j.athoracsur.2012.02.093. PMID: 22560265. Exclusion Code: X11.
833. Koike T, Koike T, Yoshiya K, et al. Risk factor analysis of locoregional recurrence after sublobar resection in patients with clinical stage IA non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2013 Aug;146(2):372-8. doi: 10.1016/j.jtcvs.2013.02.057. PMID: 23870323. Exclusion Code: X11.

834. Koizumi T, Shetty V, Yamaguchi M. Salivary cytokine panel indicative of non-small cell lung cancer. *J Int Med Res*. 2018 Sep;46(9):3570-82. doi: 10.1177/0300060518775563. PMID: 29916282. Exclusion Code: X5.
835. Kolodziejczyk M, Bujko K, Michalski W, et al. Incidence of isolated nodal failure in non-small cell lung cancer patients included in a prospective study of the value of PET-CT. *Radiother Oncol*. 2012 Jul;104(1):58-61. doi: 10.1016/j.radonc.2012.04.012. PMID: 22652096. Exclusion Code: X3.
836. Komatsu H, Izumi N, Tsukioka T, et al. Prognosis associated with synchronous or metachronous multiple primary malignancies in patients with completely resected non-small cell lung cancer. *Surg Today*. 2019 Apr;49(4):343-9. doi: 10.1007/s00595-018-1738-4. PMID: 30417262. Exclusion Code: X3.
837. Komisopoulos G, Mavroidis P, Rodriguez S, et al. Radiobiologic comparison of helical tomotherapy, intensity modulated radiotherapy, and conformal radiotherapy in treating lung cancer accounting for secondary malignancy risks. *Med Dosim*. 2014 Winter;39(4):337-47. doi: 10.1016/j.meddos.2014.06.001. PMID: 25168596. Exclusion Code: X3.
838. Konings R, van Gool MH, Bard MP, et al. Prognostic value of pre-operative glucose-corrected maximum standardized uptake value in patients with non-small cell lung cancer after complete surgical resection and 5-year follow-up. *Ann Nucl Med*. 2016 Jun;30(5):362-8. doi: 10.1007/s12149-016-1070-2. PMID: 26961089. Exclusion Code: X3.
839. Kopek N, Paludan M, Petersen J, et al. Co-morbidity index predicts for mortality after stereotactic body radiotherapy for medically inoperable early-stage non-small cell lung cancer. *Radiother Oncol*. 2009 Dec;93(3):402-7. doi: 10.1016/j.radonc.2009.06.002. PMID: 19559492. Exclusion Code: X11.
840. Korbakis D, Dimitromanolakis A, Prassas I, et al. Serum LAMC2 enhances the prognostic value of a multi-parametric panel in non-small cell lung cancer. *Br J Cancer*. 2015 Jul 28;113(3):484-91. doi: 10.1038/bjc.2015.171. PMID: 26180921. Exclusion Code: X3.
841. Korzets Ceder Y, Fenig E, Popvtzer A, et al. Stereotactic body radiotherapy for central lung tumors, yes we can! *Radiat Oncol*. 2018 Apr 25;13(1):77. doi: 10.1186/s13014-018-1017-y. PMID: 29695273. Exclusion Code: X3.
842. Koshy M, Malik R, Mahmood U, et al. Stereotactic body radiotherapy and treatment at a high volume facility is associated with improved survival in patients with inoperable stage I non-small cell lung cancer. *Radiother Oncol*. 2015 Feb;114(2):148-54. doi: 10.1016/j.radonc.2014.12.004. PMID: 25586951. Exclusion Code: X13.
843. Kovalchik SA, De Matteis S, Landi MT, et al. A regression model for risk difference estimation in population-based case-control studies clarifies gender differences in lung cancer risk of smokers and never smokers. *BMC Med Res Methodol*. 2013 Nov 19;13:143. doi: 10.1186/1471-2288-13-143. PMID: 24252624. Exclusion Code: X4.
844. Koyi H, Hillerdal G, Kolbeck KG, et al. Non-small cell lung cancer (NSCLC) in octogenarians in clinical practice. *Anticancer Res*. 2016 Oct;36(10):5397-402. doi: 10.21873/anticanres.11115. PMID: 27798905. Exclusion Code: X3.
845. Kozak A, Alchimowicz J, Safranow K, et al. The impact of the sequence of pulmonary vessel ligation during anatomic resection for lung cancer on long-term survival--a prospective randomized trial. *Adv Med Sci*. 2013;58(1):156-63. doi: 10.2478/v10039-012-0061-3. PMID: 23612700. Exclusion Code: X3.
846. Krafft SP, Rao A, Stingo F, et al. The utility of quantitative CT radiomics features for improved prediction of radiation pneumonitis. *Med Phys*. 2018 Nov;45(11):5317-24. doi: 10.1002/mp.13150. PMID: 30133809. Exclusion Code: X6.
847. Kreinbrink P, Blumenfeld P, Tolekidis G, et al. Lung stereotactic body radiation therapy (SBRT) for early-stage non-small cell lung cancer in the very elderly (>/=80years old): Extremely safe and effective. *J Geriatr Oncol*. 2017 Sep;8(5):351-5. doi: 10.1016/j.jgo.2017.07.002. PMID: 28739159. Exclusion Code: X10.

848. Kreuter M, Ehlers-Tenenbaum S, Schaaf M, et al. Treatment and outcome of lung cancer in idiopathic interstitial pneumonias. *Sarcoidosis Vasc Diffuse Lung Dis*. 2015 Jan 5;31(4):266-74. PMID: 25591137. Exclusion Code: X3.

849. Kron T, Chesson B, Hardcastle N, et al. Credentialing of radiotherapy centres in Australasia for TROG 09.02 (Chisel), a Phase III clinical trial on stereotactic ablative body radiotherapy of early stage lung cancer. *Br J Radiol*. 2018 May;91(1085):20170737. doi: 10.1259/bjr.20170737. PMID: 29446317. Exclusion Code: X6.

850. Kubik MJ, Bovbel A, Goli H, et al. Diagnostic value and accuracy of imprint cytology evaluation during image-guided core needle biopsies: Review of our experience at a large academic center. *Diagn Cytopathol*. 2015 Oct;43(10):773-9. doi: 10.1002/dc.23300. PMID: 26119885. Exclusion Code: X3.

851. Kudo S, Imai K, Ishiyama K, et al. New CT criteria for nodal staging in non-small cell lung cancer. *Clin Imaging*. 2014 Jul-Aug;38(4):448-53. doi: 10.1016/j.clinimag.2014.02.008. PMID: 24651060. Exclusion Code: X3.

852. Kuijvenhoven JC, Crombag L, Breen DP, et al. Esophageal ultrasound (EUS) assessment of T4 status in NSCLC patients. *Lung Cancer*. 2017 Dec;114:50-5. doi: 10.1016/j.lungcan.2017.10.017. PMID: 29173765. Exclusion Code: X3.

853. Kumagai S, Marumo S, Arita M, et al. Development and validation of a preoperative prognostic index independent of TNM stage in resected non-small cell lung cancer. *BMC Pulm Med*. 2017 Dec 4;17(1):166. doi: 10.1186/s12890-017-0529-9. PMID: 29202834. Exclusion Code: X3.

854. Kumar P, Gareen IF, Lathan C, et al. Racial differences in tobacco cessation and treatment usage after lung screening: an examination of the National Lung Screening Trial. *Oncologist*. 2016 Jan;21(1):40-9. doi: 10.1634/theoncologist.2015-0325. PMID: 26712960. Exclusion Code: X7.

855. Kumar S, Feddock J, Li X, et al. Update of a Prospective Study of Stereotactic Body Radiation Therapy for Post-Chemoradiation Residual Disease in Stage II/III Non-Small Cell Lung Cancer. *Int J Radiat Oncol Biol Phys*. 2017 Nov 1;99(3):652-9. doi: 10.1016/j.ijrobp.2017.07.036. PMID: 29280459. Exclusion Code: X3.

856. Kumar SG, Garg MK, Khandelwal N, et al. Role of digital tomosynthesis and dual energy subtraction digital radiography in detecting pulmonary nodules. *Eur J Radiol*. 2015 Jul;84(7):1383-91. doi: 10.1016/j.ejrad.2015.03.020. PMID: 25892052. Exclusion Code: X5.

857. Kumar V, Cohen JT, van Klaveren D, et al. Risk-targeted lung cancer screening: a cost-effectiveness analysis. *Ann Intern Med*. 2018 Jan 2doi: 10.7326/M17-1401. PMID: 29297005. Exclusion Code: X4.

858. Kundel HL. Visual search and lung nodule detection on CT scans. *Radiology*. 2015 Jan;274(1):14-6. doi: 10.1148/radiol.14142247. PMID: 25531475. Exclusion Code: X10.

859. Kuo CH, Wu CY, Lee KY, et al. Chronic obstructive pulmonary disease in stage I non-small cell lung cancer that underwent anatomic resection: the role of a recurrence promoter. *Copd*. 2014 Aug;11(4):407-13. doi: 10.3109/15412555.2013.838946. PMID: 24475998. Exclusion Code: X11.

860. Kuo E, Bharat A, Bontumasi N, et al. Impact of video-assisted thoracoscopic surgery on benign resections for solitary pulmonary nodules. *Ann Thorac Surg*. 2012 Jan;93(1):266-72; discussion 72-3. doi: 10.1016/j.athoracsur.2011.08.035. PMID: 22075217. Exclusion Code: X10.

861. Kuo SW, Chen JS, Huang PM, et al. Prognostic significance of histologic differentiation, carcinoembryonic antigen value, and lymphovascular invasion in stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2014 Oct;148(4):1200-7.e3. doi: 10.1016/j.jtcvs.2014.04.038. PMID: 24993621. Exclusion Code: X3.

862. Kuritzky AM, Aswad BI, Jones RN, et al. Lobectomy by video-assisted thoracic surgery vs muscle-sparing thoracotomy for stage I lung cancer: a critical evaluation of short- and long-term outcomes. *J Am Coll Surg*. 2015 Jun;220(6):1044-53. doi: 10.1016/j.jamcollsurg.2014.12.049. PMID: 25868407. Exclusion Code: X11.

863. Kuritzky AM, Ryder BA, Ng T. Long-term survival outcomes of Video-assisted Thoracic Surgery (VATS) lobectomy after transitioning from open lobectomy. *Ann Surg Oncol*. 2013 Aug;20(8):2734-40. doi: 10.1245/s10434-013-2929-2. PMID: 23463094. Exclusion Code: X11.

864. Kurt A, Tan S, Tatar IG, et al. The use of bronchial arteries in the characterization of primary lung cancer: an MDCT study. *J Comput Assist Tomogr*. 2014 Mar-Apr;38(2):169-73. doi: 10.1097/RCT.0b013e3182aa6753. PMID: 24448502. Exclusion Code: X3.

865. Kusk MW, Karstoft J, Mussmann BR. CT triage for lung malignancy: coronal multiplanar reformation versus images in three orthogonal planes. *Acta Radiol*. 2015 Nov;56(11):1336-41. doi: 10.1177/0284185114556928. PMID: 25406433. Exclusion Code: X3.

866. Kwan SW, Mortell KE, Hippe DS, et al. An economic analysis of sublobar resection versus thermal ablation for early-stage non-small-cell lung cancer. *J Vasc Interv Radiol*. 2014 Oct;25(10):1558-64; quiz 65. doi: 10.1016/j.jvir.2014.07.002. PMID: 25130308. Exclusion Code: X8.

867. Kwan SW, Mortell KE, Talenfeld AD, et al. Thermal ablation matches sublobar resection outcomes in older patients with early-stage non-small cell lung cancer. *J Vasc Interv Radiol*. 2014 Jan;25(1):1-9.e1. doi: 10.1016/j.jvir.2013.10.018. PMID: 24365502. Exclusion Code: X12.

868. Kwon W, Howard BA, Herndon JE, et al. FDG uptake on positron emission tomography correlates with survival and time to recurrence in patients with stage I non-small-cell lung cancer. *J Thorac Oncol*. 2015 Jun;10(6):897-902. doi: 10.1097/jto.0000000000000534. PMID: 25811445. Exclusion Code: X11.

869. Lacasse Y, Martel S, Hebert A, et al. Accuracy of virtual bronchoscopy to detect endobronchial lesions. *Ann Thorac Surg*. 2004 May;77(5):1774-80. doi: 10.1016/j.athoracsur.2003.10.068. PMID: 15111185. Exclusion Code: X3.

870. Lachelt S, Alber M, Sohn M, et al. Intensity-modulated stereotactic radiotherapy for the treatment of medically inoperable patients with NSCLC stage I. *Oncol Rep*. 2012 Oct;28(4):1309-14. doi: 10.3892/or.2012.1953. PMID: 22895737. Exclusion Code: X10.

871. Lacroix V, Mosala Nezhad Z, Kahn D, et al. Pain, quality of life, and clinical outcomes after robotic lobectomy. *Thorac Cardiovasc Surg*. 2017 Aug;65(5):344-50. doi: 10.1055/s-0036-1587590. PMID: 27575276. Exclusion Code: X11.

872. Lai CY, Chang WS, Hsieh YH, et al. Association of tissue inhibitor of metalloproteinase-1 genotypes with lung cancer risk in Taiwan. *Anticancer Res*. 2016 Jan;36(1):155-60. PMID: 26722039. Exclusion Code: X3.

873. Lai Y, Du H, Wang X, et al. Status and perspectives of clinical modes in surgical patients with lung cancer: a retrospective study. *Medicine (Baltimore)*. 2016 Jan;95(2):e2429. doi: 10.1097/md.0000000000002429. PMID: 26765424. Exclusion Code: X11.

874. Lam VK, Miller M, Dowling L, et al. Community low-dose CT lung cancer screening: a prospective cohort study. *Lung*. 2015 Feb;193(1):135-9. doi: 10.1007/s00408-014-9671-9. PMID: 25503535. Exclusion Code: X7.

875. Lammers A, Mitin T, Moghanaki D, et al. Lung cancer specialists' opinions on treatment for stage I non-small cell lung cancer: a multidisciplinary survey. *Adv Radiat Oncol*. 2018 Apr-Jun;3(2):125-9. doi: 10.1016/j.adro.2018.01.001. PMID: 29904736. Exclusion Code: X8.

876. Lamprecht B, Porsch P, Wegleitner B, et al. Electromagnetic navigation bronchoscopy (ENB): Increasing diagnostic yield. *Respir Med*. 2012 May;106(5):710-5. doi: 10.1016/j.rmed.2012.02.002. PMID: 22391437. Exclusion Code: X3.

877. Landreneau JP, Schuchert MJ, Weyant R, et al. Anatomic segmentectomy and brachytherapy mesh implantation for clinical stage I non-small cell lung cancer (NSCLC). *Surgery*. 2014 Feb;155(2):340-6. doi: 10.1016/j.surg.2013.06.055. PMID: 24314884. Exclusion Code: X6.

878. Langer SG, Graner BD, Schueler BA, et al. Sensitivity of thoracic digital tomosynthesis (DTS) for the identification of lung nodules. *J Digit Imaging*. 2016 Feb;29(1):141-7. doi: 10.1007/s10278-015-9818-0. PMID: 26349914. Exclusion Code: X3.

879. Langsenlehner U, Hofmann G, Renner W, et al. Association of vascular endothelial growth factor--a gene polymorphisms and haplotypes with breast cancer metastases. *Acta Oncol*. 2015 Mar;54(3):368-76. doi: 10.3109/0284186x.2014.948056. PMID: 25152223. Exclusion Code: X3.

880. Lanni TB, Jr., Grills IS, Kestin LL, et al. Stereotactic radiotherapy reduces treatment cost while improving overall survival and local control over standard fractionated radiation therapy for medically inoperable non-small-cell lung cancer. *Am J Clin Oncol*. 2011 Oct;34(5):494-8. doi: 10.1097/COC.0b013e3181ec63ae. PMID: 20805737. Exclusion Code: X8.

881. Lao L, Hope AJ, Maganti M, et al. Incidental prophylactic nodal irradiation and patterns of nodal relapse in inoperable early stage NSCLC patients treated with SBRT: a case-matched analysis. *Int J Radiat Oncol Biol Phys*. 2014 Sep 1;90(1):209-15. doi: 10.1016/j.ijrobp.2014.05.006. PMID: 24997639. Exclusion Code: X10.

882. Larici AR, Amato M, Ordonez P, et al. Detection of noncalcified pulmonary nodules on low-dose MDCT: comparison of the sensitivity of two CAD systems by using a double reference standard. *Radiol Med*. 2012 Sep;117(6):953-67. doi: 10.1007/s11547-012-0795-9. PMID: 22327922. Exclusion Code: X10.

883. Larke FJ, Kruger RL, Cagnon CH, et al. Estimated radiation dose associated with low-dose chest CT of average-size participants in the National Lung Screening Trial. *AJR Am J Roentgenol*. 2011 Nov;197(5):1165-9. doi: 10.2214/ajr.11.6533. PMID: 22021510. Exclusion Code: X3.

884. Lasnon C, Hicks RJ, Beauregard JM, et al. Impact of point spread function reconstruction on thoracic lymph node staging with 18F-FDG PET/CT in non-small cell lung cancer. *Clin Nucl Med*. 2012 Oct;37(10):971-6. doi: 10.1097/RLU.0b013e318251e3d1. PMID: 22899197. Exclusion Code: X6.

885. Lau YK, Caverly TJ, Cherng ST, et al. Development and validation of a personalized, web-based decision aid for lung cancer screening using mixed methods: a study protocol. *JMIR Res Protoc*. 2014 Dec 19;3(4):e78. doi: 10.2196/resprot.4039. PMID: 25532218. Exclusion Code: X5.

886. Leader JK, Warfel TE, Fuhrman CR, et al. Pulmonary nodule detection with low-dose CT of the lung: agreement among radiologists. *AJR Am J Roentgenol*. 2005 Oct;185(4):973-8. doi: 10.2214/ajr.04.1225. PMID: 16177418. Exclusion Code: X11.

887. Lee C. Screening for Lung Cancer: Effective Recruitment Methods. *AJR Am J Roentgenol*. 2018 Mar;210(3):514-7. doi: 10.2214/ajr.17.18755. PMID: 29261350. Exclusion Code: X8.

888. Lee CT, Strauss DM, Stone LE, et al. Preoperative CHA2DS2-VASc Score Predicts Postoperative Atrial Fibrillation after Lobectomy. *Thorac Cardiovasc Surg*. 2019 Mar;67(2):125-30. doi: 10.1055/s-0038-1675638. PMID: 30485896. Exclusion Code: X3.

889. Lee DS, Kim YS, Yoo Ie R, et al. Long-term clinical experience of high-dose ablative lung radiotherapy: high pre-treatment [18F]fluorodeoxyglucose-positron emission tomography maximal standardized uptake value of the primary tumor adversely affects treatment outcome. *Lung Cancer*. 2013 May;80(2):172-8. doi: 10.1016/j.lungcan.2012.12.023. PMID: 23489556. Exclusion Code: X3.

890. Lee GD, Kim HC, Kim YE, et al. Value of cytologic analysis of bronchial washings in lung cancer on the basis of bronchoscopic appearance. *Clin Respir J*. 2013 Apr;7(2):128-34. doi: 10.1111/j.1752-699X.2012.00293.x. PMID: 22568634. Exclusion Code: X8.

891. Lee H, Jeong SH, Jeong BH, et al. Incidence of brain metastasis at the initial diagnosis of lung squamous cell carcinoma on the basis of stage, excluding brain metastasis. *J Thorac Oncol*. 2016 Mar;11(3):426-31. doi: 10.1016/j.jtho.2015.11.007. PMID: 26746367. Exclusion Code: X3.

892. Lee H, Jin GY, Han YM, et al. Comparison of survival rate in primary non-small-cell lung cancer among elderly patients treated with radiofrequency ablation, surgery, or chemotherapy. *Cardiovasc Intervent Radiol*. 2012 Apr;35(2):343-50. doi: 10.1007/s00270-011-0194-y. PMID: 21626257. Exclusion Code: X11.

893. Lee HJ, Kim YT, Park PJ, et al. A novel detection method of non-small cell lung cancer using multiplexed bead-based serum biomarker profiling. *J Thorac Cardiovasc Surg*. 2012 Feb;143(2):421-7. doi: 10.1016/j.jtcvs.2011.10.046. PMID: 22104668. Exclusion Code: X5.

894. Lee HN, Lee SM, Choe J, et al. Diagnostic performance of CT-guided percutaneous transthoracic core needle biopsy using low tube voltage (100 kVp): comparison with conventional tube voltage (120 kVp). *Acta Radiol*. 2018 Apr;59(4):425-33. doi: 10.1177/0284185117719589. PMID: 28691525. Exclusion Code: X3.

895. Lee HY, Lee HY, Lee KS, et al. Reliability of small biopsy or cytology for the diagnosis of pulmonary mucinous adenocarcinoma. *J Clin Pathol*. 2014 Jul;67(7):587-91. doi: 10.1136/jclinpath-2013-202107. PMID: 24739466. Exclusion Code: X3.

896. Lee J, Kim JI, Ye SJ, et al. Dosimetric effects of roll rotational setup errors on lung stereotactic ablative radiotherapy using volumetric modulated arc therapy. *Br J Radiol*. 2015;88(1055):20140862. doi: 10.1259/bjr.20140862. PMID: 26369834. Exclusion Code: X3.

897. Lee JH, Park CM, Kim H, et al. Persistent part-solid nodules with solid part of 5 mm or smaller: Can the 'follow-up and surgical resection after interval growth' policy have a negative effect on patient prognosis? *Eur Radiol*. 2017 Jan;27(1):195-202. doi: 10.1007/s00330-016-4364-9. PMID: 27126519. Exclusion Code: X3.

898. Lee JW, Kim EY, Kim DJ, et al. The diagnostic ability of (18)F-FDG PET/CT for mediastinal lymph node staging using (18)F-FDG uptake and volumetric CT histogram analysis in non-small cell lung cancer. *Eur Radiol*. 2016 Dec;26(12):4515-23. doi: 10.1007/s00330-016-4292-8. PMID: 26943133. Exclusion Code: X3.

899. Lee K, Kim HO, Choi HK, et al. Real-world treatment patterns for patients 80 years and older with early lung cancer: a nationwide claims study. *BMC Pulm Med*. 2018 Aug 3;18(1):127. doi: 10.1186/s12890-018-0699-0. PMID: 30075770. Exclusion Code: X3.

900. Lee K, Kim HR, Kim DK, et al. Post-recurrence survival analysis of stage I non-small-cell lung cancer. *Asian Cardiovasc Thorac Ann*. 2017 Nov;25(9):623-9. doi: 10.1177/0218492317737641. PMID: 29058973. Exclusion Code: X11.

901. Lee KC, Yong HS, Lee J, et al. Is the epicardial adipose tissue area on non-ECG gated low-dose chest CT useful for predicting coronary atherosclerosis in an asymptomatic population considered for lung cancer screening? *Eur Radiol*. 2019 Feb;29(2):932-40. doi: 10.1007/s00330-018-5562-4. PMID: 29955949. Exclusion Code: X8.

902. Lee KH, Lee KW, Park JH, et al. Nodule Classification on Low-Dose Unenhanced CT and Standard-Dose Enhanced CT: Inter-Protocol Agreement and Analysis of Interchangeability. *Korean J Radiol*. 2018 May-Jun;19(3):516-25. doi: 10.3348/kjr.2018.19.3.516. PMID: 29713230. Exclusion Code: X8.

903. Lee PC, Kamel M, Nasar A, et al. Lobectomy for non-small cell lung cancer by video-assisted thoracic surgery: effects of cumulative institutional experience on adequacy of lymphadenectomy. *Ann Thorac Surg*. 2016 Mar;101(3):1116-22. doi: 10.1016/j.athoracsur.2015.09.073. PMID: 26654728. Exclusion Code: X8.

904. Lee PC, Nasar A, Port JL, et al. Long-term survival after lobectomy for non-small cell lung cancer by video-assisted thoracic surgery versus thoracotomy. *Ann Thorac Surg*. 2013 Sep;96(3):951-60; discussion 60-1. doi: 10.1016/j.athoracsur.2013.04.104. PMID: 23866808. Exclusion Code: X11.

905. Lee S, Lee JG, Lee CY, et al. Pulmonary fissure development is a prognostic factor for patients with resected stage I lung adenocarcinoma. *J Surg Oncol*. 2016 Dec;114(7):848-52. doi: 10.1002/jso.24438. PMID: 27633283. Exclusion Code: X11.

906. Lee S, Stroian G, Kopek N, et al. Analytical modelling of regional radiotherapy dose response of lung. *Phys Med Biol*. 2012 Jun 7;57(11):3309-21. doi: 10.1088/0031-9155/57/11/3309. PMID: 22572393. Exclusion Code: X3.

907. Lee SH, Park MJ, Choi SI, et al. Reactive oxygen species modulator 1 (Romo1) as a novel diagnostic marker for lung cancer-related malignant effusion. *Medicine (Baltimore)*. 2017 Jan;96(4):e5975. doi: 10.1097/md.0000000000005975. PMID: 28121949. Exclusion Code: X3.

908. Lee SH, Sung C, Lee HS, et al. Is (18)F-FDG PET/CT useful for the differential diagnosis of solitary pulmonary nodules in patients with idiopathic pulmonary fibrosis? *Ann Nucl Med*. 2018 Aug;32(7):492-8. doi: 10.1007/s12149-018-1273-9. PMID: 29974372. Exclusion Code: X8.

909. Lee SM, Goo JM, Park CM, et al. Preoperative staging of non-small cell lung cancer: prospective comparison of PET/MR and PET/CT. *Eur Radiol*. 2016 Nov;26(11):3850-7. doi: 10.1007/s00330-016-4255-0. PMID: 26883332. Exclusion Code: X3.

910. Lee SM, Park CM, Paeng JC, et al. Accuracy and predictive features of FDG-PET/CT and CT for diagnosis of lymph node metastasis of T1 non-small-cell lung cancer manifesting as a subsolid nodule. *Eur Radiol*. 2012 Jul;22(7):1556-63. doi: 10.1007/s00330-012-2395-4. PMID: 22358427. Exclusion Code: X8.

911. Lee SM, Park CM, Song YS, et al. CT assessment-based direct surgical resection of part-solid nodules with solid component larger than 5 mm without preoperative biopsy: experience at a single tertiary hospital. *Eur Radiol*. 2017 Dec;27(12):5119-26. doi: 10.1007/s00330-017-4917-6. PMID: 28656460. Exclusion Code: X11.

912. Lee SU, Moon SH, Cho KH, et al. Ablative dose proton beam therapy for stage I and recurrent non-small cell lung carcinomas : Ablative dose PBT for NSCLC. *Strahlenther Onkol*. 2016 Sep;192(9):649-57. doi: 10.1007/s00066-016-0985-9. PMID: 27282279. Exclusion Code: X6.

913. Lee SY, Hong MJ, Jeon HS, et al. Functional intronic ERCC1 polymorphism from regulomeDB can predict survival in lung cancer after surgery. *Oncotarget*. 2015 Sep 15;6(27):24522-32. doi: 10.18632/oncotarget.4083. PMID: 26056042. Exclusion Code: X17.

914. Lee T, Park JY, Lee HY, et al. Lung cancer in patients with idiopathic pulmonary fibrosis: clinical characteristics and impact on survival. *Respir Med*. 2014 Oct;108(10):1549-55. doi: 10.1016/j.rmed.2014.07.020. PMID: 25175479. Exclusion Code: X6.

915. Lee YJ, Choi SM, Lee J, et al. Utility of the National Lung Screening Trial Criteria for Estimation of Lung Cancer in the Korean Population. *Cancer Res Treat*. 2018 Jul;50(3):950-5. doi: 10.4143/crt.2017.357. PMID: 29025257. Exclusion Code: X10.

916. Leeman JE, Rimner A, Montecalvo J, et al. Histologic subtype in core lung biopsies of early-stage lung adenocarcinoma is a prognostic factor for treatment response and failure patterns after stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2017 Jan 1;97(1):138-45. doi: 10.1016/j.ijrobp.2016.09.037. PMID: 27839909. Exclusion Code: X10.

917. Lemonnier I, Guillemin F, Arveux P, et al. Quality of life after the initial treatments of non-small cell lung cancer: a persistent predictor for patients' survival. *Health Qual Life Outcomes*. 2014 May 15;12:73. doi: 10.1186/1477-7525-12-73. PMID: 24884836. Exclusion Code: X3.

918. Leng S, Liu Y, Weissfeld JL, et al. 15q12 variants, sputum gene promoter hypermethylation, and lung cancer risk: a GWAS in smokers. *J Natl Cancer Inst*. 2015 Feb 23;107(5)doi: 10.1093/jnci/djv035. PMID: 25713168. Exclusion Code: X5.

919. Lenglet A, Campeau MP, Mathieu D, et al. Risk-adapted stereotactic ablative radiotherapy for central and ultra-central lung tumours. *Radiother Oncol*. 2019 May;134:178-84. doi: 10.1016/j.radonc.2019.01.035. PMID: 31005213. Exclusion Code: X3.

920. Leong P, Deshpande S, Irving LB, et al. Endoscopic ultrasound fine-needle aspiration by experienced pulmonologists: a cusum analysis. *Eur Respir J*. 2017 Nov;50(5)doi: 10.1183/13993003.01102-2017. PMID: 29097432. Exclusion Code: X3.

921. Leroy S, Benzaquen J, Mazzetta A, et al. Circulating tumour cells as a potential screening tool for lung cancer (the AIR study): protocol of a prospective multicentre cohort study in France. *BMJ Open*. 2017 Dec 26;7(12):e018884. doi: 10.1136/bmjopen-2017-018884. PMID: 29282271. Exclusion Code: X10.

922. Levine ME, Hosgood HD, Chen B, et al. DNA methylation age of blood predicts future onset of lung cancer in the women's health initiative. *Aging (Albany NY)*. 2015 Sep;7(9):690-700. doi: 10.18632/aging.100809. PMID: 26411804. Exclusion Code: X7.
923. Lewin G, Morissette K, Dickinson J, et al. Recommendations on screening for lung cancer. *CMAJ*. 2016 Apr 05;188(6):425-32. doi: 10.1503/cmaj.151421. PMID: 26952527. Exclusion Code: X10.
924. Li B, Chen K, Tian L, et al. Detection of pulmonary nodules in CT images based on fuzzy integrated active contour model and hybrid parametric mixture model. *Comput Math Methods Med*. 2013;2013:515386. doi: 10.1155/2013/515386. PMID: 23690876. Exclusion Code: X3.
925. Li C, Liu B, Meng H, et al. Efficacy and Radiation Exposure of Ultra-Low-Dose Chest CT at 100 kVp with Tin Filtration in CT-Guided Percutaneous Core Needle Biopsy for Small Pulmonary Lesions Using a Third-Generation Dual-Source CT Scanner. *J Vasc Interv Radiol*. 2019 Jan;30(1):95-102. doi: 10.1016/j.jvir.2018.06.013. PMID: 30149997. Exclusion Code: X11.
926. Li CC, Matthews AK, Rywant MM, et al. Racial disparities in eligibility for low-dose computed tomography lung cancer screening among older adults with a history of smoking. *Cancer Causes Control*. 2019 Mar;30(3):235-40. doi: 10.1007/s10552-018-1092-2. PMID: 30377905. Exclusion Code: X8.
927. Li D, Li F, Wu Y, et al. Quantification of serum MET in non-small-cell lung cancer and its clinical significance. *Clin Biochem*. 2015 Feb;48(3):110-4. doi: 10.1016/j.clinbiochem.2014.11.021. PMID: 25489726. Exclusion Code: X3.
928. Li D, Zhu G, Di H, et al. Associations between genetic variants located in mature microRNAs and risk of lung cancer. *Oncotarget*. 2016 Jul 5;7(27):41715-24. doi: 10.18632/oncotarget.9566. PMID: 27232940. Exclusion Code: X3.
929. Li F, Arimura H, Suzuki K, et al. Computer-aided detection of peripheral lung cancers missed at CT: ROC analyses without and with localization. *Radiology*. 2005 Nov;237(2):684-90. doi: 10.1148/radiol.2372041555. PMID: 16244277. Exclusion Code: X3.
930. Li F, Li Q, Engelmann R, et al. Improving radiologists' recommendations with computer-aided diagnosis for management of small nodules detected by CT. *Acad Radiol*. 2006 Aug;13(8):943-50. doi: 10.1016/j.acra.2006.04.010. PMID: 16843846. Exclusion Code: X3.
931. Li GC, Fu YF, Cao W, et al. Computed tomography-guided percutaneous cutting needle biopsy for small (</= 20 mm) lung nodules. *Medicine (Baltimore)*. 2017 Nov;96(46):e8703. doi: 10.1097/md.0000000000008703. PMID: 29145307. Exclusion Code: X3.
932. Li H, Wang R, Zhang D, et al. Lymph node metastasis outside of a tumor-bearing lobe in primary lung cancer and the status of interlobar fissures: The necessity for removing lymph nodes from an adjacent lobe. *Medicine (Baltimore)*. 2019 Mar;98(12):e14800. doi: 10.1097/md.0000000000014800. PMID: 30896623. Exclusion Code: X3.
933. Li K, Husing A, Sookthai D, et al. Selecting high-risk individuals for lung cancer screening: a prospective evaluation of existing risk models and eligibility criteria in the German EPIC Cohort. *Cancer Prev Res (Phila)*. 2015 Sep;8(9):777-85. doi: 10.1158/1940-6207.capr-14-0424. PMID: 26076698. Exclusion Code: X17.
934. Li M, Yang D, Brock G, et al. Breath carbonyl compounds as biomarkers of lung cancer. *Lung Cancer*. 2015 Oct;90(1):92-7. doi: 10.1016/j.lungcan.2015.07.005. PMID: 26233567. Exclusion Code: X4.
935. Li N, Xu M, Cai MY, et al. Elevated serum bilirubin levels are associated with improved survival in patients with curatively resected non-small-cell lung cancer. *Cancer Epidemiol*. 2015 Oct;39(5):763-8. doi: 10.1016/j.canep.2015.06.007. PMID: 26159684. Exclusion Code: X3.
936. Li Q, Balagurunathan Y, Liu Y, et al. Comparison Between Radiological Semantic Features and Lung-RADS in Predicting Malignancy of Screen-Detected Lung Nodules in the National Lung Screening Trial. *Clin Lung Cancer*. 2018 Mar;19(2):148-56.e3. doi: 10.1016/j.cllc.2017.10.002. PMID: 29137847. Exclusion Code: X11.

937. Li Q, Fan L, Cao ET, et al. Quantitative CT analysis of pulmonary pure ground-glass nodule predicts histological invasiveness. *Eur J Radiol*. 2017 Apr;89:67-71. doi: 10.1016/j.ejrad.2017.01.024. PMID: 28267551. Exclusion Code: X3.
938. Li Q, Kim J, Balagurunathan Y, et al. CT imaging features associated with recurrence in non-small cell lung cancer patients after stereotactic body radiotherapy. *Radiat Oncol*. 2017 Sep 25;12(1):158. doi: 10.1186/s13014-017-0892-y. PMID: 28946909. Exclusion Code: X10.
939. Li R, Zhang Y, Yuan Y, et al. Dosimetric comparison of CT-guided iodine-125 seed stereotactic brachytherapy and stereotactic body radiation therapy in the treatment of NSCLC. *PLoS One*. 2017;12(11):e0187390. doi: 10.1371/journal.pone.0187390. PMID: 29121047. Exclusion Code: X3.
940. Li S, Chai H, Huang J, et al. Hybrid video-assisted thoracic surgery with segmental-main bronchial sleeve resection for non-small cell lung cancer. *Surg Innov*. 2014 Apr;21(2):180-6. doi: 10.1177/1553350613492026. PMID: 23793576. Exclusion Code: X3.
941. Li S, Wang Z, Huang J, et al. Systematic review of prognostic roles of body mass index for patients undergoing lung cancer surgery: does the 'obesity paradox' really exist? *Eur J Cardiothorac Surg*. 2017 May 1;51(5):817-28. doi: 10.1093/ejcts/ezw386. PMID: 28040677. Exclusion Code: X9.
942. Li S, Yang N, Li B, et al. A pilot study using kernelled support tensor machine for distant failure prediction in lung SBRT. *Med Image Anal*. 2018 Dec;50:106-16. doi: 10.1016/j.media.2018.09.004. PMID: 30266009. Exclusion Code: X6.
943. Li S, Zhao B, Wang X, et al. Overestimated value of (18)F-FDG PET/CT to diagnose pulmonary nodules: analysis of 298 patients. *Clin Radiol*. 2014 Aug;69(8):e352-7. doi: 10.1016/j.crad.2014.04.007. PMID: 24877581. Exclusion Code: X3.
944. Li S, Zheng Q, Ma Y, et al. Implications of false negative and false positive diagnosis in lymph node staging of NSCLC by means of (1)(8)F-FDG PET/CT. *PLoS One*. 2013;8(10):e78552. doi: 10.1371/journal.pone.0078552. PMID: 24205256. Exclusion Code: X3.
945. Li S, Zhou K, Du H, et al. Body surface area is a novel predictor for surgical complications following video-assisted thoracoscopic surgery for lung adenocarcinoma: a retrospective cohort study. *BMC Surg*. 2017 Jun 12;17(1):69. doi: 10.1186/s12893-017-0264-4. PMID: 28606134. Exclusion Code: X3.
946. Li S, Zhou K, Wang M, et al. Degree of pulmonary fissure completeness can predict postoperative cardiopulmonary complications and length of hospital stay in patients undergoing video-assisted thoracoscopic lobectomy for early-stage lung cancer. *Interact Cardiovasc Thorac Surg*. 2018 Jan 1;26(1):25-33. doi: 10.1093/icvts/ivx261. PMID: 29049746. Exclusion Code: X3.
947. Li X, Asmitananda T, Gao L, et al. Biomarkers in the lung cancer diagnosis: a clinical perspective. *Neoplasma*. 2012;59(5):500-7. doi: 10.4149/neo_2012_064. PMID: 22668014. Exclusion Code: X5.
948. Li X, Qin S, Sun X, et al. Prognostic Significance of Albumin-Globulin Score in Patients with Operable Non-Small-Cell Lung Cancer. *Ann Surg Oncol*. 2018 Nov;25(12):3647-59. doi: 10.1245/s10434-018-6715-z. PMID: 30229416. Exclusion Code: X3.
949. Li X, Zhou C, Hu W. Association between serum angiotensin-converting enzyme 2 level with postoperative morbidity and mortality after major pulmonary resection in non-small cell lung cancer patients. *Heart Lung Circ*. 2014 Jul;23(7):661-6. doi: 10.1016/j.hlc.2013.12.013. PMID: 24636159. Exclusion Code: X3.
950. Li XC, Wang W, Liu JQ, et al. Different limited resection of pulmonary lobe methods under the thoracoscopy in the treatment of early nonsmall cell lung cancer occurred in the old age. *Indian J Cancer*. 2015 Feb;51 Suppl 2:e29-32. doi: 10.4103/0019-509x.151995. PMID: 25712838. Exclusion Code: X3.
951. Li XJ, Wu QF, He DL, et al. Proteomic profiling of serum from stage I lung squamous cell carcinoma patients. *Asian Pac J Cancer Prev*. 2013;14(4):2273-6. PMID: 23725126. Exclusion Code: X3.

952. Li XQ, Zhang Y, Huang DB, et al. Value of C-arm computed tomography in radiofrequency ablation of small lung lesions. *Genet Mol Res*. 2014 Aug 7;13(3):6027-36. doi: 10.4238/2014.August.7.17. PMID: 25117360. Exclusion Code: X6.

953. Li Y, Dykstra M, Best TD, et al. Differential inflammatory response dynamics in normal lung following stereotactic body radiation therapy with protons versus photons. *Radiother Oncol*. 2019 Apr 20;136:169-75. doi: 10.1016/j.radonc.2019.04.004. PMID: 31015121. Exclusion Code: X8.

954. Li Z, Ye B, Bao M, et al. Radiologic predictors for clinical stage IA lung adenocarcinoma with ground glass components: a multi-center study of long-term outcomes. *PLoS One*. 2015;10(9):e0136616. doi: 10.1371/journal.pone.0136616. PMID: 26339917. Exclusion Code: X11.

955. Liang M, Tang W, Xu DM, et al. Low-dose CT screening for lung cancer: computer-aided detection of missed lung cancers. *Radiology*. 2016 Oct;281(1):279-88. doi: 10.1148/radiol.2016150063. PMID: 27019363. Exclusion Code: X10.

956. Liao C, Chen J, Liang J, et al. Meta-analysis study of lymph node staging by 18 F-FDG PET/CT scan in non-small cell lung cancer: comparison of TB and non-TB endemic regions (Provisional abstract). *Eur J Radiol*. 2012;81(11):3518-23. PMID: DARE-12012047008. Exclusion Code: X3.

957. Lievens Y, Obyn C, Mertens AS, et al. Stereotactic body radiotherapy for lung cancer: how much does it really cost? *J Thorac Oncol*. 2015 Mar;10(3):454-61. doi: 10.1097/jto.0000000000000421. PMID: 25376514. Exclusion Code: X8.

958. Ligor T, Pater L, Buszewski B. Application of an artificial neural network model for selection of potential lung cancer biomarkers. *J Breath Res*. 2015 May 6;9(2):027106. doi: 10.1088/1752-7155/9/2/027106. PMID: 25944812. Exclusion Code: X5.

959. Lin CC, Smeltzer MP, Jemal A, et al. Risk-adjusted margin positivity rate as a surgical quality metric for non-small cell lung cancer. *Ann Thorac Surg*. 2017 Oct;104(4):1161-70. doi: 10.1016/j.athoracsur.2017.04.033. PMID: 28709665. Exclusion Code: X8.

960. Lin KF, Wu HF, Huang WC, et al. Propensity score analysis of lung cancer risk in a population with high prevalence of non-smoking related lung cancer. *BMC Pulm Med*. 2017 Sep 6;17(1):120. doi: 10.1186/s12890-017-0465-8. PMID: 28874145. Exclusion Code: X10.

961. Lin KH, Lee RC, Liu RS, et al. The prognostic value of tumor shadow disappearance rate on integrated PET/CT evaluation of solitary pulmonary nodules with low glucose metabolism. *Nucl Med Commun*. 2016 Apr;37(4):356-62. doi: 10.1097/mnm.0000000000000446. PMID: 26796032. Exclusion Code: X8.

962. Lin L, Hu D, Zhong C, et al. Safety and efficacy of thoracoscopic wedge resection for elderly high-risk patients with stage I peripheral non-small-cell lung cancer. *J Cardiothorac Surg*. 2013 Dec 21;8:231. doi: 10.1186/1749-8090-8-231. PMID: 24359930. Exclusion Code: X3.

963. Lin Y, Lin WY, Kao CH, et al. Prognostic value of preoperative metabolic tumor volumes on PET-CT in predicting disease-free survival of patients with stage I non-small cell lung cancer. *Anticancer Res*. 2012 Nov;32(11):5087-91. PMID: 23155285. Exclusion Code: X11.

964. Linden PA, D'Amico TA, Perry Y, et al. Quantifying the safety benefits of wedge resection: a society of thoracic surgery database propensity-matched analysis. *Ann Thorac Surg*. 2014 Nov;98(5):1705-11; discussion 11-2. doi: 10.1016/j.athoracsur.2014.06.017. PMID: 25201723. Exclusion Code: X3.

965. Little MW, Chung D, Boardman P, et al. Microwave ablation of pulmonary malignancies using a novel high-energy antenna system. *Cardiovasc Intervent Radiol*. 2013 Apr;36(2):460-5. doi: 10.1007/s00270-012-0465-2. PMID: 22968596. Exclusion Code: X6.

966. Liu B, Tang Y, Yi M, et al. Genetic variants in the plasminogen activator inhibitor-1 gene are associated with an increased risk of radiation pneumonitis in lung cancer patients. *Cancer Med*. 2017 Mar;6(3):681-8. doi: 10.1002/cam4.1011. PMID: 28211612. Exclusion Code: X6.

967. Liu BJ, Dong JC, Xu CQ, et al. Accuracy of 18F-FDG PET/CT for lymph node staging in non-small-cell lung cancers. *Chin Med J (Engl)*. 2009 Aug 5;122(15):1749-54. PMID: 19781319. Exclusion Code: X3.

968. Liu H, Sintay B, Pearman K, et al. A hybrid planning strategy for stereotactic body radiation therapy of early stage non-small-cell lung cancer. *J Appl Clin Med Phys*. 2018 Nov;19(6):117-23. doi: 10.1002/acm2.12450. PMID: 30281198. Exclusion Code: X8.
969. Liu H, Ye J, Kim JJ, et al. Dosimetric comparison of two arc-based stereotactic body radiotherapy techniques for early-stage lung cancer. *Med Dosim*. 2015 Spring;40(1):76-81. doi: 10.1016/j.meddos.2014.10.004. PMID: 25499078. Exclusion Code: X10.
970. Liu HC, Huang WC, Wu CL, et al. Surgery for elderly lung cancer. *Ann Thorac Cardiovasc Surg*. 2013;19(6):416-22. PMID: 23445805. Exclusion Code: X11.
971. Liu J, Mazzone PJ, Cata JP, et al. Serum free fatty acid biomarkers of lung cancer. *Chest*. 2014 Sep;146(3):670-9. doi: 10.1378/chest.13-2568. PMID: 24743744. Exclusion Code: X3.
972. Liu L, Zhang LJ, Chen B, et al. Novel CT-guided coil localization of peripheral pulmonary nodules prior to video-assisted thoracoscopic surgery: a pilot study. *Acta Radiol*. 2014 Jul;55(6):699-706. doi: 10.1177/0284185113506136. PMID: 24078457. Exclusion Code: X3.
973. Liu M, Huang J, Xu Y, et al. MR-guided percutaneous biopsy of solitary pulmonary lesions using a 1.0-T open high-field MRI scanner with respiratory gating. *Eur Radiol*. 2017 Apr;27(4):1459-66. doi: 10.1007/s00330-016-4518-9. PMID: 27516355. Exclusion Code: X3.
974. Liu M, Wampfler JA, Dai J, et al. Chest wall resection for non-small cell lung cancer: a case-matched study of postoperative pulmonary function and quality of life. *Lung Cancer*. 2017 Apr;106:37-41. doi: 10.1016/j.lungcan.2017.01.014. PMID: 28285692. Exclusion Code: X3.
975. Liu S, Li C, Yu X, et al. Diagnostic accuracy of MRI-guided percutaneous transthoracic needle biopsy of solitary pulmonary nodules. *Cardiovasc Intervent Radiol*. 2015 Apr;38(2):416-21. doi: 10.1007/s00270-014-0915-0. PMID: 24873920. Exclusion Code: X3.
976. Liu S, Ren R, Liu M, et al. MR imaging-guided percutaneous cryotherapy for lung tumors: initial experience. *J Vasc Interv Radiol*. 2014 Sep;25(9):1456-62. doi: 10.1016/j.jvir.2014.04.025. PMID: 24985720. Exclusion Code: X6.
977. Liu Y, Tang Y, Xue Z, et al. Ratio of lymph node to primary tumor SUVmax multiplied by maximal tumor diameter on positron emission tomography/integrated computed tomography may be a predictor of mediastinal lymph node malignancy in lung cancer. *Medicine (Baltimore)*. 2016 Nov;95(46):e5457. doi: 10.1097/md.0000000000005457. PMID: 27861398. Exclusion Code: X3.
978. Liu Y, Wang H, Li Q, et al. Radiologic features of small pulmonary nodules and lung cancer risk in the national lung screening trial: a nested case-control study. *Radiology*. 2018 Jan;286(1):298-306. doi: 10.1148/radiol.2017161458. PMID: 28837413. Exclusion Code: X11.
979. Lococo F, Cesario A, Attili F, et al. Transoesophageal endoscopic ultrasound-guided fine-needle aspiration of pleural effusion for the staging of non-small cell lung cancer. *Interact Cardiovasc Thorac Surg*. 2013 Aug;17(2):237-41. doi: 10.1093/icvts/ivt166. PMID: 23615434. Exclusion Code: X11.
980. Lococo F, Galeone C, Formisano D, et al. 18F-fluorodeoxyglucose positron emission tomographic scan in solid-type p-stage-I pulmonary adenocarcinomas: what can produce false-negative results? *Eur J Cardiothorac Surg*. 2017 Apr 1;51(4):667-73. doi: 10.1093/ejcts/ezw394. PMID: 28043987. Exclusion Code: X3.
981. Loh SE, Wu DD, Venkatesh SK, et al. CT-guided thoracic biopsy: evaluating diagnostic yield and complications. *Ann Acad Med Singapore*. 2013 Jun;42(6):285-90. PMID: 23842769. Exclusion Code: X3.
982. Loo FL, Halligan AM, Port JL, et al. The emerging technique of electromagnetic navigation bronchoscopy-guided fine-needle aspiration of peripheral lung lesions: promising results in 50 lesions. *Cancer Cytopathol*. 2014 Mar;122(3):191-9. doi: 10.1002/cncy.21373. PMID: 24323803. Exclusion Code: X3.

983. Lopatin S, Tsay JC, Addrizzo-Harris D, et al. Reduced lung function in smokers in a lung cancer screening cohort with asbestos exposure and pleural plaques. *Am J Ind Med*. 2016 Mar;59(3):178-85. doi: 10.1002/ajim.22571. PMID: 26815630. Exclusion Code: X8.
984. Lopez Hanninen E, Vogl TJ, Ricke J, et al. CT-guided percutaneous core biopsies of pulmonary lesions. Diagnostic accuracy, complications and therapeutic impact. *Acta Radiol*. 2001 Mar;42(2):151-5. PMID: 11259941. Exclusion Code: X3.
985. Lopez-Padilla D, Peghini Gavilanes E, Revilla Ostolaza TY, et al. Arterial stump thrombosis after lung resection surgery: clinical presentation, treatment and progress. *Arch Bronconeumol*. 2016 Oct;52(10):512-8. doi: 10.1016/j.arbres.2016.02.009. PMID: 27156986. Exclusion Code: X3.
986. Lorenz J. Not available. *Zentralbl Chir*. 2016;141(1):11-2. PMID: CN-01263663. Exclusion Code: X1.
987. Lou F, Huang J, Sima CS, et al. Patterns of recurrence and second primary lung cancer in early-stage lung cancer survivors followed with routine computed tomography surveillance. *J Thorac Cardiovasc Surg*. 2013 Jan;145(1):75-81; discussion -2. doi: 10.1016/j.jtcvs.2012.09.030. PMID: 23127371. Exclusion Code: X3.
988. Louie A, Chen H, Werkhoven EV, et al. Caro elekta quality of life following stereotactic ablative radiotherapy for early stage lung cancer: results from the rosel randomized controlled trial and a systematic review. *Radiother Oncol*. 2016;120:S57-S8. PMID: CN-01252401. Exclusion Code: X2.
989. Louie A, Werkhoven E, Chen H, et al. Patient reported outcomes following stereotactic ablative radiotherapy or surgery for stage IA non-small-cell lung cancer: results from the ROSEL multicenter randomized trial. *Radiother Oncol*. 2015;117(1):44-8. doi: 10.1016/j.radonc.2015.08.011. PMID: CN-01105560. Exclusion Code: X8.
990. Louie AV, Senan S, Dahele M, et al. Stereotactic ablative radiation therapy for subcentimeter lung tumors: clinical, dosimetric, and image guidance considerations. *Int J Radiat Oncol Biol Phys*. 2014 Nov 15;90(4):843-9. doi: 10.1016/j.ijrobp.2014.06.064. PMID: 25585783. Exclusion Code: X3.
991. Louie BE, Farivar AS, Aye RW, et al. Early experience with robotic lung resection results in similar operative outcomes and morbidity when compared with matched video-assisted thoracoscopic surgery cases. *Ann Thorac Surg*. 2012 May;93(5):1598-604; discussion 604-5. doi: 10.1016/j.athoracsur.2012.01.067. PMID: 22440364. Exclusion Code: X3.
992. Louis E, Adriaensens P, Guedens W, et al. Detection of lung cancer through metabolic changes measured in blood plasma. *J Thorac Oncol*. 2016 Apr;11(4):516-23. doi: 10.1016/j.jtho.2016.01.011. PMID: 26949046. Exclusion Code: X5.
993. Lovinfosse P, Janvary ZL, Coucke P, et al. FDG PET/CT texture analysis for predicting the outcome of lung cancer treated by stereotactic body radiation therapy. *Eur J Nucl Med Mol Imaging*. 2016 Jul;43(8):1453-60. doi: 10.1007/s00259-016-3314-8. PMID: 26830299. Exclusion Code: X13.
994. Lu MS, Chen MF, Lin CC, et al. Is chronic kidney disease an adverse factor in lung cancer clinical outcome? A propensity score matching study. *Thorac Cancer*. 2017 Mar;8(2):106-13. doi: 10.1111/1759-7714.12414. PMID: 28207203. Exclusion Code: X11.
995. Lu Q, Cao W, Huang L, et al. CT-guided percutaneous microwave ablation of pulmonary malignancies: Results in 69 cases. *World J Surg Oncol*. 2012 May 7;10:80. doi: 10.1186/1477-7819-10-80. PMID: 22564777. Exclusion Code: X6.
996. Lucas JT, Jr., Kuremsky JG, Soike M, et al. Comparison of accelerated hypofractionation and stereotactic body radiotherapy for Stage 1 and node negative Stage 2 non-small cell lung cancer (NSCLC). *Lung Cancer*. 2014 Jul;85(1):59-65. doi: 10.1016/j.lungcan.2014.04.003. PMID: 24813936. Exclusion Code: X10.
997. Lucchiari C, Masiero M, Veronesi G, et al. Benefits of E-Cigarettes Among Heavy Smokers Undergoing a Lung Cancer Screening Program: randomized Controlled Trial Protocol. *JMIR res protoc*. 2016;5(1):e21. doi: 10.2196/resprot.4805. PMID: CN-01616880. Exclusion Code: X6.

998. Luchtenborg M, Jakobsen E, Krasnik M, et al. The effect of comorbidity on stage-specific survival in resected non-small cell lung cancer patients. *Eur J Cancer*. 2012 Dec;48(18):3386-95. doi: 10.1016/j.ejca.2012.06.012. PMID: 22795582. Exclusion Code: X3.

999. Luciano G, Stella F, Dell'Amore A, et al. Tracheo-bronchoplastic procedures for NSCLC: single-centre experience. *Heart Lung Circ*. 2015 Oct;24(10):1027-32. doi: 10.1016/j.hlc.2015.04.065. PMID: 25991393. Exclusion Code: X3.

1000. Lugg ST, Agostini PJ, Tikka T, et al. Long-term impact of developing a postoperative pulmonary complication after lung surgery. *Thorax*. 2016 Feb;71(2):171-6. doi: 10.1136/thoraxjnl-2015-207697. PMID: 26769017. Exclusion Code: X3.

1001. Lugg ST, Tikka T, Agostini PJ, et al. Smoking and timing of cessation on postoperative pulmonary complications after curative-intent lung cancer surgery. *J Cardiothorac Surg*. 2017 Jun 19;12(1):52. doi: 10.1186/s13019-017-0614-4. PMID: 28629433. Exclusion Code: X3.

1002. Luo J, Huang Q, Wang R, et al. Prognostic and predictive value of the novel classification of lung adenocarcinoma in patients with stage IB. *J Cancer Res Clin Oncol*. 2016 Sep;142(9):2031-40. doi: 10.1007/s00432-016-2192-6. PMID: 27379889. Exclusion Code: X10.

1003. Luo QQ, Lin H, Tan Q, et al. Analysis of clinical application of thoracoscopic lobectomy for lung cancer. *World J Surg Oncol*. 2014 May 21;12:157. doi: 10.1186/1477-7819-12-157. PMID: 24886331. Exclusion Code: X3.

1004. Luzzi L, Marulli G, A DEP, et al. Prognostic factors and clinical outcome in patients with surgically resected peripheral N0 adenocarcinoma <3 cm. *Minerva Chir*. 2016 Feb;71(1):1-7. PMID: 26149520. Exclusion Code: X11.

1005. Lyne C, Zaw S, King B, et al. Low rates of eligibility for lung cancer screening in patients undergoing computed tomography coronary angiography. *Intern Med J*. 2018 Oct;48(10):1265-8. doi: 10.1111/imj.14061. PMID: 30288901. Exclusion Code: X5.

1006. MA IJ, Shoni M, Siegert C, et al. Survival After Stereotactic Body Radiation Therapy for Clinically Diagnosed or Biopsy-Proven Early-Stage NSCLC: A Systematic Review and Meta-Analysis. *J Thorac Oncol*. 2019 Apr;14(4):583-95. doi: 10.1016/j.jtho.2018.12.035. PMID: 30721798. Exclusion Code: X9.

1007. Ma KF, Chu XY, Liu Y. Clinical significance of lymphatic vessel invasion in stage I non-small cell lung cancer patients. *Genet Mol Res*. 2015 Mar 13;14(1):1819-27. doi: 10.4238/2015.March.13.10. PMID: 25867327. Exclusion Code: X11.

1008. Ma S, Wang W, Xia B, et al. Multiplexed serum biomarkers for the detection of lung cancer. *EBioMedicine*. 2016 Sep;11:210-8. doi: 10.1016/j.ebiom.2016.08.018. PMID: 27575387. Exclusion Code: X5.

1009. Ma SJ, Cummings M, Serra LM, et al. Three- versus five-fraction regimens of stereotactic body radiotherapy for peripheral early-stage non-small-cell lung cancer: a two-institution propensity score-matched analysis. *Clin Lung Cancer*. 2018 May;19(3):e297-e302. doi: 10.1016/j.cllc.2017.11.007. PMID: 29254649. Exclusion Code: X10.

1010. Macdonald IK, Murray A, Healey GF, et al. Application of a high throughput method of biomarker discovery to improvement of the EarlyCDT((R))-Lung Test. *PLoS One*. 2012;7(12):e51002. doi: 10.1371/journal.pone.0051002. PMID: 23272083. Exclusion Code: X5.

1011. Macke RA, Schuchert MJ, Odell DD, et al. Parenchymal preserving anatomic resections result in less pulmonary function loss in patients with Stage I non-small cell lung cancer. *J Cardiothorac Surg*. 2015 Apr 1;10:49. doi: 10.1186/s13019-015-0253-6. PMID: 25888465. Exclusion Code: X11.

1012. Maclay JD, Farley JM, McCowan C, et al. Obtaining tissue diagnosis in lung cancer patients with poor performance status and its influence on treatment and survival. *Respir Med*. 2017 Mar;124:30-5. doi: 10.1016/j.rmed.2017.01.002. PMID: 28284318. Exclusion Code: X3.

1013. Macpherson R, Benamore R, Panakis N, et al. A proposed new imaging pathway for patients with suspected lung cancer. *Clin Radiol*. 2012 Jun;67(6):564-73. doi: 10.1016/j.crad.2011.10.032. PMID: 22300820. Exclusion Code: X5.

1014. Macpherson RE, Higgins GS, Murchison JT, et al. Non-small-cell lung cancer dimensions: CT-pathological correlation and interobserver variation. *Br J Radiol*. 2009 May;82(977):421-5. doi: 10.1259/bjr/28687035. PMID: 19153186. Exclusion Code: X3.

1015. MacRedmond R, McVey G, Lee M, et al. Screening for lung cancer using low dose CT scanning: results of 2 year follow up. *Thorax*. 2006 Jan;61(1):54-6. doi: 10.1136/thx.2004.037580. PMID: 16396954. Exclusion Code: X11.

1016. Maebayashi T, Ishibashi N, Aizawa T, et al. Significance of stereotactic body radiotherapy in older patients with early stage non-small cell lung cancer. *J Geriatr Oncol*. 2018 Mar 21doi: 10.1016/j.jgo.2018.03.005. PMID: 29573969. Exclusion Code: X10.

1017. Maeda H, Kanzaki M, Sakamoto K, et al. Effect of collagen vascular disease-associated interstitial lung disease on the outcomes of lung cancer surgery. *Surg Today*. 2017 Sep;47(9):1072-9. doi: 10.1007/s00595-017-1476-z. PMID: 28247107. Exclusion Code: X3.

1018. Mahieu J, Rinieri P, Bubenheim M, et al. Robot-assisted thoracoscopic surgery versus video-assisted thoracoscopic surgery for lung lobectomy: can a robotic approach improve short-term outcomes and operative safety? *Thorac Cardiovasc Surg*. 2016 Jun;64(4):354-62. doi: 10.1055/s-0035-1548733. PMID: 25866978. Exclusion Code: X3.

1019. Mahmood S, Bilal H, Faivre-Finn C, et al. Is stereotactic ablative radiotherapy equivalent to sublobar resection in high-risk surgical patients with stage I non-small-cell lung cancer? *Interact Cardiovasc Thorac Surg*. 2013 Nov;17(5):845-53. doi: 10.1093/icvts/ivt262. PMID: 23900381. Exclusion Code: X9.

1020. Maisonneuve P, Bagnardi V, Bellomi M, et al. Lung cancer risk prediction to select smokers for screening CT--a model based on the Italian COSMOS trial. *Cancer Prev Res (Phila)*. 2011 Nov;4(11):1778-89. doi: 10.1158/1940-6207.CAPR-11-0026. PMID: 21813406. Exclusion Code: X7.

1021. Mak RH, Hermann G, Lewis JH, et al. Outcomes by tumor histology and KRAS mutation status after lung stereotactic body radiation therapy for early-stage non-small-cell lung cancer. *Clin Lung Cancer*. 2015 Jan;16(1):24-32. doi: 10.1016/j.cllc.2014.09.005. PMID: 25450872. Exclusion Code: X13.

1022. Maki Y, Toyooka S, Soh J, et al. Early postoperative complications after middle lobe-preserving surgery for secondary lung cancer. *Surg Today*. 2017 May;47(5):601-5. doi: 10.1007/s00595-016-1413-6. PMID: 27629155. Exclusion Code: X10.

1023. Makinson A, Eymard-Duvernay S, Raffi F, et al. Feasibility and efficacy of early lung cancer diagnosis with chest computed tomography in HIV-infected smokers. *AIDS*. 2016 Feb 20;30(4):573-82. doi: 10.1097/qad.0000000000000943. PMID: 26829006. Exclusion Code: X3.

1024. Maldonado F, Boland JM, Raghunath S, et al. Noninvasive characterization of the histopathologic features of pulmonary nodules of the lung adenocarcinoma spectrum using computer-aided nodule assessment and risk yield (CANARY)--a pilot study. *J Thorac Oncol*. 2013 Apr;8(4):452-60. doi: 10.1097/JTO.0b013e3182843721. PMID: 23486265. Exclusion Code: X10.

1025. Maldonado F, Duan F, Raghunath SM, et al. Noninvasive computed tomography-based risk stratification of lung adenocarcinomas in the National Lung Screening Trial. *Am J Respir Crit Care Med*. 2015 Sep 15;192(6):737-44. doi: 10.1164/rccm.201503-0443OC. PMID: 26052977. Exclusion Code: X3.

1026. Malhotra J, Mhango G, Gomez JE, et al. Adjuvant chemotherapy for elderly patients with stage I non-small-cell lung cancer >/=4 cm in size: an SEER-Medicare analysis. *Ann Oncol*. 2015 Apr;26(4):768-73. doi: 10.1093/annonc/mdv008. PMID: 25600562. Exclusion Code: X6.

1027. Mallorie A, Goldring J, Patel A, et al. Assessment of nodal involvement in non-small-cell lung cancer with 18F-FDG-PET/CT: mediastinal blood pool cut-off has the highest sensitivity and tumour SUVmax/2 has the highest specificity. *Nucl Med Commun*. 2017 Aug;38(8):715-9. doi: 10.1097/mnm.0000000000000703. PMID: 28658052. Exclusion Code: X5.

1028. Mammarappallil JG, Hiatt KD, Ge Q, et al. Computed tomography fluoroscopy versus conventional computed tomography guidance for biopsy of intrathoracic lesions: a retrospective review of 1143 consecutive procedures. *J Thorac Imaging*. 2014 Nov;29(6):340-3. doi: 10.1097/rti.0000000000000109. PMID: 25286292. Exclusion Code: X3.

1029. Mampuya WA, Matsuo Y, Ueki N, et al. The impact of abdominal compression on outcome in patients treated with stereotactic body radiotherapy for primary lung cancer. *J Radiat Res*. 2014 Sep;55(5):934-9. doi: 10.1093/jrr/rru028. PMID: 24801474. Exclusion Code: X10.

1030. Mancini BR, Park HS, Harder EM, et al. Elderly patients undergoing SBRT for inoperable early-stage NSCLC achieve similar outcomes to younger patients. *Lung Cancer*. 2016 Jul;97:22-7. doi: 10.1016/j.lungcan.2016.04.011. PMID: 27237023. Exclusion Code: X3.

1031. Mangona VS, Aneese AM, Marina O, et al. Toxicity after central versus peripheral lung stereotactic body radiation therapy: a propensity score matched-pair analysis. *Int J Radiat Oncol Biol Phys*. 2015 Jan 1;91(1):124-32. doi: 10.1016/j.ijrobp.2014.08.345. PMID: 25442337. Exclusion Code: X3.

1032. Manners D, Hui J, Hunter M, et al. Estimating eligibility for lung cancer screening in an Australian cohort, including the effect of spirometry. *Med J Aust*. 2016 Jun 20;204(11):406. PMID: 27318396. Exclusion Code: X8.

1033. Manyam B, Videtic GM, Reddy CA, et al. Single fraction SBRT for stage i non-small cell lung cancer: treatment outcomes and effect of tumor location on chest wall toxicity. *International journal of radiation oncology biology physics*. 2017;99(2):E478-. doi: 10.1016/j.ijrobp.2017.06.1747. PMID: CN-01422977. Exclusion Code: X2.

1034. Marchiano AV, Cosentino M, Di Tolla G, et al. FNA and CNB in the diagnosis of pulmonary lesions: a single-center experience on 665 patients, comparison between two periods. *Tumori*. 2017 Jul 31;103(4):360-6. doi: 10.5301/tj.5000633. PMID: 28478642. Exclusion Code: X3.

1035. Marcus MW, Chen Y, Raji OY, et al. LLPi: Liverpool Lung Project Risk Prediction Model for Lung Cancer Incidence. *Cancer Prev Res (Phila)*. 2015 Jun;8(6):570-5. doi: 10.1158/1940-6207.capr-14-0438. PMID: 25873368. Exclusion Code: X7.

1036. Marcus MW, Raji OY, Chen Y, et al. Factors associated with dropout in a lung cancer highrisk cohort--the Liverpool lung project. *Int J Oncol*. 2014 Jun;44(6):2146-52. doi: 10.3892/ijo.2014.2371. PMID: 24714788. Exclusion Code: X8.

1037. Marcus MW, Raji OY, Duffy SW, et al. Incorporating epistasis interaction of genetic susceptibility single nucleotide polymorphisms in a lung cancer risk prediction model. *Int J Oncol*. 2016 Jul;49(1):361-70. doi: 10.3892/ijo.2016.3499. PMID: 27121382. Exclusion Code: X7.

1038. Marino KA, Sullivan JL, Weksler B. Electromagnetic navigation bronchoscopy for identifying lung nodules for thoracoscopic resection. *Ann Thorac Surg*. 2016 Aug;102(2):454-7. doi: 10.1016/j.athoracsur.2016.03.010. PMID: 27173068. Exclusion Code: X3.

1039. Markowitz SB, Manowitz A, Miller JA, et al. Yield of low-dose computerized tomography screening for lung cancer in high-risk workers: The Case of 7189 US Nuclear Weapons Workers. *Am J Public Health*. 2018 Oct;108(10):1296-302. doi: 10.2105/AJPH.2018.304518. PMID: 30138066. Exclusion Code: X7.

1040. Marshall HM, Courtney DA, Passmore LH, et al. Brief tailored smoking cessation counseling in a lung cancer screening population is feasible: a pilot randomized controlled trial. *Nicotine Tob Res*. 2016 Jul;18(7):1665-9. doi: 10.1093/ntr/ntw010. PMID: 26834052. Exclusion Code: X5.

1041. Marty-Ane CH, Canaud L, Solovei L, et al. Video-assisted thoracoscopic lobectomy: an unavoidable trend? A retrospective single-institution series of 410 cases. *Interact Cardiovasc Thorac Surg*. 2013 Jul;17(1):36-43. doi: 10.1093/icvts/ivt146. PMID: 23592725. Exclusion Code: X3.

1042. Marwaha G, Stephans KL, Woody NM, et al. Lung stereotactic body radiation therapy: regional nodal failure is not predicted by tumor size. *J Thorac Oncol*. 2014 Nov;9(11):1693-7. doi: 10.1097/jto.0000000000000313. PMID: 25185531. Exclusion Code: X13.

1043. Massion PP, Healey GF, Peek LJ, et al. Autoantibody signature enhances the positive predictive power of computed tomography and nodule-based risk models for detection of lung cancer. *J Thorac Oncol*. 2017 Mar;12(3):578-84. doi: 10.1016/j.jtho.2016.08.143. PMID: 27615397. Exclusion Code: X5.

1044. Mastrangelo G, Marangi G, Ballarin MN, et al. Lung cancer risk in past asbestos workers a few decades after exposure cessation and prospects for screening. *Arch Environ Occup Health*. 2016 Jul 3;71(4):237-44. doi: 10.1080/19338244.2015.1134423. PMID: 26730642. Exclusion Code: X7.

1045. Matsui Y, Hiraki T, Gobara H, et al. Phrenic nerve injury after radiofrequency ablation of lung tumors: retrospective evaluation of the incidence and risk factors. *J Vasc Interv Radiol*. 2012 Jun;23(6):780-5. doi: 10.1016/j.jvir.2012.02.014. PMID: 22513393. Exclusion Code: X6.

1046. Matsumura Y, Suzuki H, Ohira T, et al. Matched-pair analysis of a multi-institutional cohort reveals that epidermal growth factor receptor mutation is not a risk factor for postoperative recurrence of lung adenocarcinoma. *Lung Cancer*. 2017 Dec;114:23-30. doi: 10.1016/j.lungcan.2017.09.003. PMID: 29173761. Exclusion Code: X11.

1047. Matsumura Y, Yano M, Yoshida J, et al. Early and late recurrence after intentional limited resection for cT1aN0M0, non-small cell lung cancer: from a multi-institutional, retrospective analysis in Japan. *Interact Cardiovasc Thorac Surg*. 2016 Sep;23(3):444-9. doi: 10.1093/icvts/ivw125. PMID: 27226401. Exclusion Code: X10.

1048. Matsuo Y, Ueki N, Takayama K, et al. Evaluation of dynamic tumour tracking radiotherapy with real-time monitoring for lung tumours using a gimbal mounted linac. *Radiother Oncol*. 2014 Sep;112(3):360-4. doi: 10.1016/j.radonc.2014.08.003. PMID: 25154320. Exclusion Code: X3.

1049. Matsuoka K, Ueda M, Miyamoto Y. Risk factor for respiratory death after lung cancer surgery in octogenarians. *Asian Cardiovasc Thorac Ann*. 2015 Nov;23(9):1044-9. doi: 10.1177/0218492315605725. PMID: 26385873. Exclusion Code: X11.

1050. Matsuura Y, Mun M, Nakagawa K, et al. Efficacy and feasibility of a novel and noninvasive computed tomography-guided marking technique for peripheral pulmonary nodules. *J Thorac Cardiovasc Surg*. 2015 Apr;149(4):1208-9. doi: 10.1016/j.jtcvs.2014.11.040. PMID: 25534486. Exclusion Code: X3.

1051. Mazza F, Ferrari E, Maineri P, et al. Pleural lavage cytology predicts recurrence and survival, even in early non-small cell lung cancer. *Surg Today*. 2015 Mar;45(3):322-8. doi: 10.1007/s00595-014-0915-3. PMID: 24817060. Exclusion Code: X11.

1052. Mazza F, Ferrari E, Maineri P, et al. Pulmonary middle lobectomy for non-small-cell lung cancer: effectiveness and prognostic implications. *Eur J Cardiothorac Surg*. 2015 Dec;48(6):e117-23. doi: 10.1093/ejcts/ezv314. PMID: 26374866. Exclusion Code: X3.

1053. Mazzella A, Pardolesi A, Maisonneuve P, et al. Bronchopleural Fistula After Pneumonectomy: Risk Factors and Management, Focusing on Open-Window Thoracostomy. *Semin Thorac Cardiovasc Surg*. 2018 Spring;30(1):104-13. doi: 10.1053/j.semtcvs.2017.10.003. PMID: 29109057. Exclusion Code: X3.

1054. Mazzone PJ, Obuchowski N, Fu AZ, et al. Quality of life and healthcare use in a randomized controlled lung cancer screening study. *Ann Am Thorac Soc*. 2013 Aug;10(4):324-9. doi: 10.1513/AnnalsATS.201301-007OC. PMID: 23952850. Exclusion Code: X5.

1055. Mazzone PJ, Wang XF, Lim S, et al. Accuracy of volatile urine biomarkers for the detection and characterization of lung cancer. *BMC Cancer*. 2015 Dec 23;15:1001. doi: 10.1186/s12885-015-1996-0. PMID: 26698840. Exclusion Code: X3.

1056. McAleese J, Baluch S, Drinkwater K. The quality of curative-intent radiotherapy for non-small cell lung cancer in the UK. *Clin Oncol (R Coll Radiol)*. 2015 Sep;27(9):498-504. doi: 10.1016/j.clon.2015.05.006. PMID: 26073694. Exclusion Code: X8.

1057. McCunney RJ, Li J. Radiation risks in lung cancer screening programs: a comparison with nuclear industry workers and atomic bomb survivors. *Chest*. 2014 Mar 1;145(3):618-24. doi: 10.1378/chest.13-1420. PMID: 24590022. Exclusion Code: X10.

1058. McDevitt JL, Mouli SK, Nemcek AA, et al. Percutaneous cryoablation for the treatment of primary and metastatic lung tumors: identification of risk factors for recurrence and major complications. *J Vasc Interv Radiol*. 2016 Sep;27(9):1371-9. doi: 10.1016/j.jvir.2016.04.005. PMID: 27321886. Exclusion Code: X6.

1059. McElnay P, Casali G, Batchelor T, et al. Adopting a standardized anterior approach significantly increases video-assisted thoracoscopic surgery lobectomy rates. *Eur J Cardiothorac Surg*. 2014 Jul;46(1):100-5. doi: 10.1093/ejcts/ezt561. PMID: 24335265. Exclusion Code: X3.

1060. McElnay PJ, Molyneux M, Krishnadas R, et al. Pain and recovery are comparable after either uniportal or multiport video-assisted thoracoscopic lobectomy: an observation study. *Eur J Cardiothorac Surg*. 2015 May;47(5):912-5. doi: 10.1093/ejcts/ezu324. PMID: 25147352. Exclusion Code: X11.

1061. McGarry RC, Papiez L, Williams M, et al. Stereotactic body radiation therapy of early-stage non-small-cell lung carcinoma: phase I study. *Int J Radiat Oncol Biol Phys*. 2005 Nov 15;63(4):1010-5. doi: 10.1016/j.ijrobp.2005.03.073. PMID: 16115740. Exclusion Code: X11.

1062. McGuire AL, Hopman WM, Petsikas D, et al. Outcomes: wedge resection versus lobectomy for non-small cell lung cancer at the Cancer Centre of Southeastern Ontario 1998-2009. *Can J Surg*. 2013 Dec;56(6):E165-70. PMID: 24284157. Exclusion Code: X11.

1063. McKee BJ, Regis SM, McKee AB, et al. Performance of ACR Lung-RADS in a clinical CT lung screening program. *J Am Coll Radiol*. 2015 Mar;12(3):273-6. doi: 10.1016/j.jacr.2014.08.004. PMID: 25176499. Exclusion Code: X17.

1064. McKenna RJ, Jr., Houck W, Fuller CB. Video-assisted thoracic surgery lobectomy: experience with 1,100 cases. *Ann Thorac Surg*. 2006 Feb;81(2):421-5; discussion 5-6. doi: 10.1016/j.athoracsur.2005.07.078. PMID: 16427825. Exclusion Code: X3.

1065. McLaughlin J, Han G, Schalper KA, et al. Quantitative assessment of the heterogeneity of PD-L1 expression in non-small-cell lung cancer. *JAMA Oncol*. 2016 Jan;2(1):46-54. doi: 10.1001/jamaoncol.2015.3638. PMID: 26562159. Exclusion Code: X8.

1066. McMahon PM, Kong CY, Johnson BE, et al. Chapter 9: The MGH-HMS lung cancer policy model: tobacco control versus screening. *Risk Anal*. 2012 Jul;32 Suppl 1:S117-24. doi: 10.1111/j.1539-6924.2011.01652.x. PMID: 22882882. Exclusion Code: X4.

1067. McMahon PM, Meza R, Plevritis SK, et al. Comparing benefits from many possible computed tomography lung cancer screening programs: extrapolating from the National Lung Screening Trial using comparative modeling. *PLoS One*. 2014;9(6):e99978. doi: 10.1371/journal.pone.0099978. PMID: 24979231. Exclusion Code: X4.

1068. McWilliams JM, Dalton JB, Landrum MB, et al. Geographic variation in cancer-related imaging: Veterans Affairs health care system versus Medicare. *Ann Intern Med*. 2014 Dec 2;161(11):794-802. doi: 10.7326/m14-0650. PMID: 25437407. Exclusion Code: X3.

1069. Medbery RL, Perez SD, Force SD, et al. Video-assisted thoracic surgery lobectomy cost variability: implications for a bundled payment era. *Ann Thorac Surg*. 2014 May;97(5):1686-92; discussion 92-3. doi: 10.1016/j.athoracsur.2014.01.021. PMID: 24792254. Exclusion Code: X8.

1070. Mediratta N, Poullis M. Smoking status and 30-day mortality in patients undergoing pulmonary resections. *Asian Cardiovasc Thorac Ann*. 2016 Sep;24(7):663-9. doi: 10.1177/0218492316657252. PMID: 27365496. Exclusion Code: X7.

1071. Meena N, Bartter T. Ultrasound-guided percutaneous needle aspiration by pulmonologists: a study of factors with impact on procedural yield and complications. *J Bronchology Interv Pulmonol*. 2015 Jul;22(3):204-8. doi: 10.1097/lbr.0000000000000175. PMID: 26165890. Exclusion Code: X3.

1072. Mehta A, Cordero J, Dobersch S, et al. Non-invasive lung cancer diagnosis by detection of GATA6 and NKX2-1 isoforms in exhaled breath condensate. *EMBO Mol Med*. 2016 Dec;8(12):1380-9. doi: 10.15252/emmm.201606382. PMID: 27821429. Exclusion Code: X5.

1073. Mehta HJ, Ravenel JG, Shaftman SR, et al. The utility of nodule volume in the context of malignancy prediction for small pulmonary nodules. *Chest*. 2014 Mar 1;145(3):464-72. doi: 10.1378/chest.13-0708. PMID: 23949741. Exclusion Code: X3.

1074. Mehta RS, Lenzner D, Argiris A. Race and health disparities in patient refusal of surgery for early-stage non-small cell lung cancer: a SEER cohort study. *Ann Surg Oncol*. 2012 Mar;19(3):722-7. doi: 10.1245/s10434-011-2087-3. PMID: 21947698. Exclusion Code: X8.

1075. Meier-Schroers M, Homsi R, Skowasch D, et al. Lung cancer screening with MRI: results of the first screening round. *J Cancer Res Clin Oncol*. 2018 Jan;144(1):117-25. doi: 10.1007/s00432-017-2521-4. PMID: 28932985. Exclusion Code: X7.

1076. Meier-Schroers M, Kukuk G, Homsi R, et al. MRI of the lung using the PROPELLER technique: artifact reduction, better image quality and improved nodule detection. *Eur J Radiol*. 2016 Apr;85(4):707-13. doi: 10.1016/j.ejrad.2015.12.016. PMID: 26971412. Exclusion Code: X5.

1077. Melfi FM, Fanucchi O, Davini F, et al. Robotic lobectomy for lung cancer: evolution in technique and technology. *Eur J Cardiothorac Surg*. 2014 Oct;46(4):626-30; discussion 30-1. doi: 10.1093/ejcts/ezu079. PMID: 24616391. Exclusion Code: X3.

1078. Meng XX, Kuai XP, Dong WH, et al. Comparison of lung lesion biopsies between low-dose CT-guided and conventional CT-guided techniques. *Acta Radiol*. 2013 Oct;54(8):909-15. doi: 10.1177/0284185113485937. PMID: 23817682. Exclusion Code: X3.

1079. Merritt RE, Hoang CD, Shrager JB. Lymph node evaluation achieved by open lobectomy compared with thoracoscopic lobectomy for N0 lung cancer. *Ann Thorac Surg*. 2013 Oct;96(4):1171-7. doi: 10.1016/j.athoracsur.2013.05.044. PMID: 23915591. Exclusion Code: X11.

1080. Mets OM, Vliegenthart R, Gondrie MJ, et al. Lung cancer screening CT-based prediction of cardiovascular events. *JACC Cardiovasc Imaging*. 2013 Aug;6(8):899-907. doi: 10.1016/j.jcmg.2013.02.008. PMID: 23769488. Exclusion Code: X8.

1081. Meyers TJ, Chang SC, Chang PY, et al. Case-control study of cumulative cigarette tar exposure and lung and upper aerodigestive tract cancers. *Int J Cancer*. 2017 May 1;140(9):2040-50. doi: 10.1002/ijc.30632. PMID: 28164274. Exclusion Code: X4.

1082. Meza R, ten Haaf K, Kong CY, et al. Comparative analysis of 5 lung cancer natural history and screening models that reproduce outcomes of the NLST and PLCO trials. *Cancer*. 2014 Jun 1;120(11):1713-24. doi: 10.1002/cncr.28623. PMID: 24577803. Exclusion Code: X7.

1083. Midthun DE. Screening for lung cancer. *Clin Chest Med*. 2011 Dec;32(4):659-68. doi: 10.1016/j.ccm.2011.08.014. PMID: 22054878. Exclusion Code: X10.

1084. Migliore M, Criscione A, Calvo D, et al. Preliminary experience with video-assisted thoracic surgery lobectomy for lung malignancies: general considerations moving toward standard practice. *Future Oncol*. 2015;11(24 Suppl):43-6. doi: 10.2217/fon.15.305. PMID: 26638923. Exclusion Code: X3.

1085. Miller AT, Kruger P, Conner K, et al. Initial outcomes of a lung cancer screening program in an integrated community health system. *J Am Coll Radiol*. 2016 Jun;13(6):733-7. doi: 10.1016/j.jacr.2016.02.013. PMID: 27131618. Exclusion Code: X7.

1086. Miller CJ, Martin B, Stang K, et al. Predictors of Distant Failure After Stereotactic Body Radiation Therapy for Stages I to IIA Non-Small-Cell Lung Cancer. *Clin Lung Cancer*. 2019 Jan;20(1):37-42. doi: 10.1016/j.cllc.2018.09.002. PMID: 30279109. Exclusion Code: X13.

1087. Mimae T, Miyata Y, Mimura T, et al. Radiologic findings to predict low-grade malignant tumour among clinical T1bN0 lung adenocarcinomas: lessons from histological subtypes. *Jpn J Clin Oncol*. 2015 Aug;45(8):767-73. doi: 10.1093/jjco/hyv078. PMID: 26056324. Exclusion Code: X3.

1088. Mimae T, Suzuki K, Tsuboi M, et al. Surgical outcomes of lung cancer in patients with combined pulmonary fibrosis and emphysema. *Ann Surg Oncol*. 2015 Dec;22 Suppl 3:S1371-9. doi: 10.1245/s10434-015-4577-1. PMID: 25956575. Exclusion Code: X3.

1089. Mimae T, Tsutani Y, Miyata Y, et al. Role of lymphatic invasion in the prognosis of patients with clinical node-negative and pathologic node-positive lung adenocarcinoma. *J Thorac Cardiovasc Surg*. 2014 Jun;147(6):1820-6. doi: 10.1016/j.jtcvs.2013.11.050. PMID: 24507979. Exclusion Code: X8.

1090. Minami D, Takigawa N, Morichika D, et al. Endobronchial ultrasound-guided transbronchial biopsy with or without a guide sheath for diagnosis of lung cancer. *Respir Investig*. 2015 May;53(3):93-7. doi: 10.1016/j.resinv.2014.10.003. PMID: 25951094. Exclusion Code: X3.

1091. Minami D, Takigawa N, Oda N, et al. Endobronchial ultrasound-guided transbronchial needle aspiration of hilar and mediastinal lymph nodes detected on 18F-fluorodeoxyglucose positron emission tomography/computed tomography. *Jpn J Clin Oncol*. 2016 Jun;46(6):529-33. doi: 10.1093/jjco/hyw023. PMID: 27004902. Exclusion Code: X3.

1092. Minamimoto R, Senda M, Jinnouchi S, et al. Detection of lung cancer by FDG-PET cancer screening program: a nationwide Japanese survey. *Anticancer Res*. 2014 Jan;34(1):183-9. PMID: 24403460. Exclusion Code: X5.

1093. Ming X, Feng Y, Yang C, et al. Radiation-induced heart disease in lung cancer radiotherapy: a dosimetric update. *Medicine (Baltimore)*. 2016 Oct;95(41):e5051. doi: 10.1097/md.0000000000005051. PMID: 27741117. Exclusion Code: X9.

1094. Mitera G, Swaminath A, Rudoler D, et al. Cost-effectiveness analysis comparing conventional versus stereotactic body radiotherapy for surgically ineligible stage I non-small-cell lung cancer. *J Oncol Pract*. 2014 May;10(3):e130-6. doi: 10.1200/jop.2013.001206. PMID: 24643574. Exclusion Code: X10.

1095. Mitsuyoshi T, Nakamura M, Matsuo Y, et al. Dosimetric comparison of lung stereotactic body radiotherapy treatment plans using averaged computed tomography and end-exhalation computed tomography images: Evaluation of the effect of different dose-calculation algorithms and prescription methods. *Med Dosim*. 2016 Winter;41(4):305-9. doi: 10.1016/j.meddos.2016.07.003. PMID: 27623737. Exclusion Code: X8.

1096. Miura H, Inoue T, Shiomi H, et al. Differences in rates of radiation-induced true and false rib fractures after stereotactic body radiation therapy for Stage I primary lung cancer. *J Radiat Res*. 2015 Mar;56(2):332-7. doi: 10.1093/jrr/rru107. PMID: 25504640. Exclusion Code: X17.

1097. Miura N, Kohno M, Ito K, et al. Lung cancer surgery in patients aged 80 years or older: an analysis of risk factors, morbidity, and mortality. *Gen Thorac Cardiovasc Surg*. 2015 Jul;63(7):401-5. doi: 10.1007/s11748-015-0546-7. PMID: 25868520. Exclusion Code: X3.

1098. Miyasaka Y, Suzuki K, Oh S, et al. Cardiomegaly is a significant predictor of postoperative atelectasis following left upper superior segmentectomy. *Thorac Cardiovasc Surg*. 2015 Oct;63(7):609-13. doi: 10.1055/s-0034-1377061. PMID: 25136944. Exclusion Code: X3.

1099. Miyazaki T, Yamasaki N, Tsuchiya T, et al. Inflammation-based scoring is a useful prognostic predictor of pulmonary resection for elderly patients with clinical stage I non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2015 Apr;47(4):e140-5. doi: 10.1093/ejcts/ezu514. PMID: 25548132. Exclusion Code: X3.

1100. Miyazaki T, Yamazaki T, Nakamura D, et al. Surgery or stereotactic body radiotherapy for elderly stage I lung cancer? A propensity score matching analysis. *Surg Today*. 2017 Dec;47(12):1476-83. doi: 10.1007/s00595-017-1536-4. PMID: 28447170. Exclusion Code: X10.

1101. Modh A, Rimner A, Williams E, et al. Local control and toxicity in a large cohort of central lung tumors treated with stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2014 Dec 1;90(5):1168-76. doi: 10.1016/j.ijrobp.2014.08.008. PMID: 25303891. Exclusion Code: X3.

1102. Mohiuddin K, Haneuse S, Sofer T, et al. Relationship between margin distance and local recurrence among patients undergoing wedge resection for small (</=2 cm) non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2014 Apr;147(4):1169-75; discussion 75-7. doi: 10.1016/j.jtcvs.2013.11.056. PMID: 24507406. Exclusion Code: X11.

1103. Mohner M. An approach to adjust standardized mortality ratios for competing cause of death in cohort studies. *Int Arch Occup Environ Health*. 2016 May;89(4):593-8. doi: 10.1007/s00420-015-1097-z. PMID: 26483290. Exclusion Code: X3.

1104. Mokhles S, Nuyttens JJ, Maat AP, et al. Survival and treatment of non-small cell lung cancer stage I-II treated surgically or with stereotactic body radiotherapy: patient and tumor-specific factors affect the prognosis. *Ann Surg Oncol*. 2015 Jan;22(1):316-23. doi: 10.1245/s10434-014-3860-x. PMID: 24962941. Exclusion Code: X3.

1105. Mokhles S, Verstegen N, Maat AP, et al. Comparison of clinical outcome of stage I non-small cell lung cancer treated surgically or with stereotactic radiotherapy: results from propensity score analysis. *Lung Cancer*. 2015 Mar;87(3):283-9. doi: 10.1016/j.lungcan.2015.01.005. PMID: 25622781. Exclusion Code: X10.

1106. Moloney F, Ryan D, McCarthy L, et al. Increasing the accuracy of 18F-FDG PET/CT interpretation of "mildly positive" mediastinal nodes in the staging of non-small cell lung cancer. *Eur J Radiol*. 2014 May;83(5):843-7. doi: 10.1016/j.ejrad.2014.01.016. PMID: 24581594. Exclusion Code: X3.

1107. Montaudon M, Latrabe V, Pariente A, et al. Factors influencing accuracy of CT-guided percutaneous biopsies of pulmonary lesions. *Eur Radiol*. 2004 Jul;14(7):1234-40. doi: 10.1007/s00330-004-2250-3. PMID: 14963689. Exclusion Code: X3.

1108. Moon MH, Beck KS, Moon YK, et al. Incidence and clinical features of the incidentally found vascular stump thrombus during routine follow up after oncologic lung surgery. *PLoS One*. 2017;12(9):e0185140. doi: 10.1371/journal.pone.0185140. PMID: 28953945. Exclusion Code: X11.

1109. Moon SW, Cho DG, Cho KD, et al. Fluoroscopy-assisted thoracoscopic resection for small intrapulmonary lesions after preoperative computed tomography-guided localization using fragmented platinum microcoils. *Thorac Cardiovasc Surg*. 2012 Sep;60(6):413-8. doi: 10.1055/s-0031-1299582. PMID: 22383151. Exclusion Code: X3.

1110. Moon Y, Lee KY, Moon SW, et al. Sublobar resection margin width does not affect recurrence of clinical N0 non-small cell lung cancer presenting as GGO-predominant nodule of 3 cm or less. *World J Surg*. 2017 Feb;41(2):472-9. doi: 10.1007/s00268-016-3743-3. PMID: 27718002. Exclusion Code: X11.

1111. Moon Y, Lee KY, Park JK. Prognosis After Sublobar Resection of Small-sized Non-small Cell Lung Cancer with Visceral Pleural or Lymphovascular Invasion. *World J Surg*. 2017 Nov;41(11):2769-77. doi: 10.1007/s00268-017-4075-7. PMID: 28597091. Exclusion Code: X11.

1112. Moon Y, Park JK, Lee KY, et al. Lymphatic invasion is a more significant prognostic factor than visceral pleural invasion in non-small cell lung cancer with tumours of 3 cm or less. *Respirology*. 2017 Aug;22(6):1179-84. doi: 10.1111/resp.13029. PMID: 28382791. Exclusion Code: X8.

1113. Moon Y, Sung SW, Lee KY, et al. The importance of the lepidic component as a prognostic factor in stage I pulmonary adenocarcinoma. *World J Surg Oncol*. 2016 Feb 16;14(1):37. doi: 10.1186/s12957-016-0791-y. PMID: 26879575. Exclusion Code: X11.

1114. Moore W, Chaya Y, Chaudhry A, et al. Computed tomography assessment of ablation zone enhancement in patients with early-stage lung cancer after stereotactic ablative radiotherapy. *J Comput Assist Tomogr*. 2015 Sep-Oct;39(5):804-9. doi: 10.1097/rct.0000000000000262. PMID: 25974720. Exclusion Code: X3.

1115. Moore W, Talati R, Bhattacharji P, et al. Five-year survival after cryoablation of stage I non-small cell lung cancer in medically inoperable patients. *J Vasc Interv Radiol*. 2015 Mar;26(3):312-9. doi: 10.1016/j.jvir.2014.12.006. PMID: 25735518. Exclusion Code: X6.

1116. Moran A, Daly ME, Yip SSF, et al. Radiomics-based Assessment of Radiation-induced Lung Injury After Stereotactic Body Radiotherapy. *Clin Lung Cancer*. 2017 Nov;18(6):e425-e31. doi: 10.1016/j.cllc.2017.05.014. PMID: 28623121. Exclusion Code: X8.

1117. Moran LM, Rodriguez R, Calzado A, et al. Image quality and dose evaluation in spiral chest CT examinations of patients with lung carcinoma. *Br J Radiol*. 2004 Oct;77(922):839-46. doi: 10.1259/bjr/71539623. PMID: 15482995. Exclusion Code: X3.

1118. Mordant P, Grand B, Cazes A, et al. Adenosquamous carcinoma of the lung: surgical management, pathologic characteristics, and prognostic implications. *Ann Thorac Surg*. 2013 Apr;95(4):1189-95. doi: 10.1016/j.athoracsur.2012.12.037. PMID: 23473060. Exclusion Code: X3.

1119. More JM, Eclov NC, Chung MP, et al. Feasibility and potential utility of multicomponent exhaled breath analysis for predicting development of radiation pneumonitis after stereotactic ablative radiotherapy. *J Thorac Oncol*. 2014 Jul;9(7):957-64. doi: 10.1097/jto.0000000000000182. PMID: 24926543. Exclusion Code: X3.

1120. Morgant MC, Pages PB, Orsini B, et al. Time trends in surgery for lung cancer in France from 2005 to 2012: a nationwide study. *Eur Respir J*. 2015 Oct;46(4):1131-9. doi: 10.1183/13993003.00354-2015. PMID: 26250496. Exclusion Code: X8.

1121. Morimoto M, Okishio K, Akira M, et al. Duration of twice-daily thoracic radiotherapy and time from the start of any treatment to the end of chest irradiation as significant predictors of outcomes in limited-disease small-cell lung cancer. *Clin Lung Cancer*. 2017 Mar;18(2):e117-e27. doi: 10.1016/j.cllc.2016.09.004. PMID: 28340925. Exclusion Code: X3.

1122. Morla O, Liberge R, Arrigoni PP, et al. Pulmonary nodules and masses in lung transplant recipients: clinical and CT findings. *Eur Radiol*. 2014 Sep;24(9):2183-91. doi: 10.1007/s00330-014-3264-0. PMID: 24895041. Exclusion Code: X3.

1123. Moroga T, Yamashita S, Tokuishi K, et al. Thoracoscopic segmentectomy with intraoperative evaluation of sentinel nodes for stage I non-small cell lung cancer. *Ann Thorac Cardiovasc Surg*. 2012;18(2):89-94. PMID: 22082811. Exclusion Code: X11.

1124. Moseson EM, Wiener RS, Golden SE, et al. Patient and clinician characteristics associated with adherence. A cohort study of veterans with incidental pulmonary nodules. *Ann Am Thorac Soc*. 2016 May;13(5):651-9. doi: 10.1513/AnnalsATS.201511-745OC. PMID: 27144794. Exclusion Code: X3.

1125. Mota P, Silva HC, Soares MJ, et al. Genetic polymorphisms of phase I and phase II metabolic enzymes as modulators of lung cancer susceptibility. *J Cancer Res Clin Oncol*. 2015 May;141(5):851-60. doi: 10.1007/s00432-014-1868-z. PMID: 25388590. Exclusion Code: X7.

1126. Motoishi M, Sawai S, Hori T, et al. The preoperative HbA1c level is an independent prognostic factor for the postoperative survival after resection of non-small cell lung cancer in elderly patients. *Surg Today*. 2018 May;48(5):517-24. doi: 10.1007/s00595-017-1612-9. PMID: 29222669. Exclusion Code: X3.

1127. Moulla Y, Gradistanac T, Wittekind C, et al. Predictive risk factors for lymph node metastasis in patients with resected non-small cell lung cancer: a case control study. *J Cardiothorac Surg*. 2019 Jan 16;14(1):11. doi: 10.1186/s13019-019-0831-0. PMID: 30651112. Exclusion Code: X11.

1128. Mu JW, Gao SG, Xue Q, et al. A matched comparison study of uniportal versus triportal thoracoscopic lobectomy and sublobectomy for early-stage nonsmall cell lung cancer. *Chin Med J (Engl)*. 2015 Oct 20;128(20):2731-5. doi: 10.4103/0366-6999.167298. PMID: 26481738. Exclusion Code: X3.

1129. Muallaoglu S, Karadeniz C, Mertsoylu H, et al. The clinicopathological and survival differences between never and ever smokers with non-small cell lung cancer. *J BUON*. 2014 Apr-Jun;19(2):453-8. PMID: 24965406. Exclusion Code: X3.

1130. Muka T, Kraja B, Ruiter R, et al. Dietary mineral intake and lung cancer risk: the Rotterdam Study. *Eur J Nutr*. 2017 Jun;56(4):1637-46. doi: 10.1007/s00394-016-1210-4. PMID: 27073037. Exclusion Code: X7.

1131. Muller DC, Johansson M, Brennan P. Lung cancer risk prediction model incorporating lung function: development and validation in the UK Biobank Prospective Cohort Study. *J Clin Oncol*. 2017 Mar 10;35(8):861-9. doi: 10.1200/jco.2016.69.2467. PMID: 28095156. Exclusion Code: X4.

1132. Munir S, Koppikar S, Hopman WM, et al. Diagnostic yield for cancer and diagnostic accuracy of computed tomography-guided core needle biopsy of subsolid pulmonary lesions. *J Thorac Imaging*. 2017 Jan;32(1):50-6. doi: 10.1097/rti.0000000000000245. PMID: 27870823. Exclusion Code: X3.

1133. Murakami J, Ueda K, Sano F, et al. Pulmonary emphysema and tumor microenvironment in primary lung cancer. *J Surg Res*. 2016 Feb;200(2):690-7. doi: 10.1016/j.jss.2015.09.004. PMID: 26428090. Exclusion Code: X3.

1134. Murakawa T, Ichinose J, Hino H, et al. Long-term outcomes of open and video-assisted thoracoscopic lung lobectomy for the treatment of early stage non-small cell lung cancer are similar: a propensity-matched study. *World J Surg*. 2015 May;39(5):1084-91. doi: 10.1007/s00268-014-2918-z. PMID: 25561187. Exclusion Code: X11.

1135. Muranishi Y, Sonobe M, Hamaji M, et al. Surgery for metachronous second primary lung cancer versus surgery for primary lung cancer: a propensity score-matched comparison of postoperative complications and survival outcomes. *Interact Cardiovasc Thorac Surg*. 2018 Apr 1;26(4):631-7. doi: 10.1093/icvts/ivx389. PMID: 29253161. Exclusion Code: X3.

1136. Muranishi Y, Sonobe M, Menju T, et al. Atrial fibrillation after lung cancer surgery: incidence, severity, and risk factors. *Surg Today*. 2017 Feb;47(2):252-8. doi: 10.1007/s00595-016-1380-y. PMID: 27382978. Exclusion Code: X3.

1137. Murray L, Karakaya E, Hinsley S, et al. Lung stereotactic ablative radiotherapy (SABR): dosimetric considerations for chest wall toxicity. *Br J Radiol*. 2016;89(1058):20150628. doi: 10.1259/bjr.20150628. PMID: 26760508. Exclusion Code: X3.

1138. Murray L, Ramasamy S, Lilley J, et al. Stereotactic ablative radiotherapy (SABR) in patients with medically inoperable peripheral early stage lung cancer: outcomes for the first UK SABR cohort. *Clin Oncol (R Coll Radiol)*. 2016 Jan;28(1):4-12. doi: 10.1016/j.clon.2015.09.007. PMID: 26474546. Exclusion Code: X10.

1139. Mytelka DS, Li L, Benoit K. Post-diagnosis weight loss as a prognostic factor in non-small cell lung cancer. *J Cachexia Sarcopenia Muscle*. 2018 Feb;9(1):86-92. doi: 10.1002/jcsm.12253. PMID: 29205930. Exclusion Code: X3.

1140. Nabavizadeh N, Zhang J, Elliott DA, et al. Electromagnetic navigational bronchoscopy-guided fiducial markers for lung stereotactic body radiation therapy: analysis of safety, feasibility, and interfraction stability. *J Bronchology Interv Pulmonol*. 2014 Apr;21(2):123-30. doi: 10.1097/lbr.0000000000000065. PMID: 24739685. Exclusion Code: X3.

1141. Nagata M, Ito H, Matsuzaki T, et al. Body mass index, C-reactive protein and survival in smokers undergoing lobectomy for lung cancerdagger. *Eur J Cardiothorac Surg*. 2017 Jun 1;51(6):1164-70. doi: 10.1093/ejcts/ezx004. PMID: 28199511. Exclusion Code: X3.

1142. Nagata Y, Takayama K, Matsuo Y, et al. Clinical outcomes of a phase I/II study of 48 Gy of stereotactic body radiotherapy in 4 fractions for primary lung cancer using a stereotactic body frame. *Int J Radiat Oncol Biol Phys*. 2005 Dec 1;63(5):1427-31. doi: 10.1016/j.ijrobp.2005.05.034. PMID: 16169670. Exclusion Code: X11.

1143. Nagatani Y, Takahashi M, Ikeda M, et al. Sub-solid nodule detectability in seven observers of seventy-nine clinical cases: comparison between ultra-low-dose chest digital tomosynthesis with iterative reconstruction and chest radiography by receiver-operating characteristics analysis. *Eur J Radiol*. 2018 Oct;107:166-74. doi: 10.1016/j.ejrad.2018.08.006. PMID: 30292262. Exclusion Code: X11.

1144. Nagatani Y, Takahashi M, Ikeda M, et al. Sub-solid nodule detection performance on reduced-dose computed tomography with iterative reduction: comparison between 20 mA (7 mAs) and 120 mA (42 mAs) regarding nodular size and characteristics and association with size-specific dose estimate. *Acad Radiol*. 2017 Aug;24(8):995-1007. doi: 10.1016/j.acra.2017.01.004. PMID: 28606593. Exclusion Code: X8.

1145. Nagatani Y, Takahashi M, Murata K, et al. Lung nodule detection performance in five observers on computed tomography (CT) with adaptive iterative dose reduction using three-dimensional processing (AIDR 3D) in a Japanese multicenter study: Comparison between ultra-low-dose CT and low-dose CT by receiver-operating characteristic analysis. *Eur J Radiol*. 2015 Jul;84(7):1401-12. doi: 10.1016/j.ejrad.2015.03.012. PMID: 25892051. Exclusion Code: X3.

1146. Nagayasu T, Yamasaki N, Tsuchiya T, et al. The evolution of bronchoplasty and broncho-angioplasty as treatments for lung cancer: evaluation of 30 years of data from a single institution. *Eur J Cardiothorac Surg*. 2016 Jan;49(1):300-6. doi: 10.1093/ejcts/ezv065. PMID: 25721822. Exclusion Code: X6.

1147. Nair A, Gartland N, Barton B, et al. Comparing the performance of trained radiographers against experienced radiologists in the UK lung cancer screening (UKLS) trial. *Br J Radiol*. 2016 Oct;89(1066):20160301. doi: 10.1259/bjr.20160301. PMID: 27461068. Exclusion Code: X7.

1148. Nair VJ, MacRae R, Sirisegaram A, et al. Pretreatment [18F]-fluoro-2-deoxy-glucose positron emission tomography maximum standardized uptake value as predictor of distant metastasis in early-stage non-small cell lung cancer treated with definitive radiation therapy: rethinking the role of positron emission tomography in personalizing treatment based on risk status. *Int J Radiat Oncol Biol Phys*. 2014 Feb 1;88(2):312-8. doi: 10.1016/j.ijrobp.2013.10.029. PMID: 24411602. Exclusion Code: X6.

1149. Nakagawa M, Hara M, Sakurai K, et al. Diagnostic accuracy of 18F-2-deoxy-fluoro-D-glucose positron emission tomography for pN1 lymph nodes in patients with lung cancer. *Acta Radiol*. 2009 Jul;50(6):638-44. doi: 10.1080/02841850902971255. PMID: 19492198. Exclusion Code: X3.

1150. Nakagawa T, Negoro Y, Matsuoka T, et al. Comparison of the outcomes of stereotactic body radiotherapy and surgery in elderly patients with cT1-2N0M0 non-small cell lung cancer. *Respir Investig*. 2014 Jul;52(4):221-6. doi: 10.1016/j.resinv.2014.01.002. PMID: 24998368. Exclusion Code: X10.

1151. Nakagawa T, Tomioka Y, Toyazaki T, et al. Association between values of preoperative 6-min walk test and surgical outcomes in lung cancer patients with decreased predicted postoperative pulmonary function. *Gen Thorac Cardiovasc Surg*. 2018 Apr;66(4):220-4. doi: 10.1007/s11748-018-0888-z. PMID: 29344798. Exclusion Code: X11.

1152. Nakajima EC, Frankland MP, Johnson TF, et al. Assessing the inter-observer variability of Computer-Aided Nodule Assessment and Risk Yield (CANARY) to characterize lung adenocarcinomas. *PLoS One*. 2018;13(6):e0198118. doi: 10.1371/journal.pone.0198118. PMID: 29856852. Exclusion Code: X3.

1153. Nakajo C, Heinzer S, Montandon S, et al. Chest CT at a dose below 0.3 mSv: impact of iterative reconstruction on image quality and lung analysis. *Acta Radiol*. 2016 Mar;57(3):311-7. doi: 10.1177/0284185115578469. PMID: 25838452. Exclusion Code: X3.

1154. Nakamura H, Saji H, Marushima H, et al. Glucose uptake values in positron emission tomography are useful to predict survival after sublobar resection for lung cancer. *Thorac Cardiovasc Surg*. 2017 Mar;65(2):150-7. doi: 10.1055/s-0036-1572510. PMID: 26909560. Exclusion Code: X11.

1155. Nakamura H, Saji H, Shinmyo T, et al. Close association of IASLC/ATS/ERS lung adenocarcinoma subtypes with glucose-uptake in positron emission tomography. *Lung Cancer*. 2015 Jan;87(1):28-33. doi: 10.1016/j.lungcan.2014.11.010. PMID: 25481488. Exclusion Code: X3.

1156. Nakamura H, Sakai H, Kimura H, et al. Difference in Postsurgical Prognostic Factors between Lung Adenocarcinoma and Squamous Cell Carcinoma. *Ann Thorac Cardiovasc Surg*. 2017 Dec 20;23(6):291-7. doi: 10.5761/atcs.oa.17-00020. PMID: 28966230. Exclusion Code: X3.

1157. Nakamura M, Nishimura H, Nakayama M, et al. Dosimetric factors predicting radiation pneumonitis after CyberKnife stereotactic body radiotherapy for peripheral lung cancer. *Br J Radiol*. 2016 Dec;89(1068):20160560. doi: 10.1259/bjr.20160560. PMID: 27805837. Exclusion Code: X3.

1158. Nakamura S, Fukui T, Taniguchi T, et al. Prognostic impact of tumor size eliminating the ground glass opacity component: modified clinical T descriptors of the tumor, node, metastasis classification of lung cancer. *J Thorac Oncol*. 2013 Dec;8(12):1551-7. doi: 10.1097/jto.0000000000000020. PMID: 24389437. Exclusion Code: X11.

1159. Nakamura T, Otsuki Y, Nakamura H, et al. Pleural lavage cytology after lung resection in patients with non-small cell lung cancer and the feasibility of 20 mL saline solution. *Asian J Surg*. 2019 Jan;42(1):283-9. doi: 10.1016/j.asjsur.2018.03.001. PMID: 29628439. Exclusion Code: X3.

1160. Nakanishi R, Nakagawa M, Tokufuchi H, et al. Video-assisted thoracoscopic lobectomy for clinical stage I non-small cell lung cancer: experience with 111 consecutive patients demonstrating comorbidity. *Minerva Chir*. 2012 Feb;67(1):67-75. PMID: 22361678. Exclusion Code: X11.

1161. Nakao M, Yoshida J, Goto K, et al. Long-term outcomes of 50 cases of limited-resection trial for pulmonary ground-glass opacity nodules. *J Thorac Oncol*. 2012 Oct;7(10):1563-6. doi: 10.1097/JTO.0b013e3182641b5c. PMID: 22878750. Exclusion Code: X11.

1162. Nakatani M, Tanigawa N, Kariya S, et al. Analysis of factors influencing accuracy and complications in CT-guided lung biopsy. *Minim Invasive Ther Allied Technol*. 2012 Nov;21(6):415-22. doi: 10.3109/13645706.2012.662155. PMID: 22375617. Exclusion Code: X3.

1163. Nakayama H, Sugahara S, Tokita M, et al. Proton beam therapy for patients with medically inoperable stage I non-small-cell lung cancer at the university of tsukuba. *Int J Radiat Oncol Biol Phys*. 2010 Oct 1;78(2):467-71. doi: 10.1016/j.ijrobp.2009.07.1707. PMID: 20056349. Exclusion Code: X6.

1164. Nanda RH, Liu Y, Gillespie TW, et al. Stereotactic body radiation therapy versus no treatment for early stage non-small cell lung cancer in medically inoperable elderly patients: A National Cancer Data Base analysis. *Cancer*. 2015 Dec 1;121(23):4222-30. doi: 10.1002/cncr.29640. PMID: 26348268. Exclusion Code: X8.

1165. Narsule CK, Sales Dos Santos R, Gupta A, et al. The efficacy of electromagnetic navigation to assist with computed tomography-guided percutaneous thermal ablation of lung tumors. *Innovations (Phila)*. 2012 May-Jun;7(3):187-90. doi: 10.1097/IMI.0b013e318265b127. PMID: 22885459. Exclusion Code: X6.

1166. Nasir BS, Edwards M, Tiffault V, et al. Transesophageal pulmonary nodule biopsy using endoscopic ultrasonography. *J Thorac Cardiovasc Surg*. 2014 Sep;148(3):850-5; discussion 5. doi: 10.1016/j.jtcvs.2014.06.007. PMID: 25048631. Exclusion Code: X11.

1167. Naur TMH, Konge L, Clementsen PF. Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration for Staging of Patients with Non-Small Cell Lung Cancer without Mediastinal Involvement at Positron Emission Tomography-Computed Tomography. *Respiration*. 2017;94(3):279-84. doi: 10.1159/000477625. PMID: 28683462. Exclusion Code: X3.

1168. Navani N, Nankivell M, Lawrence DR, et al. Lung cancer diagnosis and staging with endobronchial ultrasound-guided transbronchial needle aspiration compared with conventional approaches: an open-label, pragmatic, randomised controlled trial. *Lancet Respir Med*. 2015 Apr;3(4):282-9. doi: 10.1016/s2213-2600(15)00029-6. PMID: 25660225. Exclusion Code: X3.

1169. Navarria P, Ascolese AM, Mancosu P, et al. Volumetric modulated arc therapy with flattening filter free (FFF) beams for stereotactic body radiation therapy (SBRT) in patients with medically inoperable early stage non small cell lung cancer (NSCLC). *Radiother Oncol*. 2013 Jun;107(3):414-8. doi: 10.1016/j.radonc.2013.04.016. PMID: 23725859. Exclusion Code: X10.

1170. Nawa T, Fukui K, Nakayama T, et al. A population-based cohort study to evaluate the effectiveness of lung cancer screening using low-dose CT in Hitachi city, Japan. *Jpn J Clin Oncol*. 2019 Feb 1;49(2):130-6. doi: 10.1093/jjco/hyy185. PMID: 30541133. Exclusion Code: X10.

1171. Nct. JoLT-Ca Sublobar Resection (SR) Versus Stereotactic Ablative Radiotherapy (SAbR) for Lung Cancer. *Https://clinicaltrials.gov/show/nct02468024*. 2015PMID: CN-01552762. Exclusion Code: X16.

1172. Nct. Comparison of Diagnostic and Therapeutic Efficacy of EBUS-TBNA/EUS-FNA and TEMLA in Operable NSCLC. A Randomised Controlled Trial. *Https://clinicaltrials.gov/show/nct03188562*. 2017PMID: CN-01588660. Exclusion Code: X16.

1173. Nelson G, Wu M, Hinkel C, et al. Improved targeting accuracy of lung tumor biopsies with scanning-beam digital x-ray tomosynthesis image guidance. *Med Phys*. 2016 Dec;43(12):6282. doi: 10.1118/1.4966025. PMID: 27908166. Exclusion Code: X3.

1174. Nemec U, Heidinger BH, Anderson KR, et al. Software-based risk stratification of pulmonary adenocarcinomas manifesting as pure ground glass nodules on computed tomography. *Eur Radiol*. 2018 Jan;28(1):235-42. doi: 10.1007/s00330-017-4937-2. PMID: 28710575. Exclusion Code: X3.

1175. Nentwich MF, Bohn BA, Uzunoglu FG, et al. Lymphatic invasion predicts survival in patients with early node-negative non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2013 Oct;146(4):781-7. doi: 10.1016/j.jtcvs.2013.04.037. PMID: 23778087. Exclusion Code: X11.

1176. Neroladaki A, Botsikas D, Boudabbous S, et al. Computed tomography of the chest with model-based iterative reconstruction using a radiation exposure similar to chest X-ray examination: preliminary observations. *Eur Radiol*. 2013 Feb;23(2):360-6. doi: 10.1007/s00330-012-2627-7. PMID: 22892722. Exclusion Code: X3.

1177. Netto SM, Silva AC, Nunes RA, et al. Voxel-based comparative analysis of lung lesions in CT for therapeutic purposes. *Med Biol Eng Comput*. 2017 Feb;55(2):295-314. doi: 10.1007/s11517-016-1510-0. PMID: 27180182. Exclusion Code: X5.

1178. Neves PC, Guerra M, Martins D, et al. Surgical treatment of non-small cell lung cancer in octogenarians - safety and prognosis. *Rev Port Cir Cardiotorac Vasc*. 2012 Apr-Jun;19(2):63-7. PMID: 23814772. Exclusion Code: X3.

1179. Ng CSH, MacDonald JK, Gilbert S, et al. Optimal Approach to Lobectomy for Non-Small Cell Lung Cancer: Systemic Review and Meta-Analysis. *Innovations (Phila)*. 2019 Apr;14(2):90-116. doi: 10.1177/1556984519837027. PMID: 31039680. Exclusion Code: X3.

1180. Nguyen KNB, Hause DJ, Novak J, et al. Tumor Control and Toxicity after SBRT for Ultracentral, Central, and Paramediastinal Lung Tumors. *Pract Radiat Oncol*. 2019 Mar;9(2):e196-e202. doi: 10.1016/j.prro.2018.11.005. PMID: 30496842. Exclusion Code: X3.

1181. Nguyen NP, Godinez J, Shen W, et al. Is surgery indicated for elderly patients with early stage nonsmall cell lung cancer, in the era of stereotactic body radiotherapy? *Medicine (Baltimore)*. 2016 Oct;95(43):e5212. doi: 10.1097/md.0000000000005212. PMID: 27787380. Exclusion Code: X9.

1182. Ni J, Xu L, Li W, et al. Simultaneous determination of thirteen kinds of amino acid and eight kinds of acylcarnitine in human serum by LC-MS/MS and its application to measure the serum concentration of lung cancer patients. *Biomed Chromatogr*. 2016 Nov;30(11):1796-806. doi: 10.1002/bmc.3755. PMID: 27129889. Exclusion Code: X4.

1183. Nie Y, Li Q, Li F, et al. Integrating PET and CT information to improve diagnostic accuracy for lung nodules: A semiautomatic computer-aided method. *J Nucl Med*. 2006 Jul;47(7):1075-80. PMID: 16818939. Exclusion Code: X3.

1184. Niezink AG, Dollekamp NJ, Elzinga HJ, et al. An instrument dedicated for modelling of pulmonary radiotherapy. *Radiother Oncol*. 2015 Apr;115(1):3-8. doi: 10.1016/j.radonc.2015.03.020. PMID: 25866028. Exclusion Code: X3.

1185. Nikolaidis G, Raji OY, Markopoulou S, et al. DNA methylation biomarkers offer improved diagnostic efficiency in lung cancer. *Cancer Res*. 2012 Nov 15;72(22):5692-701. doi: 10.1158/0008-5472.can-12-2309. PMID: 22962272. Exclusion Code: X7.

1186. Nishida A, Abiru H, Hayashi H, et al. Clinicoradiological outcomes of 33 cases of surgically resected pulmonary pleomorphic carcinoma: correlation with prognostic indicators. *Eur Radiol*. 2016 Jan;26(1):25-31. doi: 10.1007/s00330-015-3811-3. PMID: 25994197. Exclusion Code: X3.

1187. Nishii T, Yokose T, Miyagi Y, et al. Prognostic value of EGFR mutations in surgically resected pathological stage I lung adenocarcinoma. *Asia Pac J Clin Oncol*. 2017 Oct;13(5):e204-e11. doi: 10.1111/ajco.12512. PMID: 27349355. Exclusion Code: X11.

1188. Nishimura S, Takeda A, Sanuki N, et al. Toxicities of organs at risk in the mediastinal and hilar regions following stereotactic body radiotherapy for centrally located lung tumors. *J Thorac Oncol*. 2014 Sep;9(9):1370-6. doi: 10.1097/jto.0000000000000260. PMID: 25122433. Exclusion Code: X3.

1189. Nishio W, Yoshimura M, Maniwa Y, et al. Re-assessment of intentional extended segmentectomy for clinical T1aN0 non-small cell lung cancer. *Ann Thorac Surg*. 2016 Nov;102(5):1702-10. doi: 10.1016/j.athoracsur.2016.05.071. PMID: 27526651. Exclusion Code: X11.

1190. Nitadori J, Bograd AJ, Morales EA, et al. Preoperative consolidation-to-tumor ratio and SUVmax stratify the risk of recurrence in patients undergoing limited resection for lung adenocarcinoma </=2 cm. *Ann Surg Oncol*. 2013 Dec;20(13):4282-8. doi: 10.1245/s10434-013-3212-2. PMID: 23955584. Exclusion Code: X11.

1191. Nomori H, Cong Y, Sugimura H. Limited thoracotomy for segmentectomy: a comparison of postoperative pain with thoracoscopic lobectomy. *Surg Today*. 2016 Nov;46(11):1243-8. doi: 10.1007/s00595-015-1302-4. PMID: 26782290. Exclusion Code: X11.

1192. Nomori H, Mori T, Ikeda K, et al. Segmentectomy for selected cT1N0M0 non-small cell lung cancer: a prospective study at a single institute. *J Thorac Cardiovasc Surg*. 2012 Jul;144(1):87-93. doi: 10.1016/j.jtcvs.2012.03.034. PMID: 22502969. Exclusion Code: X11.

1193. Nomori H, Shiraishi A, Cong Y, et al. Differences in postoperative changes in pulmonary functions following segmentectomy compared with lobectomy. *Eur J Cardiothorac Surg*. 2018 Mar 1;53(3):640-7. doi: 10.1093/ejcts/ezx357. PMID: 29048464. Exclusion Code: X11.

1194. Nugent SM, Golden SE, Thomas CR, Jr., et al. Patient-clinician communication among patients with stage I lung cancer. *Support Care Cancer*. 2018 May;26(5):1625-33. doi: 10.1007/s00520-017-3992-1. PMID: 29209835. Exclusion Code: X8.

1195. Nwaejike N, Elbur E, Malagon I, et al. Is there a role for the high-risk multidisciplinary team meeting in thoracic surgery? *Interact Cardiovasc Thorac Surg*. 2016 Apr;22(4):397-400. doi: 10.1093/icvts/ivv389. PMID: 26810916. Exclusion Code: X3.

1196. Nwogu CE, D'Cunha J, Pang H, et al. VATS lobectomy has better perioperative outcomes than open lobectomy: CALGB 31001, an ancillary analysis of CALGB 140202 (Alliance). *Ann Thorac Surg*. 2015 Feb;99(2):399-405. doi: 10.1016/j.athoracsur.2014.09.018. PMID: 25499481. Exclusion Code: X3.

1197. Obuchowski NA. Predicting readers' diagnostic accuracy with a new CAD algorithm. *Acad Radiol*. 2011 Nov;18(11):1412-9. doi: 10.1016/j.acra.2011.07.007. PMID: 21917487. Exclusion Code: X5.

1198. O'Connor GT, Hatabu H. Lung cancer screening, radiation, risks, benefits, and uncertainty. *JAMA*. 2012 Jun 13;307(22):2434-5. doi: 10.1001/jama.2012.6096. PMID: 22692175. Exclusion Code: X10.

1199. Oechsner M, Chizzali B, Devecka M, et al. Interobserver variability of patient positioning using four different CT datasets for image registration in lung stereotactic body radiotherapy. *Strahlenther Onkol*. 2017 Oct;193(10):831-9. doi: 10.1007/s00066-017-1184-z. PMID: 28726056. Exclusion Code: X8.

1200. Ogawa F, Satoh Y, Iyoda A, et al. Clinical impact of lung age on postoperative readmission in non-small cell lung cancer. *J Surg Res*. 2015 Jan;193(1):442-8. doi: 10.1016/j.jss.2014.08.028. PMID: 25255723. Exclusion Code: X3.

1201. Ogawa Y, Shibamoto Y, Hashizume C, et al. Repeat stereotactic body radiotherapy (SBRT) for local recurrence of non-small cell lung cancer and lung metastasis after first SBRT. *Radiat Oncol*. 2018 Jul 28;13(1):136. doi: 10.1186/s13014-018-1080-4. PMID: 30055636. Exclusion Code: X3.

1202. Oh D, Ahn YC, Seo JM, et al. Potentially curative stereotactic body radiation therapy (SBRT) for single or oligometastasis to the lung. *Acta Oncol*. 2012 May;51(5):596-602. doi: 10.3109/0284186x.2012.681698. PMID: 22548366. Exclusion Code: X3.

1203. Oh DS, Reddy RM, Gorrepati ML, et al. Robotic-Assisted, Video-Assisted Thoracoscopic and Open Lobectomy: Propensity-Matched Analysis of Recent Premier Data. *Ann Thorac Surg*. 2017 Nov;104(5):1733-40. doi: 10.1016/j.athoracsur.2017.06.020. PMID: 29054214. Exclusion Code: X3.

1204. Oh TK, Jeon JH, Lee JM, et al. Investigation of opioid use and long-term oncologic outcomes for non-small cell lung cancer patients treated with surgery. *PLoS One*. 2017;12(7):e0181672. doi: 10.1371/journal.pone.0181672. PMID: 28732026. Exclusion Code: X11.

1205. Ohana M, Jeung MY, Bazille G, et al. Cerebral staging of lung cancer: is one single contrast-enhanced T1-weighted three-dimensional gradient-echo sequence sufficient? *Neuroradiology*. 2014 Aug;56(8):621-7. doi: 10.1007/s00234-014-1366-7. PMID: 24829164. Exclusion Code: X3.

1206. Ohno Y, Koyama H, Nogami M, et al. Whole-body MR imaging vs. FDG-PET: comparison of accuracy of M-stage diagnosis for lung cancer patients. *J Magn Reson Imaging*. 2007 Sep;26(3):498-509. doi: 10.1002/jmri.21031. PMID: 17729341. Exclusion Code: X3.

1207. Ohno Y, Koyama H, Takenaka D, et al. Dynamic MRI, dynamic multidetector-row computed tomography (MDCT), and coregistered 2-[fluorine-18]-fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET)/CT: comparative study of capability for management of pulmonary nodules. *J Magn Reson Imaging*. 2008 Jun;27(6):1284-95. doi: 10.1002/jmri.21348. PMID: 18504748. Exclusion Code: X3.

1208. Ohno Y, Koyama H, Yoshikawa T, et al. Standard-, Reduced-, and No-Dose Thin-Section Radiologic Examinations: Comparison of Capability for Nodule Detection and Nodule Type Assessment in Patients Suspected of Having Pulmonary Nodules. *Radiology*. 2017 Aug;284(2):562-73. doi: 10.1148/radiol.2017161037. PMID: 28263700. Exclusion Code: X5.

1209. Ohno Y, Nishio M, Koyama H, et al. Journal Club: Comparison of assessment of preoperative pulmonary vasculature in patients with non-small cell lung cancer by non-contrast- and 4D contrast-enhanced 3-T MR angiography and contrast-enhanced 64-MDCT. *AJR Am J Roentgenol*. 2014 Mar;202(3):493-506. doi: 10.2214/ajr.13.10833. PMID: 24555585. Exclusion Code: X8.

1210. Ohri N, Tome W, Kalnicki S, et al. Stereotactic body radiation therapy for stage I non-small cell lung cancer: The importance of treatment planning algorithm and evaluation of a tumor control probability model. *Pract Radiat Oncol*. 2018 Mar - Apr;8(2):e33-e9. doi: 10.1016/j.prro.2017.10.002. PMID: 29233523. Exclusion Code: X8.

1211. Ohtaka K, Hida Y, Kaga K, et al. Limited resection and two-staged lobectomy for non-small cell lung cancer with ground-glass opacity. *J Cardiothorac Surg*. 2013 Apr 24;8:111. doi: 10.1186/1749-8090-8-111. PMID: 23618098. Exclusion Code: X11.

1212. Okada A, Hirono T, Watanabe T. Safety and prognosis of limited surgery for octogenarians with non-small-cell lung cancer. *Gen Thorac Cardiovasc Surg*. 2012 Feb;60(2):97-103. doi: 10.1007/s11748-011-0880-3. PMID: 22327854. Exclusion Code: X11.

1213. Okada M, Tsutani Y, Ikeda T, et al. Radical hybrid video-assisted thoracic segmentectomy: long-term results of minimally invasive anatomical sublobar resection for treating lung cancer. *Interact Cardiovasc Thorac Surg*. 2012 Jan;14(1):5-11. doi: 10.1093/icvts/ivr065. PMID: 22108951. Exclusion Code: X11.

1214. Okada S, Shimada J, Kato D, et al. Prolonged air leak following lobectomy can be predicted in lung cancer patients. *Surg Today*. 2017 Aug;47(8):973-9. doi: 10.1007/s00595-016-1467-5. PMID: 28091813. Exclusion Code: X11.

1215. Okada S, Shimada J, Kato D, et al. Clinical significance of prognostic nutritional index after surgical treatment in lung cancer. *Ann Thorac Surg*. 2017 Jul;104(1):296-302. doi: 10.1016/j.athoracsur.2017.01.085. PMID: 28433217. Exclusion Code: X3.

1216. Okada S, Shimada J, Teramukai S, et al. Risk Stratification According to the Prognostic Nutritional Index for Predicting Postoperative Complications After Lung Cancer Surgery. *Ann Surg Oncol*. 2018 May;25(5):1254-61. doi: 10.1245/s10434-018-6368-y. PMID: 29450756. Exclusion Code: X3.

1217. Okamoto J, Kubokura H, Usuda J. Factors determining the choice of surgical procedure in elderly patients with non-small cell lung cancer. *Ann Thorac Cardiovasc Surg*. 2016 Jun 20;22(3):131-8. doi: 10.5761/atcs.oa.15-00365. PMID: 26822739. Exclusion Code: X11.

1218. Okamoto J, Kubokura H, Usuda J. Prognostic effect of incompletely lobulated fissures in p-Stage I non-small-cell lung cancer. *Interact Cardiovasc Thorac Surg*. 2018 Feb 1;26(2):264-70. doi: 10.1093/icvts/ivx305. PMID: 29049783. Exclusion Code: X11.

1219. Okamura K, Takayama K, Izumi M, et al. Diagnostic value of CEA and CYFRA 21-1 tumor markers in primary lung cancer. *Lung Cancer*. 2013 Apr;80(1):45-9. doi: 10.1016/j.lungcan.2013.01.002. PMID: 23352032. Exclusion Code: X5.

1220. 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 Nov 02;306(17):1865-73. doi: 10.1001/jama.2011.1591. PMID: 22031728. Exclusion Code: X5.

1221. Okereke IC, Bates MF, Jankowich MD, et al. Effects of implementation of lung cancer screening at one Veterans Affairs medical center. *Chest*. 2016 Nov;150(5):1023-9. doi: 10.1016/j.chest.2016.08.1431. PMID: 27568228. Exclusion Code: X8.

1222. Oki M, Saka H, Ando M, et al. Endoscopic ultrasound-guided fine needle aspiration and endobronchial ultrasound-guided transbronchial needle aspiration: Are two better than one in mediastinal staging of non-small cell lung cancer? *J Thorac Cardiovasc Surg*. 2014 Oct;148(4):1169-77. doi: 10.1016/j.jtcvs.2014.05.023. PMID: 24930616. Exclusion Code: X3.

1223. Olaiya B, Gilliland CA, Force SD, et al. Preoperative Computed Tomography-Guided Pulmonary Lesion Marking in Preparation for Fluoroscopic Wedge Resection-Rates of Success, Complications, and Pathology Outcomes. *Curr Probl Diagn Radiol*. 2019 Jan;48(1):27-31. doi: 10.1067/j.cpradiol.2017.10.012. PMID: 29203261. Exclusion Code: X11.

1224. Omori T, Tajiri M, Baba T, et al. Pulmonary resection for lung cancer in patients with idiopathic interstitial pneumonia. *Ann Thorac Surg*. 2015 Sep;100(3):954-60. doi: 10.1016/j.athoracsur.2015.03.094. PMID: 26116477. Exclusion Code: X3.

1225. Onaitis MW, Furnary AP, Kosinski AS, et al. Prediction of long-term survival after lung cancer surgery for elderly patients in The Society of Thoracic Surgeons General Thoracic Surgery Database. *Ann Thorac Surg*. 2018 Jan;105(1):309-16. doi: 10.1016/j.athoracsur.2017.06.071. PMID: 29174391. Exclusion Code: X3.

1226. Ong P, Grosu H, Eapen GA, et al. Endobronchial ultrasound-guided transbronchial needle aspiration for systematic nodal staging of lung cancer in patients with N0 disease by computed tomography and integrated positron emission tomography-computed tomography. *Ann Am Thorac Soc*. 2015 Mar;12(3):415-9. doi: 10.1513/AnnalsATS.201409-429OC. PMID: 25584815. Exclusion Code: X3.

1227. Onishi H, Marino K, Yamashita H, et al. Case Series of 23 Patients Who Developed Fatal Radiation Pneumonitis After Stereotactic Body Radiotherapy for Lung Cancer. *Technol Cancer Res Treat*. 2018 Jan 1;17:1533033818801323. doi: 10.1177/1533033818801323. PMID: 30286697. Exclusion Code: X3.

1228. Onishi H, Shioyama Y, Matsumoto Y, et al. Excellent survival! Multi-institutional study of stereotactic body radiation therapy for medically operable and young (70 years old or younger) patients with stage I non-small cell lung cancer. *International journal of radiation oncology*. 2016;96(2):E434-. doi: 10.1016/j.ijrobp.2016.06.1720. PMID: CN-01420424. Exclusion Code: X2.

1229. Onishi H, Shirato H, Nagata Y, et al. Stereotactic body radiotherapy (SBRT) for operable stage I non-small-cell lung cancer: can SBRT be comparable to surgery? *Int J Radiat Oncol Biol Phys*. 2011 Dec 1;81(5):1352-8. doi: 10.1016/j.ijrobp.2009.07.1751. PMID: 20638194. Exclusion Code: X11.

1230. Ooi H, Chen CY, Hsiao YC, et al. Influence of thyroid transcription factor-1 on fluorodeoxyglucose uptake and prognosis of non-small cell lung cancer. *Anticancer Res*. 2014 May;34(5):2467-75. PMID: 24778062. Exclusion Code: X3.

1231. Oor JE, Daniels JM, Debets-Ossenkopp YJ, et al. Bronchial colonization and complications after lung cancer surgery. *Langenbecks Arch Surg*. 2016 Sep;401(6):885-92. doi: 10.1007/s00423-016-1487-z. PMID: 27485548. Exclusion Code: X3.

1232. Oosterhuis JW, Verstegen N, Van Der Elst A, et al. Propensity score-matched analysis of stage I-II non-small cell lung cancer treated by video-assisted thoracoscopic lobectomy or stereotactic ablative radiotherapy. *Interact Cardiovasc Thorac Surg*. 2013;17doi: 10.1093/icvts/ivt288.1. PMID: CN-01007011. Exclusion Code: X2.

1233. Opoka L, Kunikowska J, Podgajny Z, et al. Accuracy of FDG PET/CT in the evaluation of solitary pulmonary lesions - own experience. *Pneumonol Alergol Pol*. 2014;82(3):198-205. doi: 10.5603/PiAP.2014.0027. PMID: 24793147. Exclusion Code: X3.

1234. Ose N, Sawabata N, Minami M, et al. Lymph node metastasis diagnosis using positron emission tomography with 2-[18F] fluoro-2-deoxy-D-glucose as a tracer and computed tomography in surgical cases of non-small cell lung cancer. *Eur J Cardiothorac Surg*. 2012 Jul;42(1):89-92. doi: 10.1093/ejcts/ezr287. PMID: 22290887. Exclusion Code: X6.

1235. O'Shea K, Cameron SJ, Lewis KE, et al. Metabolomic-based biomarker discovery for non-invasive lung cancer screening: a case study. *Biochim Biophys Acta*. 2016 Nov;1860(11 Pt B):2682-7. doi: 10.1016/j.bbagen.2016.07.007. PMID: 27423423. Exclusion Code: X5.

1236. Oskarsdottir GN, Halldorsson H, Sigurdsson MI, et al. Lobectomy for non-small cell lung carcinoma: a nationwide study of short- and long-term survival. *Acta Oncol*. 2017 Jul;56(7):936-42. doi: 10.1080/0284186x.2017.1304652. PMID: 28325129. Exclusion Code: X3.

1237. Oswald N, Halle-Smith J, Kerr A, et al. Perioperative immune function and pain control may underlie early hospital readmission and 90 day mortality following lung cancer resection: A prospective cohort study of 932 patients. *Eur J Surg Oncol*. 2019 May;45(5):863-9. doi: 10.1016/j.ejso.2019.02.001. PMID: 30795954. Exclusion Code: X3.

1238. Otake S, Ohtsuka T, Asakura K, et al. Impact of comorbidity index on morbidity and survival in non-small cell lung cancer. *Asian Cardiovasc Thorac Ann*. 2016 Jan;24(1):30-3. doi: 10.1177/0218492315617834. PMID: 26567555. Exclusion Code: X3.

1239. Oudkerk M, Heuvelmans MA. Screening for lung cancer by imaging: the Nelson study. *Jbr-btr*. 2013 May-Jun;96(3):163-6. PMID: 23971173. Exclusion Code: X8.
1240. Ozawa Y, Abe T, Omae M, et al. Impact of preexisting interstitial lung disease on acute, extensive radiation pneumonitis: retrospective analysis of patients with lung cancer. *PLoS One*. 2015;10(10):e0140437. doi: 10.1371/journal.pone.0140437. PMID: 26460792. Exclusion Code: X3.
1241. Ozawa Y, Hara M, Sakurai K, et al. Diagnostic accuracy of (18)F-2-deoxy-fluoro-D-glucose positron emission tomography for pN2 lymph nodes in patients with lung cancer. *Acta Radiol*. 2010 Mar;51(2):150-5. doi: 10.3109/02841850903485763. PMID: 20092375. Exclusion Code: X3.
1242. Ozeki N, Iwano S, Taniguchi T, et al. Therapeutic surgery without a definitive diagnosis can be an option in selected patients with suspected lung cancer. *Interact Cardiovasc Thorac Surg*. 2014 Nov;19(5):830-7. doi: 10.1093/icvts/ivu233. PMID: 25038121. Exclusion Code: X11.
1243. Pages PB, Delpy JP, Orsini B, et al. Propensity score analysis comparing videothoracoscopic lobectomy with thoracotomy: a French nationwide study. *Ann Thorac Surg*. 2016 Apr;101(4):1370-8. doi: 10.1016/j.athoracsur.2015.10.105. PMID: 26872732. Exclusion Code: X3.
1244. Pages PB, Mordant P, Cazes A, et al. Prognosis of lung cancer resection in patients with previous extra-respiratory solid malignancies. *Eur J Cardiothorac Surg*. 2013 Sep;44(3):534-8. doi: 10.1093/ejcts/ezt031. PMID: 23392106. Exclusion Code: X3.
1245. Pages PB, Mordant P, Grand B, et al. History of multiple previous malignancies should not be a contraindication to the surgical resection of lung cancer. *Ann Thorac Surg*. 2013 Mar;95(3):1000-5. doi: 10.1016/j.athoracsur.2012.11.072. PMID: 23375734. Exclusion Code: X3.
1246. Pairon JC, Andujar P, Rinaldo M, et al. Asbestos exposure, pleural plaques, and the risk of death from lung cancer. *Am J Respir Crit Care Med*. 2014 Dec 15;190(12):1413-20. doi: 10.1164/rccm.201406-1074OC. PMID: 25383951. Exclusion Code: X7.
1247. Pais FM, Shah RA, Vempilly JJ, et al. Transesophageal approach to lung, adrenal biopsy and fiducial placement using endoscopic ultrasonography (EUS): An interventional pulmonology experience. Initial experience of the UCSF-FRETOC (fresno tracheobronchial & oesophageal center) study group. *Respir Med*. 2018 Aug;141:52-5. doi: 10.1016/j.rmed.2018.06.019. PMID: 30053972. Exclusion Code: X11.
1248. Paks M, Leong P, Einsiedel P, et al. Ultralow dose CT for follow-up of solid pulmonary nodules: A pilot single-center study using Bland-Altman analysis. *Medicine (Baltimore)*. 2018 Aug;97(34):e12019. doi: 10.1097/md.0000000000012019. PMID: 30142849. Exclusion Code: X11.
1249. Palade E, Passlick B, Osei-Agyemang T, et al. Video-assisted vs open mediastinal lymphadenectomy for Stage I non-small-cell lung cancer: results of a prospective randomized trial. *Eur J Cardiothorac Surg*. 2013 Aug;44(2):244-9; discussion 9. doi: 10.1093/ejcts/ezs668. PMID: 23295451. Exclusion Code: X11.
1250. Palleschi A, Privitera E, Lazzeri M, et al. Prophylactic continuous positive airway pressure after pulmonary lobectomy: a randomized controlled trial. *J Thorac Dis*. 2018 May;10(5):2829-36. doi: 10.21037/jtd.2018.05.46. PMID: 29997946. Exclusion Code: X6.
1251. Palussiere J, Canella M, Cornelis F, et al. Retrospective review of thoracic neural damage during lung ablation - what the interventional radiologist needs to know about neural thoracic anatomy. *Cardiovasc Intervent Radiol*. 2013 Dec;36(6):1602-13. doi: 10.1007/s00270-013-0597-z. PMID: 23576208. Exclusion Code: X6.
1252. Palussiere J, Lagarde P, Auperin A, et al. Percutaneous lung thermal ablation of non-surgical clinical N0 non-small cell lung cancer: results of eight years' experience in 87 patients from two centers. *Cardiovasc Intervent Radiol*. 2015 Feb;38(1):160-6. doi: 10.1007/s00270-014-0999-6. PMID: 25394595. Exclusion Code: X6.
1253. Pan L, Qiang Y, Yuan J, et al. Rapid retrieval of lung nodule CT images based on hashing and pruning methods. *Biomed Res Int*. 2016;2016:3162649. doi: 10.1155/2016/3162649. PMID: 27995140. Exclusion Code: X3.

1254. Pan TW, Wu B, Xu ZF, et al. Video-assisted thoracic surgery versus thoracotomy for non-small-cell lung cancer. *Asian Pac J Cancer Prev*. 2012;13(2):447-50. PMID: 22524804. Exclusion Code: X3.

1255. Panchabhai TS, Arrossi AV, Patil PD, et al. Unexpected Neoplasms in Lungs Explanted From Lung Transplant Recipients: A Single-Center Experience and Review of Literature. *Transplant Proc*. 2018 Jan - Feb;50(1):234-40. doi: 10.1016/j.transproceed.2017.12.024. PMID: 29407315. Exclusion Code: X3.

1256. Papiashvilli M, Sasson L, Azzam S, et al. Video-assisted thoracic surgery lobectomy versus lobectomy by thoracotomy for lung cancer: pilot study. *Innovations (Phila)*. 2013 Jan-Feb;8(1):6-11. doi: 10.1097/IMI.0b013e31828d5f15. PMID: 23571787. Exclusion Code: X3.

1257. Papiashvilli M, Stav D, Cyjon A, et al. Lobectomy for non-small cell lung cancer: differences in morbidity and mortality between thoracotomy and thoracoscopy. *Innovations (Phila)*. 2012 Jan-Feb;7(1):15-22. doi: 10.1097/IMI.0b013e3182566221. PMID: 22576031. Exclusion Code: X3.

1258. Parashar B, Port J, Arora S, et al. Analysis of stereotactic radiation vs. wedge resection vs. wedge resection plus Cesium-131 brachytherapy in early stage lung cancer. *Brachytherapy*. 2015 Sep-Oct;14(5):648-54. doi: 10.1016/j.brachy.2015.04.001. PMID: 25998071. Exclusion Code: X10.

1259. Pardolesi A, Park B, Petrella F, et al. Robotic anatomic segmentectomy of the lung: technical aspects and initial results. *Ann Thorac Surg*. 2012 Sep;94(3):929-34. doi: 10.1016/j.athoracsur.2012.04.086. PMID: 22748642. Exclusion Code: X3.

1260. Park B, Lee G, Kim HK, et al. A retrospective comparative analysis of elderly and younger patients undergoing pulmonary resection for stage I non-small cell lung cancer. *World J Surg Oncol*. 2016 Jan 19;14(1):13. doi: 10.1186/s12957-015-0762-8. PMID: 26787343. Exclusion Code: X10.

1261. Park BJ. Robotic lobectomy for non-small cell lung cancer: long-term oncologic results. *Thorac Surg Clin*. 2014 May;24(2):157-62, vi. doi: 10.1016/j.thorsurg.2014.02.011. PMID: 24780419. Exclusion Code: X11.

1262. Park BJ, Melfi F, Mussi A, et al. Robotic lobectomy for non-small cell lung cancer (NSCLC): long-term oncologic results. *J Thorac Cardiovasc Surg*. 2012 Feb;143(2):383-9. doi: 10.1016/j.jtcvs.2011.10.055. PMID: 22104677. Exclusion Code: X3.

1263. Park ER, Gareen IF, Jain A, et al. Examining whether lung screening changes risk perceptions: National Lung Screening Trial participants at 1-year follow-up. *Cancer*. 2013 Apr 1;119(7):1306-13. doi: 10.1002/cncr.27925. PMID: 23280348. Exclusion Code: X11.

1264. Park HS, Harder EM, Mancini BR, et al. Central versus peripheral tumor location: influence on survival, local control, and toxicity following stereotactic body radiotherapy for primary non-small-cell lung cancer. *J Thorac Oncol*. 2015 May;10(5):832-7. doi: 10.1097/jto.0000000000000484. PMID: 25634007. Exclusion Code: X3.

1265. Park S, Nam BH, Yang HR, et al. Individualized risk prediction model for lung cancer in Korean men. *PLoS One*. 2013;8(2):e54823. doi: 10.1371/journal.pone.0054823. PMID: 23408946. Exclusion Code: X7.

1266. Park SB, Choi JY, Moon SH, et al. Prognostic value of volumetric metabolic parameters measured by [18F]fluorodeoxyglucose-positron emission tomography/computed tomography in patients with small cell lung cancer. *Cancer Imaging*. 2014 Apr 22;14:2. doi: 10.1186/1470-7330-14-2. PMID: 25609313. Exclusion Code: X3.

1267. Park SL, Fesinmeyer MD, Timofeeva M, et al. Pleiotropic associations of risk variants identified for other cancers with lung cancer risk: the PAGE and TRICL consortia. *J Natl Cancer Inst*. 2014 Apr;106(4):dju061. doi: 10.1093/jnci/dju061. PMID: 24681604. Exclusion Code: X7.

1268. Park SY, Cho A, Yu WS, et al. Prognostic value of total lesion glycolysis by 18F-FDG PET/CT in surgically resected stage IA non-small cell lung cancer. *J Nucl Med*. 2015 Jan;56(1):45-9. doi: 10.2967/jnumed.114.147561. PMID: 25525185. Exclusion Code: X11.

1269. Park SY, Lee HS, Jang HJ, et al. Wedge bronchoplastic lobectomy for non-small cell lung cancer as an alternative to sleeve lobectomy. *J Thorac Cardiovasc Surg*. 2012 Apr;143(4):825-31.e3. doi: 10.1016/j.jtcvs.2011.10.057. PMID: 22104687. Exclusion Code: X3.

1270. Pastorino U, Boffi R, Marchiano A, et al. Stopping smoking reduces mortality in low-dose computed tomography screening participants. *J Thorac Oncol*. 2016 May;11(5):693-9. doi: 10.1016/j.jtho.2016.02.011. PMID: 26921675. Exclusion Code: X8.

1271. Pastorino U, Morelli D, Marchiano A, et al. Inflammatory status and lung function predict mortality in lung cancer screening participants. *Eur J Cancer Prev*. 2018 Jul;27(4):289-95. doi: 10.1097/cej.0000000000000342. PMID: 28333763. Exclusion Code: X4.

1272. Pastorino U, Rossi M, Rosato V, et al. Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial. *Eur J Cancer Prev*. 2012 May;21(3):308-15. doi: 10.1097/CEJ.0b013e328351e1b6. PMID: 22465911. Exclusion Code: X17.

1273. Pastorino U, Silva M, Sestini S, et al. Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy. *Ann Oncol*. 2019 Jun 5doi: 10.1093/annonc/mdz169. PMID: 31168572. Exclusion Code: X17.

1274. Patel MV, Ahmed O, Jilani D, et al. Computed tomography-guided percutaneous lung biopsy: impact of lesion proximity to diaphragm on biopsy yield and pneumothorax rate. *J Thorac Imaging*. 2014 Nov;29(6):344-9. doi: 10.1097/rti.0000000000000112. PMID: 25314026. Exclusion Code: X3.

1275. Patel S, Cho A, Lamont A, et al. Implementing a community hospital lung cancer screening program: a multidisciplinary program and a standardized reporting system. *J Am Coll Radiol*. 2014 May;11(5):527-30. doi: 10.1016/j.jacr.2013.09.004. PMID: 24529982. Exclusion Code: X10.

1276. Pathak RS, Tibdewal AR, S GL, et al. Volume changes with stereotactic body radiation therapy in early lung cancer: Time trends and outcomes. *J Med Imaging Radiat Oncol*. 2016 Oct;60(5):661-7. doi: 10.1111/1754-9485.12476. PMID: 27241661. Exclusion Code: X10.

1277. Patz EF, Jr., Greco E, Gatsonis C, et al. Lung cancer incidence and mortality in National Lung Screening Trial participants who underwent low-dose CT prevalence screening: a retrospective cohort analysis of a randomised, multicentre, diagnostic screening trial. *Lancet Oncol*. 2016 May;17(5):590-9. doi: 10.1016/s1470-2045(15)00621-x. PMID: 27009070. Exclusion Code: X7.

1278. Paul S, Isaacs AJ, Treasure T, et al. Long term survival with thoracoscopic versus open lobectomy: propensity matched comparative analysis using SEER-Medicare database. *BMJ*. 2014 Oct 2;349:g5575. doi: 10.1136/bmj.g5575. PMID: 25277994. Exclusion Code: X3.

1279. Paul S, Lee PC, Mao J, et al. Long term survival with stereotactic ablative radiotherapy (SABR) versus thoracoscopic sublobar lung resection in elderly people: national population based study with propensity matched comparative analysis. *BMJ*. 2016 Jul 8;354:i3570. doi: 10.1136/bmj.i3570. PMID: 27400862. Exclusion Code: X13.

1280. Pawaroo D, Cummings NM, Musonda P, et al. Non-small cell lung carcinoma: accuracy of PET/CT in determining the size of T1 and T2 primary tumors. *AJR Am J Roentgenol*. 2011 May;196(5):1176-81. doi: 10.2214/ajr.10.4980. PMID: 21512089. Exclusion Code: X3.

1281. Paximadis P, Beebe-Dimmer JL, George J, et al. Comparing Treatment Strategies for Stage I Small-cell lung Cancer. *Clin Lung Cancer*. 2018 Sep;19(5):e559-e65. doi: 10.1016/j.cllc.2018.03.017. PMID: 29656869. Exclusion Code: X3.

1282. Pedersen JH, Petersen RH, Hansen HJ. Lung cancer screening trials: Denmark and beyond. *J Thorac Cardiovasc Surg*. 2012 Sep;144(3):S7-8. doi: 10.1016/j.jtcvs.2012.03.066. PMID: 22513316. Exclusion Code: X2.

1283. Peikert T, Duan F, Rajagopalan S, et al. Novel high-resolution computed tomography-based radiomic classifier for screen-identified pulmonary nodules in the National Lung Screening Trial. *PLoS One*. 2018;13(5):e0196910. doi: 10.1371/journal.pone.0196910. PMID: 29758038. Exclusion Code: X8.

1284. Peled N, Hakim M, Bunn PA, Jr., et al. Non-invasive breath analysis of pulmonary nodules. *J Thorac Oncol*. 2012 Oct;7(10):1528-33. doi: 10.1097/JTO.0b013e3182637d5f. PMID: 22929969. Exclusion Code: X3.

1285. Peng H, Wang J, Li J, et al. A circulating non-coding RNA panel as an early detection predictor of non-small cell lung cancer. *Life Sci*. 2016 Apr 15;151:235-42. doi: 10.1016/j.lfs.2016.03.002. PMID: 26946307. Exclusion Code: X3.

1286. Peng M, Li Z, Hu H, et al. Pulmonary ground-glass nodules diagnosis: mean change rate of peak CT number as a discriminative factor of pathology during a follow-up. *Br J Radiol*. 2016;89(1058):20150556. doi: 10.1259/bjr.20150556. PMID: 26562098. Exclusion Code: X3.

1287. Peng Z, Liu Q, Li M, et al. Comparison of (11)C-choline PET/CT and enhanced CT in the evaluation of patients with pulmonary abnormalities and locoregional lymph node involvement in lung cancer. *Clin Lung Cancer*. 2012 Jul;13(4):312-20. doi: 10.1016/j.cllc.2011.09.005. PMID: 22182444. Exclusion Code: X3.

1288. Penn A, Ma M, Chou BB, et al. Inter-reader variability when applying the 2013 Fleischner guidelines for potential solitary subsolid lung nodules. *Acta Radiol*. 2015 Oct;56(10):1180-6. doi: 10.1177/0284185114551975. PMID: 25293951. Exclusion Code: X3.

1289. Pepek JM, Marks LB, Berry MF, et al. Accuracy of positron emission tomography in identifying hilar (N1) lymph node involvement in non-small cell lung cancer: Implications for stereotactic body radiation therapy. *Pract Radiat Oncol*. 2015 Mar-Apr;5(2):79-84. doi: 10.1016/j.prro.2014.05.002. PMID: 25413417. Exclusion Code: X3.

1290. Perandini S, Soardi GA, Larici AR, et al. Multicenter external validation of two malignancy risk prediction models in patients undergoing 18F-FDG-PET for solitary pulmonary nodule evaluation. *Eur Radiol*. 2017 May;27(5):2042-6. doi: 10.1007/s00330-016-4580-3. PMID: 27631108. Exclusion Code: X3.

1291. Perandini S, Soardi GA, Motton M, et al. Limited value of logistic regression analysis in solid solitary pulmonary nodules characterization: a single-center experience on 288 consecutive cases. *J Surg Oncol*. 2014 Dec;110(7):883-7. doi: 10.1002/jso.23730. PMID: 25088475. Exclusion Code: X11.

1292. Percac-Lima S, Ashburner JM, Rigotti N, et al. Lung cancer screening patient navigation for current smokers in community health centers: a randomized controlled trial. *J Clin Oncol*. 2017;35(15)PMID: CN-01781835. Exclusion Code: X2.

1293. Percac-Lima S, Ashburner JM, Rigotti NA, et al. Patient navigation for lung cancer screening among current smokers in community health centers a randomized controlled trial. *Cancer medicine*. 2018;7(3):894-902. doi: 10.1002/cam4.1297. PMID: CN-01764144. Exclusion Code: X6.

1294. Percac-Lima S, Ashburner JM, Shepard JA, et al. Timeliness of recommended follow-up after an abnormal finding on diagnostic chest CT in smokers at high risk of developing lung cancer. *J Am Coll Radiol*. 2016 May;13(5):497-504. doi: 10.1016/j.jacr.2016.01.007. PMID: 26924163. Exclusion Code: X11.

1295. Perisinakis K, Seimenis I, Tzedakis A, et al. Radiation burden and associated cancer risk for a typical population to be screened for lung cancer with low-dose CT: A phantom study. *Eur Radiol*. 2018 Oct;28(10):4370-8. doi: 10.1007/s00330-018-5373-7. PMID: 29651767. Exclusion Code: X10.

1296. Persson GF, Nygaard DE, Hollensen C, et al. Interobserver delineation variation in lung tumour stereotactic body radiotherapy. *Br J Radiol*. 2012 Sep;85(1017):e654-60. doi: 10.1259/bjr/76424694. PMID: 22919015. Exclusion Code: X8.

1297. Peschke A, Wiedemann B, Hoffken G, et al. Forceps biopsy and suction catheter for sampling in pulmonary nodules and infiltrates. *Eur Respir J*. 2012 Jun;39(6):1432-6. doi: 10.1183/09031936.00024111. PMID: 22005922. Exclusion Code: X3.

1298. Peters S, Michielin O, Zimmermann S. Dramatic response induced by vemurafenib in a BRAF V600E-mutated lung adenocarcinoma. *J Clin Oncol*. 2013 Jul 10;31(20):e341-4. doi: 10.1200/jco.2012.47.6143. PMID: 23733758. Exclusion Code: X10.

1299. Petersen RH, Hansen HJ, Dirksen A, et al. Lung cancer screening and video-assisted thoracic surgery. *J Thorac Oncol*. 2012 Jun;7(6):1026-31. doi: 10.1097/JTO.0b013e31824fe942. PMID: 22588154. Exclusion Code: X3.

1300. Petit SF, van Elmpt W. Accurate prediction of target dose-escalation and organ-at-risk dose levels for non-small cell lung cancer patients. *Radiother Oncol*. 2015 Dec;117(3):453-8. doi: 10.1016/j.radonc.2015.07.040. PMID: 26306678. Exclusion Code: X3.

1301. Phillips M, Bauer TL, Cataneo RN, et al. Blinded validation of breath biomarkers of lung cancer, a potential ancillary to chest CT screening. *PLoS One*. 2015;10(12):e0142484. doi: 10.1371/journal.pone.0142484. PMID: 26698306. Exclusion Code: X5.

1302. Pierson C, Grinchak T, Sokolovic C, et al. Response criteria in solid tumors (PERCIST/RECIST) and SUVmax in early-stage non-small cell lung cancer patients treated with stereotactic body radiotherapy. *Radiat Oncol*. 2018 Feb 27;13(1):34. doi: 10.1186/s13014-018-0980-7. PMID: 29486779. Exclusion Code: X8.

1303. Pilyugin M, Descloux P, Andre PA, et al. BARD1 serum autoantibodies for the detection of lung cancer. *PLoS One*. 2017;12(8):e0182356. doi: 10.1371/journal.pone.0182356. PMID: 28786985. Exclusion Code: X5.

1304. Pinato DJ, Shiner RJ, Seckl MJ, et al. Prognostic performance of inflammation-based prognostic indices in primary operable non-small cell lung cancer. *Br J Cancer*. 2014 Apr 15;110(8):1930-5. doi: 10.1038/bjc.2014.145. PMID: 24667648. Exclusion Code: X3.

1305. Pine SR, Mechanic LE, Enewold L, et al. Differential serum cytokine levels and risk of lung cancer between African and European Americans. *Cancer Epidemiol Biomarkers Prev*. 2016 Mar;25(3):488-97. doi: 10.1158/1055-9965.epi-15-0378. PMID: 26711330. Exclusion Code: X7.

1306. Pinheiro LC, Reeve BB. Investigating the prognostic ability of health-related quality of life on survival: a prospective cohort study of adults with lung cancer. *Support Care Cancer*. 2018 Nov;26(11):3925-32. doi: 10.1007/s00520-018-4265-3. PMID: 29777380. Exclusion Code: X3.

1307. Pinheiro LC, Zagar TM, Reeve BB. The prognostic value of pre-diagnosis health-related quality of life on survival: a prospective cohort study of older Americans with lung cancer. *Qual Life Res*. 2017 Jul;26(7):1703-12. doi: 10.1007/s11136-017-1515-7. PMID: 28194618. Exclusion Code: X3.

1308. Pinsky PF, Dunn B, Gierada D, et al. Incidental renal tumours on low-dose CT lung cancer screening exams. *J Med Screen*. 2017 Jun;24(2):104-9. doi: 10.1177/0969141316657115. PMID: 28482765. Exclusion Code: X8.

1309. Pinsky PF, Gierada DS, Nath PH, et al. Lung cancer risk associated with new solid nodules in the National Lung Screening Trial. *AJR Am J Roentgenol*. 2017 Nov;209(5):1009-14. doi: 10.2214/ajr.17.18252. PMID: 28898131. Exclusion Code: X7.

1310. Pinsky PF, Marcus PM, Kramer BS, et al. Diagnostic procedures after a positive spiral computed tomography lung carcinoma screen. *Cancer*. 2005 Jan 1;103(1):157-63. doi: 10.1002/cncr.20746. PMID: 15529306. Exclusion Code: X8.

1311. Pinsky PF, Nath PH, Gierada DS, et al. Short- and long-term lung cancer risk associated with noncalcified nodules observed on low-dose CT. *Cancer Prev Res (Phila)*. 2014 Dec;7(12):1179-85. doi: 10.1158/1940-6207.capr-13-0438. PMID: 24755313. Exclusion Code: X8.

1312. Pinsky PF, Zhu CS, Kramer BS. Lung cancer risk by years since quitting in 30+ pack year smokers. *J Med Screen*. 2015 Sep;22(3):151-7. doi: 10.1177/0969141315579119. PMID: 25926339. Exclusion Code: X7.

1313. Planquette B, Le Pimpec-Barthes F, Trinquart L, et al. Early respiratory acidosis is a new risk factor for pneumonia after lung resection. *Interact Cardiovasc Thorac Surg*. 2012 Mar;14(3):244-8. doi: 10.1093/icvts/ivr115. PMID: 22184462. Exclusion Code: X3.

1314. Pletnikoff PP, Laukkanen JA, Tuomainen TP, et al. Cardiorespiratory fitness, C-reactive protein and lung cancer risk: a prospective population-based cohort study. *Eur J Cancer*. 2015 Jul;51(11):1365-70. doi: 10.1016/j.ejca.2015.04.020. PMID: 26008754. Exclusion Code: X4.

1315. Pletnikoff PP, Tuomainen TP, Laukkanen JA, et al. Cardiorespiratory fitness and lung cancer risk: a prospective population-based cohort study. *J Sci Med Sport*. 2016 Feb;19(2):98-102. doi: 10.1016/j.jsams.2015.02.008. PMID: 25800392. Exclusion Code: X4.

1316. Pollom EL, Qian Y, Durkee BY, et al. Hypofractionated intensity-modulated radiotherapy for patients with non-small-cell lung cancer. *Clin Lung Cancer*. 2016 Nov;17(6):588-94. doi: 10.1016/j.cllc.2016.05.024. PMID: 27378172. Exclusion Code: X6.

1317. Pompe E, de Jong PA, de Jong WU, et al. Inter-observer and inter-examination variability of manual vertebral bone attenuation measurements on computed tomography. *Eur Radiol*. 2016 Sep;26(9):3046-53. doi: 10.1007/s00330-015-4145-x. PMID: 26801161. Exclusion Code: X8.

1318. Pompe E, de Jong PA, Lynch DA, et al. Computed tomographic findings in subjects who died from respiratory disease in the National Lung Screening Trial. *Eur Respir J*. 2017 Apr;49(4)doi: 10.1183/13993003.01814-2016. PMID: 28424361. Exclusion Code: X3.

1319. Pompili C, Franks KN, Brunelli A, et al. Patient reported outcomes following video assisted thoracoscopic (VATS) resection or stereotactic ablative body radiotherapy (SABR) for treatment of non-small cell lung cancer: protocol for an observational pilot study (LiLAC). *J Thorac Dis*. 2017 Aug;9(8):2703-13. doi: 10.21037/jtd.2017.07.35. PMID: 28932579. Exclusion Code: X10.

1320. Pompili C, Salati M, Refai M, et al. Preoperative quality of life predicts survival following pulmonary resection in stage I non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2013 May;43(5):905-10. doi: 10.1093/ejcts/ezs532. PMID: 23091229. Exclusion Code: X11.

1321. Pompili C, Salati M, Refai M, et al. Recurrent air leak soon after pulmonary lobectomy: an analysis based on an electronic airflow evaluationdagger. *Eur J Cardiothorac Surg*. 2016 Apr;49(4):1091-4; discussion 4. doi: 10.1093/ejcts/ezv335. PMID: 26410629. Exclusion Code: X3.

1322. Potaris K, Athanasiou A, Konstantinou M, et al. Pulmonary hypertension after pneumonectomy for lung cancer. *Asian Cardiovasc Thorac Ann*. 2014 Nov;22(9):1072-9. doi: 10.1177/0218492314527992. PMID: 24637028. Exclusion Code: X3.

1323. Pou Ucha JL, Nogueiras Alonso JM, Alvarez Paez AM, et al. Diagnostic yield of baseline and follow-up PET/CT studies in ablative therapy for non-small cell lung cancer. *Rev Esp Med Nucl Imagen Mol*. 2012 Nov-Dec;31(6):301-7. doi: 10.1016/j.remn.2012.01.001. PMID: 23084012. Exclusion Code: X6.

1324. Poullis M, Shackcloth M, Page R, et al. Metastatic index of non-small-cell lung cancer and long-term survival. *Asian Cardiovasc Thorac Ann*. 2015 Feb;23(2):185-90. doi: 10.1177/0218492314545833. PMID: 25107893. Exclusion Code: X5.

1325. Poulou LS, Tsagouli P, Ziakas PD, et al. Computed tomography-guided needle aspiration and biopsy of pulmonary lesions: a single-center experience in 1000 patients. *Acta Radiol*. 2013 Jul;54(6):640-5. doi: 10.1177/0284185113481595. PMID: 23528565. Exclusion Code: X3.

1326. Pozo-Rodriguez F, Martin de Nicolas JL, Sanchez-Nistal MA, et al. Accuracy of helical computed tomography and [18F] fluorodeoxyglucose positron emission tomography for identifying lymph node mediastinal metastases in potentially resectable non-small-cell lung cancer. *J Clin Oncol*. 2005 Nov 20;23(33):8348-56. doi: 10.1200/jco.2004.00.6361. PMID: 16219937. Exclusion Code: X3.

1327. Pozzi P, Munarini E, Bravi F, et al. A combined smoking cessation intervention within a lung cancer screening trial: a pilot observational study. *Tumori*. 2015 May-Jun;101(3):306-11. doi: 10.5301/tj.5000282. PMID: 25838249. Exclusion Code: X7.

1328. Presley CJ, Soulos PR, Tinetti M, et al. Treatment burden of Medicare beneficiaries with stage I non-small-cell lung cancer. *J Oncol Pract*. 2017 Feb;13(2):e98-e107. doi: 10.1200/jop.2016.014100. PMID: 27997301. Exclusion Code: X8.

1329. Price A, Yellowlees A, Keerie C, et al. Radical radiotherapy with or without gemcitabine in patients with early stage medically inoperable non-small cell lung cancer. *Lung Cancer*. 2012 Sep;77(3):532-6. doi: 10.1016/j.lungcan.2012.05.089. PMID: 22672970. Exclusion Code: X6.

1330. Printz C. Off the mark: current lung cancer screening guidelines miss those most at risk. *Cancer*. 2015 Aug 01;121(15):2477-8. doi: 10.1002/cncr.28999. PMID: 26198788. Exclusion Code: X10.

1331. Priola AM, Priola SM, Cataldi A, et al. Diagnostic accuracy and complication rate of CT-guided fine needle aspiration biopsy of lung lesions: a study based on the experience of the cytopathologist. *Acta Radiol*. 2010 Jun;51(5):527-33. doi: 10.3109/02841851003691979. PMID: 20429755. Exclusion Code: X3.

1332. Priola AM, Priola SM, Giaj-Levra M, et al. Clinical implications and added costs of incidental findings in an early detection study of lung cancer by using low-dose spiral computed tomography. *Clin Lung Cancer*. 2013 Mar;14(2):139-48. doi: 10.1016/j.cllc.2012.05.005. PMID: 22868220. Exclusion Code: X7.

1333. Prionas ND, von Eyben R, Yi E, et al. Increases in serial pretreatment (18)F-FDG PET-CT metrics predict survival in early stage non-small cell lung cancer treated with stereotactic ablative radiation therapy. *Adv Radiat Oncol*. 2019 Apr-Jun;4(2):429-37. doi: 10.1016/j.adro.2018.11.006. PMID: 31011689. Exclusion Code: X13.

1334. Pritchett MA, Schampaert S, de Groot JAH, et al. Cone-Beam CT With Augmented Fluoroscopy Combined With Electromagnetic Navigation Bronchoscopy for Biopsy of Pulmonary Nodules. *J Bronchology Interv Pulmonol*. 2018 Oct;25(4):274-82. doi: 10.1097/lbr.0000000000000536. PMID: 30179922. Exclusion Code: X11.

1335. Prosch H, Stadler A, Schilling M, et al. CT fluoroscopy-guided vs. multislice CT biopsy mode-guided lung biopsies: accuracy, complications and radiation dose. *Eur J Radiol*. 2012 May;81(5):1029-33. doi: 10.1016/j.ejrad.2011.01.064. PMID: 21752567. Exclusion Code: X3.

1336. Pruitt SL, Laccetti AL, Xuan L, et al. Revisiting a longstanding clinical trial exclusion criterion: impact of prior cancer in early-stage lung cancer. *Br J Cancer*. 2017 Mar 14;116(6):717-25. doi: 10.1038/bjc.2017.27. PMID: 28196065. Exclusion Code: X8.

1337. Puri V, Crabtree T, Kymes S, et al. A comparison of surgical intervention and stereotactic body radiation therapy for stage I lung cancer in high-risk patients: a decision analysis (Structured abstract). *J Thorac Cardiovasc Surg*. 2012;143(2):428-36. PMID: NHSEED-22012003670. Exclusion Code: X10.

1338. Puri V, Patel A, Majumder K, et al. Intraoperative conversion from video-assisted thoracoscopic surgery lobectomy to open thoracotomy: a study of causes and implications. *J Thorac Cardiovasc Surg*. 2015 Jan;149(1):55-61, 2.e1. doi: 10.1016/j.jtcvs.2014.08.074. PMID: 25439768. Exclusion Code: X8.

1339. Pyenson BS, Sander MS, Jiang Y, et al. An actuarial analysis shows that offering lung cancer screening as an insurance benefit would save lives at relatively low cost. *Health Aff (Millwood)*. 2012 Apr;31(4):770-9. doi: 10.1377/hlthaff.2011.0814. PMID: 22492894. Exclusion Code: X8.

1340. Pyo JS, Kang G, Sohn JH. ALK immunohistochemistry for ALK gene rearrangement screening in non-small cell lung cancer: a systematic review and meta-analysis. *Int J Biol Markers*. 2016 Dec 23;31(4):e413-e21. doi: 10.5301/jbm.5000218. PMID: 27338643. Exclusion Code: X5.

1341. Qadri SS, Chaudhry MA, Cale A, et al. Short- and long-term outcomes of pneumonectomy in a tertiary center. *Asian Cardiovasc Thorac Ann*. 2016 Mar;24(3):250-6. doi: 10.1177/0218492316629851. PMID: 26843470. Exclusion Code: X11.

1342. Qadri SS, Jarvis M, Ariyaratnam P, et al. Could Thoracoscore predict postoperative mortality in patients undergoing pneumonectomy? *Eur J Cardiothorac Surg*. 2014 May;45(5):864-9. doi: 10.1093/ejcts/ezt517. PMID: 24212768. Exclusion Code: X3.

1343. Qi H, Wan C, Zhang L, et al. Early effective treatment of small pulmonary nodules with video-assisted thoracoscopic surgery combined with CT-guided dual-barbed hookwire localization. *Oncotarget*. 2017 Jun 13;8(24):38793-801. doi: 10.18632/oncotarget.17044. PMID: 28455967. Exclusion Code: X11.

1344. Qian DC, Han Y, Byun J, et al. A novel pathway-based approach improves lung cancer risk prediction using germline genetic variations. *Cancer Epidemiol Biomarkers Prev*. 2016 Aug;25(8):1208-15. doi: 10.1158/1055-9965.epi-15-1318. PMID: 27222311. Exclusion Code: X4.

1345. Qian H, Gao F, Wang H, et al. The efficacy and safety of crizotinib in the treatment of anaplastic lymphoma kinase-positive non-small cell lung cancer: a meta-analysis of clinical trials. *BMC Cancer*. 2014 Sep 19;14:683. doi: 10.1186/1471-2407-14-683. PMID: 25239305. Exclusion Code: X10.

1346. Qian LQ, Zhao XJ, Luo QQ, et al. Experience of segmentectomy from 36 Chinese patients with non-small cell lung cancer at stage I. *Chin Med J (Engl)*. 2013 Jul;126(14):2687-93. PMID: 23876897. Exclusion Code: X11.

1347. Qian Y, Zhu H, Pollom EL, et al. Sinoatrial node toxicity after stereotactic ablative radiation therapy to lung tumors. *Pract Radiat Oncol*. 2017 Nov - Dec;7(6):e525-e9. doi: 10.1016/j.prro.2017.04.005. PMID: 28669706. Exclusion Code: X16.

1348. Qiang G, Liang C, Guo Y, et al. Video-assisted thoracoscopic lobectomy for elderly nonsmall cell lung cancer: Short-term and long-term outcomes. *J Cancer Res Ther*. 2015 Oct-Dec;11(4):793-7. doi: 10.4103/0973-1482.140930. PMID: 26881520. Exclusion Code: X3.

1349. Qiang G, Liang C, Xiao F, et al. Impact of chronic obstructive pulmonary disease on postoperative recurrence in patients with resected non-small-cell lung cancer. *Int J Chron Obstruct Pulmon Dis*. 2016;11:43-9. doi: 10.2147/copd.s97411. PMID: 26766906. Exclusion Code: X11.

1350. Qiu C, Qu X, Shen H, et al. Evaluation of prognostic nutritional index in patients undergoing radical surgery with nonsmall cell lung cancer. *Nutr Cancer*. 2015;67(5):741-7. doi: 10.1080/01635581.2015.1032430. PMID: 25941961. Exclusion Code: X3.

1351. Qiu C, Wang G, Xu J, et al. Sublobectomy versus lobectomy for stage I non-small cell lung cancer in the elderly. *Int J Surg*. 2017 Jan;37:1-7. doi: 10.1016/j.ijsu.2016.11.090. PMID: 27890654. Exclusion Code: X11.

1352. Quadrelli S, Lyons G, Colt H, et al. Clinical characteristics and prognosis of incidentally detected lung cancers. *Int J Surg Oncol*. 2015;2015:287604. doi: 10.1155/2015/287604. PMID: 25685550. Exclusion Code: X3.

1353. Quero-Valenzuela F, Piedra-Fernandez I, Martinez-Ceres M, et al. Predictors for 30-day readmission after pulmonary resection for lung cancer. *J Surg Oncol*. 2018 May;117(6):1239-45. doi: 10.1002/jso.24973. PMID: 29355966. Exclusion Code: X11.

1354. Raghavan G, Shaverdian N, Chan S, et al. Comparing Outcomes of Patients With Early-Stage Non-Small-Cell Lung Cancer Treated With Stereotactic Body Radiotherapy Based on Frailty Status. *Clin Lung Cancer*. 2018 Sep;19(5):e759-e66. doi: 10.1016/j.cllc.2018.05.008. PMID: 29954680. Exclusion Code: X3.

1355. Raghunath S, Maldonado F, Rajagopalan S, et al. Noninvasive risk stratification of lung adenocarcinoma using quantitative computed tomography. *J Thorac Oncol*. 2014 Nov;9(11):1698-703. doi: 10.1097/jto.0000000000000319. PMID: 25170645. Exclusion Code: X3.

1356. Rai A, Doria-Rose VP, Silvestri GA, et al. Evaluating lung cancer screening uptake, outcomes, and costs in the United States: challenges with existing data and recommendations for improvement. *J Natl Cancer Inst*. 2019 Apr 1;111(4):342-9. doi: 10.1093/jnci/djy228. PMID: 30698792. Exclusion Code: X10.

1357. Raji O, Agbaje OF, Duffy SW, et al. The predictive ability of LLP lung cancer risk model with and without seizure 6-Like (SEZ6L) gene. *J Thorac Oncol*. 2009(4):S408-9. Exclusion Code: X2.

1358. Raji OY, Agbaje OF, Duffy SW, et al. Incorporation of a genetic factor into an epidemiologic model for prediction of individual risk of lung cancer: the Liverpool Lung Project. *Cancer Prev Res (Phila)*. 2010 May;3(5):664-9. doi: 10.1158/1940-6207.CAPR-09-0141. PMID: 20424129. Exclusion Code: X4.

1359. Raji OY, Duffy SW, Agbaje OF, et al. Predictive accuracy of the Liverpool Lung Project risk model for stratifying patients for computed tomography screening for lung cancer: a case-control and cohort validation study. *Ann Intern Med*. 2012 Aug 21;157(4):242-50. doi: 10.7326/0003-4819-157-4-201208210-00004. PMID: 22910935. Exclusion Code: X7.

1360. Ramella S, Spoto S, Fiore M, et al. A clinical score, including biohumoral parameters, is a useful pretest index to discriminate pulmonary infections from radiation damage in chemoradiation-treated lung cancer patients. *Cancer Invest*. 2014 May;32(4):110-4. doi: 10.3109/07357907.2014.883525. PMID: 24548301. Exclusion Code: X3.

1361. Ramos R, Girard P, Masuet C, et al. Mediastinal lymph node dissection in early-stage non-small cell lung cancer: totally thoracoscopic vs thoracotomy. *Eur J Cardiothorac Surg*. 2012 Jun;41(6):1342-8; discussion 8. doi: 10.1093/ejcts/ezr220. PMID: 22228841. Exclusion Code: X3.

1362. Ramos R, Masuet C, Gossot D. Lobectomy for early-stage lung carcinoma: a cost analysis of full thoracoscopy versus posterolateral thoracotomy. *Surg Endosc*. 2012 Feb;26(2):431-7. doi: 10.1007/s00464-011-1891-y. PMID: 21898011. Exclusion Code: X11.

1363. Ramos R, Nadal E, Peiro I, et al. Preoperative nutritional status assessment predicts postoperative outcomes in patients with surgically resected non-small cell lung cancer. *Eur J Surg Oncol*. 2018 Sep;44(9):1419-24. doi: 10.1016/j.ejso.2018.03.026. PMID: 29685760. Exclusion Code: X11.

1364. Rangel MP, Antonangelo L, Acencio MMP, et al. Detection of sputum cofilin-1 as indicator of malignancy. *Braz J Med Biol Res*. 2018;51(8):e7138. doi: 10.1590/1414-431x20187138. PMID: 29846436. Exclusion Code: X10.

1365. Rangel MP, de Sa VK, Martins V, et al. Tissue hyaluronan expression, as reflected in the sputum of lung cancer patients, is an indicator of malignancy. *Braz J Med Biol Res*. 2015 Jun;48(6):557-67. doi: 10.1590/1414-431x20144300. PMID: 25992645. Exclusion Code: X4.

1366. Rauschenbach BM, Mackowiak L, Malhotra HK. A dosimetric comparison of three-dimensional conformal radiotherapy, volumetric-modulated arc therapy, and dynamic conformal arc therapy in the treatment of non-small cell lung cancer using stereotactic body radiotherapy. *J Appl Clin Med Phys*. 2014 Sep 8;15(5):4898. doi: 10.1120/jacmp.v15i5.4898. PMID: 25207575. Exclusion Code: X8.

1367. Rebonato A, Maiettini D, Andolfi M, et al. CT-Guided Percutaneous Trans-scapular Lung Biopsy in the Diagnosis of Peripheral Pulmonary Lesion Nodules of the Superior Lobes Using Large Needles. *Cardiovasc Intervent Radiol*. 2018 Feb;41(2):284-90. doi: 10.1007/s00270-017-1768-0. PMID: 28808757. Exclusion Code: X3.

1368. Redberg RF, O'Malley PG. Important questions about lung cancer screening programs when incidental findings exceed lung cancer nodules by 40 to 1. *JAMA Intern Med*. 2017 Mar 1;177(3):311-2. doi: 10.1001/jamainternmed.2016.9446. PMID: 28135358. Exclusion Code: X10.

1369. Reddy RM, Murlidhar V, Zhao L, et al. Pulmonary venous blood sampling significantly increases the yield of circulating tumor cells in early-stage lung cancer. *J Thorac Cardiovasc Surg*. 2016 Mar;151(3):852-8. doi: 10.1016/j.jtcvs.2015.09.126. PMID: 26614417. Exclusion Code: X8.

1370. Reichert M, Steiner D, Kerber S, et al. A standardized technique of systematic mediastinal lymph node dissection by video-assisted thoracoscopic surgery (VATS) leads to a high rate of nodal upstaging in early-stage non-small cell lung cancer. *Surg Endosc*. 2016 Mar;30(3):1119-25. doi: 10.1007/s00464-015-4312-9. PMID: 26169635. Exclusion Code: X11.

1371. Remick JS, Schonewolf C, Gabriel P, et al. First clinical report of proton beam therapy for postoperative radiotherapy for non-small-cell lung cancer. *Clin Lung Cancer*. 2017 Jul;18(4):364-71. doi: 10.1016/j.cllc.2016.12.009. PMID: 28162946. Exclusion Code: X3.

1372. Rena O, Massera F, Boldorini R, et al. Non-small cell lung cancer in surgically treated women. *Tumori*. 2013 Nov-Dec;99(6):661-6. doi: 10.1700/1390.15453. PMID: 24503788. Exclusion Code: X3.

1373. Rennert G, Kremer R, Rennert HS, et al. Lower lung cancer rates in Jewish smokers in Israel and the USA. *Int J Cancer*. 2015 Nov 1;137(9):2155-62. doi: 10.1002/ijc.29587. PMID: 25924736. Exclusion Code: X3.

1374. Reshko LB, Kalman NS, Hugo GD, et al. Cardiac radiation dose distribution, cardiac events and mortality in early-stage lung cancer treated with stereotactic body radiation therapy (SBRT). *J Thorac Dis*. 2018 Apr;10(4):2346-56. doi: 10.21037/jtd.2018.04.42. PMID: 29850140. Exclusion Code: X3.

1375. Revel MP, Mannes I, Benzakoun J, et al. Subsolid lung nodule classification: a CT criterion for improving interobserver agreement. *Radiology*. 2018 Jan;286(1):316-25. doi: 10.1148/radiol.2017170044. PMID: 28796590. Exclusion Code: X3.

1376. Ricardi U, Filippi AR, Guarneri A, et al. Stereotactic body radiation therapy for early stage non-small cell lung cancer: results of a prospective trial. *Lung Cancer*. 2010 Apr;68(1):72-7. doi: 10.1016/j.lungcan.2009.05.007. PMID: 19556022. Exclusion Code: X11.

1377. Ricardi U, Frezza G, Filippi AR, et al. Stereotactic Ablative Radiotherapy for stage I histologically proven non-small cell lung cancer: an Italian multicenter observational study. *Lung Cancer*. 2014 Jun;84(3):248-53. doi: 10.1016/j.lungcan.2014.02.015. PMID: 24681279. Exclusion Code: X10.

1378. Ricke J, Jurgens JH, Deschamps F, et al. Irreversible electroporation (IRE) fails to demonstrate efficacy in a prospective multicenter phase II trial on lung malignancies: the ALICE trial. *Cardiovasc Intervent Radiol*. 2015 Apr;38(2):401-8. doi: 10.1007/s00270-014-1049-0. PMID: 25609208. Exclusion Code: X3.

1379. Rico M, Martinez E, Pellejero S, et al. Influence of different treatment techniques and clinical factors over the intrafraction variation on lung stereotactic body radiotherapy. *Clin Transl Oncol*. 2016 Oct;18(10):1011-8. doi: 10.1007/s12094-015-1475-8. PMID: 26758718. Exclusion Code: X8.

1380. Ridge CA, Silk M, Petre EN, et al. Radiofrequency ablation of T1 lung carcinoma: comparison of outcomes for first primary, metachronous, and synchronous lung tumors. *J Vasc Interv Radiol*. 2014 Jul;25(7):989-96. doi: 10.1016/j.jvir.2014.02.021. PMID: 24703321. Exclusion Code: X6.

1381. Ridge CA, Yildirim A, Boiselle PM, et al. Differentiating between subsolid and solid pulmonary nodules at CT: inter- and intraobserver agreement between experienced thoracic radiologists. *Radiology*. 2016 Mar;278(3):888-96. doi: 10.1148/radiol.2015150714. PMID: 26458208. Exclusion Code: X3.

1382. Rieber J, Tonndorf-Martini E, Schramm O, et al. Establishing stereotactic body radiotherapy with flattening filter free techniques in the treatment of pulmonary lesions - initial experiences from a single institution. *Radiat Oncol*. 2016 Jun 8;11:80. doi: 10.1186/s13014-016-0648-0. PMID: 27411832. Exclusion Code: X3.

1383. Rintoul RC, Glover MJ, Jackson C, et al. Cost effectiveness of endosonography versus surgical staging in potentially resectable lung cancer: a health economics analysis of the ASTER trial from a European perspective. *Thorax*. 2014 Jul;69(7):679-81. doi: 10.1136/thoraxjnl-2013-204374. PMID: 24064440. Exclusion Code: X3.

1384. Riquet M, Mordant P, Pricopi C, et al. A review of 250 ten-year survivors after pneumonectomy for non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2014 May;45(5):876-81. doi: 10.1093/ejcts/ezt494. PMID: 24132299. Exclusion Code: X3.

1385. Riquet M, Rivera C, Pricopi C, et al. Is the lymphatic drainage of lung cancer lobe-specific? A surgical appraisal. *Eur J Cardiothorac Surg*. 2015 Mar;47(3):543-9. doi: 10.1093/ejcts/ezu226. PMID: 24875885. Exclusion Code: X3.

1386. Ritchie AJ, Sanghera C, Jacobs C, et al. Computer vision tool and technician as first reader of lung cancer screening CT scans. *J Thorac Oncol*. 2016 May;11(5):709-17. doi: 10.1016/j.jtho.2016.01.021. PMID: 26994641. Exclusion Code: X5.

1387. Roach MC, Rehman S, DeWees TA, et al. It's never too late: smoking cessation after stereotactic body radiation therapy for non-small cell lung carcinoma improves overall survival. *Pract Radiat Oncol*. 2016 Jan-Feb;6(1):12-8. doi: 10.1016/j.prro.2015.09.005. PMID: 26598909. Exclusion Code: X13.

1388. Robbins HA, Berg CD, Cheung LC, et al. Identification of candidates for longer lung cancer screening intervals following a negative low-dose computed tomography result. *J Natl Cancer Inst*. 2019 Apr 12doi: 10.1093/jnci/djz041. PMID: 30976808. Exclusion Code: X4.

1389. Robinson JW, Brennan PC, Mello-Thoms C, et al. Reporting instructions significantly impact false positive rates when reading chest radiographs. *Eur Radiol*. 2016 Oct;26(10):3654-9. doi: 10.1007/s00330-015-4194-1. PMID: 26780639. Exclusion Code: X3.

1390. Robinson JW, Ryan JT, McEntee MF, et al. Grey-scale inversion improves detection of lung nodules. *Br J Radiol*. 2013 Jan;86(1021):20110812. doi: 10.1259/bjr/2796154510.1259/bjr.20110812. PMID: 23239692. Exclusion Code: X3.

1391. Robson JM, Vaidyanathan S, Cheyne L, et al. Occult nodal disease in patients with non-small-cell lung cancer who are suitable for stereotactic ablative body radiation. *Clin Lung Cancer*. 2014 Nov;15(6):466-9. doi: 10.1016/j.cllc.2014.07.006. PMID: 25220208. Exclusion Code: X8.

1392. Rocha RD, Azevedo AA, Falsarella PM, et al. Cerebral air embolism during CT-guided lung biopsy. *Thorax*. 2015 Nov;70(11):1099-100. doi: 10.1136/thoraxjnl-2015-207205. PMID: 26024689. Exclusion Code: X3.

1393. Rodgers-Fischl PM, Martin JT, Saha SP. Video-assisted thoracoscopic versus open lobectomy: costs and outcomes. *South Med J*. 2017 Mar;110(3):229-33. doi: 10.14423/smj.0000000000000620. PMID: 28257551. Exclusion Code: X3.

1394. Rodriguez F, Seijo LM, Sanchez PA, et al. Modified technique for obtaining mediastinal samples with endobronchial ultrasound-guided transbronchial needle aspiration: results from a prospective observational study. *Arch Bronconeumol*. 2013 Apr;49(4):135-9. doi: 10.1016/j.arbres.2012.10.006. PMID: 23265621. Exclusion Code: X3.

1395. Rodriguez M, Gomez Hernandez MT, Novoa NM, et al. Poorer survival in stage IB lung cancer patients after pneumonectomy. *Arch Bronconeumol*. 2015 May;51(5):223-6. doi: 10.1016/j.arbres.2014.09.007. PMID: 25454899. Exclusion Code: X11.

1396. Roesel C, Terjung S, Weinreich G, et al. Sarcomatoid carcinoma of the lung: a rare histological subtype of non-small cell lung cancer with a poor prognosis even at earlier tumour stages. *Interact Cardiovasc Thorac Surg*. 2017 Mar 1;24(3):407-13. doi: 10.1093/icvts/ivw392. PMID: 28025310. Exclusion Code: X3.

1397. Rojas-Solano JR, Ugalde-Gamboa L, Machuzak M. Robotic Bronchoscopy for Diagnosis of Suspected Lung Cancer: A Feasibility Study. *J Bronchology Interv Pulmonol*. 2018 Jul;25(3):168-75. doi: 10.1097/lbr.0000000000000499. PMID: 29762461. Exclusion Code: X11.

1398. Roman M, Labbouz S, Valtzoglou V, et al. Lobectomy vs. segmentectomy. A propensity score matched comparison of outcomes. *Eur J Surg Oncol*. 2019 May;45(5):845-50. doi: 10.1016/j.ejso.2018.10.534. PMID: 30409440. Exclusion Code: X3.

1399. Ronit A, Kristensen T, Klitbo DM, et al. Incidental lung cancers and positive computed tomography images in people living with HIV. *AIDS*. 2017 Sep 10;31(14):1973-7. doi: 10.1097/qad.0000000000001600. PMID: 28857778. Exclusion Code: X10.

1400. Ros-Mazurczyk M, Jelonek K, Marczyk M, et al. Serum lipid profile discriminates patients with early lung cancer from healthy controls. *Lung Cancer*. 2017 Oct;112:69-74. doi: 10.1016/j.lungcan.2017.07.036. PMID: 29191603. Exclusion Code: X11.

1401. Rossi MM, Peulen HM, Belderbos JS, et al. Intrafraction motion in stereotactic body radiation therapy for non-small cell lung cancer: intensity modulated radiation therapy versus volumetric modulated arc therapy. *Int J Radiat Oncol Biol Phys*. 2016 Jun 1;95(2):835-43. doi: 10.1016/j.ijrobp.2016.01.060. PMID: 27131084. Exclusion Code: X8.

1402. Rostambeigi N, Scanlon P, Flanagan S, et al. CT Fluoroscopic-Guided Coil Localization of Lung Nodules prior to Video-Assisted Thoracoscopic Surgical Resection Reduces Complications Compared to Hook Wire Localization. *J Vasc Interv Radiol*. 2019 Mar;30(3):453-9. doi: 10.1016/j.jvir.2018.10.013. PMID: 30819493. Exclusion Code: X11.

1403. Rotolo N, Floridi C, Imperatori A, et al. Comparison of cone-beam CT-guided and CT fluoroscopy-guided transthoracic needle biopsy of lung nodules. *Eur Radiol*. 2016 Feb;26(2):381-9. doi: 10.1007/s00330-015-3861-6. PMID: 26045345. Exclusion Code: X3.

1404. Ryoo JJ, Malin JL, Ordin DL, et al. Facility characteristics and quality of lung cancer care in an integrated health care system. *J Thorac Oncol*. 2014 Apr;9(4):447-55. doi: 10.1097/jto.0000000000000108. PMID: 24736065. Exclusion Code: X8.

1405. Sa YJ, Kim JJ, Du Kim Y, et al. A new protocol for concomitant needle aspiration biopsy and localization of solitary pulmonary nodules. *J Cardiothorac Surg*. 2015 Jul 29;10:104. doi: 10.1186/s13019-015-0312-z. PMID: 26219285. Exclusion Code: X11.

1406. Safi S, Rauch G, op den Winkel J, et al. Sublobar resection, radiofrequency ablation or radiotherapy in stage I non-small cell lung cancer. *Respiration*. 2015;89(6):550-7. doi: 10.1159/000381555. PMID: 25968471. Exclusion Code: X11.

1407. Saghir Z, Ashraf H, Dirksen A, et al. Contamination during 4 years of annual CT screening in the Danish Lung Cancer Screening Trial (DLCST). *Lung Cancer*. 2011 Mar;71(3):323-7. doi: 10.1016/j.lungcan.2010.06.006. PMID: 20619924. Exclusion Code: X8.

1408. Saito H, Konno H, Atari M, et al. Management of intersegmental plane on pulmonary segmentectomy concerning postoperative complications. *Ann Thorac Surg*. 2017 Jun;103(6):1773-80. doi: 10.1016/j.athoracsur.2017.01.014. PMID: 28366465. Exclusion Code: X11.

1409. Saito H, Nakagawa T, Ito M, et al. Pulmonary function after lobectomy versus segmentectomy in patients with stage I non-small cell lung cancer. *World J Surg*. 2014 Aug;38(8):2025-31. doi: 10.1007/s00268-014-2521-3. PMID: 24682312. Exclusion Code: X11.

1410. Saji H, Ueno T, Nakamura H, et al. A proposal for a comprehensive risk scoring system for predicting postoperative complications in octogenarian patients with medically operable lung cancer: JACS1303. *Eur J Cardiothorac Surg*. 2018 Apr 1;53(4):835-41. doi: 10.1093/ejcts/ezx415. PMID: 29240884. Exclusion Code: X3.

1411. Sakaguchi M, Maebayashi T, Aizawa T, et al. Patient outcomes of monotherapy with hypofractionated three-dimensional conformal radiation therapy for stage T2 or T3 non-small cell lung cancer: a retrospective study. *Radiat Oncol*. 2016 Jan 19;11:3. doi: 10.1186/s13014-016-0582-1. PMID: 26781290. Exclusion Code: X6.

1412. Salati M, Brunelli A, Decaluwe H, et al. Report from the European Society of Thoracic Surgeons Database 2017: patterns of care and perioperative outcomes of surgery for malignant lung neoplasm. *Eur J Cardiothorac Surg*. 2017 Dec 1;52(6):1041-8. doi: 10.1093/ejcts/ezx272. PMID: 28950348. Exclusion Code: X3.

1413. Salhi B, Huysse W, Van Maele G, et al. The effect of radical treatment and rehabilitation on muscle mass and strength: a randomized trial in stages I-III lung cancer patients. *Lung Cancer*. 2014 Apr;84(1):56-61. doi: 10.1016/j.lungcan.2014.01.011. PMID: 24560331. Exclusion Code: X6.

1414. Samson P, Keogan K, Crabtree T, et al. Interpreting survival data from clinical trials of surgery versus stereotactic body radiation therapy in operable Stage I non-small cell lung cancer patients. *Lung cancer (Amsterdam, Netherlands)*. 2017;103:6-10. doi: 10.1016/j.lungcan.2016.11.005. PMID: CN-01243643. Exclusion Code: X10.

1415. Samson P, Rehman S, Juloori A, et al. Local control for clinical stage I non-small cell lung cancer treated with 5-fraction stereotactic body radiation therapy is not associated with treatment schedule. *Pract Radiat Oncol*. 2018 Nov - Dec;8(6):404-13. doi: 10.1016/j.prro.2018.04.004. PMID: 29907514. Exclusion Code: X8.

1416. Samson P, Robinson CG, Bradley J, et al. The National Surgical Quality Improvement Program risk calculator does not adequately stratify risk for patients with clinical stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2016 Mar;151(3):697-705.e1. doi: 10.1016/j.jtcvs.2015.08.058. PMID: 26410001. Exclusion Code: X11.

1417. Sancheti MS, Chihara RK, Perez SD, et al. Hospitalization costs after surgery in high-risk patients with early stage lung cancer. *Ann Thorac Surg*. 2018 Jan;105(1):263-70. doi: 10.1016/j.athoracsur.2017.08.038. PMID: 29174780. Exclusion Code: X11.

1418. Sancheti MS, Lee R, Ahmed SU, et al. Percutaneous fiducial localization for thoracoscopic wedge resection of small pulmonary nodules. *Ann Thorac Surg*. 2014 Jun;97(6):1914-8; discussion 9. doi: 10.1016/j.athoracsur.2014.02.028. PMID: 24725836. Exclusion Code: X3.

1419. Sancheti MS, Melvan JN, Medbery RL, et al. Outcomes after surgery in high-risk patients with early stage lung cancer. *Ann Thorac Surg*. 2016 Mar;101(3):1043-50; Discussion 51. doi: 10.1016/j.athoracsur.2015.08.088. PMID: 26572255. Exclusion Code: X11.

1420. Sanchez de Cos Escuin J, Serra Mitjans M, Hernandez Hernandez J, et al. The Spanish Society of Pulmonology and Thoracic Surgery Lung Cancer Cooperative Group-II registry. A descriptive study. *Arch Bronconeumol*. 2013 Nov;49(11):462-7. doi: 10.1016/j.arbres.2013.05.002. PMID: 23838409. Exclusion Code: X8.

1421. Sanchez-Salcedo P, Berto J, de-Torres JP, et al. Lung cancer screening: fourteen year experience of the Pamplona early detection program (P-IELCAP). *Arch Bronconeumol*. 2015 Apr;51(4):169-76. doi: 10.1016/j.arbres.2014.09.019. PMID: 25641356. Exclusion Code: X7.

1422. Sanderson B, McWilliam A, Faivre-Finn C, et al. Using the Malthus programme to predict the recruitment of patients to MR-linac research trials in prostate and lung cancer. *Radiother Oncol*. 2017 Jan;122(1):159-62. doi: 10.1016/j.radonc.2016.11.014. PMID: 27939554. Exclusion Code: X5.

1423. Sandhu AP, Lau SK, Rahn D, et al. Stereotactic body radiation therapy in octogenarians with stage I lung cancer. *Clin Lung Cancer*. 2014 Mar;15(2):131-5. doi: 10.1016/j.cllc.2013.08.007. PMID: 24157245. Exclusion Code: X10.

1424. Sandri A, Papagiannopoulos K, Milton R, et al. High-risk patients and postoperative complications following video-assisted thoracic surgery lobectomy: a case-matched comparison with lower-risk counterpartsdagger. *Interact Cardiovasc Thorac Surg*. 2015 Dec;21(6):761-5. doi: 10.1093/icvts/ivv254. PMID: 26362624. Exclusion Code: X11.

1425. Sanford L, Molloy J, Kumar S, et al. Evaluation of plan quality and treatment efficiency for single-isocenter/two-lesion lung stereotactic body radiation therapy. *J Appl Clin Med Phys*. 2019 Jan;20(1):118-27. doi: 10.1002/acm2.12500. PMID: 30548205. Exclusion Code: X8.

1426. Sangha BS, Hague CJ, Jessup J, et al. Transthoracic computed tomography-guided lung nodule biopsy: comparison of core needle and fine needle aspiration techniques. *Can Assoc Radiol J*. 2016 Aug;67(3):284-9. doi: 10.1016/j.carj.2015.10.005. PMID: 27005931. Exclusion Code: X11.

1427. Sas-Korczynska B, Luczynska E, Kamzol W, et al. Analysis of risk factors for pulmonary complications in patients with limited-stage small cell lung cancer : A single-centre retrospective study. *Strahlenther Onkol*. 2017 Feb;193(2):141-9. doi: 10.1007/s00066-016-1069-6. PMID: 27785518. Exclusion Code: X3.

1428. Sato A, Hamada S, Urashima Y, et al. The effect of false-positive results on subsequent participation in chest x-ray screening for lung cancer. *J Epidemiol*. 2016 Dec 5;26(12):646-53. doi: 10.2188/jea.JE20150106. PMID: 27374136. Exclusion Code: X10.

1429. Sato H, Toyooka S, Soh J, et al. Advantage of induction chemoradiotherapy for lung cancer in securing cancer-free bronchial margin. *Ann Thorac Surg*. 2017 Sep;104(3):971-8. doi: 10.1016/j.athoracsur.2017.03.045. PMID: 28610882. Exclusion Code: X3.

1430. Sato S, Koike T, Hashimoto T, et al. Surgical outcomes of lung cancer patients with combined pulmonary fibrosis and emphysema and those with idiopathic pulmonary fibrosis without emphysema. *Ann Thorac Cardiovasc Surg*. 2016 Aug 23;22(4):216-23. doi: 10.5761/atcs.oa.15-00315. PMID: 27052999. Exclusion Code: X11.

1431. Sato T, Kondo H, Watanabe A, et al. A simple risk scoring system for predicting acute exacerbation of interstitial pneumonia after pulmonary resection in lung cancer patients. *Gen Thorac Cardiovasc Surg*. 2015 Mar;63(3):164-72. doi: 10.1007/s11748-014-0487-6. PMID: 25352311. Exclusion Code: X3.

1432. Sato T, Teramukai S, Kondo H, et al. Impact and predictors of acute exacerbation of interstitial lung diseases after pulmonary resection for lung cancer. *J Thorac Cardiovasc Surg*. 2014 May;147(5):1604-11.e3. doi: 10.1016/j.jtcvs.2013.09.050. PMID: 24267779. Exclusion Code: X10.

1433. Sato T, Watanabe A, Kondo H, et al. Long-term results and predictors of survival after surgical resection of patients with lung cancer and interstitial lung diseases. *J Thorac Cardiovasc Surg*. 2015 Jan;149(1):64-9, 70.e1-2. doi: 10.1016/j.jtcvs.2014.08.086. PMID: 25439777. Exclusion Code: X10.

1434. Satoh Y, Motosugi U, Nambu A, et al. Prognostic value of semiautomatic CT volumetry in patients with stage I Non-small cell lung cancer treated with stereotactic body radiation therapy. *J Comput Assist Tomogr*. 2016 May-Jun;40(3):343-50. doi: 10.1097/rct.0000000000000368. PMID: 26854414. Exclusion Code: X10.

1435. Satoh Y, Motosugi U, Saito A, et al. Pretreatment (18)F-fluorodeoxyglucose Uptake in the Lung Parenchyma Predicts Poor Survival After Stereotactic Body Radiation Therapy in Patients With Stage I Non-Small Cell Lung Cancer. *Technol Cancer Res Treat*. 2018 Jan 1;17:1533033818794934. doi: 10.1177/1533033818794934. PMID: 30222060. Exclusion Code: X13.

1436. Satoh Y, Onishi H, Nambu A, et al. Volume-based parameters measured by using FDG PET/CT in patients with stage I NSCLC treated with stereotactic body radiation therapy: prognostic value. *Radiology*. 2014 Jan;270(1):275-81. doi: 10.1148/radiol.13130652. PMID: 24029640. Exclusion Code: X10.

1437. Sawabata N, Kanzaki R, Sakamoto T, et al. Clinical predictor of pre- or minimally invasive pulmonary adenocarcinoma: possibility of sub-classification of clinical T1a. *Eur J Cardiothorac Surg*. 2014 Feb;45(2):256-61. doi: 10.1093/ejcts/ezt329. PMID: 23868951. Exclusion Code: X11.

1438. Sawicki LM, Grueneisen J, Buchbender C, et al. Evaluation of the outcome of lung nodules missed on 18F-FDG PET/MRI compared with 18F-FDG PET/CT in patients with known malignancies. *J Nucl Med*. 2016 Jan;57(1):15-20. doi: 10.2967/jnumed.115.162966. PMID: 26514173. Exclusion Code: X3.

1439. Sayan M, Satir Turk M, Celik A, et al. Surgical outcomes of early-stage small-cell lung cancer: single-center experience. *Asian Cardiovasc Thorac Ann*. 2019 Mar;27(3):187-91. doi: 10.1177/0218492319826724. PMID: 30661378. Exclusion Code: X3.

1440. Saydam O, Gokce M, Kilicgun A, et al. Accuracy of positron emission tomography in mediastinal node assessment in coal workers with lung cancer. *Med Oncol*. 2012 Jun;29(2):589-94. doi: 10.1007/s12032-011-9879-y. PMID: 21380783. Exclusion Code: X3.

1441. Schaal M, Severac F, Labani A, et al. Diagnostic performance of ultra-low-dose computed tomography for detecting asbestos-related pleuropulmonary diseases: prospective study in a screening setting. *PLoS One*. 2016;11(12):e0168979. doi: 10.1371/journal.pone.0168979. PMID: 28033378. Exclusion Code: X11.

1442. Schaefer JF, Vollmar J, Schick F, et al. Solitary pulmonary nodules: dynamic contrast-enhanced MR imaging--perfusion differences in malignant and benign lesions. *Radiology*. 2004 Aug;232(2):544-53. doi: 10.1148/radiol.2322030515. PMID: 15215548. Exclusion Code: X3.

1443. Schalekamp S, van Ginneken B, Heggelman B, et al. New methods for using computer-aided detection information for the detection of lung nodules on chest radiographs. *Br J Radiol*. 2014 Apr;87(1036):20140015. doi: 10.1259/bjr.20140015. PMID: 24625084. Exclusion Code: X5.

1444. Schanne DH, Nestle U, Allgauer M, et al. Stereotactic body radiotherapy for centrally located stage I NSCLC: a multicenter analysis. *Strahlenther Onkol*. 2015 Feb;191(2):125-32. doi: 10.1007/s00066-014-0739-5. PMID: 25159135. Exclusion Code: X3.

1445. Schillaci O, Travascio L, Bolacchi F, et al. Accuracy of early and delayed FDG PET-CT and of contrast-enhanced CT in the evaluation of lung nodules: a preliminary study on 30 patients. *Radiol Med*. 2009 Sep;114(6):890-906. doi: 10.1007/s11547-009-0400-z. PMID: 19579015. Exclusion Code: X3.

1446. Schmocker RK, Vanness DJ, Macke RA, et al. Outpatient air leak management after lobectomy: a CMS cost analysis. *J Surg Res*. 2016 Jun 15;203(2):390-7. doi: 10.1016/j.jss.2016.03.043. PMID: 27363648. Exclusion Code: X3.

1447. Schneider L, Farrokhyar F, Schieman C, et al. The burden of death following discharge after lobectomydagger. *Eur J Cardiothorac Surg*. 2015 Jul;48(1):65-70. doi: 10.1093/ejcts/ezu427. PMID: 25422293. Exclusion Code: X3.

1448. Schneider T, Puderbach M, Kunz J, et al. Simultaneous computed tomography-guided biopsy and radiofrequency ablation of solitary pulmonary malignancy in high-risk patients. *Respiration*. 2012;84(6):501-8. doi: 10.1159/000342874. PMID: 23037897. Exclusion Code: X6.

1449. Scholten ET, de Jong PA, de Hoop B, et al. Towards a close computed tomography monitoring approach for screen detected subsolid pulmonary nodules? *Eur Respir J*. 2015 Mar;45(3):765-73. doi: 10.1183/09031936.00005914. PMID: 25431271. Exclusion Code: X7.

1450. Scholten ET, Mali WP, Prokop M, et al. Non-solid lung nodules on low-dose computed tomography: comparison of detection rate between 3 visualization techniques. *Cancer Imaging*. 2013 Apr 15;13:150-4. doi: 10.1102/1470-7330.2013.0016. PMID: 23598304. Exclusion Code: X8.

1451. Schonewolf CA, Verma V, Post CM, et al. Outcomes of invasive mediastinal nodal staging versus positron emission tomography staging alone for early-stage non-small cell lung cancer treated with stereotactic body radiation therapy. *Lung Cancer*. 2018 Mar;117:53-9. doi: 10.1016/j.lungcan.2017.07.005. PMID: 28800837. Exclusion Code: X13.

1452. Schreuder A, van Ginneken B, Scholten ET, et al. Classification of CT Pulmonary Opacities as Perifissural Nodules: Reader Variability. *Radiology*. 2018 Sep;288(3):867-75. doi: 10.1148/radiol.2018172771. PMID: 29969076. Exclusion Code: X8.

1453. Schroeder MC, Tien YY, Wright K, et al. Geographic variation in the use of adjuvant therapy among elderly patients with resected non-small cell lung cancer. *Lung Cancer*. 2016 May;95:28-34. doi: 10.1016/j.lungcan.2016.02.010. PMID: 27040848. Exclusion Code: X8.

1454. Schuhmann M, Bostanci K, Bugalho A, et al. Endobronchial ultrasound-guided cryobiopsies in peripheral pulmonary lesions: a feasibility study. *Eur Respir J*. 2014 Jan;43(1):233-9. doi: 10.1183/09031936.00011313. PMID: 23900983. Exclusion Code: X3.

1455. Schwartz RM, Yip R, Flores RM, et al. The impact of resection method and patient factors on quality of life among stage IA non-small cell lung cancer surgical patients. *J Surg Oncol*. 2017 Feb;115(2):173-80. doi: 10.1002/jso.24478. PMID: 27790715. Exclusion Code: X11.

1456. Sconfienza LM, Mauri G, Grossi F, et al. Pleural and peripheral lung lesions: comparison of US- and CT-guided biopsy. *Radiology*. 2013 Mar;266(3):930-5. doi: 10.1148/radiol.12112077. PMID: 23204543. Exclusion Code: X3.

1457. Scotti V, Bruni A, Francolini G, et al. Stereotactic Ablative Radiotherapy as an Alternative to Lobectomy in Patients With Medically Operable Stage I NSCLC: A Retrospective, Multicenter Analysis. *Clin Lung Cancer*. 2019 Jan;20(1):e53-e61. doi: 10.1016/j.cllc.2018.09.003. PMID: 30348595. Exclusion Code: X13.

1458. Segmen F, Aktas Z, Ozturk A, et al. How many samples would be optimal for endobronchial cryobiopsy? *Surg Endosc*. 2017 Mar;31(3):1219-24. doi: 10.1007/s00464-016-5095-3. PMID: 27412127. Exclusion Code: X3.

1459. Sekine Y, Sakairi Y, Yoshino M, et al. The impact of combined pulmonary fibrosis and chronic obstructive pulmonary disease on long-term survival after lung cancer surgery. *Thorac Cardiovasc Surg*. 2014 Jun;62(4):332-7. doi: 10.1055/s-0033-1363478. PMID: 24879070. Exclusion Code: X11.

1460. Semaan RW, Lee HJ, Feller-Kopman D, et al. Same-day computed tomographic chest imaging for pulmonary nodule targeting with electromagnetic navigation bronchoscopy may decrease unnecessary procedures. *Ann Am Thorac Soc*. 2016 Dec;13(12):2223-8. doi: 10.1513/AnnalsATS.201607-522BC. PMID: 27925781. Exclusion Code: X8.

1461. Senan S, Verstegen NE, Palma D, et al. Stages I-II non-small cell lung cancer treated using either lobectomy by video-assisted thoracoscopic surgery (VATS) or stereotactic ablative radiotherapy (SABR): outcomes of a propensity score-matched analysis. *J Clin Oncol*. 2012;30(15)PMID: CN-01008197. Exclusion Code: X2.

1462. Senbaklavaci O. Lobar lung resection in elderly patients with non-small cell lung carcinoma: impact of chronic obstructive pulmonary disease on surgical outcome. *Int Surg*. 2014 Jul-Aug;99(4):319-24. doi: 10.9738/intsurg-d-14-00015.1. PMID: 25058759. Exclusion Code: X3.

1463. Senthi S, Dahele M, van de Ven PM, et al. Late radiologic changes after stereotactic ablative radiotherapy for early stage lung cancer: a comparison of fixed-beam versus arc delivery techniques. *Radiother Oncol*. 2013 Oct;109(1):77-81. doi: 10.1016/j.radonc.2013.08.034. PMID: 24060174. Exclusion Code: X10.

1464. Senthi S, Haasbeek CJ, Slotman BJ, et al. Outcomes of stereotactic ablative radiotherapy for central lung tumours: a systematic review. *Radiother Oncol*. 2013 Mar;106(3):276-82. doi: 10.1016/j.radonc.2013.01.004. PMID: 23462705. Exclusion Code: X9.

1465. Senthi S, Lagerwaard FJ, Haasbeek CJ, et al. Patterns of disease recurrence after stereotactic ablative radiotherapy for early stage non-small-cell lung cancer: a retrospective analysis. *Lancet Oncol*. 2012 Aug;13(8):802-9. doi: 10.1016/s1470-2045(12)70242-5. PMID: 22727222. Exclusion Code: X3.

1466. Seok Y, Cho S, Kim K, et al. Partly solid pulmonary nodules: waiting for change or surgery outright? *Interact Cardiovasc Thorac Surg*. 2014 Oct;19(4):556-60. doi: 10.1093/icvts/ivu205. PMID: 24981106. Exclusion Code: X3.

1467. Seok Y, Cho S, Lee JY, et al. The effect of postoperative change in bronchial angle on postoperative pulmonary function after upper lobectomy in lung cancer patients. *Interact Cardiovasc Thorac Surg*. 2014 Feb;18(2):183-8. doi: 10.1093/icvts/ivt463. PMID: 24243734. Exclusion Code: X3.

1468. Serra Fortuny M, Gallego M, Berna L, et al. FDG-PET parameters predicting mediastinal malignancy in lung cancer. *BMC Pulm Med*. 2016 Dec 8;16(1):177. doi: 10.1186/s12890-016-0338-6. PMID: 27931198. Exclusion Code: X3.

1469. Sestini S, Boeri M, Marchiano A, et al. Circulating microRNA signature as liquid-biopsy to monitor lung cancer in low-dose computed tomography screening. *Oncotarget*. 2015 Oct 20;6(32):32868-77. doi: 10.18632/oncotarget.5210. PMID: 26451608. Exclusion Code: X5.

1470. Shafiek H, Valera JL, Togores B, et al. Risk of postoperative complications in chronic obstructive lung diseases patients considered fit for lung cancer surgery: beyond oxygen consumption. *Eur J Cardiothorac Surg*. 2016 Oct;50(4):772-9. doi: 10.1093/ejcts/ezw104. PMID: 27059429. Exclusion Code: X3.

1471. Shah C, Grills IS, Kestin LL, et al. Intrafraction variation of mean tumor position during image-guided hypofractionated stereotactic body radiotherapy for lung cancer. *Int J Radiat Oncol Biol Phys*. 2012 Apr 1;82(5):1636-41. doi: 10.1016/j.ijrobp.2011.02.011. PMID: 21489715. Exclusion Code: X8.

1472. Shao F, Liu Z, Pan Y, et al. Bronchoplasty using continuous suture in complete monitor view: a suitable method of thoracoscopic sleeve lobectomy for non-small cell lung cancer. *World J Surg Oncol*. 2016 Apr 30;14:134. doi: 10.1186/s12957-016-0895-4. PMID: 27130332. Exclusion Code: X3.

1473. Shapiro M, Kadakia S, Lim J, et al. Lobe-specific mediastinal nodal dissection is sufficient during lobectomy by video-assisted thoracic surgery or thoracotomy for early-stage lung cancer. *Chest*. 2013 Nov;144(5):1615-21. doi: 10.1378/chest.12-3069. PMID: 23828253. Exclusion Code: X11.

1474. Sharifi H, van Elmpt W, Oberije C, et al. Quantification of CT-assessed radiation-induced lung damage in lung cancer patients treated with or without chemotherapy and cetuximab. *Acta Oncol*. 2016;55(2):156-62. doi: 10.3109/0284186x.2015.1080856. PMID: 26399389. Exclusion Code: X3.

1475. Sharma A, McDermott S, Mathisen DJ, et al. Preoperative localization of lung nodules with fiducial markers: feasibility and technical considerations. *Ann Thorac Surg*. 2017 Apr;103(4):1114-20. doi: 10.1016/j.athoracsur.2016.09.112. PMID: 28131426. Exclusion Code: X3.

1476. Sharma R, Wang Y, Chen L, et al. Utility of a novel triple marker (combination of thyroid transcription factor 1, Napsin A, and P40) in the subclassification of non-small cell lung carcinomas using fine-needle aspiration cases. *Hum Pathol*. 2016 Aug;54:8-16. doi: 10.1016/j.humpath.2016.02.027. PMID: 27045515. Exclusion Code: X5.

1477. Shaverdian N, Tenn S, Veruttipong D, et al. The significance of PTV dose coverage on cancer control outcomes in early stage non-small cell lung cancer patients treated with highly ablative stereotactic body radiation therapy. *Br J Radiol*. 2016;89(1059):20150963. doi: 10.1259/bjr.20150963. PMID: 26764282. Exclusion Code: X10.

1478. Shaverdian N, Veruttipong D, Wang J, et al. Location matters: stage I non-small-cell carcinomas of the lower lobes treated with stereotactic body radiation therapy are associated with poor outcomes. *Clin Lung Cancer*. 2017 Mar;18(2):e137-e42. doi: 10.1016/j.cllc.2016.09.001. PMID: 27908620. Exclusion Code: X10.

1479. Shaverdian N, Veruttipong D, Wang J, et al. Pretreatment immune parameters predict for overall survival and toxicity in early-stage non-small-cell lung cancer patients treated with stereotactic body radiation therapy. *Clin Lung Cancer*. 2016 Jan;17(1):39-46. doi: 10.1016/j.cllc.2015.07.007. PMID: 26372098. Exclusion Code: X3.

1480. Shaverdian N, Wang PC, Steinberg M, et al. The patient's perspective on stereotactic body radiation therapy (SBRT) vs. surgery for treatment of early stage non-small cell lung cancer (NSCLC). *Lung Cancer*. 2015 Nov;90(2):230-3. doi: 10.1016/j.lungcan.2015.07.009. PMID: 26358313. Exclusion Code: X10.

1481. She Y, Zhang L, Zhu H, et al. The predictive value of CT-based radiomics in differentiating indolent from invasive lung adenocarcinoma in patients with pulmonary nodules. *Eur Radiol*. 2018 Dec;28(12):5121-8. doi: 10.1007/s00330-018-5509-9. PMID: 29869172. Exclusion Code: X3.

1482. Sheel AR, McShane J, Poullis MP. Survival of patients with or without symptoms undergoing potentially curative resections for primary lung cancer. *Ann Thorac Surg*. 2013 Jan;95(1):276-84. doi: 10.1016/j.athoracsur.2012.09.051. PMID: 23200231. Exclusion Code: X3.

1483. Sheikhbahaei S, Mena E, Yanamadala A, et al. The value of FDG PET/CT in treatment response assessment, follow-up, and surveillance of lung cancer. *AJR Am J Roentgenol*. 2017 Feb;208(2):420-33. doi: 10.2214/ajr.16.16532. PMID: 27726427. Exclusion Code: X3.

1484. Shelver J, Wendt CH, McClure M, et al. Effect of an automated tracking registry on the rate of tracking failure in incidental pulmonary nodules. *J Am Coll Radiol*. 2017 Jun;14(6):773-7. doi: 10.1016/j.jacr.2017.02.001. PMID: 28434846. Exclusion Code: X8.

1485. Shen J, Liao J, Guarnera MA, et al. Analysis of MicroRNAs in sputum to improve computed tomography for lung cancer diagnosis. *J Thorac Oncol*. 2014 Jan;9(1):33-40. doi: 10.1097/jto.0000000000000025. PMID: 24305007. Exclusion Code: X5.

1486. Sherman SM, Lane EL. Awareness of risk factors for breast, lung and cervical cancer in a UK student population. *J Cancer Educ*. 2015 Dec;30(4):660-3. doi: 10.1007/s13187-014-0770-3. PMID: 25510367. Exclusion Code: X5.

1487. Shi GL, Chen Y, Sun Y, et al. Significance of serum MicroRNAs in the auxiliary diagnosis of non-small cell lung cancer. *Clin Lab*. 2017 Jan 1;63(1):133-40. doi: 10.7754/Clin.Lab.2016.160710. PMID: 28164492. Exclusion Code: X4.

1488. Shi Q, Wang XS, Vaporciyan AA, et al. Patient-reported symptom interference as a measure of postsurgery functional recovery in lung cancer. *J Pain Symptom Manage*. 2016 Dec;52(6):822-31. doi: 10.1016/j.jpainsymman.2016.07.005. PMID: 27521528. Exclusion Code: X3.

1489. Shiels MS, Katki HA, Hildesheim A, et al. Circulating inflammation markers, risk of lung cancer, and utility for risk stratification. *J Natl Cancer Inst*. 2015 Oct;107(10)doi: 10.1093/jnci/djv199. PMID: 26220734. Exclusion Code: X3.

1490. Shiels MS, Pfeiffer RM, Hildesheim A, et al. Circulating inflammation markers and prospective risk for lung cancer. *J Natl Cancer Inst*. 2013 Dec 18;105(24):1871-80. doi: 10.1093/jnci/djt309. PMID: 24249745. Exclusion Code: X4.

1491. Shien K, Toyooka S, Soh J, et al. Clinicopathological characteristics and lymph node metastasis pathway of non-small-cell lung cancer located in the left lingular division. *Interact Cardiovasc Thorac Surg*. 2015 Jun;20(6):791-6. doi: 10.1093/icvts/ivv062. PMID: 25805399. Exclusion Code: X3.

1492. Shim SS, Oh YW, Kong KA, et al. Pulmonary nodule size evaluation with chest tomosynthesis and CT: a phantom study. *Br J Radiol*. 2015 Mar;88(1047):20140040. doi: 10.1259/bjr.20140040. PMID: 25605344. Exclusion Code: X4.

1493. Shimada Y, Saji H, Kato Y, et al. The frequency and prognostic impact of pathological microscopic vascular invasion according to tumor size in non-small cell lung cancer. *Chest*. 2016 Mar;149(3):775-85. doi: 10.1378/chest.15-0559. PMID: 26379115. Exclusion Code: X3.

1494. Shimamura Y, Sasaki S, Shimohira M, et al. New technique of percutaneous CT fluoroscopy-guided marking before video-assisted thoracoscopic surgery for small lung lesions: feasibility of using a 25-gauge needle without local anaesthesia. *Br J Radiol*. 2018 Feb;91(1083):20170692. doi: 10.1259/bjr.20170692. PMID: 29172683. Exclusion Code: X3.

1495. Shimizu K, Mogi A, Yajima T, et al. Thoracoscopic subsuperior segment segmentectomy. *Ann Thorac Surg*. 2017 Nov;104(5):e407-e10. doi: 10.1016/j.athoracsur.2017.07.007. PMID: 29054241. Exclusion Code: X3.

1496. Shimizu K, Nagashima T, Yajima T, et al. Thoracoscopic medial-basal segment segmentectomy. *Ann Thorac Surg*. 2017 Nov;104(5):e403-e6. doi: 10.1016/j.athoracsur.2017.07.006. PMID: 29054240. Exclusion Code: X6.

1497. Shin JY, Yoon JK, Marwaha G. Progress in the treatment and outcomes for early-stage non-small cell lung cancer. *Lung*. 2018 Jun;196(3):351-8. doi: 10.1007/s00408-018-0110-1. PMID: 29550987. Exclusion Code: X3.

1498. Shin KE, Lee KS, Yi CA, et al. Subcentimeter lung nodules stable for 2 years at LDCT: long-term follow-up using volumetry. *Respirology*. 2014 Aug;19(6):921-8. doi: 10.1111/resp.12337. PMID: 24934105. Exclusion Code: X8.

1499. Shin S, Kim HK, Choi YS, et al. Prognosis of unexpected and expected pathologic N1 non-small cell lung cancer. *Ann Thorac Surg*. 2013 Sep;96(3):969-75; discussion 75-6. doi: 10.1016/j.athoracsur.2013.04.070. PMID: 23916803. Exclusion Code: X3.

1500. Shin S, Park HY, Kim H, et al. Joint effect of airflow limitation and emphysema on postoperative outcomes in early-stage nonsmall cell lung cancer. *Eur Respir J*. 2016 Dec;48(6):1743-50. doi: 10.1183/13993003.01148-2016. PMID: 27811074. Exclusion Code: X11.

1501. Shin S, Park JS, Kim HK, et al. Approach to metastasis-suspected nodule accompanying operable non-small cell lung cancer. *Thorac Cardiovasc Surg*. 2014 Oct;62(7):616-23. doi: 10.1055/s-0033-1363767. PMID: 24752828. Exclusion Code: X3.

1502. Shingyoji M, Nakajima T, Yoshino M, et al. Endobronchial ultrasonography for positron emission tomography and computed tomography-negative lymph node staging in non-small cell lung cancer. *Ann Thorac Surg*. 2014 Nov;98(5):1762-7. doi: 10.1016/j.athoracsur.2014.05.078. PMID: 25149044. Exclusion Code: X8.

1503. Shintani Y, Inoue M, Funaki S, et al. Clinical usefulness of free subcutaneous fat pad for reduction of intraoperative air leakage during thoracoscopic pulmonary resection in lung cancer cases. *Surg Endosc*. 2015 Oct;29(10):2910-3. doi: 10.1007/s00464-014-4019-3. PMID: 25537378. Exclusion Code: X3.

1504. Shiono S, Abiko M, Sato T. Limited resection for clinical stage IA non-small-cell lung cancers based on a standardized-uptake value index. *Eur J Cardiothorac Surg*. 2013 Jan;43(1):e7-e12. doi: 10.1093/ejcts/ezs573. PMID: 23129358. Exclusion Code: X11.

1505. Shiono S, Katahira M, Abiko M, et al. Smoking is a perioperative risk factor and prognostic factor for lung cancer surgery. *Gen Thorac Cardiovasc Surg*. 2015 Feb;63(2):93-8. doi: 10.1007/s11748-014-0461-3. PMID: 25085320. Exclusion Code: X3.

1506. Shiono S, Yanagawa N, Abiko M, et al. Detection of non-aggressive stage IA lung cancer using chest computed tomography and positron emission tomography/computed tomography. *Interact Cardiovasc Thorac Surg*. 2014 Oct;19(4):637-43. doi: 10.1093/icvts/ivu188. PMID: 24994703. Exclusion Code: X11.

1507. Shiono S, Yanagawa N, Abiko M, et al. Noninvasive differential diagnosis of pulmonary nodules using the Standardized Uptake Value Index. *Ann Thorac Cardiovasc Surg*. 2015;21(3):236-41. doi: 10.5761/atcs.oa.14-00241. PMID: 25740450. Exclusion Code: X3.

1508. Shioyama Y, Onishi H, Takayama K, et al. Clinical outcomes of stereotactic body radiotherapy for patients with stage I small-cell lung cancer: analysis of a subset of the japanese radiological society multi-institutional SBRT study group database. *Technol Cancer Res Treat*. 2018 Jan 1;17:1533033818783904. doi: 10.1177/1533033818783904. PMID: 29983096. Exclusion Code: X3.

1509. Shirata Y, Jingu K, Koto M, et al. Prognostic factors for local control of stage I non-small cell lung cancer in stereotactic radiotherapy: a retrospective analysis. *Radiat Oncol*. 2012 Oct 31;7:182. doi: 10.1186/1748-717x-7-182. PMID: 23110967. Exclusion Code: X13.

1510. Shlomi D, Peled N, Schwarz YA, et al. Non-invasive early detection of malignant pulmonary nodules by FISH-based sputum test. *Cancer Genet*. 2018 Oct;226-227:1-10. doi: 10.1016/j.cancergen.2018.04.118. PMID: 30005848. Exclusion Code: X3.

1511. Shoji F, Haratake N, Akamine T, et al. The preoperative controlling nutritional status score predicts survival after curative surgery in patients with pathological stage I non-small cell lung cancer. *Anticancer Res*. 2017 Feb;37(2):741-7. doi: 10.21873/anticanres.11372. PMID: 28179325. Exclusion Code: X8.

1512. Shoji F, Matsubara T, Kozuma Y, et al. Preoperative Geriatric Nutritional Risk Index: A predictive and prognostic factor in patients with pathological stage I non-small cell lung cancer. *Surg Oncol*. 2017 Dec;26(4):483-8. doi: 10.1016/j.suronc.2017.09.006. PMID: 29113668. Exclusion Code: X10.

1513. Shoji F, Miura N, Matsubara T, et al. Prognostic significance of immune-nutritional parameters for surgically resected elderly lung cancer patients: a multicentre retrospective study. *Interact Cardiovasc Thorac Surg*. 2018 Mar 1;26(3):389-94. doi: 10.1093/icvts/ivx337. PMID: 29049803. Exclusion Code: X10.

1514. Shoji F, Yamazaki K, Kouso H, et al. The impact of pleural lavage cytology both before and after lung resection on recurrence of non-small cell lung cancer. *Ann Thorac Surg*. 2016 Jun;101(6):2141-6. doi: 10.1016/j.athoracsur.2015.12.037. PMID: 27012585. Exclusion Code: X6.

1515. Shrager J. Invited commentary. *Ann Thorac Surg*. 2016 Jun;101(6):2146-7. doi: 10.1016/j.athoracsur.2016.01.034. PMID: 27211933. Exclusion Code: X10.
1516. Shroyer AL, Quin JA, Grau-Sepulveda MV, et al. Geographic variations in lung cancer lobectomy outcomes: The General Thoracic Surgery Database. *Ann Thorac Surg*. 2017 Nov;104(5):1650-5. doi: 10.1016/j.athoracsur.2017.05.066. PMID: 28935347. Exclusion Code: X8.
1517. Shultz DB, Jang SS, Hanlon AL, et al. The effect of arm position on the dosimetry of thoracic stereotactic ablative radiation therapy using volumetric modulated arc therapy. *Pract Radiat Oncol*. 2014 May-Jun;4(3):192-7. doi: 10.1016/j.prro.2013.07.010. PMID: 24766687. Exclusion Code: X8.
1518. Shultz DB, Trakul N, Abelson JA, et al. Imaging features associated with disease progression after stereotactic ablative radiotherapy for stage I non-small-cell lung cancer. *Clin Lung Cancer*. 2014 Jul;15(4):294-301.e3. doi: 10.1016/j.cllc.2013.12.011. PMID: 24594400. Exclusion Code: X13.
1519. Shultz DB, Trakul N, Maxim PG, et al. Vagal and recurrent laryngeal neuropathy following stereotactic ablative radiation therapy in the chest. *Pract Radiat Oncol*. 2014 Jul-Aug;4(4):272-8. doi: 10.1016/j.prro.2013.08.005. PMID: 25012837. Exclusion Code: X3.
1520. Shusharina N, Liao Z, Mohan R, et al. Differences in lung injury after IMRT or proton therapy assessed by (18)FDG PET imaging. *Radiother Oncol*. 2018 Jul;128(1):147-53. doi: 10.1016/j.radonc.2017.12.027. PMID: 29352608. Exclusion Code: X3.
1521. Siegelman JW, Supanich MP, Gavrielides MA. Pulmonary nodules with ground-glass opacity can be reliably measured with low-dose techniques regardless of iterative reconstruction: results of a phantom study. *AJR Am J Roentgenol*. 2015 Jun;204(6):1242-7. doi: 10.2214/ajr.14.13820. PMID: 26001234. Exclusion Code: X3.
1522. Sigel K, Wisnivesky J, Crothers K, et al. Immunological and infectious risk factors for lung cancer in US veterans with HIV: a longitudinal cohort study. *Lancet HIV*. 2017 Feb;4(2):e67-e73. doi: 10.1016/s2352-3018(16)30215-6. PMID: 27916584. Exclusion Code: X3.
1523. Sihoe AD, Hiranandani R, Wong H, et al. Operating on a suspicious lung mass without a preoperative tissue diagnosis: pros and cons. *Eur J Cardiothorac Surg*. 2013 Aug;44(2):231-7; discussion 7. doi: 10.1093/ejcts/ezs671. PMID: 23299236. Exclusion Code: X11.
1524. Silva M, Galeone C, Sverzellati N, et al. Screening with low-dose computed tomography does not improve survival of small cell lung cancer. *J Thorac Oncol*. 2016 Feb;11(2):187-93. doi: 10.1016/j.jtho.2015.10.014. PMID: 26845115. Exclusion Code: X3.
1525. Silva M, Sverzellati N, Manna C, et al. Long-term surveillance of ground-glass nodules: evidence from the MILD trial. *J Thorac Oncol*. 2012 Oct;7(10):1541-6. doi: 10.1097/JTO.0b013e3182641bba. PMID: 22968185. Exclusion Code: X11.
1526. Silvestri GA, Vachani A, Whitney D, et al. A bronchial genomic classifier for the diagnostic evaluation of lung cancer. *N Engl J Med*. 2015 Jul 16;373(3):243-51. doi: 10.1056/NEJMoa1504601. PMID: 25981554. Exclusion Code: X5.
1527. Sim YT, Goh YG, Dempsey MF, et al. PET-CT evaluation of solitary pulmonary nodules: correlation with maximum standardized uptake value and pathology. *Lung*. 2013 Dec;191(6):625-32. doi: 10.1007/s00408-013-9500-6. PMID: 24013495. Exclusion Code: X3.
1528. Simone CB, 2nd, Wildt B, Haas AR, et al. Stereotactic body radiation therapy for lung cancer. *Chest*. 2013 Jun;143(6):1784-90. doi: 10.1378/chest.12-2580. PMID: 23732589. Exclusion Code: X10.
1529. Simonsen DF, Sogaard M, Bozi I, et al. Risk factors for postoperative pneumonia after lung cancer surgery and impact of pneumonia on survival. *Respir Med*. 2015 Oct;109(10):1340-6. doi: 10.1016/j.rmed.2015.07.008. PMID: 26209227. Exclusion Code: X3.

1530. Sin DD, Tammemagi CM, Lam S, et al. Pro-surfactant protein B as a biomarker for lung cancer prediction. *J Clin Oncol*. 2013 Dec 20;31(36):4536-43. doi: 10.1200/jco.2013.50.6105. PMID: 24248694. Exclusion Code: X7.

1531. Singh S, Pinsky P, Fineberg NS, et al. Evaluation of reader variability in the interpretation of follow-up CT scans at lung cancer screening. *Radiology*. 2011 Apr;259(1):263-70. doi: 10.1148/radiol.10101254. PMID: 21248232. Exclusion Code: X11.

1532. Singh SP, Gierada DS, Pinsky P, et al. Reader variability in identifying pulmonary nodules on chest radiographs from the national lung screening trial. *J Thorac Imaging*. 2012 Jul;27(4):249-54. doi: 10.1097/RTI.0b013e318256951e. PMID: 22627615. Exclusion Code: X5.

1533. Sinicrope PS, Rabe KG, Brockman TA, et al. Perceptions of lung cancer risk and beliefs in screening accuracy of spiral computed tomography among high-risk lung cancer family members. *Acad Radiol*. 2010 Aug;17(8):1012-25. doi: 10.1016/j.acra.2010.04.003. PMID: 20599157. Exclusion Code: X11.

1534. Sio TT, Jensen AR, Miller RC, et al. Influence of patient's physiologic factors and immobilization choice with stereotactic body radiotherapy for upper lung tumors. *J Appl Clin Med Phys*. 2014 Sep 8;15(5):4931. doi: 10.1120/jacmp.v15i5.4931. PMID: 25207580. Exclusion Code: X8.

1535. Siva S, Callahan J, Kron T, et al. A prospective observational study of Gallium-68 ventilation and perfusion PET/CT during and after radiotherapy in patients with non-small cell lung cancer. *BMC Cancer*. 2014 Oct 2;14:740. doi: 10.1186/1471-2407-14-740. PMID: 25277150. Exclusion Code: X10.

1536. Siva S, Kirby K, Caine H, et al. Comparison of single-fraction and multi-fraction stereotactic radiotherapy for patients with 18F-fluorodeoxyglucose positron emission tomography-staged pulmonary oligometastases. *Clin Oncol (R Coll Radiol)*. 2015 Jun;27(6):353-61. doi: 10.1016/j.clon.2015.01.004. PMID: 25698068. Exclusion Code: X3.

1537. Sivapalan P, Naur TMH, Colella S, et al. Impact of EBUS-TBNA on PET-CT imaging of mediastinal nodes. *J Bronchology Interv Pulmonol*. 2017 Jul;24(3):188-92. doi: 10.1097/lbr.0000000000000373. PMID: 28696964. Exclusion Code: X3.

1538. Sivrikoz CM, Ak I, Simsek FS, et al. Is mediastinoscopy still the gold standard to evaluate mediastinal lymph nodes in patients with non-small cell lung carcinoma? *Thorac Cardiovasc Surg*. 2012 Mar;60(2):116-21. doi: 10.1055/s-0030-1271148. PMID: 21692019. Exclusion Code: X3.

1539. Slatore C, Sullivan D, Pappas M, et al. Patient-centered outcomes among lung cancer screening recipients with computed tomography: a systematic review (Provisional abstract). *Database of Abstracts of Reviews of Effects*. 2014(2):927-34. PMID: DARE-12014038387. Exclusion Code: X9.

1540. Slatore CG, Golden SE, Ganzini L, et al. Distress and patient-centered communication among veterans with incidental (not screen-detected) pulmonary nodules. A cohort study. *Ann Am Thorac Soc*. 2015 Feb;12(2):184-92. doi: 10.1513/AnnalsATS.201406-283OC. PMID: 25521482. Exclusion Code: X3.

1541. Slatore CG, Wiener RS, Golden SE, et al. Longitudinal assessment of distress among veterans with incidental pulmonary nodules. *Ann Am Thorac Soc*. 2016 Nov;13(11):1983-91. doi: 10.1513/AnnalsATS.201607-555OC. PMID: 27599153. Exclusion Code: X3.

1542. Slattery MM, Foley C, Kenny D, et al. Long-term follow-up of non-calcified pulmonary nodules (<10 mm) identified during low-dose CT screening for lung cancer. *Eur Radiol*. 2012 Sep;22(9):1923-8. doi: 10.1007/s00330-012-2443-0. PMID: 22538626. Exclusion Code: X10.

1543. Slavova-Azmanova NS, Lizama C, Johnson CE, et al. Impact of the introduction of EBUS on time to management decision, complications, and invasive modalities used to diagnose and stage lung cancer: a pragmatic pre-post study. *BMC Cancer*. 2016 Jan 28;16:44. doi: 10.1186/s12885-016-2081-z. PMID: 26822160. Exclusion Code: X3.

1544. Smeltzer MP, Faris NR, Ray MA, et al. Survival Before and After Direct Surgical Quality Feedback in a Population-Based Lung Cancer Cohort. *Ann Thorac Surg*. 2019 May;107(5):1487-93. doi: 10.1016/j.athoracsur.2018.11.058. PMID: 30594579. Exclusion Code: X3.

1545. Smith CB, Kale M, Mhango G, et al. Comparative outcomes of elderly stage I lung cancer patients treated with segmentectomy via video-assisted thoracoscopic surgery versus open resection. *J Thorac Oncol*. 2014 Mar;9(3):383-9. doi: 10.1097/jto.0000000000000083. PMID: 24495998. Exclusion Code: X11.

1546. Smith CB, Swanson SJ, Mhango G, et al. Survival after segmentectomy and wedge resection in stage I non-small-cell lung cancer. *J Thorac Oncol*. 2013 Jan;8(1):73-8. doi: 10.1097/JTO.0b013e31827451c4. PMID: 23164939. Exclusion Code: X8.

1547. Smith SL, Bowers D, Jennings P, et al. Pulmonary radiofrequency ablation in a district general hospital: is it a safe and effective treatment? *Clin Radiol*. 2016 Sep;71(9):939.e1-8. doi: 10.1016/j.crad.2016.03.021. PMID: 27157314. Exclusion Code: X3.

1548. Snee MP, McParland L, Collinson F, et al. The SABRTooth feasibility trial protocol: a study to determine the feasibility and acceptability of conducting a phase III randomised controlled trial comparing stereotactic ablative radiotherapy (SABR) with surgery in patients with peripheral stage I non-small cell lung cancer (NSCLC) considered to be at higher risk of complications from surgical resection. *Pilot Feasibility Stud*. 2016;2:5. doi: 10.1186/s40814-016-0046-2. PMID: 27965826. Exclusion Code: X10.

1549. Snee MP, McParland L, Collinson F, et al. Erratum to: The SABRTooth feasibility trial protocol: a study to determine the feasibility and acceptability of conducting a phase III randomised controlled trial comparing stereotactic ablative radiotherapy (SABR) with surgery in patients with peripheral stage I non-small cell lung cancer (NSCLC) considered to be at higher risk of complications from surgical resection. *Pilot Feasibility Stud*. 2016;2:55. doi: 10.1186/s40814-016-0095-6. PMID: 27976752. Exclusion Code: X10.

1550. Soardi GA, Perandini S, Larici AR, et al. Multicentre external validation of the BIMC model for solid solitary pulmonary nodule malignancy prediction. *Eur Radiol*. 2017 May;27(5):1929-33. doi: 10.1007/s00330-016-4538-5. PMID: 27553937. Exclusion Code: X3.

1551. Soda M, Isobe K, Inoue A, et al. A prospective PCR-based screening for the EML4-ALK oncogene in non-small cell lung cancer. *Clin Cancer Res*. 2012 Oct 15;18(20):5682-9. doi: 10.1158/1078-0432.ccr-11-2947. PMID: 22908099. Exclusion Code: X3.

1552. Soderman C, Johnsson AA, Vikgren J, et al. Evaluation of accuracy and precision of manual size measurements in chest tomosynthesis using simulated pulmonary nodules. *Acad Radiol*. 2015 Apr;22(4):496-504. doi: 10.1016/j.acra.2014.11.012. PMID: 25601303. Exclusion Code: X3.

1553. Sofocleous CT, Garg SK, Cohen P, et al. Ki 67 is an independent predictive biomarker of cancer specific and local recurrence-free survival after lung tumor ablation. *Ann Surg Oncol*. 2013 Dec;20 Suppl 3:S676-83. doi: 10.1245/s10434-013-3140-1. PMID: 23897007. Exclusion Code: X3.

1554. Solli P, Casiraghi M, Brambilla D, et al. Surgical treatment of superior sulcus tumors: a 15-year single-center experience. *Semin Thorac Cardiovasc Surg*. 2017 Spring;29(1):79-88. doi: 10.1053/j.semtcvs.2017.01.010. PMID: 28684003. Exclusion Code: X3.

1555. Solomon J, Mileto A, Nelson RC, et al. Quantitative features of liver lesions, lung nodules, and renal stones at multi-detector row CT examinations: dependency on radiation dose and reconstruction algorithm. *Radiology*. 2016 Apr;279(1):185-94. doi: 10.1148/radiol.2015150892. PMID: 26624973. Exclusion Code: X3.

1556. Sommer G, Tremper J, Koenigkam-Santos M, et al. Lung nodule detection in a high-risk population: comparison of magnetic resonance imaging and low-dose computed tomography. *Eur J Radiol*. 2014 Mar;83(3):600-5. doi: 10.1016/j.ejrad.2013.11.012. PMID: 24364923. Exclusion Code: X7.

1557. Sommer G, Wiese M, Winter L, et al. Preoperative staging of non-small-cell lung cancer: comparison of whole-body diffusion-weighted magnetic resonance imaging and 18F-fluorodeoxyglucose-positron emission tomography/computed tomography. *Eur Radiol*. 2012 Dec;22(12):2859-67. doi: 10.1007/s00330-012-2542-y. PMID: 22772365. Exclusion Code: X8.

1558. Sommer MS, Trier K, Vibe-Petersen J, et al. Perioperative rehabilitation in operation for lung cancer (PROLUCA) - rationale and design. *BMC Cancer*. 2014 Jun 4;14:404. doi: 10.1186/1471-2407-14-404. PMID: 24898680. Exclusion Code: X10.

1559. Son JY, Lee HY, Kim JH, et al. Quantitative CT analysis of pulmonary ground-glass opacity nodules for distinguishing invasive adenocarcinoma from non-invasive or minimally invasive adenocarcinoma: the added value of using iodine mapping. *Eur Radiol*. 2016 Jan;26(1):43-54. doi: 10.1007/s00330-015-3816-y. PMID: 25981222. Exclusion Code: X3.

1560. Son JY, Lee HY, Lee KS, et al. Quantitative CT analysis of pulmonary ground-glass opacity nodules for the distinction of invasive adenocarcinoma from pre-invasive or minimally invasive adenocarcinoma. *PLoS One*. 2014;9(8):e104066. doi: 10.1371/journal.pone.0104066. PMID: 25102064. Exclusion Code: X3.

1561. Song S, Chang JH, Kim HJ, et al. Survey of the patterns of using stereotactic ablative radiotherapy for early-stage non-small cell lung cancer in Korea. *Cancer Res Treat*. 2017 Jul;49(3):688-94. doi: 10.4143/crt.2016.219. PMID: 27809459. Exclusion Code: X8.

1562. Song SY, Choi W, Shin SS, et al. Fractionated stereotactic body radiation therapy for medically inoperable stage I lung cancer adjacent to central large bronchus. *Lung Cancer*. 2009 Oct;66(1):89-93. doi: 10.1016/j.lungcan.2008.12.016. PMID: 19168260. Exclusion Code: X11.

1563. Sozzi G, Boeri M, Rossi M, et al. Clinical utility of a plasma-based miRNA signature classifier within computed tomography lung cancer screening: a correlative MILD trial study. *J Clin Oncol*. 2014 Mar 10;32(8):768-73. doi: 10.1200/jco.2013.50.4357. PMID: 24419137. Exclusion Code: X5.

1564. Speicher PJ, Gu L, Wang X, et al. Adjuvant chemotherapy after lobectomy for T1-2N0 non-small cell lung cancer: are the guidelines supported? *J Natl Compr Canc Netw*. 2015 Jun;13(6):755-61. PMID: 26085391. Exclusion Code: X6.

1565. Spencer K, Kennedy M, Lummis K, et al. Equivalent cancer-specific survival following surgical resection or SABR for stage I lung cancer. *Radiother Oncol*. 2018;127:S244-S5. PMID: CN-01630579. Exclusion Code: X2.

1566. Spiro S, Shah P, Rintoul R, et al. Lungsearch: a randomised controlled trial of surveillance for the early detection of lung cancer in a high risk group. *Thorax*. 2016;71:A76-. doi: 10.1136/thoraxjnl-2016-209333.134. PMID: CN-01360140. Exclusion Code: X2.

1567. Spiro SG, Hackshaw A. Research in progress--LungSEARCH: a randomised controlled trial of surveillance for the early detection of lung cancer in a high-risk group. *Thorax*. 2016 Jan;71(1):91-3. doi: 10.1136/thoraxjnl-2015-207433. PMID: 26138736. Exclusion Code: X5.

1568. Spitz MR, Amos CI, Land S, et al. Role of selected genetic variants in lung cancer risk in African Americans. *J Thorac Oncol*. 2013 Apr;8(4):391-7. doi: 10.1097/JTO.0b013e318283da29. PMID: 23454887. Exclusion Code: X4.

1569. Spitz MR, Etzel CJ, Dong Q, et al. An expanded risk prediction model for lung cancer. *Cancer Prev Res (Phila)*. 2008 Sep;1(4):250-4. doi: 10.1158/1940-6207.CAPR-08-0060. PMID: 19138968. Exclusion Code: X4.

1570. Spitz MR, Hong WK, Amos CI, et al. A risk model for prediction of lung cancer. *J Natl Cancer Inst*. 2007 May 02;99(9):715-26. doi: 10.1093/jnci/djk153. PMID: 17470739. Exclusion Code: X7.

1571. Splatt AM, Steinke K. Major complications of high-energy microwave ablation for percutaneous CT-guided treatment of lung malignancies: Single-centre experience after 4 years. *J Med Imaging Radiat Oncol*. 2015 Oct;59(5):609-16. doi: 10.1111/1754-9485.12345. PMID: 26238653. Exclusion Code: X6.

1572. Spratt DE, Wu AJ, Adeseye V, et al. Recurrence patterns and second primary lung cancers after stereotactic body radiation therapy for early-stage non-small-cell lung cancer: implications for surveillance. *Clin Lung Cancer*. 2016 May;17(3):177-83.e2. doi: 10.1016/j.cllc.2015.09.006. PMID: 26602271. Exclusion Code: X10.

1573. Srisomboon C, Koizumi K, Haraguchi S, et al. Complete video-assisted thoracoscopic surgery for lung cancer in 400 patients. *Asian Cardiovasc Thorac Ann*. 2013 Dec;21(6):700-7. doi: 10.1177/0218492313479038. PMID: 24569329. Exclusion Code: X3.

1574. St Julien JB, Pinkerman R, Aldrich MC, et al. Poor survival for veterans with pathologic stage I non-small-cell lung cancer. *Am J Surg*. 2012 Nov;204(5):637-42. doi: 10.1016/j.amjsurg.2012.07.008. PMID: 22906246. Exclusion Code: X11.

1575. Stahl JM, Ross R, Harder EM, et al. The effect of biologically effective dose and radiation treatment schedule on overall survival in stage I non-small cell lung cancer patients treated with stereotactic body radiation therapy. *Int J Radiat Oncol Biol Phys*. 2016 Dec 1;96(5):1011-20. doi: 10.1016/j.ijrobp.2016.08.033. PMID: 27869080. Exclusion Code: X10.

1576. Stam B, Tijhuis A, Rossi M, et al. Cardiac sparing in stereotactic body radiotherapy of early stage NSCLC patients. *J Thorac Oncol*. 2018;13(10):S1009-. doi: 10.1016/j.jtho.2018.08.1924. PMID: CN-01654361. Exclusion Code: X2.

1577. Stamenovic D, Messerschmidt A, Schneider T. Surgery for lung tumors in the elderly: A retrospective cohort study on the influence of advanced age (over 80 years) on the development of complications by using a multivariate risk model. *Int J Surg*. 2018 Apr;52:141-8. doi: 10.1016/j.ijsu.2018.02.008. PMID: 29486244. Exclusion Code: X3.

1578. Stefani A, Nesci J, Casali C, et al. Wedge resection versus lobectomy for T1N0 non-small cell lung cancer. *Minerva Chir*. 2012 Dec;67(6):489-98. PMID: 23334112. Exclusion Code: X11.

1579. Steger V, Veit S, Walker T, et al. Does dose matter? Effect of two different neoadjuvant protocols in advanced NSCLC. *Thorac Cardiovasc Surg*. 2013 Mar;61(2):109-15. doi: 10.1055/s-0032-1311529. PMID: 22821672. Exclusion Code: X3.

1580. Steinfort DP, Farmer MW, Irving LB, et al. Pulmonologist-performed per-esophageal needle aspiration of parenchymal lung lesions using an EBUS bronchoscope: diagnostic utility and safety. *J Bronchology Interv Pulmonol*. 2017 Apr;24(2):117-24. doi: 10.1097/lbr.0000000000000350. PMID: 28005836. Exclusion Code: X3.

1581. Steinfort DP, Leong TL, Laska IF, et al. Diagnostic utility and accuracy of rapid on-site evaluation of bronchoscopic brushings. *Eur Respir J*. 2015 Jun;45(6):1653-60. doi: 10.1183/09031936.00111314. PMID: 25537567. Exclusion Code: X3.

1582. Steinhauser Motta JP, Kempa AT, Pinto Cardoso A, et al. Endobronchial ultrasound in real life: primary diagnosis and mediastinal staging of lung cancer in patients submitted to thoracic surgery. *BMC Pulm Med*. 2016 Jul 19;16(1):101. doi: 10.1186/s12890-016-0264-7. PMID: 27435209. Exclusion Code: X3.

1583. Stephans KL, Djemil T, Diaconu C, et al. Esophageal dose tolerance to hypofractionated stereotactic body radiation therapy: risk factors for late toxicity. *Int J Radiat Oncol Biol Phys*. 2014 Sep 1;90(1):197-202. doi: 10.1016/j.ijrobp.2014.05.011. PMID: 25015204. Exclusion Code: X3.

1584. Stephans KL, Djemil T, Reddy CA, et al. A comparison of two stereotactic body radiation fractionation schedules for medically inoperable stage I non-small cell lung cancer: the Cleveland Clinic experience. *J Thorac Oncol*. 2009 Aug;4(8):976-82. doi: 10.1097/JTO.0b013e3181adf509. PMID: 19633473. Exclusion Code: X11.

1585. Steunenberg B, Aerts B, De Groot H, et al. Quality assessment of video mediastinoscopy performed for staging in non-small cell lung cancer. *Thorac Cardiovasc Surg*. 2016 Sep;64(6):520-5. doi: 10.1055/s-0035-1556082. PMID: 26220697. Exclusion Code: X3.

1586. Stevens H, Bakker PF, Schlosser NJ, et al. Use of a dual-head coincidence camera and 18F-FDG for detection and nodal staging of non-small cell lung cancer: accuracy as determined by 2 independent observers. *J Nucl Med*. 2003 Mar;44(3):336-40. PMID: 12620997. Exclusion Code: X3.

1587. Stigt JA, Uil SM, Oostdijk AH, et al. A diagnostic program for patients suspected of having lung cancer. *Clin Lung Cancer*. 2012 Nov;13(6):475-81. doi: 10.1016/j.cllc.2012.03.001. PMID: 22498114. Exclusion Code: X3.

1588. Stolz AJ, Harustiak T, Simonek J, et al. Pneumonectomy for non-small cell lung cancer: predictors of early mortality and morbidity. *Acta Chir Belg*. 2014 Jan-Feb;114(1):25-30. PMID: 24720134. Exclusion Code: X11.

1589. Stolzmann P, Veit-Haibach P, Chuck N, et al. Detection rate, location, and size of pulmonary nodules in trimodality PET/CT-MR: comparison of low-dose CT and Dixon-based MR imaging. *Invest Radiol*. 2013 May;48(5):241-6. doi: 10.1097/RLI.0b013e31826f2de9. PMID: 23070096. Exclusion Code: X3.

1590. Stornaiuolo M, La Regina G, Passacantilli S, et al. Structure-based lead optimization and biological evaluation of BAX direct activators as novel potential anticancer agents. *J Med Chem*. 2015 Mar 12;58(5):2135-48. doi: 10.1021/jm501123r. PMID: 25668341. Exclusion Code: X6.

1591. Strano S, Lupo A, Lococo F, et al. Prognostic significance of vascular and lymphatic emboli in resected pulmonary adenocarcinoma. *Ann Thorac Surg*. 2013 Apr;95(4):1204-10. doi: 10.1016/j.athoracsur.2012.12.024. PMID: 23415237. Exclusion Code: X3.

1592. Su CT, Bhargava A, Shah CD, et al. Screening Patterns and Mortality Differences in Patients With Lung Cancer at an Urban Underserved Community. *Clin Lung Cancer*. 2018 Sep;19(5):e767-e73. doi: 10.1016/j.cllc.2018.05.019. PMID: 29937386. Exclusion Code: X10.

1593. Subotic D, Molins L, Soldatovic I, et al. Completion pneumonectomy: a valuable option for lung cancer recurrence or new primaries. *World J Surg Oncol*. 2018 May 28;16(1):98. doi: 10.1186/s12957-018-1398-2. PMID: 29807542. Exclusion Code: X3.

1594. Subotic D, Savic M, Atanasijadis N, et al. Standard versus extended pneumonectomy for lung cancer: what really matters? *World J Surg Oncol*. 2014 Aug 3;12:248. doi: 10.1186/1477-7819-12-248. PMID: 25086948. Exclusion Code: X3.

1595. Sugiura H, Takeda A, Hoshi T, et al. Acute exacerbation of usual interstitial pneumonia after resection of lung cancer. *Ann Thorac Surg*. 2012 Mar;93(3):937-43. doi: 10.1016/j.athoracsur.2011.12.010. PMID: 22305054. Exclusion Code: X3.

1596. Sui X, Meinel FG, Song W, et al. Detection and size measurements of pulmonary nodules in ultra-low-dose CT with iterative reconstruction compared to low dose CT. *Eur J Radiol*. 2016 Mar;85(3):564-70. doi: 10.1016/j.ejrad.2015.12.013. PMID: 26860668. Exclusion Code: X11.

1597. Sui X, Zhao H, Yang F, et al. Analysis of factors affecting successful microcoil localization for pulmonary nodules. *J Surg Res*. 2018 Apr;224:193-9. doi: 10.1016/j.jss.2017.12.020. PMID: 29506840. Exclusion Code: X10.

1598. Sullivan DR, Forsberg CW, Ganzini L, et al. Longitudinal changes in depression symptoms and survival among patients with lung cancer: a national cohort assessment. *J Clin Oncol*. 2016 Nov 20;34(33):3984-91. doi: 10.1200/jco.2016.66.8459. PMID: 27996350. Exclusion Code: X3.

1599. Sullivan FM, Farmer E, Mair FS, et al. Detection in blood of autoantibodies to tumour antigens as a case-finding method in lung cancer using the EarlyCDT®-Lung Test (ECLS): study protocol for a randomized controlled trial. *BMC Cancer*. 2017;17(1):187. doi: 10.1186/s12885-017-3175-y. PMID: CN-01443602. Exclusion Code: X8.

1600. Sumitomo R, Fukui T, Marumo S, et al. Effects of vessel interruption sequence during thoracoscopic lobectomy for non-small cell lung cancer. *Gen Thorac Cardiovasc Surg*. 2018 Aug;66(8):464-70. doi: 10.1007/s11748-018-0943-9. PMID: 29802566. Exclusion Code: X11.

1601. Sun B, Wang Y, Kota K, et al. Telomere length variation: A potential new telomere biomarker for lung cancer risk. *Lung Cancer*. 2015 Jun;88(3):297-303. doi: 10.1016/j.lungcan.2015.03.011. PMID: 25840848. Exclusion Code: X4.

1602. Sun V, Kim JY, Williams AC, et al. Quality of life and symptoms following stereotactic body radiotherapy in early-stage lung cancer patients. *J Community Support Oncol*. 2014 Nov;12(11):407-14. PMID: 25789332. Exclusion Code: X13.

1603. Sun Y, Duan Q, Chen X, et al. Comparative efficacy and toxicity of induction chemotherapy with concurrent stereotactic body radiotherapy and stereotactic body radiotherapy with subsequent chemotherapy in patients with clinical stage T1-3N0M0 non-small cell lung carcinoma. *Clin Transl Oncol*. 2017 Dec;19(12):1498-506. doi: 10.1007/s12094-017-1694-2. PMID: 28589432. Exclusion Code: X6.

1604. Sun Y, Yang M, Mao D, et al. Low-dose volume perfusion computed tomography (VPCT) for diagnosis of solitary pulmonary nodules. *Eur J Radiol*. 2016 Jun;85(6):1208-18. doi: 10.1016/j.ejrad.2016.03.026. PMID: 27161072. Exclusion Code: X3.

1605. Sung SY, Kwak YK, Lee SW, et al. Lymphovascular Invasion Increases the Risk of Nodal and Distant Recurrence in Node-Negative Stage I-IIA Non-Small-Cell Lung Cancer. *Oncology*. 2018;95(3):156-62. doi: 10.1159/000488859. PMID: 29847825. Exclusion Code: X10.

1606. Suo S, Cheng J, Cao M, et al. Assessment of heterogeneity difference between edge and core by using texture analysis: differentiation of malignant from inflammatory pulmonary nodules and masses. *Acad Radiol*. 2016 Sep;23(9):1115-22. doi: 10.1016/j.acra.2016.04.009. PMID: 27298058. Exclusion Code: X3.

1607. Suresh S, Salama GR, Ramjit A, et al. CT-Guided Fine-Needle Aspiration Biopsy of Pulmonary Nodules 8 mm or Less Has a Higher Diagnostic Accuracy than Positron Emission Tomography-CT. *J Vasc Interv Radiol*. 2018 Apr;29(4):520-3. doi: 10.1016/j.jvir.2017.10.004. PMID: 29287961. Exclusion Code: X3.

1608. Suzuki H, Morimoto J, Mizobuchi T, et al. Does segmentectomy really preserve the pulmonary function better than lobectomy for patients with early-stage lung cancer? *Surg Today*. 2017 Apr;47(4):463-9. doi: 10.1007/s00595-016-1387-4. PMID: 27484067. Exclusion Code: X8.

1609. Suzuki O, Mitsuyoshi T, Miyazaki M, et al. Dose-volume-response analysis in stereotactic radiotherapy for early lung cancer. *Radiother Oncol*. 2014 Aug;112(2):262-6. doi: 10.1016/j.radonc.2014.07.004. PMID: 25107554. Exclusion Code: X3.

1610. Suzuki Y, Okamoto T, Fujishita T, et al. Clinical implications of sarcopenia in patients undergoing complete resection for early non-small cell lung cancer. *Lung Cancer*. 2016 Nov;101:92-7. doi: 10.1016/j.lungcan.2016.08.007. PMID: 27794415. Exclusion Code: X11.

1611. Swaminath A, Wierzbicki M, Parpia S, et al. Canadian phase III randomized trial of stereotactic body radiotherapy versus conventionally hypofractionated radiotherapy for stage I, medically inoperable non-small-cell lung cancer - rationale and protocol design for the Ontario Clinical Oncology Group (OCOG)-LUSTRE Trial. *Clin Lung Cancer*. 2017 Mar;18(2):250-4. doi: 10.1016/j.cllc.2016.08.002. PMID: 27876603. Exclusion Code: X10.

1612. Swanick CW, Allen PK, Tao R, et al. Incidence and predictors of chest wall toxicity after high-dose radiation therapy in 15 fractions. *Pract Radiat Oncol*. 2017 Jan - Feb;7(1):63-71. doi: 10.1016/j.prro.2016.05.009. PMID: 27637136. Exclusion Code: X3.

1613. Tachibana K, Nakazato Y, Tsuchida S, et al. Immediate cytology improves accuracy and decreases complication rate in real-time computed tomography-guided needle lung biopsy. *Diagn Cytopathol*. 2013 Dec;41(12):1063-8. doi: 10.1002/dc.22940. PMID: 23239643. Exclusion Code: X3.

1614. Tachihara M, Tamura D, Kiriu T, et al. Bronchoscopy Using Virtual Navigation and Endobronchial Ultrasonography with a Guide Sheath (EBUS-GS) with or without Fluoroscopy for Peripheral Pulmonary Lesions. *Kobe J Med Sci*. 2018 Mar 27;63(4):E99-e104. PMID: 29955020. Exclusion Code: X3.

1615. Tada A, Hiraki T, Iguchi T, et al. Influence of radiofrequency ablation of lung cancer on pulmonary function. *Cardiovasc Intervent Radiol*. 2012 Aug;35(4):860-7. doi: 10.1007/s00270-011-0221-z. PMID: 21725672. Exclusion Code: X6.

1616. Tagawa T, Iwata T, Nakajima T, et al. Evolution of a lung-sparing strategy with sleeve lobectomy and induction therapy for non-small cell lung cancer: 20-year experience at a single institution. *World J Surg*. 2016 Apr;40(4):906-12. doi: 10.1007/s00268-015-3330-z. PMID: 26711642. Exclusion Code: X3.

1617. Tajima Y, Nakayama H, Itonaga T, et al. Dosimetric evaluation of compensator intensity modulation-based stereotactic body radiotherapy for Stage I non-small-cell lung cancer. *Br J Radiol*. 2015 Aug;88(1052):20150122. doi: 10.1259/bjr.20150122. PMID: 25996577. Exclusion Code: X8.

1618. Takahashi EA, Koo CW, White DB, et al. Prospective Pilot Evaluation of Radiologists and Computer-aided Pulmonary Nodule Detection on Ultra-low-Dose CT With Tin Filtration. *J Thorac Imaging*. 2018 Nov;33(6):396-401. doi: 10.1097/rti.0000000000000348. PMID: 30048344. Exclusion Code: X3.

1619. Takahashi N, Sawabata N, Kawamura M, et al. Multicenter prospective study of sublobar resection for c-stage I non-small cell lung cancer patients unable to undergo lobectomy (KLSG-0801): complete republication. *Gen Thorac Cardiovasc Surg*. 2016 Aug;64(8):470-5. doi: 10.1007/s11748-016-0662-z. PMID: 27234224. Exclusion Code: X11.

1620. Takahashi Y, Horio H, Hato T, et al. Prognostic significance of preoperative neutrophil-lymphocyte ratios in patients with stage I non-small cell lung cancer after complete resection. *Ann Surg Oncol*. 2015 Dec;22 Suppl 3:S1324-31. doi: 10.1245/s10434-015-4735-5. PMID: 26198075. Exclusion Code: X3.

1621. Takashima S, Sone S, Li F, et al. Small solitary pulmonary nodules (< or =1 cm) detected at population-based CT screening for lung cancer: Reliable high-resolution CT features of benign lesions. *AJR Am J Roentgenol*. 2003 Apr;180(4):955-64. PMID: 12646435. Exclusion Code: X8.

1622. Takeda A, Enomoto T, Sanuki N, et al. Reassessment of declines in pulmonary function >/=1 year after stereotactic body radiotherapy. *Chest*. 2013 Jan;143(1):130-7. doi: 10.1378/chest.12-0207. PMID: 22722234. Exclusion Code: X3.

1623. Takeda A, Kunieda E, Fujii H, et al. Evaluation for local failure by 18F-FDG PET/CT in comparison with CT findings after stereotactic body radiotherapy (SBRT) for localized non-small-cell lung cancer. *Lung Cancer*. 2013 Mar;79(3):248-53. doi: 10.1016/j.lungcan.2012.11.008. PMID: 23246123. Exclusion Code: X8.

1624. Takeda A, Kunieda E, Ohashi T, et al. Severe COPD is correlated with mild radiation pneumonitis following stereotactic body radiotherapy. *Chest*. 2012 Apr;141(4):858-66. doi: 10.1378/chest.11-1193. PMID: 21885726. Exclusion Code: X3.

1625. Takeda A, Sanuki N, Fujii H, et al. Maximum standardized uptake value on FDG-PET is a strong predictor of overall and disease-free survival for non-small-cell lung cancer patients after stereotactic body radiotherapy. *J Thorac Oncol*. 2014 Jan;9(1):65-73. doi: 10.1097/jto.0000000000000031. PMID: 24346094. Exclusion Code: X10.

1626. Takeda Y, Miura K, Sato T, et al. Clinically simplified screening methods to evaluate maximum standard uptake value from F-18-FDG-PET/CT in patients with non-small-cell lung cancer. *Medicine (Baltimore)*. 2018 Jun;97(26):e11226. doi: 10.1097/md.0000000000011226. PMID: 29952981. Exclusion Code: X3.

1627. Takenaka R, Shibamoto Y, Miyakawa A, et al. The fate of residual tumor masses that persist after stereotactic body radiotherapy for solitary lung nodules: will they recur? *Clin Lung Cancer*. 2016 Sep;17(5):406-11. doi: 10.1016/j.cllc.2015.12.003. PMID: 26781347. Exclusion Code: X8.

1628. Takenaka T, Inamasu E, Yoshida T, et al. Influence of the distance between home and the hospital on patients with surgically resected non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2016 Mar;49(3):842-6. doi: 10.1093/ejcts/ezv253. PMID: 26201956. Exclusion Code: X11.

1629. Takenaka T, Takenoyama M, Toyozawa R, et al. Concurrent chemoradiotherapy for patients with postoperative recurrence of surgically resected non-small-cell lung cancer. *Clin Lung Cancer*. 2015 Jan;16(1):51-6. doi: 10.1016/j.cllc.2014.06.001. PMID: 25038000. Exclusion Code: X3.

1630. Takeuchi K, Togashi Y, Kamihara Y, et al. Prospective and clinical validation of ALK immunohistochemistry: results from the phase I/II study of alectinib for ALK-positive lung cancer (AF-001JP study). *Ann Oncol*. 2016 Jan;27(1):185-92. doi: 10.1093/annonc/mdv501. PMID: 26487585. Exclusion Code: X5.

1631. Takx RA, Vliegenthart R, Mohamed Hoesein FA, et al. Pulmonary function and CT biomarkers as risk factors for cardiovascular events in male lung cancer screening participants: the NELSON study. *Eur Radiol*. 2015 Jan;25(1):65-71. doi: 10.1007/s00330-014-3384-6. PMID: 25182625. Exclusion Code: X5.

1632. Talapatra K, Majumder D, Chadha P, et al. Stereotactic body radiotherapy for lung tumors: Dosimetric analysis and clinical outcome. *Indian J Cancer*. 2018 Apr-Jun;55(2):170-5. doi: 10.4103/ijc.IJC_555_17. PMID: 30604731. Exclusion Code: X3.

1633. Talwar A, Rahman NM, Kadir T, et al. A retrospective validation study of three models to estimate the probability of malignancy in patients with small pulmonary nodules from a tertiary oncology follow-up centre. *Clin Radiol*. 2017 Feb;72(2):177.e1-.e8. doi: 10.1016/j.crad.2016.09.014. PMID: 27908443. Exclusion Code: X3.

1634. Talwar A, Willaime JMY, Pickup LC, et al. Pulmonary nodules: Assessing the imaging biomarkers of malignancy in a "coffee-break". *Eur J Radiol*. 2018 Apr;101:82-6. doi: 10.1016/j.ejrad.2018.02.004. PMID: 29571806. Exclusion Code: X3.

1635. Tamburini N, Maniscalco P, Mazzara S, et al. Multidisciplinary management improves survival at 1 year after surgical treatment for non-small-cell lung cancer: a propensity score-matched study. *Eur J Cardiothorac Surg*. 2018 Jun 1;53(6):1199-204. doi: 10.1093/ejcts/ezx464. PMID: 29293943. Exclusion Code: X3.

1636. Tammemagi CM, Pinsky PF, Caporaso NE, et al. Lung cancer risk prediction: Prostate, Lung, Colorectal And Ovarian Cancer Screening Trial models and validation. *J Natl Cancer Inst*. 2011 Jul 6;103(13):1058-68. doi: 10.1093/jnci/djr173. PMID: 21606442. Exclusion Code: X7.

1637. Tammemagi MC, Berg CD, Riley TL, et al. Impact of lung cancer screening results on smoking cessation. *J Natl Cancer Inst*. 2014 Jun;106(6):dju084. doi: 10.1093/jnci/dju084. PMID: 24872540. Exclusion Code: X5.

1638. Tammemagi MC, Lam SC, McWilliams AM, et al. Incremental value of pulmonary function and sputum DNA image cytometry in lung cancer risk prediction. *Cancer Prev Res (Phila)*. 2011 Apr;4(4):552-61. doi: 10.1158/1940-6207.CAPR-10-0183. PMID: 21411501. Exclusion Code: X7.

1639. Tammemagi MC, ten Haaf K, Toumazis I, et al. Development and validation of a multivariable lung cancer risk prediction model that includes low-dose computed tomography screening results: a secondary analysis of data from the National Lung Screening Trial. *JAMA Netw Open*. 2019 Mar 1;2(3):e190204. doi: 10.1001/jamanetworkopen.2019.0204. PMID: 30821827. Exclusion Code: X7.

1640. Tamura A, Suzuki J, Fukami T, et al. Chronic pulmonary aspergillosis as a sequel to lobectomy for lung cancer. *Interact Cardiovasc Thorac Surg*. 2015 Nov;21(5):650-6. doi: 10.1093/icvts/ivv239. PMID: 26323287. Exclusion Code: X3.

1641. Tamura M, Matsumoto I, Saito D, et al. Mean computed tomography value to predict the tumor invasiveness in clinical stage IA lung cancer. *Ann Thorac Surg*. 2017 Jul;104(1):261-6. doi: 10.1016/j.athoracsur.2017.01.060. PMID: 28410633. Exclusion Code: X8.

1642. Tane S, Nishio W, Okuma H, et al. Operative outcomes of thoracoscopic lobectomy for non-small-cell lung cancer. *Asian Cardiovasc Thorac Ann*. 2015 Oct;23(8):950-7. doi: 10.1177/0218492315596657. PMID: 26207005. Exclusion Code: X11.

1643. Tang C, Welsh JW, de Groot P, et al. Ipilimumab with stereotactic ablative radiation therapy: Phase I results and immunologic correlates from peripheral T cells. *Clin Cancer Res*. 2017 Mar 15;23(6):1388-96. doi: 10.1158/1078-0432.ccr-16-1432. PMID: 27649551. Exclusion Code: X3.

1644. Taniguchi D, Yamasaki N, Miyazaki T, et al. The surgical outcomes of lung cancer combined with interstitial pneumonia: a single-institution report. *Surg Today*. 2017 Nov;47(11):1397-404. doi: 10.1007/s00595-017-1551-5. PMID: 28589262. Exclusion Code: X3.

1645. Tanner NT, Aggarwal J, Gould MK, et al. Management of pulmonary nodules by community pulmonologists: a multicenter observational study. *Chest*. 2015 Dec;148(6):1405-14. doi: 10.1378/chest.15-0630. PMID: 26087071. Exclusion Code: X3.

1646. Tanner NT, Egede LE, Shamblin C, et al. Attitudes and beliefs toward lung cancer screening among US Veterans. *Chest*. 2013 Dec;144(6):1783-7. doi: 10.1378/chest.13-0056. PMID: 23764896. Exclusion Code: X8.

1647. Tao G, Jingying Y, Tan G, et al. A novel CT-guided technique using medical adhesive for localization of small pulmonary ground-glass nodules and mixed ground-glass nodules (</=20 mm) before video-assisted thoracoscopic surgery. *Diagn Interv Radiol*. 2018 Jul;24(4):209-12. doi: 10.5152/dir.2018.17315. PMID: 30091711. Exclusion Code: X3.

1648. Tao H, Hayashi T, Sano F, et al. Prognostic impact of lymphovascular invasion compared with that of visceral pleural invasion in patients with pN0 non-small-cell lung cancer and a tumor diameter of 2 cm or smaller. *J Surg Res*. 2013 Nov;185(1):250-4. doi: 10.1016/j.jss.2013.05.104. PMID: 23830361. Exclusion Code: X11.

1649. Tao H, Onoda H, Okabe K, et al. The impact of coexisting lung diseases on outcomes in patients with pathological Stage I non-small-cell lung cancer. *Interact Cardiovasc Thorac Surg*. 2018 Jun 1;26(6):1009-15. doi: 10.1093/icvts/ivx441. PMID: 29394349. Exclusion Code: X10.

1650. Tartar A, Kilic N, Akan A. Classification of pulmonary nodules by using hybrid features. *Comput Math Methods Med*. 2013;2013:148363. doi: 10.1155/2013/148363. PMID: 23970942. Exclusion Code: X3.

1651. Taton O, Bondue B, Gevenois PA, et al. Diagnostic Yield of Combined Pulmonary Cryobiopsies and Electromagnetic Navigation in Small Pulmonary Nodules. *Pulm Med*. 2018;2018:6032974. doi: 10.1155/2018/6032974. PMID: 30581621. Exclusion Code: X3.

1652. Taus A, Aguilo R, Curull V, et al. Impact of 18F-FDG PET/CT in the treatment of patients with non-small cell lung cancer. *Arch Bronconeumol*. 2014 Mar;50(3):99-104. doi: 10.1016/j.arbres.2013.09.017. PMID: 24360985. Exclusion Code: X3.

1653. Taverner J, Cheang MY, Antippa P, et al. Negative EBUS-TBNA predicts very low prevalence of mediastinal disease in staging of non-small cell lung cancer. *J Bronchology Interv Pulmonol*. 2016 Apr;23(2):177-80. doi: 10.1097/lbr.0000000000000234. PMID: 26905440. Exclusion Code: X8.

1654. Tay JH, Irving L, Antippa P, et al. Radial probe endobronchial ultrasound: factors influencing visualization yield of peripheral pulmonary lesions. *Respirology*. 2013 Jan;18(1):185-90. doi: 10.1111/j.1440-1843.2012.02276.x. PMID: 23035636. Exclusion Code: X3.

1655. Taylor MD, LaPar DJ, Isbell JM, et al. Marginal pulmonary function should not preclude lobectomy in selected patients with non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2014 Feb;147(2):738-44; Discussion 44-6. doi: 10.1016/j.jtcvs.2013.09.064. PMID: 24252944. Exclusion Code: X3.

1656. Tchouta LN, Park HS, Boffa DJ, et al. Hospital volume and outcomes of robot-assisted lobectomies. *Chest*. 2017 Feb;151(2):329-39. doi: 10.1016/j.chest.2016.09.008. PMID: 27687847. Exclusion Code: X3.

1657. Tekatli H, Duijm M, Oomen-de Hoop E, et al. Normal Tissue Complication Probability Modeling of Pulmonary Toxicity After Stereotactic and Hypofractionated Radiation Therapy for Central Lung Tumors. *Int J Radiat Oncol Biol Phys*. 2018 Mar 1;100(3):738-47. doi: 10.1016/j.ijrobp.2017.11.022. PMID: 29413285. Exclusion Code: X3.

1658. Tekatli H, van 't Hof S, Nossent EJ, et al. Use of stereotactic ablative radiotherapy (SABR) in non-small cell lung cancer measuring more than 5 cm. *J Thorac Oncol*. 2017 Jun;12(6):974-82. doi: 10.1016/j.jtho.2017.02.021. PMID: 28286243. Exclusion Code: X3.

1659. Tembhekar AR, Wright CL, Daly ME. Cardiac dose and survival after stereotactic body radiotherapy for early-stage non-small-cell lung cancer. *Clin Lung Cancer*. 2017 May;18(3):293-8. doi: 10.1016/j.cllc.2016.12.007. PMID: 28089158. Exclusion Code: X10.

1660. Temming S, Kocher M, Stoelben E, et al. Risk-adapted robotic stereotactic body radiation therapy for inoperable early-stage non-small-cell lung cancer. *Strahlenther Onkol*. 2018 Feb;194(2):91-7. doi: 10.1007/s00066-017-1194-x. PMID: 28812120. Exclusion Code: X3.

1661. ten Haaf K, de Koning HJ. Should never-smokers at increased risk for lung cancer be screened? *J Thorac Oncol*. 2015 Sep;10(9):1285-91. doi: 10.1097/jto.0000000000000593. PMID: 26287320. Exclusion Code: X4.

1662. ten Haaf K, van Rosmalen J, de Koning HJ. Lung cancer detectability by test, histology, stage, and gender: estimates from the NLST and the PLCO trials. *Cancer Epidemiol Biomarkers Prev*. 2015 Jan;24(1):154-61. doi: 10.1158/1055-9965.epi-14-0745. PMID: 25312998. Exclusion Code: X8.

1663. Teramoto A, Fujita H, Yamamuro O, et al. Automated detection of pulmonary nodules in PET/CT images: Ensemble false-positive reduction using a convolutional neural network technique. *Med Phys*. 2016 Jun;43(6):2821-7. doi: 10.1118/1.4948498. PMID: 27277030. Exclusion Code: X5.

1664. Terzi A, Bertolaccini L, Viti A, et al. Lung cancer detection with digital chest tomosynthesis: baseline results from the observational study SOS. *J Thorac Oncol*. 2013 Jun;8(6):685-92. doi: 10.1097/JTO.0b013e318292bdef. PMID: 23612466. Exclusion Code: X5.

1665. Thibault I, Poon I, Yeung L, et al. Predictive factors for local control in primary and metastatic lung tumours after four to five fraction stereotactic ablative body radiotherapy: a single institution's comprehensive experience. *Clin Oncol (R Coll Radiol)*. 2014 Nov;26(11):713-9. doi: 10.1016/j.clon.2014.06.018. PMID: 25085765. Exclusion Code: X3.

1666. Thomas DC, Arnold BN, Hoag JR, et al. Timing and Risk Factors Associated With Venous Thromboembolism After Lung Cancer Resection. *Ann Thorac Surg*. 2018 May;105(5):1469-75. doi: 10.1016/j.athoracsur.2018.01.072. PMID: 29501644. Exclusion Code: X3.

1667. Thomas PA, Berbis J, Baste JM, et al. Pneumonectomy for lung cancer: contemporary national early morbidity and mortality outcomes. *J Thorac Cardiovasc Surg*. 2015 Jan;149(1):73-82. doi: 10.1016/j.jtcvs.2014.09.063. PMID: 25439468. Exclusion Code: X3.

1668. Thomas PA, Falcoz PE, Bernard A, et al. Bilobectomy for lung cancer: contemporary national early morbidity and mortality outcomes. *Eur J Cardiothorac Surg*. 2016 Feb;49(2):e38-43; discussion e. doi: 10.1093/ejcts/ezv407. PMID: 27070154. Exclusion Code: X3.

1669. Thornton AA, Owen JE, Kernstine K, et al. Predictors of finding benefit after lung cancer diagnosis. *Psychooncology*. 2012 Apr;21(4):365-73. doi: 10.1002/pon.1904. PMID: 21254308. Exclusion Code: X3.

1670. Thorsteinsson H, Alexandersson A, Oskarsdottir GN, et al. Resection rate and outcome of pulmonary resections for non-small-cell lung cancer: a nationwide study from Iceland. *J Thorac Oncol*. 2012 Jul;7(7):1164-9. doi: 10.1097/JTO.0b013e318252d022. PMID: 22592213. Exclusion Code: X11.

1671. Timmerman R, McGarry R, Yiannoutsos C, et al. Excessive toxicity when treating central tumors in a phase II study of stereotactic body radiation therapy for medically inoperable early-stage lung cancer. *J Clin Oncol*. 2006 Oct 20;24(30):4833-9. doi: 10.1200/jco.2006.07.5937. PMID: 17050868. Exclusion Code: X11.

1672. Timmerman R, Papiez L, McGarry R, et al. Extracranial stereotactic radioablation: results of a phase I study in medically inoperable stage I non-small cell lung cancer. *Chest*. 2003 Nov;124(5):1946-55. PMID: 14605072. Exclusion Code: X11.

1673. Timmerman RD, Kavanagh BD. Stereotactic body radiation therapy. *Curr Probl Cancer*. 2005 May-Jun;29(3):120-57. doi: 10.1016/j.currproblcancer.2005.05.001. PMID: 16059851. Exclusion Code: X10.

1674. Tirzite M, Bukovskis M, Strazda G, et al. Detection of lung cancer in exhaled breath with an electronic nose using support vector machine analysis. *J Breath Res*. 2017 Aug 21;11(3):036009. doi: 10.1088/1752-7163/aa7799. PMID: 28585921. Exclusion Code: X5.

1675. Tjulandin S, Imyanitov E, Moiseyenko V, et al. Prospective cohort study of clinical characteristics and management patterns for patients with non-small-cell lung cancer in the Russian Federation: EPICLIN-Lung. *Curr Med Res Opin*. 2015 Jun;31(6):1117-27. doi: 10.1185/03007995.2015.1036015. PMID: 25867537. Exclusion Code: X3.

1676. Toba H, Kondo K, Miyoshi T, et al. Fluoroscopy-assisted thoracoscopic resection after computed tomography-guided bronchoscopic metallic coil marking for small peripheral pulmonary lesions. *Eur J Cardiothorac Surg*. 2013 Aug;44(2):e126-32. doi: 10.1093/ejcts/ezt220. PMID: 23598353. Exclusion Code: X3.

1677. Tockman M. Survival and mortality from lung cancer in a screened population: The Johns Hopkins study. *Chest*. 1986;89(Suppl):325s-6s. Exclusion Code: X2.

1678. Tokoro Y, Yasuo M, Kobayashi T, et al. Computed tomography-guided bronchoscopy in the diagnosis of small peripheral pulmonary lesions: A retrospective study of 240 examinations in a single academic center. *Respir Investig*. 2016 Sep;54(5):347-54. doi: 10.1016/j.resinv.2016.04.004. PMID: 27566383. Exclusion Code: X3.

1679. Tomita M, Ayabe T, Chosa E, et al. Impact of smoking on outcome of resected lung adenocarcinoma. *Gen Thorac Cardiovasc Surg*. 2015 Nov;63(11):608-12. doi: 10.1007/s11748-015-0579-y. PMID: 26243355. Exclusion Code: X3.

1680. Tomita M, Ayabe T, Nakamura K. The advanced lung cancer inflammation index is an independent prognostic factor after surgical resection in patients with non-small-cell lung cancer. *Interact Cardiovasc Thorac Surg*. 2018 Feb 1;26(2):288-92. doi: 10.1093/icvts/ivx329. PMID: 29049691. Exclusion Code: X3.

1681. Tomizawa K, Shimizu S, Ohara S, et al. Clinical significance of tumor cavitation in surgically resected early-stage primary lung cancer. *Lung Cancer*. 2017 Oct;112:57-61. doi: 10.1016/j.lungcan.2017.08.004. PMID: 29191601. Exclusion Code: X3.

1682. Tong AN, Yan P, Yuan GH, et al. Advantages of CyberKnife for inoperable stage I peripheral non-small-cell lung cancer compared to three-dimensional conformal radiotherapy. *Mol Clin Oncol*. 2015 Mar;3(2):442-8. doi: 10.3892/mco.2014.475. PMID: 25798283. Exclusion Code: X14.

1683. Tong BC, Kosinski AS, Burfeind WR, Jr., et al. Sex differences in early outcomes after lung cancer resection: analysis of the Society of Thoracic Surgeons General Thoracic Database. *J Thorac Cardiovasc Surg*. 2014 Jul;148(1):13-8. doi: 10.1016/j.jtcvs.2014.03.012. PMID: 24726742. Exclusion Code: X3.

1684. Tong LC, Rudomina D, Rekhtman N, et al. Impact of touch preparations on core needle biopsies. *Cancer Cytopathol*. 2014 Nov;122(11):851-4. doi: 10.1002/cncy.21447. PMID: 24946755. Exclusion Code: X3.

1685. Toosi K, Velez-Cubian FO, Glover J, et al. Upstaging and survival after robotic-assisted thoracoscopic lobectomy for non-small cell lung cancer. *Surgery*. 2016 Nov;160(5):1211-8. doi: 10.1016/j.surg.2016.08.003. PMID: 27665362. Exclusion Code: X3.

1686. Torchio R, Mazzucco A, Guglielmo M, et al. Minute ventilation to carbon dioxide output (V'E/V'CO2 slope) is the strongest death predictor before larger lung resections. *Monaldi Arch Chest Dis*. 2017 Sep 22;87(3):817. doi: 10.4081/monaldi.2017.817. PMID: 29424191. Exclusion Code: X3.

1687. Torres EL, Fiorina E, Pennazio F, et al. Large scale validation of the M5L lung CAD on heterogeneous CT datasets. *Med Phys*. 2015 Apr;42(4):1477-89. doi: 10.1118/1.4907970. PMID: 25832038. Exclusion Code: X3.

1688. Toyokawa G, Yamada Y, Tagawa T, et al. Significance of spread through air spaces in early-stage lung adenocarcinomas undergoing limited resection. *Thorac Cancer*. 2018 Oct;9(10):1255-61. doi: 10.1111/1759-7714.12828. PMID: 30079987. Exclusion Code: X11.

1689. Toyooka S, Okumura N, Nakamura H, et al. A Multicenter Randomized Controlled Study of Paclitaxel plus Carboplatin versus Oral Uracil-Tegafur as the Adjuvant Chemotherapy in Resected Non-Small Cell Lung Cancer. *J Thorac Oncol*. 2018;13(5):699-706. doi: 10.1016/j.jtho.2018.02.015. PMID: CN-01913780. Exclusion Code: X3.

1690. Tramontano AC, Cipriano LE, Kong CY, et al. Microsimulation model predicts survival benefit of radiofrequency ablation and stereotactic body radiotherapy versus radiotherapy for treating inoperable stage I non-small cell lung cancer. *AJR Am J Roentgenol*. 2013 May;200(5):1020-7. doi: 10.2214/ajr.12.8968. PMID: 23617484. Exclusion Code: X3.

1691. Tramontano AC, Sheehan DF, McMahon PM, et al. Evaluating the impacts of screening and smoking cessation programmes on lung cancer in a high-burden region of the USA: a simulation modelling study. *BMJ Open*. 2016 Feb 29;6(2):e010227. doi: 10.1136/bmjopen-2015-010227. PMID: 26928026. Exclusion Code: X7.

1692. Tran AA, Brown SB, Rosenberg J, et al. Tract embolization with gelatin sponge slurry for prevention of pneumothorax after percutaneous computed tomography-guided lung biopsy. *Cardiovasc Intervent Radiol*. 2014 Dec;37(6):1546-53. doi: 10.1007/s00270-013-0823-8. PMID: 24366313. Exclusion Code: X3.

1693. Tremblay A, Taghizadeh N, McWilliams AM, et al. Low prevalence of high-grade lesions detected with autofluorescence bronchoscopy in the setting of lung cancer screening in the Pan-Canadian Lung Cancer Screening Study. *Chest*. 2016 Nov;150(5):1015-22. doi: 10.1016/j.chest.2016.04.019. PMID: 27142184. Exclusion Code: X5.

1694. Tresoldi S, Flor N, Luciani A, et al. Contrast enhanced chest-MDCT in oncologic patients. Prospective evaluation of the prevalence of incidental pulmonary embolism and added value of thin reconstructions. *Eur Radiol*. 2015 Nov;25(11):3200-6. doi: 10.1007/s00330-015-3739-7. PMID: 25899418. Exclusion Code: X3.

1695. Trivino A, Congregado M, Loscertales J, et al. Experience and development of the video-assisted thoracic surgery lobectomy technique: comparative study with conventional surgery in stage I non-small cell lung cancer. *Arch Bronconeumol*. 2014 Feb;50(2):57-61. doi: 10.1016/j.arbres.2013.05.007. PMID: 23890810. Exclusion Code: X11.

1696. Trudgen K, Khattar NH, Bensadoun E, et al. Autoantibody profiling for lung cancer screening longitudinal retrospective analysis of CT screening cohorts. *PLoS One*. 2014;9(2):e87947. doi: 10.1371/journal.pone.0087947. PMID: 24498409. Exclusion Code: X5.

1697. Tseng TS, Park JY, Zabaleta J, et al. Role of nicotine dependence on the relationship between variants in the nicotinic receptor genes and risk of lung adenocarcinoma. *PLoS One*. 2014;9(9):e107268. doi: 10.1371/journal.pone.0107268. PMID: 25233467. Exclusion Code: X10.

1698. Tsubamoto M, Nishida T, Higaki N, et al. Separation between the chest wall and subpleural lung lesions: A two-step method to preoperatively exclude invasion or focal pleural adhesion by multidetector computed tomography. *Eur J Radiol*. 2019 Mar;112:180-5. doi: 10.1016/j.ejrad.2019.01.027. PMID: 30777208. Exclusion Code: X3.

1699. Tsukioka T, Izumi N, Mizuguchi S, et al. Impact of multiple malignancies on surgical outcomes in patients with 1 cm or smaller non-small cell lung cancer. *Int J Clin Oncol*. 2018 Feb;23(1):66-72. doi: 10.1007/s10147-017-1185-z. PMID: 28864833. Exclusion Code: X3.

1700. Tsunezuka H, Kato D, Okada S, et al. Surgical outcome of wide wedge resection in poor-risk patients with clinical-N0 non-small cell lung cancer. *Gen Thorac Cardiovasc Surg*. 2017 Oct;65(10):581-6. doi: 10.1007/s11748-017-0803-z. PMID: 28748318. Exclusion Code: X11.

1701. Tsutani Y, Miyata Y, Kushitani K, et al. Propensity score-matched analysis of adjuvant chemotherapy for stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg*. 2014 Oct;148(4):1179-85. doi: 10.1016/j.jtcvs.2014.05.084. PMID: 25112928. Exclusion Code: X10.

1702. Tsutani Y, Miyata Y, Nakayama H, et al. Oncologic outcomes of segmentectomy compared with lobectomy for clinical stage IA lung adenocarcinoma: propensity score-matched analysis in a multicenter study. *J Thorac Cardiovasc Surg*. 2013 Aug;146(2):358-64. doi: 10.1016/j.jtcvs.2013.02.008. PMID: 23477694. Exclusion Code: X11.

1703. Tsutani Y, Miyata Y, Nakayama H, et al. Appropriate sublobar resection choice for ground glass opacity-dominant clinical stage IA lung adenocarcinoma: wedge resection or segmentectomy. *Chest*. 2014 Jan;145(1):66-71. doi: 10.1378/chest.13-1094. PMID: 24551879. Exclusion Code: X8.

1704. Tu Q, Yang Z, Gan J, et al. Transcutaneous Electrical Acupoint Stimulation Improves Immunological Function During the Perioperative Period in Patients With Non-Small Cell Lung Cancer Undergoing Video-Assisted Thoracic Surgical Lobectomy. *Technol Cancer Res Treat*. 2018 Jan 1;17:1533033818806477. doi: 10.1177/1533033818806477. PMID: 30381011. Exclusion Code: X6.

1705. Tucker SL, Liao Z, Dinh J, et al. Is there an impact of heart exposure on the incidence of radiation pneumonitis? Analysis of data from a large clinical cohort. *Acta Oncol*. 2014 May;53(5):590-6. doi: 10.3109/0284186x.2013.831185. PMID: 23992110. Exclusion Code: X3.

1706. Tvilum M, Khalil AA, Moller DS, et al. Clinical outcome of image-guided adaptive radiotherapy in the treatment of lung cancer patients. *Acta Oncol*. 2015;54(9):1430-7. doi: 10.3109/0284186x.2015.1062544. PMID: 26206515. Exclusion Code: X3.

1707. Uchida Y, Tsugawa T, Tanaka-Mizuno S, et al. Exclusion of emphysematous lung from dose-volume estimates of risk improves prediction of radiation pneumonitis. *Radiat Oncol*. 2017 Oct 2;12(1):160. doi: 10.1186/s13014-017-0891-z. PMID: 28969651. Exclusion Code: X3.

1708. Ueda K, Hayashi M, Tanaka N, et al. Surgery for undiagnosed ground glass pulmonary nodules: decision making using serial computed tomography. *World J Surg*. 2015 Jun;39(6):1452-9. doi: 10.1007/s00268-015-2979-7. PMID: 25651958. Exclusion Code: X3.

1709. Ueda K, Murakami J, Sano F, et al. Similar radiopathological features, but different postoperative recurrence rates, between Stage I lung cancers arising in emphysematous lungs and those arising in nonemphysematous lungs. *Eur J Cardiothorac Surg*. 2015 May;47(5):905-11. doi: 10.1093/ejcts/ezu311. PMID: 25123673. Exclusion Code: X11.

1710. Ueda K, Sano F, Murakami J, et al. Does pulmonary resection promote the progression of unresected ground-glass nodules? *Anticancer Res*. 2014 Dec;34(12):7401-6. PMID: 25503180. Exclusion Code: X3.

1711. Uehara H, Matsuura Y, Nakao M, et al. Prognostic significance of clinical/pathological stage IA non-small-cell lung cancer showing partially solid or solid tumours on radiological exam. *Ann Thorac Cardiovasc Surg*. 2015;21(4):338-44. doi: 10.5761/atcs.oa.14-00242. PMID: 25740451. Exclusion Code: X11.

1712. Uehara H, Tsutani Y, Okumura S, et al. Prognostic role of positron emission tomography and high-resolution computed tomography in clinical stage IA lung adenocarcinoma. *Ann Thorac Surg*. 2013 Dec;96(6):1958-65. doi: 10.1016/j.athoracsur.2013.06.086. PMID: 24021765. Exclusion Code: X8.

1713. Ueki N, Matsuo Y, Togashi Y, et al. Impact of pretreatment interstitial lung disease on radiation pneumonitis and survival after stereotactic body radiation therapy for lung cancer. *J Thorac Oncol*. 2015 Jan;10(1):116-25. doi: 10.1097/jto.0000000000000359. PMID: 25376512. Exclusion Code: X10.

1714. Uribe-Etxebarria Lugariza-Aresti N, Barcelo Galindez R, Pac Ferrer J, et al. Biopsy of the sentinel node in lung cancer. *Med Clin (Barc)*. 2017 Mar 22;148(6):257-9. doi: 10.1016/j.medcli.2016.10.034. PMID: 27993403. Exclusion Code: X3.

1715. Usuda K, Funasaki A, Sekimura A, et al. FDG-PET/CT and diffusion-weighted imaging for resected lung cancer: correlation of maximum standardized uptake value and apparent diffusion coefficient value with prognostic factors. *Med Oncol*. 2018 Apr 9;35(5):66. doi: 10.1007/s12032-018-1128-1. PMID: 29633024. Exclusion Code: X3.

1716. Uzun C, Akkaya Z, Dusunceli Atman E, et al. Diagnostic accuracy and safety of CT-guided fine needle aspiration biopsy of pulmonary lesions with non-coaxial technique: a single center experience with 442 biopsies. *Diagn Interv Radiol*. 2017 Mar-Apr;23(2):137-43. doi: 10.5152/dir.2016.16173. PMID: 28029638. Exclusion Code: X3.

1717. Vagn-Hansen C, Pedersen MR, Rafaelsen SR. Diagnostic yield and complications of transthoracic computed tomography-guided biopsies. *Dan Med J*. 2016 Jun;63(6)PMID: 27264940. Exclusion Code: X3.

1718. Valan CD, Slagsvold JE, Halvorsen TO, et al. Survival in limited disease small cell lung cancer according to N3 lymph node involvement. *Anticancer Res*. 2018 Feb;38(2):871-6. doi: 10.21873/anticanres.12296. PMID: 29374714. Exclusion Code: X3.

1719. Valdes G, Robinson C, Lee P, et al. Tumor control probability and the utility of 4D vs 3D dose calculations for stereotactic body radiotherapy for lung cancer. *Med Dosim*. 2015 Spring;40(1):64-9. doi: 10.1016/j.meddos.2014.10.002. PMID: 25542785. Exclusion Code: X11.

1720. Valdes G, Solberg TD, Heskel M, et al. Using machine learning to predict radiation pneumonitis in patients with stage I non-small cell lung cancer treated with stereotactic body radiation therapy. *Phys Med Biol*. 2016 Aug 21;61(16):6105-20. doi: 10.1088/0031-9155/61/16/6105. PMID: 27461154. Exclusion Code: X10.

1721. van Boerdonk RA, Daniels JM, Snijders PJ, et al. DNA copy number aberrations in endobronchial lesions: a validated predictor for cancer. *Thorax*. 2014 May;69(5):451-7. doi: 10.1136/thoraxjnl-2013-203821. PMID: 24227199. Exclusion Code: X7.

1722. van Boerdonk RA, Smesseim I, Heideman DA, et al. Close surveillance with long-term follow-up of subjects with preinvasive endobronchial lesions. *Am J Respir Crit Care Med*. 2015 Dec 15;192(12):1483-9. doi: 10.1164/rccm.201504-0822OC. PMID: 26275031. Exclusion Code: X3.

1723. van den Berg LL, Klinkenberg TJ, Groen HJ, et al. Patterns of recurrence and survival after surgery or stereotactic radiotherapy for early stage NSCLC. *J Thorac Oncol*. 2015 May;10(5):826-31. doi: 10.1097/jto.0000000000000483. PMID: 25629639. Exclusion Code: X10.

1724. van der Aalst CM, van Klaveren RJ, de Koning HJ. Does participation to screening unintentionally influence lifestyle behaviour and thus lifestyle-related morbidity? *Best Pract Res Clin Gastroenterol*. 2010 Aug;24(4):465-78. doi: 10.1016/j.bpg.2010.06.001. PMID: 20833350. Exclusion Code: X9.

1725. van der Heijden EH, Hoefsloot W, van Hees HW, et al. High definition bronchoscopy: a randomized exploratory study of diagnostic value compared to standard white light bronchoscopy and autofluorescence bronchoscopy. *Respir Res*. 2015 Mar 7;16:33. doi: 10.1186/s12931-015-0193-7. PMID: 25848883. Exclusion Code: X3.

1726. van der Linden N, Bongers ML, Coupe VMH, et al. Treatment patterns and differences in survival of non-small cell lung cancer patients between academic and non-academic hospitals in the Netherlands. *Clin Lung Cancer*. 2017 Sep;18(5):e341-e7. doi: 10.1016/j.cllc.2015.11.011. PMID: 28347579. Exclusion Code: X3.

1727. 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 randomised lung cancer multi-slice CT screening trial (NELSON). *Int J Cancer*. 2007 Feb 15;120(4):868-74. doi: 10.1002/ijc.22134. PMID: 17131307. Exclusion Code: X8.

1728. van Riel SJ, Ciompi F, Jacobs C, et al. Malignancy risk estimation of screen-detected nodules at baseline CT: comparison of the PanCan model, Lung-RADS and NCCN guidelines. *Eur Radiol*. 2017 Oct;27(10):4019-29. doi: 10.1007/s00330-017-4767-2. PMID: 28293773. Exclusion Code: X3.

1729. van Riel SJ, Ciompi F, Winkler Wille MM, et al. Malignancy risk estimation of pulmonary nodules in screening CTs: comparison between a computer model and human observers. *PLoS One*. 2017;12(11):e0185032. doi: 10.1371/journal.pone.0185032. PMID: 29121063. Exclusion Code: X5.

1730. VanderWalde NA, Deal AM, Comitz E, et al. Geriatric assessment as a predictor of tolerance, quality of life, and outcomes in older patients with head and neck cancers and lung cancers receiving radiation therapy. *Int J Radiat Oncol Biol Phys*. 2017 Jul 15;98(4):850-7. doi: 10.1016/j.ijrobp.2016.11.048. PMID: 28258889. Exclusion Code: X3.

1731. Vansteenkiste JF, Cho BC, Vanakesa T, et al. Efficacy of the MAGE-A3 cancer immunotherapeutic as adjuvant therapy in patients with resected MAGE-A3-positive non-small-cell lung cancer (MAGRIT): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2016 Jun;17(6):822-35. doi: 10.1016/s1470-2045(16)00099-1. PMID: 27132212. Exclusion Code: X6.

1732. Van't Westeinde SC, Horeweg N, De Leyn P, et al. Complications following lung surgery in the Dutch-Belgian randomized lung cancer screening trial. *Eur J Cardiothorac Surg*. 2012 Sep;42(3):420-9. doi: 10.1093/ejcts/ezs081. PMID: 22491665. Exclusion Code: X11.

1733. Varadarajulu S, Schmulewitz N, Wildi SM, et al. Accuracy of EUS in staging of T4 lung cancer. *Gastrointest Endosc*. 2004 Mar;59(3):345-8. PMID: 14997129. Exclusion Code: X3.

1734. Vardhanabhuti V, Pang CL, Tenant S, et al. Prospective intra-individual comparison of standard dose versus reduced-dose thoracic CT using hybrid and pure iterative reconstruction in a follow-up cohort of pulmonary nodules-Effect of detectability of pulmonary nodules with lowering dose based on nodule size, type and body mass index. *Eur J Radiol*. 2017 Jun;91:130-41. doi: 10.1016/j.ejrad.2017.04.006. PMID: 28629559. Exclusion Code: X5.

1735. Varela G, Gomez-Hernandez MT. Stereotactic ablative radiotherapy for early stage non-small cell lung cancer: a word of caution. *Transl Lung Cancer Res*. 2016 Feb;5(1):102-5. doi: 10.3978/j.issn.2218-6751.2015.10.10. PMID: 26958502. Exclusion Code: X10.

1736. Varlotto J, Fakiris A, Flickinger J, et al. Matched-pair and propensity score comparisons of outcomes of patients with clinical stage I non-small cell lung cancer treated with resection or stereotactic radiosurgery. *Cancer*. 2013 Aug 1;119(15):2683-91. doi: 10.1002/cncr.28100. PMID: 23605504. Exclusion Code: X10.

1737. Vassallo L, Traverso A, Agnello M, et al. A cloud-based computer-aided detection system improves identification of lung nodules on computed tomography scans of patients with extra-thoracic malignancies. *Eur Radiol*. 2019 Jan;29(1):144-52. doi: 10.1007/s00330-018-5528-6. PMID: 29948089. Exclusion Code: X3.

1738. Vaz AP, Fernandes G, Souto Moura C, et al. Integrated PET/CT in non small cell lung cancer staging--clinical and pathological agreement. *Rev Port Pneumol*. 2012 May-Jun;18(3):109-14. doi: 10.1016/j.rppneu.2012.01.004. PMID: 22405953. Exclusion Code: X11.

1739. Vehmas T. Visually scored calcifications in thoracic arteries predict death: follow-up study after lung cancer CT screening. *Acta Radiol*. 2012 Jul;53(6):643-7. doi: 10.1258/ar.2012.120247. PMID: 22761343. Exclusion Code: X10.

1740. Velcheti V, Schalper KA, Carvajal DE, et al. Programmed death ligand-1 expression in non-small cell lung cancer. *Lab Invest*. 2014 Jan;94(1):107-16. doi: 10.1038/labinvest.2013.130. PMID: 24217091. Exclusion Code: X7.

1741. Veluswamy RR, Ezer N, Mhango G, et al. Limited resection versus lobectomy for older patients with early-stage lung cancer: impact of histology. *J Clin Oncol*. 2015 Oct 20;33(30):3447-53. doi: 10.1200/jco.2014.60.6624. PMID: 26240229. Exclusion Code: X7.

1742. Venkitaraman B, Karunanithi S, Kumar A, et al. Role of 68Ga-DOTATOC PET/CT in initial evaluation of patients with suspected bronchopulmonary carcinoid. *Eur J Nucl Med Mol Imaging*. 2014 May;41(5):856-64. doi: 10.1007/s00259-013-2659-5. PMID: 24435773. Exclusion Code: X5.

1743. Verma A, Abisheganaden J, Light RW. Identifying malignant pleural effusion by a cancer ratio (serum LDH: pleural fluid ADA ratio). *Lung*. 2016 Feb;194(1):147-53. doi: 10.1007/s00408-015-9831-6. PMID: 26678281. Exclusion Code: X3.

1744. Verma A, Lim AY, Tai DY, et al. Timeliness of diagnosing lung cancer: number of procedures and time needed to establish diagnosis: being right the first time. *Medicine (Baltimore)*. 2015 Jul;94(29):e1216. doi: 10.1097/md.0000000000001216. PMID: 26200646. Exclusion Code: X3.

1745. Verma S, Chan J, Chew C, et al. PET-SUV Max and Upstaging of Lung Cancer. *Heart Lung Circ*. 2019 Mar;28(3):436-42. doi: 10.1016/j.hlc.2017.12.011. PMID: 29428202. Exclusion Code: X3.

1746. Verma V, Shostrom VK, Zhen W, et al. Influence of fractionation scheme and tumor location on toxicities after stereotactic body radiation therapy for large (>/=5 cm) non-small cell lung cancer: a multi-institutional analysis. *Int J Radiat Oncol Biol Phys*. 2017 Mar 15;97(4):778-85. doi: 10.1016/j.ijrobp.2016.11.049. PMID: 28244414. Exclusion Code: X3.

1747. Verma V, Simone CB, 2nd, Allen PK, et al. Multi-institutional experience of stereotactic ablative radiation therapy for stage I small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2017 Feb 1;97(2):362-71. doi: 10.1016/j.ijrobp.2016.10.041. PMID: 28011047. Exclusion Code: X3.

1748. Veronesi G, Maisonneuve P, Rampinelli C, et al. Computed tomography screening for lung cancer: results of ten years of annual screening and validation of cosmos prediction model. *Lung Cancer*. 2013 Dec;82(3):426-30. doi: 10.1016/j.lungcan.2013.08.026. PMID: 24099665. Exclusion Code: X4.

1749. Verstegen NE, Lagerwaard FJ, Hashemi SM, et al. Patterns of disease recurrence after SABR for early stage non-small-cell lung cancer: optimizing follow-up schedules for salvage therapy. *J Thorac Oncol*. 2015 Aug;10(8):1195-200. doi: 10.1097/jto.0000000000000576. PMID: 26200274. Exclusion Code: X8.

1750. Verstegen NE, Oosterhuis JW, Palma DA, et al. Stage I-II non-small-cell lung cancer treated using either stereotactic ablative radiotherapy (SABR) or lobectomy by video-assisted thoracoscopic surgery (VATS): outcomes of a propensity score-matched analysis. *Ann Oncol*. 2013 Jun;24(6):1543-8. doi: 10.1093/annonc/mdt026. PMID: 23425947. Exclusion Code: X3.

1751. Vest MT, Herrin J, Soulos PR, et al. Use of new treatment modalities for non-small cell lung cancer care in the Medicare population. *Chest*. 2013 Feb 1;143(2):429-35. doi: 10.1378/chest.12-1149. PMID: 23187634. Exclusion Code: X8.

1752. Vial MR, Khan KA, O'Connell O, et al. Endobronchial ultrasound-guided transbronchial needle aspiration in the nodal staging of stereotactic ablative body radiotherapy patients. *Ann Thorac Surg*. 2017 May;103(5):1600-5. doi: 10.1016/j.athoracsur.2016.09.106. PMID: 28027732. Exclusion Code: X3.

1753. Videtic GMM, Donington J, Giuliani M, et al. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline. *Pract Radiat Oncol*. 2017 Sep - Oct;7(5):295-301. doi: 10.1016/j.prro.2017.04.014. PMID: 28596092. Exclusion Code: X16.

1754. Videtic GMM, Woody NM, Reddy CA, et al. Never too old: a single-institution experience of stereotactic body radiation therapy for patients 90 years and older with early stage lung cancer. *Pract Radiat Oncol*. 2017 Nov - Dec;7(6):e543-e9. doi: 10.1016/j.prro.2017.06.011. PMID: 28867545. Exclusion Code: X3.

1755. Vinogradskiy Y, Diot Q, Kavanagh B, et al. Spatial and dose-response analysis of fibrotic lung changes after stereotactic body radiation therapy. *Med Phys*. 2013 Aug;40(8):081712. doi: 10.1118/1.4813916. PMID: 23927309. Exclusion Code: X8.

1756. Vis DC, Kelly MM, Lee AG, et al. Contralateral recurrence of inflammatory myofibroblastic tumour of the lung 10 years after pneumonectomy. *Thorax*. 2018 Nov;73(11):1089-90. doi: 10.1136/thoraxjnl-2018-211645. PMID: 29884625. Exclusion Code: X10.

1757. Viti A, Socci L, Congregado M, et al. The everlasting issue of prolonged air leaks after lobectomy for non-small cell lung cancer: A data-driven prevention planning model in the era of minimally invasive approaches. *J Surg Oncol*. 2018 Dec;118(8):1285-91. doi: 10.1002/jso.25289. PMID: 30399200. Exclusion Code: X3.

1758. Volk RJ, Linder SK, Leal VB, et al. Feasibility of a patient decision aid about lung cancer screening with low-dose computed tomography. *Prev Med*. 2014 May;62:60-3. doi: 10.1016/j.ypmed.2014.02.006. PMID: 24518006. Exclusion Code: X5.

1759. Voltolini L, Bongiolatti S, Luzzi L, et al. Impact of interstitial lung disease on short-term and long-term survival of patients undergoing surgery for non-small-cell lung cancer: analysis of risk factors. *Eur J Cardiothorac Surg*. 2013 Jan;43(1):e17-23. doi: 10.1093/ejcts/ezs560. PMID: 23129356. Exclusion Code: X11.

1760. von Reibnitz D, Shaikh F, Wu AJ, et al. Stereotactic body radiation therapy (SBRT) improves local control and overall survival compared to conventionally fractionated radiation for stage I non-small cell lung cancer (NSCLC). *Acta Oncol*. 2018 Nov;57(11):1567-73. doi: 10.1080/0284186x.2018.1481292. PMID: 29873277. Exclusion Code: X13.

1761. Wakeam E, Acuna SA, Leighl NB, et al. Surgery versus chemotherapy and radiotherapy for early and locally advanced small cell lung cancer: a propensity-matched analysis of survival. *Lung Cancer*. 2017 Jul;109:78-88. doi: 10.1016/j.lungcan.2017.04.021. PMID: 28577955. Exclusion Code: X3.

1762. Walker PR, Cykert S, Edwards L, et al. An intervention study to reduce black-white treatment disparities in early stage non-small cell lung cancer. *J Clin Oncol*. 2017;35(15)PMID: CN-01781395. Exclusion Code: X2.

1763. Walter JE, Heuvelmans MA, Bock GH, et al. Characteristics of new solid nodules detected in incidence screening rounds of low-dose CT lung cancer screening: the NELSON study. *Thorax*. 2018 Aug;73(8):741-7. doi: 10.1136/thoraxjnl-2017-211376. PMID: 29661918. Exclusion Code: X8.

1764. Walter JE, Heuvelmans MA, ten Haaf K, et al. Persisting new nodules in incidence rounds of the NELSON CT lung cancer screening study. *Thorax*. 2019 Mar;74(3):247-53. doi: 10.1136/thoraxjnl-2018-212152. PMID: 30591535. Exclusion Code: X8.

1765. Walts AE, Marchevsky AM. Potential errors in staging primary pulmonary adenocarcinomas by sublobar resection. *Ann Diagn Pathol*. 2013 Dec;17(6):471-5. doi: 10.1016/j.anndiagpath.2013.05.006. PMID: 23810206. Exclusion Code: X8.

1766. Wang BY, Liu CY, Hsu PK, et al. Single-incision versus multiple-incision thoracoscopic lobectomy and segmentectomy: a propensity-matched analysis. *Ann Surg*. 2015 Apr;261(4):793-9. doi: 10.1097/sla.0000000000000712. PMID: 24836148. Exclusion Code: X3.

1767. Wang BY, Tu CC, Liu CY, et al. Single-incision thoracoscopic lobectomy and segmentectomy with radical lymph node dissection. *Ann Thorac Surg*. 2013 Sep;96(3):977-82. doi: 10.1016/j.athoracsur.2013.05.002. PMID: 23870694. Exclusion Code: X3.

1768. Wang C, Duan Q, Kelly M, et al. Accuracy of bronchial brush and wash specimens prepared by the ThinPrep method in the diagnosis of pulmonary small cell carcinoma. *Cancer Cytopathol*. 2014 Aug;122(8):577-85. doi: 10.1002/cncy.21435. PMID: 24824569. Exclusion Code: X5.

1769. Wang CC, Tseng CC, Hsiao CC, et al. Circulating endothelial-derived activated microparticle: a useful biomarker for predicting one-year mortality in patients with advanced non-small cell lung cancer. *Biomed Res Int*. 2014;2014:173401. doi: 10.1155/2014/173401. PMID: 25061601. Exclusion Code: X3.

1770. Wang D, Koh ES, Descallar J, et al. Application of novel quantitative techniques for fluorodeoxyglucose positron emission tomography/computed tomography in patients with non-small-cell lung cancer. *Asia Pac J Clin Oncol*. 2016 Dec;12(4):349-58. doi: 10.1111/ajco.12587. PMID: 27550522. Exclusion Code: X3.

1771. Wang H, Shi J, Liu H, et al. Clinical and diagnostic features of angiosarcoma with pulmonary metastases: A retrospective observational study. *Medicine (Baltimore)*. 2017 Sep;96(36):e8033. doi: 10.1097/md.0000000000008033. PMID: 28885371. Exclusion Code: X3.

1772. Wang L, Anraku M, Sato M, et al. Impact of the 8th Edition of the UICC-TNM Classification on Clinical Stage 0-IA Lung Adenocarcinoma: Does the New Classification Predict Postoperative Prognosis More Precisely than the Previous One? *Ann Thorac Cardiovasc Surg*. 2018 Oct 19;24(5):223-9. doi: 10.5761/atcs.oa.18-00051. PMID: 29848840. Exclusion Code: X11.

1773. Wang L, Chen Y, Tang K, et al. The Value of (18)F-FDG PET/CT Mathematical Prediction Model in Diagnosis of Solitary Pulmonary Nodules. *Biomed Res Int*. 2018;2018:9453967. doi: 10.1155/2018/9453967. PMID: 29789808. Exclusion Code: X10.

1774. Wang L, Pei Y, Li S, et al. Left sleeve lobectomy versus left pneumonectomy for the management of patients with non-small cell lung cancer. *Thorac Cancer*. 2018 Mar;9(3):348-52. doi: 10.1111/1759-7714.12583. PMID: 29341464. Exclusion Code: X3.

1775. Wang L, Yin X, Wang F, et al. The usefulness of combined diagnostic CT and (99m)Tc-octreotide somatostatin receptor SPECT/CT imaging on pulmonary nodule characterization in patients. *Cancer Biother Radiopharm*. 2013 Dec;28(10):731-6. doi: 10.1089/cbr.2013.1482. PMID: 24094076. Exclusion Code: X8.

1776. Wang P, Zhang D, Guo XG, et al. A propensity-matched analysis of surgery and stereotactic body radiotherapy for early stage non-small cell lung cancer in the elderly. *Medicine (Baltimore)*. 2016 Dec;95(52):e5723. doi: 10.1097/md.0000000000005723. PMID: 28033277. Exclusion Code: X14.

1777. Wang S, Ye Q, Lu X. Plasma apolipoprotein E level is associated with the risk of endobronchial biopsy-induced bleeding in patients with lung cancer. *Lipids Health Dis*. 2018 Jul 21;17(1):166. doi: 10.1186/s12944-018-0821-6. PMID: 30031394. Exclusion Code: X3.

1778. Wang S, Zhang J, Lu X. Non-linear association of plasma level of high-density lipoprotein cholesterol with endobronchial biopsy bleeding in patients with lung cancer. *Lipids Health Dis*. 2019 Jan 18;18(1):17. doi: 10.1186/s12944-019-0966-y. PMID: 30658636. Exclusion Code: X3.

1779. Wang W, Dou S, Dong W, et al. Impact of COPD on prognosis of lung cancer: from a perspective on disease heterogeneity. *Int J Chron Obstruct Pulmon Dis*. 2018;13:3767-76. doi: 10.2147/copd.s168048. PMID: 30538439. Exclusion Code: X3.

1780. Wang W, Feng X, Duan X, et al. Establishment of two data mining models of lung cancer screening based on three gene promoter methylations combined with telomere damage. *Int J Biol Markers*. 2017 Mar 2;32(1):e141-e6. doi: 10.5301/jbm.5000232. PMID: 27716889. Exclusion Code: X7.

1781. Wang W, Liu M, Wang J, et al. Analysis of the discriminative methods for diagnosis of benign and malignant solitary pulmonary nodules based on serum markers. *Oncol Res Treat*. 2014;37(12):740-6. doi: 10.1159/000369488. PMID: 25531720. Exclusion Code: X5.

1782. Wang X, Li H, Zhu XR, et al. Multiple-CT optimization of intensity-modulated proton therapy - Is it possible to eliminate adaptive planning? *Radiother Oncol*. 2018 Jul;128(1):167-73. doi: 10.1016/j.radonc.2017.09.032. PMID: 29054378. Exclusion Code: X6.

1783. Wang X, Liu H, Shen Y, et al. Low-dose computed tomography (LDCT) versus other cancer screenings in early diagnosis of lung cancer: A meta-analysis. *Medicine (Baltimore)*. 2018 Jul;97(27):e11233. doi: 10.1097/md.0000000000011233. PMID: 29979385. Exclusion Code: X9.

1784. Wang X, Ma K, Cui J, et al. An individual risk prediction model for lung cancer based on a study in a Chinese population. *Tumori*. 2015 Jan-Feb;101(1):16-23. doi: 10.5301/tj.5000205. PMID: 25702657. Exclusion Code: X4.

1785. Wang X, Zamdborg L, Ye H, et al. A matched-pair analysis of stereotactic body radiotherapy (SBRT) for oligometastatic lung tumors from colorectal cancer versus early stage non-small cell lung cancer. *BMC Cancer*. 2018 Oct 10;18(1):962. doi: 10.1186/s12885-018-4865-9. PMID: 30305131. Exclusion Code: X10.

1786. Wang XY, Zhao YF, Liu Y, et al. Prognostic value of metabolic variables of [18F]FDG PET/CT in surgically resected stage I lung adenocarcinoma. *Medicine (Baltimore)*. 2017 Sep;96(35):e7941. doi: 10.1097/md.0000000000007941. PMID: 28858121. Exclusion Code: X3.

1787. Wang XY, Zhao YF, Liu Y, et al. Comparison of different automated lesion delineation methods for metabolic tumor volume of 18F-FDG PET/CT in patients with stage I lung adenocarcinoma. *Medicine (Baltimore)*. 2017 Dec;96(51):e9365. doi: 10.1097/md.0000000000009365. PMID: 29390527. Exclusion Code: X5.

1788. Wang Y, Hu Y, Wang D, et al. The analysis of volatile organic compounds biomarkers for lung cancer in exhaled breath, tissues and cell lines. *Cancer Biomark*. 2012;11(4):129-37. doi: 10.3233/cbm-2012-00270. PMID: 23144150. Exclusion Code: X5.

1789. Wang Y, Liu B, Cao P, et al. Comparison between computed tomography-guided percutaneous microwave ablation and thoracoscopic lobectomy for stage I non-small cell lung cancer. *Thorac Cancer*. 2018 Nov;9(11):1376-82. doi: 10.1111/1759-7714.12842. PMID: 30152596. Exclusion Code: X10.

1790. Wang Y, McKay JD, Rafnar T, et al. Rare variants of large effect in BRCA2 and CHEK2 affect risk of lung cancer. *Nat Genet*. 2014 Jul;46(7):736-41. doi: 10.1038/ng.3002. PMID: 24880342. Exclusion Code: X3.

1791. Wang Y, Wang R, Zheng D, et al. Predicting the recurrence risk factors and clinical outcomes of peripheral pulmonary adenocarcinoma </=3 cm with wedge resection. *J Cancer Res Clin Oncol*. 2017 Jun;143(6):1043-51. doi: 10.1007/s00432-016-2337-7. PMID: 28204972. Exclusion Code: X14.

1792. Wang Y, Wang R, Zheng D, et al. The indication of completion lobectomy for lung adenocarcinoma </=3 cm after wedge resection during surgical operation. *J Cancer Res Clin Oncol*. 2017 Oct;143(10):2095-104. doi: 10.1007/s00432-017-2452-0. PMID: 28616702. Exclusion Code: X14.

1793. Wang Y, Zheng D, Zheng J, et al. Predictors of recurrence and survival of pathological T1N0M0 invasive adenocarcinoma following lobectomy. *J Cancer Res Clin Oncol*. 2018 Jun;144(6):1015-23. doi: 10.1007/s00432-018-2622-8. PMID: 29532227. Exclusion Code: X10.

1794. Wang Z, Zhang J, Cheng Z, et al. Factors affecting major morbidity after video-assisted thoracic surgery for lung cancer. *J Surg Res*. 2014 Dec;192(2):628-34. doi: 10.1016/j.jss.2014.07.051. PMID: 25167779. Exclusion Code: X14.

1795. Wargo JJ, Kim AH, Hart A, et al. It took a village: good's syndrome. *Am J Med*. 2015 Jul;128(7):699-701. doi: 10.1016/j.amjmed.2015.03.002. PMID: 25796418. Exclusion Code: X3.

1796. Warren WA, Hagaman JT. Endobronchial ultrasound-guided transbronchial needle aspiration for mediastinal staging in a community medical center. *Ann Am Thorac Soc*. 2016 Oct;13(10):1802-7. doi: 10.1513/AnnalsATS.201603-216BC. PMID: 27409724. Exclusion Code: X3.

1797. Warth A, Cortis J, Soltermann A, et al. Tumour cell proliferation (Ki-67) in non-small cell lung cancer: a critical reappraisal of its prognostic role. *Br J Cancer*. 2014 Sep 9;111(6):1222-9. doi: 10.1038/bjc.2014.402. PMID: 25051406. Exclusion Code: X3.

1798. Warwick R, Mediratta N, Shackcloth M, et al. Wedge resection verses lobectomy for stage 1 non-small-cell lung cancer. *Asian Cardiovasc Thorac Ann*. 2013 Oct;21(5):566-73. doi: 10.1177/0218492312466861. PMID: 24570559. Exclusion Code: X8.

1799. Warwick R, Shackcloth M, Mediratta N, et al. Female sex and long-term survival post curative resection for non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2013 Oct;44(4):624-30. doi: 10.1093/ejcts/ezt139. PMID: 23509234. Exclusion Code: X8.

1800. Watanabe I, Kanauchi N, Watanabe H. Preoperative prognostic nutritional index as a predictor of outcomes in elderly patients after surgery for lung cancer. *Jpn J Clin Oncol*. 2018 Apr 1;48(4):382-7. doi: 10.1093/jjco/hyy014. PMID: 29528442. Exclusion Code: X10.

1801. Way T, Chan HP, Hadjiiski L, et al. Computer-aided diagnosis of lung nodules on CT scans: ROC study of its effect on radiologists' performance. *Acad Radiol*. 2010 Mar;17(3):323-32. doi: 10.1016/j.acra.2009.10.016. PMID: 20152726. Exclusion Code: X3.

1802. Wei B, Broussard B, Bryant A, et al. Left upper lobectomy after coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2015 Sep;150(3):531-5. doi: 10.1016/j.jtcvs.2015.05.066. PMID: 26149098. Exclusion Code: X3.

1803. Wei B, D'Amico T, Samad Z, et al. The impact of pulmonary hypertension on morbidity and mortality following major lung resection. *Eur J Cardiothorac Surg*. 2014 Jun;45(6):1028-33. doi: 10.1093/ejcts/ezt495. PMID: 24132298. Exclusion Code: X11.

1804. Weksler B, Kosinski AS, Burfeind WR, et al. Racial and ethnic differences in lung cancer surgical stage: an STS database study. *Thorac Cardiovasc Surg*. 2015 Oct;63(7):538-43. doi: 10.1055/s-0035-1546295. PMID: 25984780. Exclusion Code: X8.

1805. Welch BT, Brinjikji W, Schmit GD, et al. A national analysis of the complications, cost, and mortality of percutaneous lung ablation. *J Vasc Interv Radiol*. 2015 Jun;26(6):787-91. doi: 10.1016/j.jvir.2015.02.019. PMID: 25866239. Exclusion Code: X3.

1806. Wen SW, Han L, Lv HL, et al. A propensity-matched analysis of outcomes of patients with clinical stage I non-small cell lung cancer treated surgically or with stereotactic radiotherapy: a meta-analysis. *J Invest Surg*. 2019 Jan;32(1):27-34. doi: 10.1080/08941939.2017.1370519. PMID: 28985095. Exclusion Code: X9.

1807. Wesolowski SP, Boros PW, Orlowski TM, et al. Use the lower limit of normal, not 80% predicted, in judging eligibility for lung resection. *Respiration*. 2016;92(2):65-71. doi: 10.1159/000447974. PMID: 27428328. Exclusion Code: X3.

1808. White CS, Dharaiya E, Campbell E, et al. The Vancouver Lung Cancer Risk Prediction Model: assessment by using a subset of the National Lung Screening Trial Cohort. *Radiology*. 2017 Apr;283(1):264-72. doi: 10.1148/radiol.2016152627. PMID: 27740906. Exclusion Code: X3.

1809. Widder J, Postmus D, Ubbels JF, et al. Survival and quality of life after stereotactic or 3D-conformal radiotherapy for inoperable early-stage lung cancer. *Int J Radiat Oncol Biol Phys*. 2011 Nov 15;81(4):e291-7. doi: 10.1016/j.ijrobp.2011.03.052. PMID: 21640503. Exclusion Code: X13.

1810. Widlak P, Pietrowska M, Polanska J, et al. Serum mass profile signature as a biomarker of early lung cancer. *Lung Cancer*. 2016 Sep;99:46-52. doi: 10.1016/j.lungcan.2016.06.011. PMID: 27565913. Exclusion Code: X4.

1811. Wiener RS, Gould MK, Slatore CG, et al. Resource use and guideline concordance in evaluation of pulmonary nodules for cancer: too much and too little care. *JAMA Intern Med*. 2014 Jun;174(6):871-80. doi: 10.1001/jamainternmed.2014.561. PMID: 24710850. Exclusion Code: X3.

1812. Wiener RS, Gould MK, Woloshin S, et al. 'The thing is not knowing': patients' perspectives on surveillance of an indeterminate pulmonary nodule. *Health Expect*. 2015 Jun;18(3):355-65. doi: 10.1111/hex.12036. PMID: 23252477. Exclusion Code: X3.

1813. Wikoff WR, Hanash S, DeFelice B, et al. Diacetylspermine is a novel prediagnostic serum biomarker for non-small-cell lung cancer and has additive performance with pro-surfactant protein B. *J Clin Oncol*. 2015 Nov 20;33(33):3880-6. doi: 10.1200/jco.2015.61.7779. PMID: 26282655. Exclusion Code: X10.

1814. Wilbur DC, Meyer MG, Presley C, et al. Automated 3-dimensional morphologic analysis of sputum specimens for lung cancer detection: Performance characteristics support use in lung cancer screening. *Cancer Cytopathol*. 2015 Sep;123(9):548-56. doi: 10.1002/cncy.21565. PMID: 26153135. Exclusion Code: X5.

1815. Williams CD, Gajra A, Ganti AK, et al. Use and impact of adjuvant chemotherapy in patients with resected non-small cell lung cancer. *Cancer*. 2014 Jul 1;120(13):1939-47. doi: 10.1002/cncr.28679. PMID: 24668613. Exclusion Code: X6.

1816. Williams CD, Salama JK, Moghanaki D, et al. Impact of race on treatment and survival among U.S. veterans with early-stage lung cancer. *J Thorac Oncol*. 2016 Oct;11(10):1672-81. doi: 10.1016/j.jtho.2016.05.030. PMID: 27296104. Exclusion Code: X3.

1817. Williams CD, Stechuchak KM, Zullig LL, et al. Influence of comorbidity on racial differences in receipt of surgery among US veterans with early-stage non-small-cell lung cancer. *J Clin Oncol*. 2013 Feb 1;31(4):475-81. doi: 10.1200/jco.2012.44.1170. PMID: 23269988. Exclusion Code: X8.

1818. Williams SP, Kinshuck AJ, Williams C, et al. Incidental head and neck findings on 18F-fluoro-deoxy-glucose positron emission tomography computed tomography. *J Laryngol Otol*. 2015 Sep;129(9):898-902. doi: 10.1017/s0022215115001826. PMID: 26206309. Exclusion Code: X3.

1819. Wilshire CL, Louie BE, Manning KA, et al. Radiologic evaluation of small lepidic adenocarcinomas to guide decision making in surgical resection. *Ann Thorac Surg*. 2015 Sep;100(3):979-88. doi: 10.1016/j.athoracsur.2015.04.030. PMID: 26231858. Exclusion Code: X11.

1820. Wilson DO, Ryan A, Fuhrman C, et al. Doubling times and CT screen-detected lung cancers in the Pittsburgh Lung Screening Study. *Am J Respir Crit Care Med*. 2012 Jan 1;185(1):85-9. doi: 10.1164/rccm.201107-1223OC. PMID: 21997335. Exclusion Code: X11.

1821. Wilson DO, Weissfeld J. A simple model for predicting lung cancer occurrence in a lung cancer screening program: The Pittsburgh Predictor. *Lung Cancer*. 2015 Jul;89(1):31-7. doi: 10.1016/j.lungcan.2015.03.021. PMID: 25863905. Exclusion Code: X7.

1822. Wimaleswaran H, Farmer MW, Irving LB, et al. Pulmonologist-performed transoesophageal sampling for lung cancer staging using an endobronchial ultrasound video-bronchoscope: an Australian experience. *Intern Med J*. 2017 Feb;47(2):205-10. doi: 10.1111/imj.13330. PMID: 27860078. Exclusion Code: X3.

1823. Winkler Wille MM, van Riel SJ, Saghir Z, et al. Predictive accuracy of the PanCan Lung Cancer Risk Prediction Model-external validation based on CT from the Danish Lung Cancer Screening Trial. *Eur Radiol*. 2015 Oct;25(10):3093-9. doi: 10.1007/s00330-015-3689-0. PMID: 25764091. Exclusion Code: X4.

1824. Wisnivesky JP, Bonomi M, Henschke C, et al. Radiation therapy for the treatment of unresected stage I-II non-small cell lung cancer. *Chest*. 2005 Sep;128(3):1461-7. doi: 10.1378/chest.128.3.1461. PMID: 16162744. Exclusion Code: X6.

1825. Witte B, Stenz C, Vahl CF, et al. Comparative intention-to-treat analysis of the video-assisted thoracoscopic surgery approach to pulmonary segmentectomy for lung carcinomadouble dagger. *Interact Cardiovasc Thorac Surg*. 2015 Sep;21(3):276-83. doi: 10.1093/icvts/ivv143. PMID: 26063694. Exclusion Code: X3.

1826. Wolf A, Liu B, Leoncini E, et al. Outcomes for Thoracoscopy Versus Thoracotomy Not Just Technique Dependent: A Study of 9,787 Patients. *Ann Thorac Surg*. 2018 Mar;105(3):886-91. doi: 10.1016/j.athoracsur.2017.09.059. PMID: 29397101. Exclusion Code: X3.

1827. Wolf AS, Swanson SJ, Yip R, et al. The impact of margins on outcomes after wedge resection for stage I non-small cell lung cancer. *Ann Thorac Surg*. 2017 Oct;104(4):1171-8. doi: 10.1016/j.athoracsur.2017.04.024. PMID: 28669499. Exclusion Code: X3.

1828. Wolf FJ, Aswad B, Ng T, et al. Intraoperative microwave ablation of pulmonary malignancies with tumor permittivity feedback control: ablation and resection study in 10 consecutive patients. *Radiology*. 2012 Jan;262(1):353-60. doi: 10.1148/radiol.11110015. PMID: 22106348. Exclusion Code: X6.

1829. Wolff HB, Alberts L, Kastelijn EA, et al. Differences in longitudinal health utility between stereotactic body radiation therapy and surgery in stage I non-small cell lung cancer. *J Thorac Oncol*. 2018 May;13(5):689-98. doi: 10.1016/j.jtho.2018.01.021. PMID: 29391288. Exclusion Code: X3.

1830. Wong OY, Yau V, Kang J, et al. Survival Impact of Cardiac Dose Following Lung Stereotactic Body Radiotherapy. *Clin Lung Cancer*. 2018 Mar;19(2):e241-e6. doi: 10.1016/j.cllc.2017.08.002. PMID: 28941961. Exclusion Code: X3.

1831. Wood DE, Eapen GA, Ettinger DS, et al. Lung cancer screening. *J Natl Compr Canc Netw*. 2012 Feb;10(2):240-65. PMID: 22308518. Exclusion Code: X10.

1832. Woody NM, Stephans KL, Andrews M, et al. A histologic basis for the efficacy of SBRT to the lung. *J Thorac Oncol*. 2017 Mar;12(3):510-9. doi: 10.1016/j.jtho.2016.11.002. PMID: 28017592. Exclusion Code: X13.

1833. Woody NM, Stephans KL, Andrews M, et al. A biological basis for local failure after lung stereotactic body radiation therapy. *International journal of radiation oncology biology physics. Conference: 58th annual meeting of the american society for radiation oncology, ASTRO 2016. United states*. 2016;96(2 Supplement 1):E421-E2. PMID: CN-01463389. Exclusion Code: X2.

1834. Woody NM, Stephans KL, Marwaha G, et al. Stereotactic body radiation therapy for non-small cell lung cancer tumors greater than 5 cm: safety and efficacy. *Int J Radiat Oncol Biol Phys*. 2015 Jun 1;92(2):325-31. doi: 10.1016/j.ijrobp.2015.01.045. PMID: 25841625. Exclusion Code: X3.

1835. Woody NM, Videtic GM, Stephans KL, et al. Predicting chest wall pain from lung stereotactic body radiotherapy for different fractionation schemes. *Int J Radiat Oncol Biol Phys*. 2012 May 1;83(1):427-34. doi: 10.1016/j.ijrobp.2011.06.1971. PMID: 22197087. Exclusion Code: X3.

1836. Wormanns D, Ludwig K, Beyer F, et al. Detection of pulmonary nodules at multirow-detector CT: effectiveness of double reading to improve sensitivity at standard-dose and low-dose chest CT. *Eur Radiol*. 2005 Jan;15(1):14-22. doi: 10.1007/s00330-004-2527-6. PMID: 15526207. Exclusion Code: X3.

1837. Wozniak MB, Scelo G, Muller DC, et al. Circulating MicroRNAs as non-invasive biomarkers for early detection of non-small-cell lung cancer. *PLoS One*. 2015;10(5):e0125026. doi: 10.1371/journal.pone.0125026. PMID: 25965386. Exclusion Code: X3.

1838. Wu AJ, Williams E, Modh A, et al. Dosimetric predictors of esophageal toxicity after stereotactic body radiotherapy for central lung tumors. *Radiother Oncol*. 2014 Aug;112(2):267-71. doi: 10.1016/j.radonc.2014.07.001. PMID: 25064471. Exclusion Code: X3.

1839. Wu CF, Fernandez R, de la Torre M, et al. Mid-term survival outcome of single-port video-assisted thoracoscopic anatomical lung resection: a two-centre experience. *Eur J Cardiothorac Surg*. 2018 Aug 1;54(2):252-9. doi: 10.1093/ejcts/ezy067. PMID: 29514185. Exclusion Code: X3.

1840. Wu CY, Chen JS, Lin YS, et al. Feasibility and safety of nonintubated thoracoscopic lobectomy for geriatric lung cancer patients. *Ann Thorac Surg*. 2013 Feb;95(2):405-11. doi: 10.1016/j.athoracsur.2012.10.082. PMID: 23245449. Exclusion Code: X3.

1841. Wu CY, Fu JY, Wu CF, et al. Survival prediction model using clinico-pathologic characteristics for nonsmall cell lung cancer patients after curative resection. *Medicine (Baltimore)*. 2015 Nov;94(45):e2013. doi: 10.1097/md.0000000000002013. PMID: 26559298. Exclusion Code: X3.

1842. Wu F, Tian SP, Jin X, et al. CT and histopathologic characteristics of lung adenocarcinoma with pure ground-glass nodules 10 mm or less in diameter. *Eur Radiol*. 2017 Oct;27(10):4037-43. doi: 10.1007/s00330-017-4829-5. PMID: 28386719. Exclusion Code: X10.

1843. Wu HY, Goan YG, Chang YH, et al. Qualification and verification of serological biomarker candidates for lung adenocarcinoma by targeted mass spectrometry. *J Proteome Res*. 2015 Aug 7;14(8):3039-50. doi: 10.1021/pr501195t. PMID: 26120931. Exclusion Code: X3.

1844. Wu YL, Herbst RS, Mann H, et al. ADAURA: phase III, Double-blind, Randomized Study of Osimertinib Versus Placebo in EGFR Mutation-positive Early-stage NSCLC After Complete Surgical Resection. *Clin Lung Cancer*. 2018;19(4):e533-e6. doi: 10.1016/j.cllc.2018.04.004. PMID: CN-01708182. Exclusion Code: X3.

1845. Wurstbauer K, Deutschmann H, Dagn K, et al. DART-bid (Dose-differentiated accelerated radiation therapy, 1.8 Gy twice daily)--a novel approach for non-resected NSCLC: final results of a prospective study, correlating radiation dose to tumor volume. *Radiat Oncol*. 2013 Mar 5;8:49. doi: 10.1186/1748-717x-8-49. PMID: 23497555. Exclusion Code: X6.

1846. Xia B, Chen GY, Cai XW, et al. Is involved-field radiotherapy based on CT safe for patients with limited-stage small-cell lung cancer? *Radiother Oncol*. 2012 Feb;102(2):258-62. doi: 10.1016/j.radonc.2011.10.003. PMID: 22056536. Exclusion Code: X6.

1847. Xia H, Sun Z, Deng L, et al. Prognostic significance of the preoperative lymphocyte to monocyte ratio in patients with stage I non-small cell lung cancer undergoing complete resection. *Cancer Invest*. 2016 Sep 13;34(8):378-84. doi: 10.1080/07357907.2016.1213276. PMID: 27558529. Exclusion Code: X3.

1848. Xiao F, Yu Q, Zhang Z, et al. Novel perspective to evaluate the safety of segmentectomy: clinical significance of lobar and segmental lymph node metastasis in cT1N0M0 lung adenocarcinoma. *Eur J Cardiothorac Surg*. 2018 Jan 1;53(1):228-34. doi: 10.1093/ejcts/ezx263. PMID: 28950357. Exclusion Code: X11.

1849. Xiao H, Zhang L, Zhou H, et al. Proteomic analysis of human saliva from lung cancer patients using two-dimensional difference gel electrophoresis and mass spectrometry. *Mol Cell Proteomics*. 2012 Feb;11(2):M111.012112. doi: 10.1074/mcp.M111.012112. PMID: 22096114. Exclusion Code: X3.

1850. Xie X, Dijkstra AE, Vonk JM, et al. Chronic respiratory symptoms associated with airway wall thickening measured by thin-slice low-dose CT. *AJR Am J Roentgenol*. 2014 Oct;203(4):W383-90. doi: 10.2214/ajr.13.11536. PMID: 25247967. Exclusion Code: X8.

1851. Xie X, Willemink MJ, de Jong PA, et al. Small irregular pulmonary nodules in low-dose CT: observer detection sensitivity and volumetry accuracy. *AJR Am J Roentgenol*. 2014 Mar;202(3):W202-9. doi: 10.2214/ajr.13.10830. PMID: 24555615. Exclusion Code: X3.

1852. Xing L, Su J, Guarnera MA, et al. Sputum microRNA biomarkers for identifying lung cancer in indeterminate solitary pulmonary nodules. *Clin Cancer Res*. 2015 Jan 15;21(2):484-9. doi: 10.1158/1078-0432.ccr-14-1873. PMID: 25593345. Exclusion Code: X5.

1853. Xing R, Chen KB, Xuan Y, et al. RBX1 expression is an unfavorable prognostic factor in patients with non-small cell lung cancer. *Surg Oncol*. 2016 Sep;25(3):147-51. doi: 10.1016/j.suronc.2016.05.006. PMID: 27566015. Exclusion Code: X3.

1854. Xu CH, Cao L, Wei Y, et al. Serum cripto-1 as a clinical marker for lung cancer. *Int J Biol Markers*. 2015 Nov 11;30(4):e369-73. doi: 10.5301/jbm.5000155. PMID: 26109366. Exclusion Code: X3.

1855. Xu CH, Wang Q, Zhan P, et al. GSTP1 Ile105Val polymorphism is associated with lung cancer risk among Asian population and smokers: an updated meta-analysis. *Mol Biol Rep*. 2014 Jul;41(7):4199-212. doi: 10.1007/s11033-014-3290-7. PMID: 24566690. Exclusion Code: X10.

1856. Xu CH, Wang W, Wei Y, et al. Prognostic value of the new International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society classification in stage IB lung adenocarcinoma. *Eur J Surg Oncol*. 2015 Oct;41(10):1430-6. doi: 10.1016/j.ejso.2015.06.004. PMID: 26123994. Exclusion Code: X11.

1857. Xu DM, Lee IJ, Zhao S, et al. CT screening for lung cancer: value of expert review of initial baseline screenings. *AJR Am J Roentgenol*. 2015 Feb;204(2):281-6. doi: 10.2214/ajr.14.12526. PMID: 25349980. Exclusion Code: X11.

1858. Xu DM, van der Zaag-Loonen HJ, Oudkerk M, et al. Smooth or attached solid indeterminate nodules detected at baseline CT screening in the NELSON study: cancer risk during 1 year of follow-up. *Radiology*. 2009 Jan;250(1):264-72. doi: 10.1148/radiol.2493070847. PMID: 18984780. Exclusion Code: X11.

1859. Xu DM, Yip R, Smith JP, et al. Retrospective review of lung cancers diagnosed in annual rounds of CT screening. *AJR Am J Roentgenol*. 2014 Nov;203(5):965-72. doi: 10.2214/ajr.13.12115. PMID: 25247825. Exclusion Code: X3.

1860. Xu H, Zhang L. The Feasibility of Thoracoscopic Left Pneumonectomy. *Thorac Cardiovasc Surg*. 2019 Mar;67(2):137-41. doi: 10.1055/s-0038-1642618. PMID: 29715708. Exclusion Code: X3.

1861. Xu H, Zhang L. The Bronchus First and Vessels Simultaneously Stapled Technique: A Safe and Simple Method for Video-Assisted Right Upper Lobe Lobectomy. *Thorac Cardiovasc Surg*. 2019 Mar;67(2):131-6. doi: 10.1055/s-0037-1620276. PMID: 29381881. Exclusion Code: X3.

1862. Xu N, Wang M, Zhu Z, et al. Integrated positron emission tomography and computed tomography in preoperative lymph node staging of non-small cell lung cancer. *Chin Med J (Engl)*. 2014;127(4):607-13. PMID: 24534208. Exclusion Code: X3.

1863. Xu Y, Sun H, Zhang Z, et al. Assessment of relationship between CT features and serum tumor marker index in early-stage lung adenocarcinoma. *Acad Radiol*. 2016 Nov;23(11):1342-8. doi: 10.1016/j.acra.2016.06.005. PMID: 27426977. Exclusion Code: X3.

1864. Yaffe D, Koslow M, Haskiya H, et al. A novel technique for CT-guided transthoracic biopsy of lung lesions: improved biopsy accuracy and safety. *Eur Radiol*. 2015 Nov;25(11):3354-60. doi: 10.1007/s00330-015-3750-z. PMID: 25903714. Exclusion Code: X3.

1865. Yaffe D, Shitrit D, Gottfried M, et al. Ipsilateral opposite-side aspiration in resistant pneumothorax after CT image guided lung biopsy: complementary role after simple needle aspiration. *Chest*. 2013 Sep;144(3):947-51. doi: 10.1378/chest.12-2790. PMID: 23681216. Exclusion Code: X3.

1866. Yamagami T, Yoshimatsu R, Miura H, et al. Diagnostic performance of percutaneous lung biopsy using automated biopsy needles under CT-fluoroscopic guidance for ground-glass opacity lesions. *Br J Radiol*. 2013 Feb;86(1022):20120447. doi: 10.1259/bjr.20120447. PMID: 23385998. Exclusion Code: X3.

1867. Yamaguchi M, Furuya A, Edagawa M, et al. How should we manage small focal pure ground-glass opacity nodules on high-resolution computed tomography? A single institute experience. *Surg Oncol*. 2015 Sep;24(3):258-63. doi: 10.1016/j.suronc.2015.08.004. PMID: 26298200. Exclusion Code: X3.

1868. Yamamoto T, Jingu K, Shirata Y, et al. Outcomes after stereotactic body radiotherapy for lung tumors, with emphasis on comparison of primary lung cancer and metastatic lung tumors. *BMC Cancer*. 2014 Jun 23;14:464. doi: 10.1186/1471-2407-14-464. PMID: 24957478. Exclusion Code: X3.

1869. Yamamoto T, Kadoya N, Morishita Y, et al. Assessment and agreement of the CT appearance pattern and its severity grading of radiation-induced lung injury after stereotactic body radiotherapy for lung cancer. *PLoS One*. 2018;13(10):e0204734. doi: 10.1371/journal.pone.0204734. PMID: 30286105. Exclusion Code: X3.

1870. Yamamoto T, Kadoya N, Sato Y, et al. Prognostic Value of Radiation Pneumonitis After Stereotactic Body Radiotherapy: Effect of Pulmonary Emphysema Quantitated Using CT Images. *Clin Lung Cancer*. 2018 Jan;19(1):e85-e90. doi: 10.1016/j.cllc.2017.05.022. PMID: 28655592. Exclusion Code: X3.

1871. Yamamoto T, Kadoya N, Shirata Y, et al. Formula corrected maximal standardized uptake value in FDG-PET for partial volume effect and motion artifact is not a prognostic factor in stage I non-small cell lung cancer treated with stereotactic body radiotherapy. *Ann Nucl Med*. 2015 Oct;29(8):666-73. doi: 10.1007/s12149-015-0991-5. PMID: 26040413. Exclusion Code: X10.

1872. Yamamoto T, Kadoya N, Shirata Y, et al. Impact of tumor attachment to the pleura measured by a pretreatment CT image on outcome of stage I NSCLC treated with stereotactic body radiotherapy. *Radiat Oncol*. 2015 Feb 7;10:35. doi: 10.1186/s13014-015-0343-6. PMID: 25886315. Exclusion Code: X10.

1873. Yamamoto T, Suzuki H, Nagato K, et al. Is left upper lobectomy for lung cancer a risk factor for cerebral infarction? *Surg Today*. 2016 Jul;46(7):780-4. doi: 10.1007/s00595-015-1233-0. PMID: 26272485. Exclusion Code: X3.

1874. Yamanashi K, Okumura N, Yamamoto Y, et al. Adjuvant chemotherapy for elderly patients with non-small-cell lung cancer. *Asian Cardiovasc Thorac Ann*. 2017 Jun;25(5):371-7. doi: 10.1177/0218492317714669. PMID: 28592139. Exclusion Code: X6.

1875. Yamao Y, Yamakado K, Takaki H, et al. CT-fluoroscopy in chest interventional radiology: sliding scale of imaging parameters based on radiation exposure dose and factors increasing radiation exposure dose. *Clin Radiol*. 2013 Feb;68(2):162-6. doi: 10.1016/j.crad.2012.05.020. PMID: 22906574. Exclusion Code: X3.

1876. Yamashita S, Tokuishi K, Anami K, et al. Thoracoscopic segmentectomy for T1 classification of non-small cell lung cancer: a single center experience. *Eur J Cardiothorac Surg*. 2012 Jul;42(1):83-8. doi: 10.1093/ejcts/ezr254. PMID: 22228839. Exclusion Code: X11.

1877. Yamashita Y, Mukaida H, Harada H, et al. Post-thoracotomy pain and long-term survival associated with video-assisted thoracic surgery lobectomy methods for clinical T1N0 lung cancer: a patient-oriented, prospective cohort study. *Eur J Cardiothorac Surg*. 2013 Jul;44(1):e71-6. doi: 10.1093/ejcts/ezt107. PMID: 23509236. Exclusion Code: X11.

1878. Yan B, Zhang W, Lu F, et al. Safety of polyethylene glycol recombinant human granulocyte colony-stimulating factor in treating non-small cell lung cancer patients at I b stage. *Asian Pac J Trop Med*. 2013 Nov;6(11):912-5. doi: 10.1016/s1995-7645(13)60163-7. PMID: 24083590. Exclusion Code: X6.

1879. Yan S, Qian W, Guan Y, et al. Improving lung cancer prognosis assessment by incorporating synthetic minority oversampling technique and score fusion method. *Med Phys*. 2016 Jun;43(6):2694-703. doi: 10.1118/1.4948499. PMID: 27277016. Exclusion Code: X4.

1880. Yanagawa M, Honda O, Kikuyama A, et al. Pulmonary nodules: effect of adaptive statistical iterative reconstruction (ASIR) technique on performance of a computer-aided detection (CAD) system-comparison of performance between different-dose CT scans. *Eur J Radiol*. 2012 Oct;81(10):2877-86. doi: 10.1016/j.ejrad.2011.09.011. PMID: 21982461. Exclusion Code: X3.

1881. Yanagawa N, Shiono S, Abiko M, et al. Positive intraoperative pleural lavage cytology is a predictive marker of disease recurrence in stage I lung adenocarcinoma. *Interact Cardiovasc Thorac Surg*. 2014 May;18(5):621-5. doi: 10.1093/icvts/ivu015. PMID: 24532312. Exclusion Code: X11.

1882. Yang B, Jhun BW, Shin SH, et al. Comparison of four models predicting the malignancy of pulmonary nodules: A single-center study of Korean adults. *PLoS One*. 2018;13(7):e0201242. doi: 10.1371/journal.pone.0201242. PMID: 30063725. Exclusion Code: X3.

1883. Yang CC, Fong Y, Lin LC, et al. The age-adjusted Charlson comorbidity index is a better predictor of survival in operated lung cancer patients than the Charlson and Elixhauser comorbidity indices. *Eur J Cardiothorac Surg*. 2018 Jan 1;53(1):235-40. doi: 10.1093/ejcts/ezx215. PMID: 29106506. Exclusion Code: X3.

1884. Yang CJ, Wang H, Kumar A, et al. Impact of timing of lobectomy on survival for clinical stage IA lung squamous cell carcinoma. *Chest*. 2017 Dec;152(6):1239-50. doi: 10.1016/j.chest.2017.07.032. PMID: 28800867. Exclusion Code: X3.

1885. Yang DW, Zhang Y, Hong QY, et al. Role of a serum-based biomarker panel in the early diagnosis of lung cancer for a cohort of high-risk patients. *Cancer*. 2015 Sep 1;121 Suppl 17:3113-21. doi: 10.1002/cncr.29551. PMID: 26331818. Exclusion Code: X4.

1886. Yang H, Sun Y, Yao F, et al. Surgical therapy for bilateral multiple primary lung cancer. *Ann Thorac Surg*. 2016 Mar;101(3):1145-52. doi: 10.1016/j.athoracsur.2015.09.028. PMID: 26602007. Exclusion Code: X11.

1887. Yang HX, Woo KM, Sima CS, et al. Long-term survival based on the surgical approach to lobectomy for clinical stage I nonsmall cell lung cancer: comparison of robotic, video-assisted thoracic surgery, and thoracotomy lobectomy. *Ann Surg*. 2017 Feb;265(2):431-7. doi: 10.1097/sla.0000000000001708. PMID: 28059973. Exclusion Code: X11.

1888. Yang J, Lin J, Liu T, et al. Analysis of lncRNA expression profiles in non-small cell lung cancers (NSCLC) and their clinical subtypes. *Lung Cancer*. 2014 Aug;85(2):110-5. doi: 10.1016/j.lungcan.2014.05.011. PMID: 24906504. Exclusion Code: X5.

1889. Yang J, Xu T, Gomez DR, et al. Polymorphisms in BMP2/BMP4, with estimates of mean lung dose, predict radiation pneumonitis among patients receiving definitive radiotherapy for non-small cell lung cancer. *Oncotarget*. 2017 Jun 27;8(26):43080-90. doi: 10.18632/oncotarget.17904. PMID: 28574846. Exclusion Code: X3.

1890. Yang P, Wang Y, Wampfler JA, et al. Trends in Subpopulations at High Risk for Lung Cancer. *J Thorac Oncol*. 2016 Feb;11(2):194-202. doi: 10.1016/j.jtho.2015.10.016. PMID: 26811226. Exclusion Code: X3.

1891. Yang R, Jiao W, Zhao Y, et al. Lymph node evaluation in totally thoracoscopic lobectomy with two-port for clinical early-stage nonsmall-cell lung cancer: Single-center experience of 1086 cases. *Indian J Cancer*. 2015 Dec;52 Suppl 2:e134-9. doi: 10.4103/0019-509x.172511. PMID: 26728672. Exclusion Code: X10.

1892. Yang SC, Lai WW, Lin CC, et al. Cost-effectiveness of implementing computed tomography screening for lung cancer in Taiwan. *Lung Cancer*. 2017 Jun;108:183-91. doi: 10.1016/j.lungcan.2017.04.001. PMID: 28625633. Exclusion Code: X8.

1893. Yang W, Qian F, Teng J, et al. Community-based lung cancer screening with low-dose CT in China: results of the baseline screening. *Lung Cancer*. 2018 Mar;117:20-6. doi: 10.1016/j.lungcan.2018.01.003. PMID: 29496251. Exclusion Code: X14.

1894. Yang W, Sun W, Li Q, et al. Diagnostic accuracy of CT-guided transthoracic needle biopsy for solitary pulmonary nodules. *PLoS One*. 2015;10(6):e0131373. doi: 10.1371/journal.pone.0131373. PMID: 26110775. Exclusion Code: X3.

1895. Yang X, Ye X, Zheng A, et al. Percutaneous microwave ablation of stage I medically inoperable non-small cell lung cancer: clinical evaluation of 47 cases. *J Surg Oncol*. 2014 Nov;110(6):758-63. doi: 10.1002/jso.23701. PMID: 24965604. Exclusion Code: X6.

1896. Yang Y, Zhou Z, Niu XM, et al. Clinical analysis of postoperative venous thromboembolism risk factors in lung cancer patients. *J Surg Oncol*. 2012 Nov;106(6):736-41. doi: 10.1002/jso.23190. PMID: 22711667. Exclusion Code: X11.

1897. Yano M, Yoshida J, Koike T, et al. Survival of 1737 lobectomy-tolerable patients who underwent limited resection for cStage IA non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2015 Jan;47(1):135-42. doi: 10.1093/ejcts/ezu138. PMID: 24699203. Exclusion Code: X10.

1898. Yano T, Kawashima O, Takeo S, et al. A Prospective Observational Study of Pulmonary Resection for Non-small Cell Lung Cancer in Patients Older Than 75 Years. *Semin Thorac Cardiovasc Surg*. 2017 Winter;29(4):540-7. doi: 10.1053/j.semtcvs.2017.05.004. PMID: 29698655. Exclusion Code: X3.

1899. Yano T, Shimokawa M, Kawashima O, et al. The influence of comorbidity on the postoperative survival in elderly (>/= 75 years old) with lung cancer. *Gen Thorac Cardiovasc Surg*. 2018 Jun;66(6):344-50. doi: 10.1007/s11748-018-0919-9. PMID: 29616463. Exclusion Code: X3.

1900. Yao F, Wang J, Yao J, et al. Three-dimensional image reconstruction with free open-source OsiriX software in video-assisted thoracoscopic lobectomy and segmentectomy. *Int J Surg*. 2017 Mar;39:16-22. doi: 10.1016/j.ijsu.2017.01.079. PMID: 28115296. Exclusion Code: X11.

1901. Yao F, Wang J, Yao J, et al. Early Experience with Video-Assisted Thoracoscopic Anatomic Segmentectomy. *J Laparoendosc Adv Surg Tech A*. 2018 Jul;28(7):819-26. doi: 10.1089/lap.2017.0680. PMID: 29424636. Exclusion Code: X11.

1902. Yao F, Wang J, Yao J, et al. Reevaluation of the efficacy of preoperative computed tomography-guided hook wire localization: A retrospective analysis. *Int J Surg*. 2018 Mar;51:24-30. doi: 10.1016/j.ijsu.2018.01.014. PMID: 29367030. Exclusion Code: X3.

1903. Yao W, Lu M, Fan W, et al. Comparison between microwave ablation and lobectomy for stage I non-small cell lung cancer: a propensity score analysis. *Int J Hyperthermia*. 2018 Dec;34(8):1329-36. doi: 10.1080/02656736.2018.1434901. PMID: 29378462. Exclusion Code: X11.

1904. Yasaka K, Katsura M, Hanaoka S, et al. High-resolution CT with new model-based iterative reconstruction with resolution preference algorithm in evaluations of lung nodules: Comparison with conventional model-based iterative reconstruction and adaptive statistical iterative reconstruction. *Eur J Radiol*. 2016 Mar;85(3):599-606. doi: 10.1016/j.ejrad.2016.01.001. PMID: 26860673. Exclusion Code: X3.

1905. Ye B, Cheng M, Ge XX, et al. Factors that predict lymph node status in clinical stage T1aN0M0 lung adenocarcinomas. *World J Surg Oncol*. 2014 Feb 21;12:42. doi: 10.1186/1477-7819-12-42. PMID: 24559138. Exclusion Code: X8.

1906. Ye B, Cheng M, Li W, et al. Predictive factors for lymph node metastasis in clinical stage IA lung adenocarcinoma. *Ann Thorac Surg*. 2014 Jul;98(1):217-23. doi: 10.1016/j.athoracsur.2014.03.005. PMID: 24841547. Exclusion Code: X8.

1907. Yeginsu A, Vayvada M, Karademir BC, et al. Combined Off-Pump Coronary Artery Bypass Grafting and Lung Resection in Patients with Lung Cancer Accompanied by Coronary Artery Disease. *Braz J Cardiovasc Surg*. 2018 Sep-Oct;33(5):483-9. doi: 10.21470/1678-9741-2018-0126. PMID: 30517257. Exclusion Code: X3.

1908. Yegya-Raman N, Kim S, Deek MP, et al. Daily Image Guidance With Cone Beam Computed Tomography May Reduce Radiation Pneumonitis in Unresectable Non-Small Cell Lung Cancer. *Int J Radiat Oncol Biol Phys*. 2018 Aug 1;101(5):1104-12. doi: 10.1016/j.ijrobp.2018.03.025. PMID: 29730063. Exclusion Code: X3.

1909. Yegya-Raman N, Reyhan M, Kim S, et al. Association of Target Volume Margins With Locoregional Control and Acute Toxicities for Non-small cell lung cancer Treated With Concurrent Chemoradiation Therapy. *Pract Radiat Oncol*. 2019 Jan;9(1):e74-e82. doi: 10.1016/j.prro.2018.08.007. PMID: 30144583. Exclusion Code: X3.

1910. Yendamuri S, Battoo A, Attwood K, et al. Concomitant Mediastinoscopy Increases the Risk of Postoperative Pneumonia After Pulmonary Lobectomy. *Ann Surg Oncol*. 2018 May;25(5):1269-76. doi: 10.1245/s10434-018-6397-6. PMID: 29488189. Exclusion Code: X3.

1911. Yendamuri S, Battoo A, Dy G, et al. Transcervical extended mediastinal lymphadenectomy: experience from a North American cancer center. *Ann Thorac Surg*. 2017 Nov;104(5):1644-9. doi: 10.1016/j.athoracsur.2017.05.022. PMID: 28942077. Exclusion Code: X3.

1912. Yendamuri S, Sharma R, Demmy M, et al. Temporal trends in outcomes following sublobar and lobar resections for small (</= 2 cm) non-small cell lung cancers--a Surveillance Epidemiology End Results database analysis. *J Surg Res*. 2013 Jul;183(1):27-32. doi: 10.1016/j.jss.2012.11.052. PMID: 23260233. Exclusion Code: X8.

1913. Yeo J, Crawford EL, Zhang X, et al. A lung cancer risk classifier comprising genome maintenance genes measured in normal bronchial epithelial cells. *BMC Cancer*. 2017 May 2;17(1):301. doi: 10.1186/s12885-017-3287-4. PMID: 28464886. Exclusion Code: X5.

1914. Yi CA, Lee KS, Lee HY, et al. Coregistered whole body magnetic resonance imaging-positron emission tomography (MRI-PET) versus PET-computed tomography plus brain MRI in staging resectable lung cancer: comparisons of clinical effectiveness in a randomized trial. *Cancer*. 2013 May 15;119(10):1784-91. doi: 10.1002/cncr.28000. PMID: 23423920. Exclusion Code: X3.

1915. Yi E, Bae MK, Cho S, et al. Pathological prognostic factors of recurrence in early stage lung adenocarcinoma. *ANZ J Surg*. 2018 Apr;88(4):327-31. doi: 10.1111/ans.14033. PMID: 28702948. Exclusion Code: X11.

1916. Yildirim D, Tamam M, Sanli Y, et al. Virtual bronchoscopy using FDG-PET/CT images for the evaluation of lung cancer. *Eur Rev Med Pharmacol Sci*. 2012 Dec;16(14):1951-60. PMID: 23242722. Exclusion Code: X8.

1917. Yilmaz A, Uskul TB, Bayramgurler B, et al. Cell type accuracy of transthoracic fine needle aspiration material in primary lung cancer. *Respirology*. 2001 Jun;6(2):91-4. PMID: 11422887. Exclusion Code: X3.

1918. Yip PY, Cooper WA, Kohonen-Corish MR, et al. Phosphorylated Akt expression is a prognostic marker in early-stage non-small cell lung cancer. *J Clin Pathol*. 2014 Apr;67(4):333-40. doi: 10.1136/jclinpath-2013-201870. PMID: 24265323. Exclusion Code: X11.

1919. Yip R, Henschke CI, Yankelevitz DF, et al. The impact of the regimen of screening on lung cancer cure: a comparison of I-ELCAP and NLST. *Eur J Cancer Prev*. 2015 May;24(3):201-8. doi: 10.1097/cej.0000000000000065. PMID: 25089376. Exclusion Code: X7.

1920. Yip R, Yankelevitz DF, Hu M, et al. Lung cancer deaths in the National Lung Screening Trial attributed to nonsolid nodules. *Radiology*. 2016 Nov;281(2):589-96. doi: 10.1148/radiol.2016152333. PMID: 27378239. Exclusion Code: X3.

1921. Yong JR, Qi S, van Triest HJ, et al. Automatic segmentation of juxta-pleural tumors from CT images based on morphological feature analysis. *Biomed Mater Eng*. 2014;24(6):3137-44. doi: 10.3233/bme-141136. PMID: 25227023. Exclusion Code: X3.

1922. Yoo SS, Jin C, Jung DK, et al. Putative functional variants of XRCC1 identified by RegulomeDB were not associated with lung cancer risk in a Korean population. *Cancer Genet*. 2015 Jan-Feb;208(1-2):19-24. doi: 10.1016/j.cancergen.2014.11.004. PMID: 25592768. Exclusion Code: X3.

1923. Yoon HJ, Chung MJ, Hwang HS, et al. Adaptive statistical iterative reconstruction-applied ultra-low-dose CT with radiography-comparable radiation dose: usefulness for lung nodule detection. *Korean J Radiol*. 2015 Sep-Oct;16(5):1132-41. doi: 10.3348/kjr.2015.16.5.1132. PMID: 26357505. Exclusion Code: X6.

1924. Yoshida J, Ishii G, Hishida T, et al. Limited resection trial for pulmonary ground-glass opacity nodules: case selection based on high-resolution computed tomography-interim results. *Jpn J Clin Oncol*. 2015 Jul;45(7):677-81. doi: 10.1093/jjco/hyv057. PMID: 25900903. Exclusion Code: X11.

1925. Yoshida Y, Kage H, Murakawa T, et al. Worse prognosis for stage IA lung cancer patients with smoking history and more severe chronic obstructive pulmonary disease. *Ann Thorac Cardiovasc Surg*. 2015;21(3):194-200. doi: 10.5761/atcs.oa.14-00200. PMID: 25641032. Exclusion Code: X11.

1926. Yoshida Y, Murayama T, Sato Y, et al. Gender differences in long-term survival after surgery for non-small cell lung cancer. *Thorac Cardiovasc Surg*. 2016 Sep;64(6):507-14. doi: 10.1055/s-0035-1558995. PMID: 26366891. Exclusion Code: X3.

1927. Yoshimatsu R, Yamagami T, Tanaka O, et al. Comparison of fully automated and semi-automated biopsy needles for lung biopsy under CT fluoroscopic guidance. *Br J Radiol*. 2012 Mar;85(1011):208-13. doi: 10.1259/bjr/15132704. PMID: 21828150. Exclusion Code: X3.

1928. Yoshitake T, Nakamura K, Shioyama Y, et al. Stereotactic body radiation therapy for stage I non-small cell lung cancer patients with chronic respiratory insufficiency requiring domiciliary oxygen therapy. *Anticancer Res*. 2012 Sep;32(9):4041-4. PMID: 22993357. Exclusion Code: X10.

1929. Young RP, Hopkins RJ. A review of the Hispanic paradox: time to spill the beans? *Eur Respir Rev*. 2014 Dec;23(134):439-49. doi: 10.1183/09059180.00000814. PMID: 25445942. Exclusion Code: X6.

1930. Young RP, Hopkins RJ, Hay BA, et al. Lung cancer susceptibility model based on age, family history and genetic variants. *PLoS One*. 2009;4(4):e5302. doi: 10.1371/journal.pone.0005302. PMID: 19390575. Exclusion Code: X7.

1931. Yousaf-Khan U, van der Aalst C, de Jong PA, et al. Final screening round of the NELSON lung cancer screening trial: the effect of a 2.5-year screening interval. *Thorax*. 2017 Jan;72(1):48-56. doi: 10.1136/thoraxjnl-2016-208655. PMID: 27364640. Exclusion Code: X17.

1932. Yu V, Kishan AU, Cao M, et al. Dose impact in radiographic lung injury following lung SBRT: statistical analysis and geometric interpretation. *Med Phys*. 2014 Mar;41(3):031701. doi: 10.1118/1.4863483. PMID: 24593705. Exclusion Code: X3.

Appendix C. Excluded Studies

1933. Yu X, Li Y, Shi C, et al. Risk factors of lymph node metastasis in patients with non-small cell lung cancer </= 2 cm in size: A monocentric population-based analysis. *Thorac Cancer*. 2018 Jan;9(1):3-9. doi: 10.1111/1759-7714.12490. PMID: 29034994. Exclusion Code: X10.

1934. Yu YC, Hsu PK, Yeh YC, et al. Surgical results of synchronous multiple primary lung cancers: similar to the stage-matched solitary primary lung cancers? *Ann Thorac Surg*. 2013 Dec;96(6):1966-74. doi: 10.1016/j.athoracsur.2013.04.142. PMID: 24021769. Exclusion Code: X3.

1935. Yuan ST, Brown RK, Zhao L, et al. Timing and intensity of changes in FDG uptake with symptomatic esophagitis during radiotherapy or chemo-radiotherapy. *Radiat Oncol*. 2014 Jan 27;9(1):37. doi: 10.1186/1748-717x-9-37. PMID: 24467939. Exclusion Code: X3.

1936. Yuan X, Zhang J, Quan C, et al. Differentiation of malignant and benign pulmonary nodules with first-pass dual-input perfusion CT. *Eur Radiol*. 2013 Sep;23(9):2469-74. doi: 10.1007/s00330-013-2842-x. PMID: 23793548. Exclusion Code: X3.

1937. Yuan Y, Matsumoto T, Hiyama A, et al. Role of high-resolution CT in the diagnosis of small pulmonary nodules coexisting with potentially operable lung cancer. *Radiat Med*. 2002 Sep-Oct;20(5):237-45. PMID: 12450103. Exclusion Code: X3.

1938. Yun JK, Kim MA, Choi CM, et al. Surgical Outcomes after Pulmonary Resection for Non-Small Cell Lung Cancer with Localized Pleural Seeding First Detected during Surgery. *Thorac Cardiovasc Surg*. 2018 Mar;66(2):142-9. doi: 10.1055/s-0035-1564928. PMID: 26669768. Exclusion Code: X3.

1939. Yung RC, Zeng MY, Stoddard GJ, et al. Transcutaneous computed bioconductance measurement in lung cancer: a treatment enabling technology useful for adjunctive risk stratification in the evaluation of suspicious pulmonary lesions. *J Thorac Oncol*. 2012 Apr;7(4):681-9. doi: 10.1097/JTO.0b013e31824a8dcd. PMID: 22425917. Exclusion Code: X3.

1940. Zanon M, Pacini GS, de Souza VVS, et al. Early detection of lung cancer using ultra-low-dose computed tomography in coronary CT angiography scans among patients with suspected coronary heart disease. *Lung Cancer*. 2017 Dec;114:1-5. doi: 10.1016/j.lungcan.2017.10.004. PMID: 29173759. Exclusion Code: X3.

1941. Zehentmayr F, Wurstbauer K, Deutschmann H, et al. DART-bid: dose-differentiated accelerated radiation therapy, 1.8 Gy twice daily: high local control in early stage (I/II) non-small-cell lung cancer. *Strahlenther Onkol*. 2015 Mar;191(3):256-63. doi: 10.1007/s00066-014-0754-6. PMID: 25245469. Exclusion Code: X3.

1942. Zeliadt SB, Hoffman RM, Birkby G, et al. Challenges implementing lung cancer screening in federally qualified health centers. *Am J Prev Med*. 2018 Apr;54(4):568-75. doi: 10.1016/j.amepre.2018.01.001. PMID: 29429606. Exclusion Code: X8.

1943. Zeng Q, Liu M, Zhou N, et al. Serum human epididymis protein 4 (HE4) may be a better tumor marker in early lung cancer. *Clin Chim Acta*. 2016 Apr 1;455:102-6. doi: 10.1016/j.cca.2016.02.002. PMID: 26851650. Exclusion Code: X3.

1944. Zer A, Domachevsky L, Rapson Y, et al. The Role of 18F-FDG PET/CT on staging and prognosis in patients with small cell lung cancer. *Eur Radiol*. 2016 Sep;26(9):3155-61. doi: 10.1007/s00330-015-4132-2. PMID: 26685851. Exclusion Code: X3.

1945. Zhang B, Lee SW, Chen S, et al. Action Levels on Dose and Anatomic Variation for Adaptive Radiation Therapy Using Daily Offline Plan Evaluation: Preliminary Results. *Pract Radiat Oncol*. 2019 Jan;9(1):49-54. doi: 10.1016/j.prro.2018.08.006. PMID: 30142442. Exclusion Code: X6.

1946. Zhang C, Yu H, Li X, et al. Diagnostic value of computed tomography scanning in differentiating malignant from benign solitary pulmonary nodules: a meta-analysis (Provisional abstract). *Database of Abstracts of Reviews of Effects*. 2014(2):8551-8. PMID: DARE-12014034768. Exclusion Code: X9.

Appendix C. Excluded Studies

1947. Zhang F, Ying L, Jin J, et al. The C-reactive protein/albumin ratio predicts long-term outcomes of patients with operable non-small cell lung cancer. *Oncotarget*. 2017 Jan 31;8(5):8835-42. doi: 10.18632/oncotarget.13053. PMID: 27823974. Exclusion Code: X3.

1948. Zhang G, Zou L, Xu H. Anodic alumina coating for extraction of volatile organic compounds in human exhaled breath vapor. *Talanta*. 2015 Jan;132:528-34. doi: 10.1016/j.talanta.2014.09.035. PMID: 25476340. Exclusion Code: X5.

1949. Zhang H, Gao S, Chen B, et al. Comparison of the accuracy of ^{99m}Tc-3P<inf>4</inf>-RGD<inf>2</inf> SPECT and CT in diagnosing solitary pulmonary nodules. *Oncol Lett*. 2016;12(4):2517-23. doi: 10.3892/ol.2016.5030. PMID: CN-01211975. Exclusion Code: X3.

1950. Zhang J, Li B, Ding X, et al. Genetic variants in inducible nitric oxide synthase gene are associated with the risk of radiation-induced lung injury in lung cancer patients receiving definitive thoracic radiation. *Radiother Oncol*. 2014 May;111(2):194-8. doi: 10.1016/j.radonc.2014.03.001. PMID: 24746566. Exclusion Code: X6.

1951. Zhang J, Xu J, Lu H, et al. Altered phosphatidylcholines expression in sputum for diagnosis of non-small cell lung cancer. *Oncotarget*. 2016 Sep 27;7(39):63158-65. doi: 10.18632/oncotarget.11283. PMID: 27542233. Exclusion Code: X5.

1952. Zhang J, Xue ZQ, Chu XY, et al. Surgical treatment and prognosis of octogenarians with non-small cell lung cancer. *Asian Pac J Trop Med*. 2012 Jun;5(6):465-8. doi: 10.1016/s1995-7645(12)60079-0. PMID: 22575979. Exclusion Code: X3.

1953. Zhang L, Ren Y, Liu Y. Comparison of the effects of lobectomy on immunologic function between video-assisted thoracoscopic surgery and traditional open surgery for non-small-cell lung cancer. *Am J Ther*. 2016 Nov/Dec;23(6):e1406-e13. doi: 10.1097/mjt.0000000000000254. PMID: 25909924. Exclusion Code: X3.

1954. Zhang M, Yoshizawa A, Kawakami S, et al. The histological characteristics and clinical outcomes of lung cancer in patients with combined pulmonary fibrosis and emphysema. *Cancer Med*. 2016 Oct;5(10):2721-30. doi: 10.1002/cam4.858. PMID: 27546810. Exclusion Code: X3.

1955. Zhang R, Kyriss T, Dippon J, et al. American Society of Anesthesiologists physical status facilitates risk stratification of elderly patients undergoing thoracoscopic lobectomy. *Eur J Cardiothorac Surg*. 2018 May 1;53(5):973-9. doi: 10.1093/ejcts/ezx436. PMID: 29228138. Exclusion Code: X11.

1956. Zhang S, Liu Y. Computer-based three-dimensional reconstruction of lung cancer using 64-slice CT scanning data and virtual surgery. *Nan fang yi ke da xue xue bao [Journal of Southern Medical University]*. 2016;36(4):562-6. PMID: CN-01167967. Exclusion Code: X1.

1957. Zhang X, Zhang F, Qiao W, et al. Low Hematocrit Is a Strong Predictor of Poor Prognosis in Lung Cancer Patients. *Biomed Res Int*. 2018;2018:6804938. doi: 10.1155/2018/6804938. PMID: 30417013. Exclusion Code: X3.

1958. Zhang Y, Elgizouli M, Schottker B, et al. Smoking-associated DNA methylation markers predict lung cancer incidence. *Clin Epigenetics*. 2016;8:127. doi: 10.1186/s13148-016-0292-4. PMID: 27924164. Exclusion Code: X7.

1959. Zhang Y, Ma Y, Li Y, et al. Are exon 19 deletions and L858R different in early stage lung adenocarcinoma? *J Cancer Res Clin Oncol*. 2018 Jan;144(1):165-71. doi: 10.1007/s00432-017-2526-z. PMID: 29026990. Exclusion Code: X3.

1960. Zhang Y, Schottker B, Ordonez-Mena J, et al. F2RL3 methylation, lung cancer incidence and mortality. *Int J Cancer*. 2015 Oct 1;137(7):1739-48. doi: 10.1002/ijc.29537. PMID: 25821117. Exclusion Code: X7.

1961. Zhang Y, Sun Y, Chen H. A propensity score matching analysis of survival following segmentectomy or wedge resection in early-stage lung invasive adenocarcinoma or squamous cell carcinoma. *Oncotarget*. 2016 Mar 22;7(12):13880-5. doi: 10.18632/oncotarget.7284. PMID: 26871600. Exclusion Code: X8.

1962. Zhang Y, Zhang L, Li R, et al. Genetic variations in cancer-related significantly mutated genes and lung cancer susceptibility. *Ann Oncol*. 2017 Jul 1;28(7):1625-30. doi: 10.1093/annonc/mdx161. PMID: 28383694. Exclusion Code: X7.

1963. Zhang Z, Feng H, Xiao F, et al. Limited resection in clinical stage I non-small cell lung cancer patients aged 75 years old or more: a meta-analysis. *Ann Transl Med*. 2018 Sep;6(18):359. doi: 10.21037/atm.2018.08.35. PMID: 30370286. Exclusion Code: X9.

1964. Zhang Z, Gao S, Mao Y, et al. Surgical outcomes of synchronous multiple primary non-small cell lung cancers. *Sci Rep*. 2016 Jun 2;6:23252. doi: 10.1038/srep23252. PMID: 27254665. Exclusion Code: X11.

1965. Zhao B, James LP, Moskowitz CS, et al. Evaluating variability in tumor measurements from same-day repeat CT scans of patients with non-small cell lung cancer. *Radiology*. 2009 Jul;252(1):263-72. doi: 10.1148/radiol.2522081593. PMID: 19561260. Exclusion Code: X3.

1966. Zhao DP, Yang CL, Zhou X, et al. Association between CLPTM1L polymorphisms (rs402710 and rs401681) and lung cancer susceptibility: evidence from 27 case-control studies. *Mol Genet Genomics*. 2014 Oct;289(5):1001-12. doi: 10.1007/s00438-014-0868-7. PMID: 24907075. Exclusion Code: X3.

1967. Zhao H, Marshall HM, Yang IA, et al. Screen-detected subsolid pulmonary nodules: long-term follow-up and application of the PanCan lung cancer risk prediction model. *Br J Radiol*. 2016;89(1060):20160016. doi: 10.1259/bjr.20160016. PMID: 26882046. Exclusion Code: X8.

1968. Zhao L, Tong L, Lin J, et al. Characterization of solitary pulmonary nodules with 18F-FDG PET/CT relative activity distribution analysis. *Eur Radiol*. 2015 Jul;25(7):1837-44. doi: 10.1007/s00330-015-3592-8. PMID: 25636419. Exclusion Code: X3.

1969. Zhao S, Jiang T, Zhang L, et al. Clinicopathological and prognostic significance of regulatory T cells in patients with non-small cell lung cancer: A systematic review with meta-analysis. *Oncotarget*. 2016 Jun 14;7(24):36065-73. doi: 10.18632/oncotarget.9130. PMID: 27153545. Exclusion Code: X3.

1970. Zhao W, Wang H, Xie J, et al. A Clinicopathological Study of Small Lung Adenocarcinoma 1 cm or Less in Size: Emphasis on Histological Subtypes Associated With Lymph Node Metastasis and Recurrence. *Int J Surg Pathol*. 2018 Feb;26(1):4-11. doi: 10.1177/1066896917721649. PMID: 28805108. Exclusion Code: X3.

1971. Zhao X, Qian L, Luo Q, et al. Segmentectomy as a safe and equally effective surgical option under complete video-assisted thoracic surgery for patients of stage I non-small cell lung cancer. *J Cardiothorac Surg*. 2013 Apr 29;8:116. doi: 10.1186/1749-8090-8-116. PMID: 23628209. Exclusion Code: X11.

1972. Zhao Y, de Bock GH, Vliegenthart R, et al. Performance of computer-aided detection of pulmonary nodules in low-dose CT: comparison with double reading by nodule volume. *Eur Radiol*. 2012 Oct;22(10):2076-84. doi: 10.1007/s00330-012-2437-y. PMID: 22814824. Exclusion Code: X11.

1973. Zhao ZR, Xi SY, Li W, et al. Prognostic impact of pattern-based grading system by the new IASLC/ATS/ERS classification in Asian patients with stage I lung adenocarcinoma. *Lung Cancer*. 2015 Dec;90(3):604-9. doi: 10.1016/j.lungcan.2015.10.026. PMID: 26547801. Exclusion Code: X11.

1974. Zheng A, Wang X, Yang X, et al. Major complications after lung microwave ablation: a single-center experience on 204 sessions. *Ann Thorac Surg*. 2014 Jul;98(1):243-8. doi: 10.1016/j.athoracsur.2014.03.008. PMID: 24793688. Exclusion Code: X6.

1975. Zheng A, Ye X, Yang X, et al. Local efficacy and survival after microwave ablation of lung tumors: a retrospective study in 183 patients. *J Vasc Interv Radiol*. 2016 Dec;27(12):1806-14. doi: 10.1016/j.jvir.2016.08.013. PMID: 27789077. Exclusion Code: X6.

1976. Zheng H, Jiang S, Chen C. Stepwise tactile localization and wedge resections for deep pulmonary nodules during video-assisted thoracoscopic surgery. *Thorac Cardiovasc Surg*. 2016 Mar;64(2):182-6. doi: 10.1055/s-0035-1545262. PMID: 25785763. Exclusion Code: X11.

Appendix C. Excluded Studies

1977. Zheng X, Xiong H, Li Y, et al. Application of quantitative autofluorescence bronchoscopy image analysis method in identifying bronchopulmonary cancer. *Technol Cancer Res Treat*. 2017 Aug;16(4):482-7. doi: 10.1177/1533034616656466. PMID: 27436838. Exclusion Code: X3.
1978. Zheng Y, Shi A, Wang W, et al. Posttreatment Immune Parameters Predict Cancer Control and Pneumonitis in Stage I Non-Small-Cell Lung Cancer Patients Treated With Stereotactic Ablative Radiotherapy. *Clin Lung Cancer*. 2018 Jul;19(4):e399-e404. doi: 10.1016/j.cllc.2017.12.012. PMID: 29519614. Exclusion Code: X10.
1979. Zhong C, Fang W, Mao T, et al. Comparison of thoracoscopic segmentectomy and thoracoscopic lobectomy for small-sized stage IA lung cancer. *Ann Thorac Surg*. 2012 Aug;94(2):362-7. doi: 10.1016/j.athoracsur.2012.04.047. PMID: 22727321. Exclusion Code: X11.
1980. Zhong C, Yao F, Zhao H. Clinical outcomes of thoracoscopic lobectomy for patients with clinical N0 and pathologic N2 non-small cell lung cancer. *Ann Thorac Surg*. 2013 Mar;95(3):987-92. doi: 10.1016/j.athoracsur.2012.10.083. PMID: 23261117. Exclusion Code: X3.
1981. Zhong Y, Xu XQ, Pan XL, et al. Retrospective evaluation of safety, efficacy and risk factors for pneumothorax in simultaneous localizations of multiple pulmonary nodules using hook wire system. *Cardiovasc Intervent Radiol*. 2017 Sep;40(9):1408-14. doi: 10.1007/s00270-017-1631-3. PMID: 28357573. Exclusion Code: X11.
1982. Zhou H, Tapias LF, Gaissert HA, et al. Lymph node assessment and impact on survival in video-assisted thoracoscopic lobectomy or segmentectomy. *Ann Thorac Surg*. 2015 Sep;100(3):910-6. doi: 10.1016/j.athoracsur.2015.04.034. PMID: 26165483. Exclusion Code: X17.
1983. Zhou S, Pei G, Han Y, et al. Sleeve lobectomy by video-assisted thoracic surgery versus thoracotomy for non-small cell lung cancer. *J Cardiothorac Surg*. 2015 Sep 10;10:116. doi: 10.1186/s13019-015-0318-6. PMID: 26357875. Exclusion Code: X3.
1984. Zhou T, Lu H, Zhang J, et al. Pulmonary nodule detection model based on SVM and CT image feature-level fusion with rough sets. *Biomed Res Int*. 2016;2016:8052436. doi: 10.1155/2016/8052436. PMID: 27722173. Exclusion Code: X3.
1985. Zhu H, Zhang L, Wang Y, et al. Improved image quality and diagnostic potential using ultra-high-resolution computed tomography of the lung with small scan FOV: A prospective study. *PLoS One*. 2017;12(2):e0172688. doi: 10.1371/journal.pone.0172688. PMID: 28231320. Exclusion Code: X3.
1986. Zhu J, Zhang HP, Ni J, et al. Endobronchial ultrasound-guided transbronchial needle aspiration for diagnosing mediastinal lymphadenectasis: a cohort study from a single center. *Clin Respir J*. 2017 Mar;11(2):159-67. doi: 10.1111/crj.12317. PMID: 25918974. Exclusion Code: X3.
1987. Zhuang YP, Wang HY, Zhang J, et al. Diagnostic accuracy and safety of CT-guided fine needle aspiration biopsy in cavitary pulmonary lesions. *Eur J Radiol*. 2013 Jan;82(1):182-6. doi: 10.1016/j.ejrad.2012.09.011. PMID: 23079048. Exclusion Code: X3.
1988. Zimmermann M, Nickl S, Lambers C, et al. Discrimination of clinical stages in non-small cell lung cancer patients by serum HSP27 and HSP70: a multi-institutional case-control study. *Clin Chim Acta*. 2012 Jul 11;413(13-14):1115-20. doi: 10.1016/j.cca.2012.03.008. PMID: 22465083. Exclusion Code: X7.
1989. Zinovev D, Duo Y, Raicu DS, et al. Consensus versus disagreement in imaging research: a case study using the LIDC database. *J Digit Imaging*. 2012 Jun;25(3):423-36. doi: 10.1007/s10278-011-9445-3. PMID: 22193755. Exclusion Code: X3.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Ackerson, 2018[295] N/A Fair	NA	Medium	Low	Low	NI	Medium	Low	Nearly a quarter (24%) of SBRT patients lacked pathologic confirmation of NSCLC; ROB stemming from this small study with some data collected retrospectively (70 SBRT patients).
Allibhai, 2013[259] NA Fair	NA	Low	Low	NI	NI	Low	High	There was no information on deviations from the intended SBRT therapy or on missing data reported in the article. Additionally, the only adverse event reported was radiation pneumonitis.
Anderson, 2009[150] ELCAP Fair	NA	Medium	Low	Low	Low	Medium	Low	Risk of selection bias and self-reported outcome
Arnold, 2017[199] NCDB: 2003-2012 Fair	NA	Medium	Low	NI	Low	Low	Low	Risk of selection bias, as reported by the authors, and lack of information on deviations from treatment before entry into the study.
Badellino, 2017[270] NA Fair	NA	Low	Low	Low	NI	Medium	Medium	Risk for information and reporting bias related to the outcomes and no information on missing data.
Baine, 2019[232] NCDB: 2004-2014 Fair	NA	Low	Low	NI	Low	Medium	Low	Risk of outcome measurement bias; lack of detail about systems for outcome ascertainment.
Ball, 2019[293] CHISEL Fair	NA	Medium	Low	Low	Low	Low	Medium	Risk of selection bias because nearly half (43%) of the SBRT sample had a history of previous cancer, and also risk of reporting bias because the trial protocol did not require the recording of toxicities occurring after local treatment failure

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Barriger, 2012[290] N/A Fair	NA	Medium	Medium	NI	Medium	Medium	Low	Risk of selection bias; unclear how many patients had histologically confirmed NSCLC; ROB due to intervention classification because different treatment planning systems were used depending on the year of treatment; potential missing data bias because of the exclusion of patients with incomplete dosimetry data.
Baumann, 2006[227] N/A Fair	NA	Low	Low	NI	Low	Medium	Low	Risk of outcome measurement bias because of ascertainment methods used.
Berry, 2018[216] California Cancer Registry: 2013-2014 Fair	NA	Medium	Low	NI	Low	Low	Low	Risk of selection bias; no detail was given about how patients' cancers were staged; no information about potential deviation from intended surgeries.
Bibault, 2015[254] NA Fair	NA	Medium	Low	NI	NI	Low	Low	No information for multiple domains and risk of selection bias due to inclusion of patients with previous treatment of lung cancer (surgery and SBRT).
Bongers, 2011[286] N/A Fair	NA	Medium	Low	Low	Low	Medium	Low	Risk of outcome measurement bias; a "high proportion" of patients returned to their pulmonology outpatient clinics (number not reported) for longer-term followup; unclear how many patients or how their referring institutions collected data about chest wall toxicity that could be used in this analysis.
Brooks, 2017[204] NA Fair	NA	Low	Low	NI	NI	Low	Low	Sparse information was reported for multiple domains; it is unclear what the data source was for survival outcomes.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Brunelli, 2015[181] NA Good	NA	Low	Low	NI	Low	Low	Low	NA
Bryant, 2018[196] VINCI: 2006-2015 Fair	NA	Low	Medium	NI	Medium	Low	Low	Potential misclassification of surgical approach subtype or bias related to missing data.
Byrne, 2008[161] PLuSS Fair	NA	Medium	Low	Low	Medium	Medium	Low	Risk of selection bias, missing data, and outcome measurement
Chang, 2007[192] SEER: 1988-1997 Fair	NA	Low	Low	NI	NI	Low	Low	No information from multiple domains.
Chang, 2012[282] N/A Fair	NA	Low	Low	Medium	NI	Low	Low	Deviation from the SBRT protocol for patients with centrally located tumors close to critical structures; no information about whether any patients were excluded during sample selection.
Chung, 2017[132] NLST Good	Low	Medium	Low	Low	Low	Low	Low	NA
Cox, 2003[154] Mayo Lung Project Fair	NA	Medium	Low	Low	Low	Medium	Low	Risk of selection and outcome measurement bias
Cox, 2017[186] NCDB: 2003-2006 Fair	NA	Low	Low	NI	NI	NI	Low	No information reported for several ROB domains.
Crabtree/ Timmeran, 2013,[265] 2010[272] RTOG 0236 Good	NA	Low	Low	Low	NI	Low	Low	NA
Crucitti, 2015[111] “Un repiro per la vita” Good	NA	Low	Low	Low	NI	Low	Low	NA

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Cummings, 2018[233] N/A Fair	NA	Low	Low	NI	NI	Medium	Medium	Risk of outcome measurement bias due to ascertainment methods and a short followup period in the single-fraction SBRT arm; risk of selective outcome reporting bias in that Grade 1-2 toxicities were not recorded or reported.
Detillon, 2019[231] Netherlands Cancer Registry Fair	NA	Medium	Medium	NI	NI	Low	Low	Risk of selection bias in that nearly half of the sample (48%) lacked histological confirmation of NSCLC; no information reported about SBRT dosing used to treat the sample.
Dhanasopon, 2017[386] NCDB, 2004-2013 Poor	Medium	High	Low	Low	High	Low	Low	Risk of selection bias due to confounding by indication, and bias due to missing data, in that some patients were excluded from the analysis for missing data, but the authors did not report how many.
Dunn, 2017[163] UKLS Fair	Medium	Medium	Low	Low	Low	Low	Low	Risk of confounding and selection bias.
Dziedzic, 2017[217] Polish National Lung Cancer Registry Fair	NA	Medium	Low	NI	Medium	Low	Low	Risk of selection bias in that a "significant number of patients" did not receive PET staging of their tumors; ROB due to exclusion of patients with missing or "inconsistent" data without details about the criteria for that process.
Eba, 2016[201] NA Fair	NA	Low	Low	NI	Low	NI	Medium	Lack of information on multiple domains; risk of reporting bias due to the identification of 3-yr OS as the primary endpoint but the reporting of results for 5-yr OS.
Ezer, 2018[273] SEER: 2000-2009 Fair	NA	Low	Low	NI	NI	Low	Low	No information from multiple domains, including deviation from intended intervention and missing data.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Fair	NA	Low	Low	NI	NI	Medium	Low	Risk of outcome measurement bias that may have led to an underestimation of toxicity events due to the study's short median followup time, reliance on retrospective review of hospital medical records for some ascertainment, and small sample (N=74 patients with 78 tumors).
Fernandez, 2012[188] SEER-Medicare: 1998-2005 Fair	NA	Low	Low	NI	NI	Low	Low	No information on multiple domains.
Ferrero, 2015[262] NA Fair	NA	NI	Low	Low	Medium	Low	Low	Medium ROB due to missing data over the course of followup and no information on potential sources of selection bias.
Fischer-Valuck, 2013[281] N/A Fair	NA	Low	Low	Low	NI	NI	Low	No or minimal information on multiple domains.
Gareen, 2014[156] NLST Fair	NA	Medium	Medium	Low	Low	Low	Medium	Risk of selection bias because selection was related to outcome, but with adjustment. Potential for selective reporting bias in that results are inconsistent with a priori plan.
Goya, 2005[195] Japanese Joint Committee of Lung Cancer Registry Fair	NA	Medium	Low	NI	Low	NI	Low	Potential selection bias as the type of hospital may be related to survival outcomes; little information reported about the source(s) of the data from individual hospitals.
Grills, 2012[256] NA Fair	NA	Medium	Medium	Low	NI	Low	Low	Risk of selection and intervention classification bias across multiple institutions; lack of information on missing data; unclear how harms were included or excluded in the reporting

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Guckenberger, 2013[280] N/A Fair	NA	Medium	Low	NI	Medium	Medium	Low	Risk of selection bias because the study may have included patients with secondary tumors; exclusion of one of 13 centers from the toxicity analysis may have introduced bias related to missing data; risk of measurement bias because not all participating centers had in-house databases for managing the data of SBRT patients; no information about adherence to SBRT protocols.
Guerrera, 2015[171] NA Fair	NA	Low	Low	Low	NI	NI	Low	Lack of information for several domains.
Haasbeek, 2010[291] N/A Fair	NA	Medium	Low	Low	NI	Medium	Low	Risk of selection bias in that majority of sample (61%) lacked histological confirmation of NSCLC; risk of outcome measurement bias due to a short median followup period and some reliance on referring lung physicians or GPs for the toxicity data of patients opting out of followup at the study center.
Haidar, 2014[257] NA Fair	NA	Low	Low	Low	Medium	Low	Low	Some missing data related to pathologic confirmation of disease.
Handa, 2018[218] N/A Fair	NA	Low	Low	NI	NI	Medium	Low	Risk of outcome measurement bias because of reliance on a single hospital's existing data; no information from multiple domains.
Henschke, 2006[128] I-ELCAP Fair	NA	Medium	Low	Low	Medium	Low	Low	Patient selection, decreased patients in annual screening
Henschke, 2006[129] I-ELCAP Fair	NA	Medium	Low	Low	Low	Low	Low	Risk of selection bias

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Henschke, 2006[131] I-ELCAP Fair	NA	Medium	Low	Low	Low	Low	Low	Risk of selection bias
Henschke, 2013[107] I-ELCAP Good	NA	Low	Low	Low	Low	Low	NI	NA
Heuvelmans, 2015[325] NELSON Fair	NA	Low	Low	Low	Low	Medium	Medium	Risk of outcome measurement bias; unclear if assessments were done with knowledge of patient's position in study; risk for selective reporting bias.
Husain, 2015[239] NCDB: 2003-2011 Fair	NA	Low	Low	Low	NI	Low	Medium	No information on missing data and potential for reporting bias with limited harms data reported.
Infante, 2011[140] DANTE Fair	NA	Medium	Low	Low	Low	Low	Medium	Risk of selection bias because enrollment was related to outcome; risk of outcome measurement bias because unclear if assessment done with knowledge of patient's position in study; risk of selective reporting bias in that outcomes were inconsistent with a priori plan.
Inoue, 2013[224] N/A Fair	NA	Low	Low	Low	NI	Medium	Low	Risk of outcome measurement bias with short followup period for survival outcomes; no information about missing data.
Jeon, 2018[268] NA Fair	NA	Low	Low	Low	NI	Low	Low	No information related to missing data. Authors retrospectively analyzed data that seemed to have been collected prospectively, but there is minimal description of the data ascertainment methods employed.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Jeppesen, 2013[223] N/A Fair	NA	Medium	Low	NI	NI	Low	Low	Missing information about multiple domains. Risk for selection bias in that some patients may have had Stage II cancer, depending on which classification system the investigators applied to the sample.
Jeppesen, 2018[203] NA Fair	NA	Low	Low	Low	NI	Medium	Medium	No information on missing data and potential for information bias related to outcomes, which were ascertained from medical records and only selectively reported.
Kaerlev, 2012[157] DLCST Good	NA	Low	Low	Low	Low	Low	Low	NA
Karasawa, 2018[229] N/A Fair	NA	Low	Low	Low	Medium	Medium	Low	Risk of bias from exclusion of 33% of eligible SBRT patients because of a dose difference due to a difference in calculation method; risk of outcome measurement bias.
Katoh, 2017[255] NA Fair	NA	Low	Low	Low	NI	Low	Medium	No information on missing data and very little information was provided on harms, except radiation pneumonitis, other than reporting that 1 grade 2 dermatitis and 10 grade 2 thoracic wall pain cases, no other toxicities were reported; data were not presented for Stage 1 patients only.
Khullar, 2015[178] NCDB: 2003-2006 Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information for multiple domains.
Khullar, 2015[189] NCDB: 2003-2011 Fair	NA	Low	Low	NI	Medium	NI	Low	No information for several ROB domains. Patient characteristics are presented for the entire cohort of patients but not the subcohort that contributed to the long-term survival analyses.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Kinsinger, 2017[38] VA Population (LCSDP) Fair	NA	Medium	NI	NI	Low	NI	Low	Risk of selection bias because not all eligible patients (veterans) participated
Koshy, 2015[200] NCDB: 2003-2006 Fair	NA	Medium	Low	Low	NI	Low	Low	Risk of selection bias (only 64% of patients receiving SBRT were included) and lack of information related to missing data.
Lagerwaard, 2008[292] N/A Fair	NA	Medium	Low	Low	NI	Medium	Low	Risk of selection bias because most patients lacked histopathological confirmation of NSCLC; unclear how many of the 18% of patients with a prior lung cancer were actually experiencing a secondary tumor or recurrence (vs. a primary tumor); risk of outcome measurement bias due to short median followup period and at least some reliance on referring lung physicians or GPs for toxicity data of patients opting out of followup at the study center.
Lagerwaard, 2012[283] N/A Fair	NA	Low	Low	Low	Medium	Medium	Low	Risk of bias due to missing data that may have affected toxicity results; HRQOL data were missing for a large percentage of patients at 18- and 24-month time points; unclear how many patients were missing toxicity data, but the reasons for attrition, such as patients returning to their local hospitals, likely also reduced the availability of toxicity data.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Lagerwaard, 2012[225] N/A Fair	NA	Medium	Low	Low	NI	Medium	Low	Risk of selection bias in that probable operability of patients for selection into study was determined post hoc; risk of outcome measurement bias because investigators relied on referring physicians for toxicity data for an unknown number of patients opting out of followup at the study center.
Lakha, 2014[175] SEER: 2004-2010 Fair	NA	Low	Low	NI	NI	Low	Low	No information on multiple domains.
Lam, 2018[202] NCDB: 2004-2014 Fair	NA	Low	Low	NI	NI	NI	Low	No information provided related to several domains.
Landreneau, 2014[176] NA Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information related to intervention deviation and missing data. The analysis was among propensity-score matched groups defined by surgical approach; this isn't a selection bias but might impact generalizability (e.g., unmatched had surgery earlier than matched, were less likely to have COPD, and had larger tumors).
Lee, 2015[387] RegulomeDB Poor	NA (KQs 6 & 7)	NI	NI	NI	NI	NI	NI	Uncontrolled study with very little information reported that was relevant to ROB assessment.
Lee, 2018[234] N/A Fair	NA	Low	Low	NI	Medium	Medium	Low	ROB due to exclusion of patients not followed up at the study's hospital, and also potential outcome measurement bias due to the post hoc nature of the analysis.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Licht, 2013[249] DLCR: 2007-2011 Fair	NA	Medium	Low	Low	Low	Low	Low	Risk of selection bias because authors only included standard lobectomies in the study in an "attempt to make VATS and thoracotomy groups more comparable." Authors did not provide their definition of a nonstandard lobectomy.
Lindberg, 2015[207] NA Fair	NA	Low	Low	Low	NI	Low	Low	Lack of information on missing data.
Liu, 2018[219] SEER: 2000-2013 Fair	NA	Low	Low	NI	Medium	Low	Low	ROB due to missing data because patients were excluded for missing examinable lymph node counts and clinical features.
Louie, 2016[238] STS-GTS: 2009-2013 Fair	NA	Medium	Low	Low	NI	NI	Low	No information for multiple domains and potential selection bias resulting from exclusion of cases from low-volume centers.
Lutz, 2019[220] N/A Fair	NA	Low	Low	NI	Low	Medium	Low	No information on intervention deviation; risk of outcome measurement bias because no statistical methods or adjustments were used to explore the impact of including 140 patients (22.5% of the 621 in the study sample) who were upstaged in the analysis.
Lv, 2018[221] SEER: 2004-2014 Fair	NA	Low	Low	NI	NI	Low	Medium	No information from multiple domains; risk of reporting bias because the study's only eligible survival data, 5-year OS, were reported for the total sample, not the lobectomy or SLR arms, for which overall survival curves were compared.
Ma, 2017[269] NA Fair	NA	Low	Low	NI	NI	Low	Medium	Medium risk of reporting bias due to certain data points not being collected and no information on multiple other domains.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Maeda, 2010[191] NA Fair	NA	Low	Low	NI	NI	Low	Low	No information on multiple domains.
Maeda, 2012[184] NA Fair	NA	Low	Low	NI	NI	Low	Low	No information on multiple domains.
Manyam, 2019[230] N/A Fair	NA	Low	Low	Low	NI	Medium	Low	Risk of outcome measurement bias for 5-year OS due to a short followup period (median 23.8 months).
Mascalchi, 2006[136] ITALUNG Fair	NA	Medium	Low	Low	Low	Low	Low	Risk of selection bias
Mathieu, 2014[260] NA Fair	NA	Low	Low	Low	Medium	Low	Medium	ROB related to exclusion of patients with disease recurrence from analysis and reporting of only some toxicities.
Matsuo, 2012[285] N/A Fair	NA	Low	Low	Low	NI	Medium	Low	No information on missing data; risk of outcome measurement bias in that the analysis was based on post hoc ascertainment.
Matsuo, 2014[198] NA Fair	NA	Medium	Low	NI	NI	Low	Low	No information for multiple domains and some concern over selection of patients given that the original trial was stopped early due to slow patient enrollment.
Mediratta, 2014[177] NA Good	NA	Low	Low	NI	Low	Low	Low	NA
Melvan, 2015[243] NCDB: 2003-2011 Fair	NA	Low	Low	NI	Medium	Low	Low	Medium ROB related missing data and no information on intervention deviation.
Menezes, 2010[121] NA Fair	NA	Medium	Low	Low	Medium	Low	Low	Unclear selection, poor followup after 1st annual screening

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Miura, 2015[388] NA Poor	NA	High	Low	Low	NI	Low	Low	Restricting the study sample to patients with at least 12 months of followup CT scans after SBRT (i.e., a minimum of 4 followup scans) introduces a high risk of selection bias; unclear why this criterion was applied since all radiation-induced rib fractures after the first day of SBRT were included; unclear how many cases of rib fractures were missed as a result of the exclusion. Additionally, more than half of the patients had multiple cancers (some lung, some other sites).
Moon, 2018[214] SEER: 2000-2014 Fair	NA	Low	Medium	NI	NI	Low	Low	ROB due to intervention classification in that it was unclear how many segmentectomy patients received "intentional" vs. "compromised" procedures based on their comorbidities, and potential bias due to lack of information about missing data.
Morgan, 2017[167] NA Fair	NA	Medium	NI	Low	Low	Low	Low	Risk of selection bias.
Mutter, 2012[287] N/A Fair	NA	Low	Low	Low	NI	Medium	Low	Risk of outcome measurement bias in that median followup time (16 months) was shorter than the median time to rib fracture diagnosis (27 months).
Nagata, 2015[205] JCOG0403 Fair	NA	Low	Low	NI	NI	Medium	Medium	Long-term followup methods unclear, lack of information on missingness of data, and potential reporting bias related to grade 1-2 harms.
Nakamura, 2015[173] NA Fair	NA	Low	Low	NI	NI	NI	Medium	Post hoc analysis focused on intraoperative blood loss and lack of information on multiple domains.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Nguyen, 2016[166] NLST Fair	NA	Low	Low	Low	Low	NI	Low	Medium risk of selection bias due to possible healthy-volunteer bias, and potential outcome measurement bias because definition of "potentially significant" extrapulmonary findings was left up to radiologists interpreting CT scans to decide.
Nyman, 2016[267] SPACE† Fair	NA	Low	Low	Medium	Medium	Low	Low	A small percentage of patients did not receive SBRT as intended, data sources are unclear, and there is some missing data, though it is not thoroughly described.
Okada, 2006[193] NA Fair	NA	Low	Low	Medium	NI	Low	Low	ROB related to deviations from intended surgical approach and unknown attrition/missing data.
Olsen, 2011[288] N/A Fair	NA	Low	Low	Low	NI	Medium	Low	Risk of outcome measurement bias in that median followup time (range of 11 to 16 months) was short and may not have been enough time for some toxicity events to occur.
Onishi, 2007[226] N/A Fair	NA	Low	Low	NI	NI	Medium	Low	Potential risk of outcome measurement bias due to post hoc use data from 14 different hospitals. Missing information on multiple domains.
Palma, 2010[289] Amsterdam Cancer Registry Fair	NA	Medium	Medium	NI	NI	Medium	Low	Risk of selection bias due to lack of histologic confirmation of NSCLC among 33% of RT patients (and unknown proportion of those receiving SBRT). At least some risk of intervention misclassification because no dosing information was available for RT treatments given. Post hoc analysis of data from population-based registry. No information for several domains.
Pegna, 2013[99] ITALUNG Good	NA	Low	Low	Low	Low	Low	Low	NA

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Pinsky, 2014[64] NLST Fair	NA	Low	Low	Low	Low	Low	Medium	Post hoc analysis
Pinsky, 2015[100] NLST Fair	NA	Medium	Low	NI	NI	Medium	Low	Medium risk of outcome measurement bias because of difference in how radiologists were instructed to assess nodule growth using Lung-RADS criteria vs. NLST criteria. They applied Lung-RADS criteria in a post-hoc fashion to patients previously screened using NLST criteria, which created the potential for discrepancy in terms of how nodes discovered at baseline were later classified as having growth during post-baseline scans. A sensitivity analysis was done assuming that all nodules reported with growth in NLST met Lung-RADS criteria for growth, but that assumption may have been incorrect in at least some cases.
Puri, 2014[242] NA Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information for multiple domains. This is a post hoc analysis of two trial datasets that prospectively collected data.
Puri, 2015[252] NCDB: 1998-2010 Fair	NA	Medium	Low	Medium	NI	Low	Medium	Risk of selection bias in terms of the patients that completed followup; authors were unable to explain the large difference in median survival between the surgical and SBRT groups. No information provided on missingness of data. Author utilized propensity-score matching to compare surgery to SBRT, but results were only presented for surgery overall and SLR.
Pinsky, 2018[139] NLST Fair	Medium	Low	Low	Low	Low	Medium	Low	Post hoc analysis of NLST RCT, looking at intervention arm of study.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Rampinelli, 2017[134] COSMOS Fair	Yes	Low	Low	Low	NI	NI	NI	Bias due to the source of harms data; data on the harm of radiation-induced cancer from LDCT program were estimated (not measured) based on an assumed relationship (which in turn is based on data from other studies of radiation therapy) that appears to be controversial.
Razi, 2016[180] SEER: 1998-2007 Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information for multiple domains.
Robinson, 2013[266] NA Fair	NA	Low	Low	NI	NI	NI	Low	There was no information for several domains.
Rosen, 2014[244] NCDB: 2004-2009 Fair	NA	Low	Low	NI	Medium	Low	Low	Medium ROB related to missing data (both in terms of how missingness of some variables resulted in exclusion from study and in unknown stage data) and lack of information on intervention deviation.
Rosen, 2014[258] NA Fair	NA	Low	Low	Low	NI	Low	Medium	Risk of reporting bias and lack of information on missing data.
Rosen, 2016[185] NCDB: 2008-2012 Good	NA	Low	Low	Low	NI	Low	Low	NA
Samson, 2015[240] NCDB: 1998-2010; Washington SOM 2000-2012 Fair	NA	Low	Low	NI	NI	NI	Low	Lack of information for several domains.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Samson, 2017[245] NCDB: 2004-2013 Fair	NA	Medium	Low	NI	NI	Low	Low	Medium risk of selection bias and lack of information on several additional domains.
Sawabata, 2011[190] Japanese Joint Committee of Lung Cancer Registry Fair	NA	Low	Low	NI	Low	NI	Low	No information for multiple domains and few details provided by the authors, except as they related to tumor characteristics.
Scheel, 2015[170] NA Fair	NA	Low	Low	Low	NI	Medium	Low	No information on extent of missing data and potential for outcome misclassification.
Schuchert, 2012[248] NA Fair	NA	Medium	Low	NI	NI	Low	Low	Patients were identified from multiple databases, including billing records. Authors report that patients who received incomplete resections were not included; if incomplete resection is associated with poorer outcomes, there could be selection bias present. Lack of information related to several other domains.
Sekihara, 2018[222] N/A Fair	NA	Low	Low	NI	NI	Medium	Low	Risk of outcome measurement bias in that the study relied on a post hoc analysis of a single hospital's data, and no information from multiple domains.
Shapiro, 2012[247] SEER: 1992-2002 Fair	NA	Low	Low	NI	Medium	Low	Low	Medium ROB related to missing data.
Shibamoto, 2012[236] N/A Good	NA	Low	Low	Low	Low	Low	Low	NA

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Shirvani, 2012[237] SEER: 2001-2007 Fair	NA	Low	Low	NI	NI	Low	Low	No information on multiple domains.
Shirvani, 2014[241] SEER: 2003-2009 Fair	NA	Medium	Low	Low	NI	Low	Low	Risk of selection bias resulting from exclusion of patients with incomplete Medicare records. Lack of information on missing outcomes data.
Speicher, 2016[187] NCDB: 2003-2006 Fair	NA	Low	Low	NI	Medium	NI	Low	No information for several ROB domains. Patient characteristics are presented for the entire cohort of patients but not the subcohort that contributed to the long-term survival analyses.
Stanic, 2014[279] RTOG 0236 Fair	NA	Medium	Low	NI	Medium	Medium	Low	Risk of self-selection bias indicated by fact that most of the sample was female when majority of NSCLC patients in the population are male. Potential bias from missing data for PFT outcomes due to test noncompliance at each timepoint of interest. Potential bias from outcome measurement for PFT outcomes in that large variation occurred in the timing of assessments.
Stephens, 2014[182] NA Fair	NA	Low	Low	Medium	NI	Low	Low	ROB related to patients who crossed over from one surgical approach to another and lack of information related to missing data.
Stokes, 2018[251] NCDB: 2004-2013 Fair	NA	Medium	NI	NI	Low	NI	Low	No information provided related to several domains. Missing data informed selection of patients into the analysis (i.e., complete case analysis).
Strand, 2006[194] Cancer Registry of Norway Good	NA	Low	Low	Low	Low	Low	Low	NA

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Styn, 2009[151] PLuSS Fair	NA	Medium	Low	Low	Low	Medium	Low	Potential bias from outcomes and patient selection.
Su, 2014[174] ACOSOG Z0030 (Alliance) Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information on several domains.
Sun, 2017[197] NA Fair	NA	Medium	Low	Low	Low	NI	Low	Risk of selection bias with respect to inclusion of patients with a prior history of lung or other cancers. Additionally, 5% of the enrolled patients had no followup imaging or records and were not included in the analysis.
Swensen, 2002[168] NA Fair	NA	Medium	Low	Low	Low	Low	Low	Potential bias from patient selection.
Swensen, 2005[130] NA Fair	NA	Medium	Low	Low	Medium	Low	Low	Potential bias from patient selection and missing data.
Taremi, 2012[261] NA Fair	NA	Medium	Low	NI	NI	Low	Low	Medium risk of selection bias related to short followup periods and lack of information related to missing data.
Taremi, 2012[264] NA Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information for multiple domains.
Thalanayar, 2015[143] PLuSS Fair	NA	Medium	Low	Low	Low	Medium	Low	Potential bias due to patient selection and outcome.
Townsend, 2005[152] Mayo Lung Project Fair	NA	Medium	Low	Low	Medium	Medium	Low	Possible selection, outcome and missing data bias as listed.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Toyoda, 2008[126] NA Fair	NA	Medium	Low	Low	Low	Low	Low	Potential bias due to patient selection.
Tsushima, 2008[123] NA Fair	NA	Medium	Low	Low	Low	Low	Low	Potential bias due to patient selection.
Tsutani, 2014[179] NA Good	NA	Low	Low	NI	Low	Low	Low	NA
Ubels, 2015[206] NA Fair	NA	Medium	Low	NI	NI	Low	Low	Lack of information for multiple domains. The study included a small number of patients; almost 10% of them were excluded after enrollment for reasons that may be associated with poorer outcomes.
Ueda, 2018[274] N/A Fair	NA	Low	Low	NI	NI	Medium	Low	No information in multiple domains; risk of outcome measurement bias because ECG was inconsistently used to identify POAF, the study's primary outcome of interest, and more broadly, this was a small post hoc analysis of a single hospital's data.
Uhlig, 2018[228] NCDB: 2004-2013 Fair	NA	Low	Low	NI	Low	Medium	Low	Risk of outcome measurement bias due to the post hoc nature of the analysis and lack of detail about systems for outcome ascertainment.
Valle, 2016[246] NCCN: 2007-2011 Fair	NA	Medium	Low	NI	Medium	NI	Low	Risk of selection bias and bias due to missing data; no information provided for additional domains.
Veronesi, 2008[124] COSMOS Fair	NA	Medium	Low	Low	Low	Low	Low	Risk of patient selection bias.
Veronesi, 2008[127] COSMOS Fair	NA	Medium	Low	Low	Low	Low	Low	Risk of selection bias.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Veronesi, 2012[135] COSMOS Fair	Medium	Low	Low	Low	Medium	Medium	Medium	ROB likely affects the size of effects this study demonstrates: namely, that (for scenario A) greater VDT is associated with lower LC mortality (and likely overdiagnosis), as well as for scenario B) that LDCT screening finds indolent lesions, i.e., those with long VDT. Sources of bias include confounding, missing data, outcomes measurement, and selective reporting.
Videtic, 2014[271] NA Fair	NA	Medium	Low	Low	NI	Low	Low	Risk of selection bias and lack of information on missingness of data.
Wagnetz, 2012[118] NA Fair	NA	Medium	Low	Low	NI	Low	Low	Risk of selection bias and no information on missing data.
Walker, 2015[133] NA Fair	NA	Medium	Low	Low	Low	Low	Low	ROB due to patient selection.
Walter, 2016[78] NELSON Good	NA	Low	Low	Low	Low	Low	Low	NA
Westover, 2012[284] N/A Fair	NA	Low	Low	Low	Low	Medium	Low	Medium risk of outcome measurement bias; study relied on a database and drew data from a very small sample of 15 patients.
Wilson, 2008[137] PLuSS Fair	NA	Medium	Low	Low	Low	Low	Low	ROB due to patient selection.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Wink, 2019[235] N/A Fair	NA	Medium	Medium	NI	NI	Medium	Low	Missing information for multiple domains; post hoc analysis with short followup period for 5-year OS (median 48.1 months for surviving patients); risk of outcome measurement bias; OS data were retrieved from national databases, and unclear how comprehensively they captured mortality; risk of selection bias because majority (68%) of sample did not have histologic confirmation of NSCLC; variation in how SBRT was planned across the study's treating institutions.
Yang, 2016[250] NCDB: 2010-2012 Fair	NA	Low	Low	NI	NI	NI	Low	No information on multiple domains. Authors report that outcomes of surgical approach were evaluated with intent-to-treat analysis but provide no additional information.
Ye, 2018[294] N/A Fair	NA	Medium	Low	Low	NI	Low	Low	Risk of selection bias in that nearly a fifth (19%) of SBRT patients lacked pathologic confirmation of NSCLC.
Yousaf-Khan, 2017[389] NELSON Poor	Low	Medium	Low	Low	Medium	Low	Low	High risk of self-selection bias for the fourth round of screening, the focus of this substudy. Enrollment of 78% of eligible patients from 3rd round of screening (about 70% of initial sample) and confirmation in the article that the fourth round's patients differed significantly from the initial sample in several ways (e.g., more current smokers in the fourth round).
Zhai, 2014[172] NA Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information for several domains.
Zhao, 2014[109] NELSON Fair	NA	Low	Low	Medium	Low	Low	NI	This longitudinal study did not apply the same imaging followup protocol to all patients in terms of the intervals between scans.

Appendix D Table 1. Risk of Bias and Overall Quality Assessment Ratings for Nonrandomized Studies

First Author, Year Study Name Quality Rating	Confounding*	Participant Selection	Intervention Classification	Intervention Deviation	Missing Data	Outcome Measurement	Reporting	Comments for Fair- or Poor-Quality Studies
Zhao, 2017[183] SEER: 2004-2012 Fair	NA	Low	Low	NI	NI	Low	Low	Lack of information related to several domains.
Zhou, 2015[390] Mass General Hospital Database Poor	NA	High	Low	NI	Medium	NI	Medium	High risk of selection bias, medium ROB related to missing data/patient attrition and reporting of harms (i.e., 'complications'), and lack of information on additional domains.
Zhou, 2018[215] SEER: 2004-2013 Fair	NA	Medium	Low	NI	Low	Low	Low	Risk of selection bias because no detail was given about how patients' cancers were staged, and no information about potential deviation from intended interventions.

* Bias due to confounding did not apply to KQ6/7 studies.

† Only the SBRT arm of the study was eligible for this review.

Abbreviations: ACOSOG=American College of Surgeons Oncology Group; CHISEL=A Randomised Phase III Trial of Highly Conformal Hypofractionated Image Guided ("Stereotactic") Radiotherapy (HypoRT) Versus Conventionally Fractionated Radiotherapy (ConRT) for Inoperable Early Stage I Non-small Cell Lung Cancer; COPD=chronic obstructive pulmonary disease; COSMOS=Continuous Observation of Smoking Subjects study; CT=computed tomography; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology trial; DLCR=Danish Lung Cancer Registry; ECG=electrocardiogram; GP=general practitioner; HRQOL=health-related quality of life; I-ELCAP=International Early Lung Cancer Action Project; ITALUNG=The Italian Lung Study; JCOG=Japan Clinical Oncology Group; KQ=Key Question; LC=lung cancer; LDCT=low-dose computed tomography; LCSDP=Lung Cancer Screening Demonstration Project; Lung-RADS=ACR Lung Imaging Reporting and Data System; NA=not applicable; NCCN=National Comprehensive Cancer Network; NCDB=National Cancer Database; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial; NI=no information; NLST=National Lung Screening Trial; OS=overall surgery; PFT=pulmonary function test; POAF=postoperative atrial fibrillation; RCT=randomized, controlled trial; ROB=risk of bias; RT=radiotherapy; RTOG=Radiation Therapy Oncology Group; SBRT=stereotactic body radiation therapy; SEER=Surveillance, Epidemiology, and End Results; SLR=sublobar resection; SOM=School of Medicine; SPACE=Stereotactic Precision And Conventional Radiotherapy Evaluation; STS-GTS=Society of Thoracic Surgeons General Thoracic Surgery Database; VATS=video-assisted thoracoscopic surgery; VDT=volume doubling time; VINCI=Veteran's Affairs Informatics and Computing Infrastructure; vs.=versus.

Appendix D Table 2. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 1

First Author, Year Study Name Quality Rating	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Eligibility criteria specified?	Were outcome measurements equal, reliable and valid?	Were outcome accessors masked?	Were care providers masked?	Were Patients masked?
Aberle, 2011[32] NLST Good	Yes	Yes	Yes	Yes	Yes	LC mortality: Yes LC incidence: unclear (but likely)	Unclear (but unlikely)	No
Aberle, 2013[58] NLST Good	Yes	Yes	Yes	Yes	Yes	LC mortality: Yes LC incidence: Unclear (but likely)	Unclear (but unlikely)	No
Aggestrup, 2012[160] DLCST Fair	Yes	Yes	Yes	Yes	Yes	Unclear	No	No
Ashraf, 2009[145] DLCST Fair	Yes	Yes	Yes	Yes	Yes	Unclear	No	No
Ashraf, 2014[147] DLCST Good	Yes	Unclear	Yes	Yes	Yes	Unclear (but unlikely to bias smoking cessation)	Unclear (but unlikely to bias smoking cessation)	No
Becker, 2012[60] LUSI Good	Yes	Unclear	Yes	Yes	Yes	NR	No (but unlikely to bias baseline screening results)	No
Becker, 2015[59], 2019[73] LUSI Fair	Yes	Unclear	Yes	Yes	Yes	NR	No	No
Brain, 2016[391] UKLS Poor	Yes	Yes	Yes	Yes	Yes	NR	No	No
Brain, 2017[392] UKLS Poor	Yes	Yes	Yes	Yes	Unclear	Not reported	No	No
Church, 2013[57] NLST Good	Yes	Yes	Yes	Yes	Yes	LC mortality: Yes LC incidence: Unclear (but likely)	Unclear (but unlikely)	No
Clark, 2016[149] NLST Fair	Yes	Yes	Yes	Yes	Unclear	Yes	Unclear (but unlikely)	No

Appendix D Table 2. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 1

First Author, Year Study Name Quality Rating	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Eligibility criteria specified?	Were outcome measurements equal, reliable and valid?	Were outcome accessors masked?	Were care providers masked?	Were Patients masked?
Croswell, 2010[119] NA Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
De Koning, 2020[76]	Yes*	Yes*	Yes	Yes	Unclear	Yes	Unclear	No
Field, 2016[97] UKLS Fair	Yes	Unclear	Yes	Yes	No	Unclear	Unclear	No
Field, 2016[117] UKLS Fair	Yes	Yes	Yes	Yes	Yes	NR	No	No
Gohagan, 2004[70] LSS Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
Gohagan, 2005[69] LSS Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
Heleno, 2018[141] DLCST Fair	Yes	NR	Mostly (slightly higher risk)	Yes	Yes	NR	No	No
Horeweg, 2013[98] NELSON Poor	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	No
Horeweg, 2014[33] NELSON Poor	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	No
Infante, 2008[72] DANTE Fair	Yes	Yes	Yes	Yes	Yes	Unclear	No	No
Infante, 2009[71] DANTE Fair	Yes	Yes	Yes	Yes	Yes	Unclear	No	No

Appendix D Table 2. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 1

First Author, Year Study Name Quality Rating	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Eligibility criteria specified?	Were outcome measurements equal, reliable and valid?	Were outcome accessors masked?	Were care providers masked?	Were Patients masked?
Infante, 2015[61] DANTE Fair	Yes	No	Yes	Yes	Yes	Unclear	Unclear	No
Lopes Penga, 2009[125] ITALUNG Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
National Lung Screening Trial Research Team, 2019[74] NLST Fair	Yes	Yes	Yes	Yes	Unclear; ascertainment methods differed for trial years (when outcome verification committee was involved) and post-trial years	Unclear	Unclear (but unlikely)	No
O'Grady, 2014[169] PLCO, NLST Good	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Paci, 2017[62] ITALUNG Fair	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Pastorino, 2012[80] and 2019[75, 81] MILD Poor	No	Unclear	No	Yes	Unclear	Unclear	No	No
Patz, 2014[142] NLST Fair	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Pedersen, 2009[122] DLCST Good	Yes	Yes	Yes	Yes	Yes	Unclear	No	No
Pinsky, 2005[393], Doroudi, 2018[75] LSS Fair	Yes	Yes	Yes	Yes	Yes	No	No	No

Appendix D Table 2. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 1

First Author, Year Study Name Quality Rating	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Eligibility criteria specified?	Were outcome measurements equal, reliable and valid?	Were outcome accessors masked?	Were care providers masked?	Were Patients masked?
Pinsky, 2013[63] NLST Fair	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Rasmussen, 2014[158] DLCST Fair	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Saghir, 2012[65] DLCST Fair	Yes	Yes	Yes	Yes	Yes	Unclear	No	No
Sverzellati, 2016[82] MILD Fair	Yes (for annual vs. Biennial)	Unclear	Yes	Yes	Yes	Unclear	No	No
Tanner, 2015[66] NLST Fair	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Taylor, 2007[155] NLST/LSS Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
van den Bergh, 2010[162] NELSON Fair	Yes	Yes	Yes	Yes	Yes	Unclear	No	No
van den Bergh, 2011[159] NELSON Fair	Yes	Yes	Yes	Yes	Unclear	Yes	No	No
van der Aalst, 2010[148] NELSON Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
van der Aalst, 2011[153] NELSON Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
van Klaveren, 2009[120] NELSON Good	Yes	Yes	Yes	Yes	Yes	No	No	No

Appendix D Table 2. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 1

First Author, Year Study Name Quality Rating	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Eligibility criteria specified?	Were outcome measurements equal, reliable and valid?	Were outcome accessors masked?	Were care providers masked?	Were Patients masked?
van't Westeinde, 2012[138] NELSON Fair	Yes	Yes	Yes	Yes	Yes	No	No	No
Videtic, 2015[263] RTOG 0915 Fair	Unclear	Unclear	Unclear	Yes	Yes	Unclear	No	No
Wille, 2016[67] DLCST Good	Yes	Yes	Yes	Yes	Yes	Unclear	No	No
Young, 2015[144] NLST Fair	Yes	Yes	Yes	Yes	Yes	Yes	No	No

***** Details of randomization and allocation concealment were not published but were obtained by written personal communication from the first author. In short, all invited persons were given an 8-character random number by an external consultant. For persons responding with informed consent, these personal identification numbers were shifted by 1-8 positions (blindly, randomly computer generated), and then sorted again (ascending numbers) to be randomized. No investigator had control nor insight into this random process, and it also ensured that the consultant could not influence this process.

Abbreviations: CT=computed tomography; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology trial; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=The Italian Lung Study; LC=lung cancer; LUSI=German Lung Cancer Screening Intervention Trial; MILD=Multicentric Italian Lung Detection trial; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial; NLST=National Lung Screening Trial; NR=Not reported; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; RTOG=Radiation Therapy Oncology Group; UKLS=UK Lung Cancer Screening trial; vs.=versus

Appendix D Table 3. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 2

First Author, Year Study Name Quality Rating	What was the reported adherence to the intervention?	Did the study have crossovers or contamination?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition >10% or overall high attrition, raising concerns for bias?
Aberle, 2011[32] NLST Good	CT: 95% CXR: 93%	Minimal (average annual rate of CT in CXR group: 4.3%)	Average over three screening rounds: 6.1%	Average over three screening rounds: LDCT: 5% CXR: 7% T0: LDCT: 1.5% CXR: 2.6% T1: LDCT: 6.0% CXR: 8.8% T2: LDCT: 7.1% CXR: 10.6%	No
Aberle, 2013[58] NLST Good	T1: LDCT: 94% CXR: 91.2% T2: LDCT: 92.9% CXR: 89.4%	NR for T1 and T2 screens; over three rounds, 4.3% (per Aberle 75)	Overall: T1: 7.4% T2: 8.8%	T1: LDCT: 6.0% CXR: 8.8% T2: LDCT: 7.1% CXR: 10.6%	No
Aggestrup, 2012[160] DLCST Fair	94.3%	NR	5.6%	CT: 2.9% Control: 8.2%	No
Ashraf, 2009[145] DLCST Fair	NR	NR	8.3%	CT: 5.3% Control: 11.6%	11.6% of the control group had missing data
Ashraf, 2014[147] DLCST Good	Year 5: 89% CT: 90% Control: 89% (Higher for years 1-4)	Yes	Year 5: 14.6%	CT: 6% Control: 12%	No Sensitivity analysis complete case vs. imputation LOCF same results
Becker, 2012[60] LUSI Good	CT: 99.9% Control: 99.9%	No (baseline screen)	0% (baseline screen)	None	No

Appendix D Table 3. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 2

First Author, Year Study Name Quality Rating	What was the reported adherence to the intervention?	Did the study have crossovers or contamination?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition >10% or overall high attrition, raising concerns for bias?
Becker, 2015[59], 2019[73] LUSI Fair	Year 3: CT: 93.4% Control: 94.5% Year 2: CT: 94.6% Control: 91.5% Year 1: CT: 99.9% Control: 99.9%	NR	Over five years: 0.1% - 6.9%	Year 3: CT: 6.6% Control: 5.5% Year 2: CT: 5.4% Control: 8.5% Year 1: CT: 0.1% Control: 0.1%	No
Brain, 2016[391] UKLS Poor	For psychosocial outcomes, adherence to followup surveys: T0: 99.9% T1: CT: 84% Control: 78% T2: CT: 82% Control: 65%	NR	For psychosocial outcomes: T0: 0.01% T1: CT: 16% Control: 22% T2: CT: 18% Control: 35%	Psychosocial outcomes: T0: 0.01% T1: CT: 16% Control: 22% T2: CT: 18% Control: 35%	Yes
Brain, 2017[392] UKLS Poor	For smoking cessation outcomes, adherence to followup surveys: T1: 65% T2: 57%	NR	T1: 35% T2: 43%	T1: CT: 31% Control: 39% T2: CT: 35% Control: 51%	Yes
Church, 2013[57] NLST Good	98%	NR for baseline scree, over three rounds, 4.3% (per Aberle 75)	2%	LDCT: 1.5% CXR: 2.6%	No
Clark, 2016[149] NLST Fair	NR for this subset of ACRIN centers; likely >90% given overall study adherence	NR for ACRIN centers subset; but for overall study 4.3%	NR for ACRIN center subset; likely similar to overall study	NR	No
Croswell, 2010[119] NA Fair	84.2%	NR	15.8%	CT: 15.8%	Yes

Appendix D Table 3. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 2

First Author, Year Study Name Quality Rating	What was the reported adherence to the intervention?	Did the study have crossovers or contamination?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition >10% or overall high attrition, raising concerns for bias?
De Koning, 2020[76]	90% among men for all rounds (95.8% for round 1 of screening); NR for women	Unclear	Missing data <2% for the primary outcome from linkages with national registries	<2%	No
Field, 2016[97] UKLS Fair	98.30%	NR	1.70%	Unclear	Unclear
Field, 2016[117] UKLS Fair	98%	NR	For psychosocial outcomes: T0: 0.01% T1: CT: 16% Control: 22% T2: CT: 18% Control: 35%	For psychosocial outcomes: Baseline: 0% T1 (2 weeks after LDCT or control notification): 6% T2 (10–27 months): 17%	T1: No T2: Yes
Gohagan, 2004[70] LSS Fair	95.5%	0.90%	4.5%	CT: 4.5%	No
Gohagan, 2005[69] LSS Fair	85.8%	NR	14.2%	CT: 14.2%	Yes
Heleno, 2018[141] DLCST Fair	NR	Yes	NR	NR	No
Horeweg, 2013[98] NELSON Poor	For all three waves: ~90-95%	Unclear	3.80%	Unclear	Unclear
Horeweg, 2014[33] NELSON Poor	90%	NR	3.80%	Unclear	Unclear
Infante, 2008[72] DANTE Fair	Baseline only: 100%	No	0%	0%	No

Appendix D Table 3. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 2

First Author, Year Study Name Quality Rating	What was the reported adherence to the intervention?	Did the study have crossovers or contamination?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition >10% or overall high attrition, raising concerns for bias?
Infante, 2009[71] DANTE Fair	90.9%	<10% (presented as combined arms needing CT)	9.1%	CT: 9.1%	No
Infante, 2015[61] DANTE Fair	94%	Yes	6%	Unclear	NA
Lopes Penga, 2009[125] ITALUNG Fair	87.2%	NR	12.7%	CT: 12.7%	Yes
National Lung Screening Trial Research Team, 2019[74] NLST Fair	NR in this article, and post-trial screening was unclear, but original NLST reported CT: 95% CXR: 93%	Unclear; post-trial screening was not ascertained	11/33 centers (representing 12.4% of trial participants) did not have a home state cancer registry for linkage for lung cancer incidence; for mortality, linkage to national death index was available for all but 2.2%	NR	Unclear for lung cancer incidence; no for lung cancer mortality and all-cause mortality
O'Grady, 2014[169] PLCO, NLST Good	High	Some	Unclear	Unclear	Unclear
Paci, 2017[62] ITALUNG Fair	Across 4 rounds of LDCT screening: 81%	Yes (but minimal)	Low (conducted ITT analysis)	Low	No

Appendix D Table 3. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 2

First Author, Year Study Name Quality Rating	What was the reported adherence to the intervention?	Did the study have crossovers or contamination?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition >10% or overall high attrition, raising concerns for bias?
Pastorino, 2012[80] and 2019[81] MILD Poor	>95%	Unclear for 5-year followup; by 10-year followup, 1.2% of control group had LDCT	Low (conducted ITT analysis) for loss to followup, but many people in control group had shorter followup duration.	Unclear for loss to followup, but less followup among control group (e.g., 44.9 vs. 56 months in 5-year followup study); percentage of subjects with available data at 10 years: 46.2% (805/1723) controls vs. 81.4% (1934/2376) LDCT	Yes, when considering differential followup, 35.2% fewer people from the control group had 10-year followup than in the LDCT group
Patz, 2014[142] NLST Fair	NR in this paper	NR	Low	No	No
Pedersen, 2009[122] DLCST Good	Unclear but appears to be 100% for baseline CT	NR	Number of CTs obtained NR	NR	It was NR whether any of the 2,052 patients did not have a CT
Pinsky, 2005[393] Doroudi, 2018[75] LSS Fair	85.8%	NR	14.2%	CT: 14.2%	Yes
Pinsky, 2013[63] NLST Fair	NR in this paper	NR	Low	No	No
Rasmussen, 2014[158] DLCST Fair	Unclear	Not much	Moderate for COS-LC	None at baseline, somewhat lower for COS-LC survey completion in control arm in subsequent rounds	Depends on which round of screening you are referring to
Saghir, 2012[65] DLCST Fair	High, mean annual participation 95.5%	Minimal	Low	Low	No
Sverzellati, 2016[82] MILD Fair	High, until years T5 and T6	NR	Low in early years, then moderate	Unclear	In later years, yes

Appendix D Table 3. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 2

First Author, Year Study Name Quality Rating	What was the reported adherence to the intervention?	Did the study have crossovers or contamination?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition >10% or overall high attrition, raising concerns for bias?
Tanner, 2015[66] NLST Fair	High in NLST	NR	Low	Low	No
Taylor, 2007[155] NLST/LSS Fair	79.7%	NR	20.3%	For entire survey group: 20.3%	Yes
van den Bergh, 2010[162] NELSON Fair	For all, 86.7% CT at T0: 91.0% (630/692) T1: 93.6% (641/685) T2: 93.0% (620/667) T3: 87.7% (600/684)	NR	13.3%	13.3%	Yes, at third annual screen
van den Bergh, 2011[159] NELSON Fair	NR in this paper	No	T0, All: 87.9% LDCT: 89.8% Control: 85.9% T1 Screen: 87.7% T2, All: 78.9% LDCT: 89.3%, Control 64.7%	LDCT: 89% vs. Control: 65%	Yes
van der Aalst, 2010[148] NELSON Fair	92.1%	No	NA	NA	NA
van der Aalst, 2011[153] NELSON Fair	92.1%	No	NA	NA	NA
van Klaveren, 2009[120] NELSON Good	96.4%	NR	3.5%	CT: 3.5%	No
van't Westeinde, 2012[138] NELSON Fair	NR in this publication (but >90% in other NELSON publications)	NR	NR	NR	NR

Appendix D Table 3. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 2

First Author, Year Study Name Quality Rating	What was the reported adherence to the intervention?	Did the study have crossovers or contamination?	What was the overall attrition?	What was the differential attrition?	Did the study have differential attrition >10% or overall high attrition, raising concerns for bias?
Videtic, 2015[263] RTOG 0915 Fair	100% of analyzable patients	No	10/94 (11%) patients were excluded post-randomization due to withdrawal of consent, protocol violations, or RT dosing not met	34Gy group: 8/47 (17%) 48Gy group: 2/47 (4%)	Yes
Wille, 2016[67] DLCST Good	NR in this paper	No	Low	Low (LDCT: 20; Control: 14)	No
Young, 2015[144] NLST Fair	High in NLST	NR	Low	Low	No

Abbreviations: ACRIN=American College of Radiology Imaging Network; COS-LC=consequences of screening-lung cancer; CT=computed tomography; CXR=chest X-ray; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology trial; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=The Italian Lung Study; ITT=intention-to-treat; LDCT=low-dose computed tomography; LOCF: last observation carried forward; LUSI=German Lung Cancer Screening Intervention Trial; MILD=Multicentric Italian Lung Detection trial; NA=not applicable; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial; NLST=National Lung Screening Trial; NR=not reported; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; RTOG=Radiation Therapy Oncology Group; T=timepoint; UKLS=UK Lung Cancer Screening trial; vs.=versus.

Appendix D Table 4. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 3

First Author, Year Study Name Quality Rating	What was the method used to handle missing data?	Did the study use intention to screen analysis or ITT (e.g., rather than per protocol)?	Were ascertainment techniques for outcomes adequately described?	Were ascertainment techniques equal, valid, and reliable?	Overall Rating	Comments for Poor-Quality Studies
Aberle, 2011[32] NLST Good	NR, (small amount of missing data from baseline questionnaires) Missing data from Aberle 2010: 0.4%, similar each arm	Yes	Yes	Yes	Good	NA
Aberle, 2013[58] NLST Good	Missing data excluded from screening accuracy calculations	Yes	Yes	Yes	Good	NA
Aggestrup, 2012[160] DLCST Fair	NR	ITT	NR	NA	Fair	NA
Ashraf, 2009[145] DLCST Fair	Functioned under the assumption that they were still smokers	ITT	No	NA	Fair	NA
Ashraf, 2014[147] DLCST Good	Complete case and LOCF imputation	Yes	Yes	Yes	Good	NA
Becker, 2012[60] LUSI Good	Missing data NR, but baseline data appears complete	Yes	Yes	Yes	Good	NA
Becker, 2015[59], 2019[73] LUSI Fair	NR, but less than 10 participants each round were lost to followup, so complete case analysis would likely not bias results	Yes	Yes	Yes	Fair	NA

Appendix D Table 4. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 3

First Author, Year Study Name Quality Rating	What was the method used to handle missing data?	Did the study use intention to screen analysis or ITT (e.g., rather than per protocol)?	Were ascertainment techniques for outcomes adequately described?	Were ascertainment techniques equal, valid, and reliable?	Overall Rating	Comments for Poor-Quality Studies
Brain, 2016[391] UKLS Poor	For individual instruments: mean replacement imputation within domain if <35% missing data If > 35% missing data within domain, dropped from analysis. For participants lost to followup - complete case analysis. Sensitivity analysis performed where inverse probability weighting used to adjust for missing data	Yes	Yes	Yes	Poor	Poor quality rating is due to high attrition for psychosocial outcomes and greater loss to followup, as well as lack of reporting contamination and cross-overs in the control group.
Brain, 2017[392] UKLS Poor	Imputed all missing followup as smokers; sensitivity analysis of complete case with unclear use of inverse probability weighting to account for nonresponse	Yes	Yes	Yes	Poor	Poor quality rating due to high attrition for smoking cessation outcomes, single imputation conducted under the assumption that smoking status was positive, and unclear use of IPW
Church, 2013[57] NLST Good	Missing data excluded from screening accuracy calculations	Yes	Yes	Yes	Good	NA
Clark, 2016[149] NLST Fair	Complete case for smoking status data (5.8% missing followup forms)	Yes	Yes	Unclear	Fair	NA
Croswell, 2010[119] NA Fair	NR	No	NR	NA	Fair	NA
De Koning, 2020[76]	None (but missing data very low)	Yes	Mostly, but some details NR	Unclear	Fair	NA

Appendix D Table 4. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 3

First Author, Year Study Name Quality Rating	What was the method used to handle missing data?	Did the study use intention to screen analysis or ITT (e.g., rather than per protocol)?	Were ascertainment techniques for outcomes adequately described?	Were ascertainment techniques equal, valid, and reliable?	Overall Rating	Comments for Poor-Quality Studies
Field, 2016[97] UKLS Poor	Unclear	No	No	NA	Poor	Poor quality rating due to numerous unclear domains, including allocation concealment and accessor and provider masking, differential attrition, and methods used to handle missing data. No reporting on crossovers or contamination. This study did not report on the control arm
Field, 2016[117] UKLS Fair	Mean replacement strategy was used when participants were missing data for psychosocial variables	Yes	Yes	Yes	Fair	NA
Gohagan, 2004[70] LSS Fair	NR	No	NR	NA	Fair	NA
Gohagan, 2005[69] LSS Fair	NR	No	NR	NA	Fair	NA
Heleno, 2018[141] DLCST Fair	NR	Yes	Elsewhere	Presumably	Fair	NA
Horeweg, 2013[98] NELSON Poor	Did not include patients without a CT	No	No	NA	Poor	Poor quality rating due to numerous unclear domains, including allocation concealment, masking, crossover and contamination. No data from the control arm is reported in this study.
Horeweg, 2014[33] NELSON Poor	Excluded from analysis	No	No	NA	Poor	Poor quality rating due to lack of control arm inclusion, and because several groups were not reported due to unavailable data.
Infante, 2008[72] DANTE Fair	NR	Yes	NR	NA	Fair	NA

Appendix D Table 4. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 3

First Author, Year Study Name Quality Rating	What was the method used to handle missing data?	Did the study use intention to screen analysis or ITT (e.g., rather than per protocol)?	Were ascertainment techniques for outcomes adequately described?	Were ascertainment techniques equal, valid, and reliable?	Overall Rating	Comments for Poor-Quality Studies
Infante, 2009[71] DANTE Fair	NI	No	NR	NA	Fair	NA
Infante, 2015[61] DANTE Fair	Unclear	Yes	No	NA	Fair	NA
Lopes Penga, 2009[125] ITALUNG Fair	NR	No	NR	NA	Fair	NA
National Lung Screening Trial Research Team, 2019[74] NLST Fair	NR	Yes	Yes	Unclear for lung cancer incidence; yes for lung cancer mortality and all-cause mortality	Fair	NA
O'Grady, 2014[169] PLCO, NLST Good	Use of missing indicator variable	Yes	Yes	Yes	Good	NA
Paci, 2017[62] ITALUNG Fair	NA	Yes	Yes	Unclear (31 deaths of 335 in the trial underwent cause-of-death review; the other deaths did not undergo the same rigorous evaluation based on an algorithm with uncertain validity)	Fair	NA

Appendix D Table 4. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 3

First Author, Year Study Name Quality Rating	What was the method used to handle missing data?	Did the study use intention to screen analysis or ITT (e.g., rather than per protocol)?	Were ascertainment techniques for outcomes adequately described?	Were ascertainment techniques equal, valid, and reliable?	Overall Rating	Comments for Poor-Quality Studies
Pastorino, 2012[80] and 2019[81] MILD Poor	Unclear	Yes	No	Unclear	Poor	Poor-quality rating due to high risk of selection bias, unclear methods of randomization and allocation concealment, changing protocol and addition of a control arm later in the trial, lack of similar groups at baseline for important variables (e.g., proportion of current smokers), differential followup between groups, and high risk of measurement bias.
Patz, 2014[142] NLST Fair	NR in this paper	Yes	Yes	Yes	Fair	NA
Pedersen, 2009[122] DLCST Good	NR	Appears all had a CT in intervention arm	NR	NA	Good	NA
Pinsky, 2005[393] Doroudi, 2018[75] LSS Fair	NR	NR	NR	Unclear	Fair	NA
Pinsky, 2013[63] NLST Fair	NR in this paper	Yes	Yes	Yes	Fair	NA
Rasmussen, 2014[158] DLCST Fair	Imputation	Yes	Yes	Yes	Fair	NA
Saghir, 2012[65] DLCST Fair	NR	Yes	Yes	Yes	Fair	NA
Sverzellati, 2016[82] MILD Fair	NR in this paper	Unclear	Yes	Unclear	Fair	NA
Tanner, 2015[66] NLST Fair	NR	Yes	Yes (in other publications)	Yes	Fair	NA

Appendix D Table 4. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 3

First Author, Year Study Name Quality Rating	What was the method used to handle missing data?	Did the study use intention to screen analysis or ITT (e.g., rather than per protocol)?	Were ascertainment techniques for outcomes adequately described?	Were ascertainment techniques equal, valid, and reliable?	Overall Rating	Comments for Poor-Quality Studies
Taylor, 2007[155] NLST/LSS Fair	NR	No	NR	NA	Fair	NA
van den Bergh, 2010[162] NELSON Fair	Not used for each round	No	NR	NA	Fair	NA
van den Bergh, 2011[159] NELSON Fair	NR	Yes	Yes (in other publications)	Yes	Fair	NA
van der Aalst, 2010[148] NELSON Fair	NI	No	NR	NA	Fair	NA
van der Aalst, 2011[153] NELSON Fair	NI	No	NR	NA	Fair	NA
van Klaveren, 2009[120] NELSON Good	NI	No	NR	NA	Good	NA
van't Westeinde, 2012[138] NELSON Fair	Took only positive results from NELSON, thus missing data NR	No	NR	NA	Fair	NA
Videtic, 2015[263] RTOG 0915 Fair	Unclear	Yes	Yes	Yes	Fair	NA
Wille, 2016[67] DLCST Good	NA	Yes	Yes	Yes	Good	NA
Young, 2015[144] NLST Fair	NR in this paper	Yes	Yes (in other publications)	Yes	Fair	NA

Appendix D Table 4. Risk of Bias and Overall Quality Assessment Ratings for Randomized Studies: Part 3

Abbreviations: ACRIN=American College of Radiology Imaging Network; COPD=chronic obstructive pulmonary disease; CT=computed tomography; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology trial; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=The Italian Lung Study; IPW=inverse probability weighting; ITT=Intention-to-treat; KQ=Key Question; LDCT=low-dose computed tomography; LOCF: Last observation carried forward; LUSI=German Lung Cancer Screening Intervention Trial; MILD=Multicentric Italian Lung Detection trial; NA=Not applicable; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial; NI=Not included; NLST=National Lung Screening Trial; NR=Not reported; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; RTOG=Radiation Therapy Oncology Group; UKLS=UK Lung Cancer Screening trial.

Appendix D Table 5. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 1

First Author, Year Model Name Quality Rating	Does study sample adequately capture the population of interest?	Was there selective inclusion of participants in the model based on data availability?	Enrolled consecutive patients or a random sample?	Selection criteria clearly described?	Was followup duration for the cohort the same as the time horizon of the prediction reported?	Is a valid and reliable definition and method for measurement of the outcomes reported?	Was the same outcome definition (and method for measurement) used in all patients?
De-Torres, 2015[88] COPD-LUCSS Fair	Maybe	Some	Yes	Yes	Yes	Yes	Somewhat
Katki, 2016[84] PLCO, NLST, NHIS Good	Yes	Some	Yes	Yes	Somewhat	Yes	Yes
Kovalckik, 2013[56] NLST Good	Yes	No	Yes	Yes	Yes	Yes	Yes
Landy, 2019[89] NHIS Fair	Yes (NHIS)	NR	No, complex sampling survey design	Yes, based on model development papers[84, 85]	NA – modeling study	NR/NA - modeling study	NA – modeling study
Li, 2015[394] EPIC Cohort Poor	No	Yes	No	Yes	No (only for 1 of the models)	Yes	Yes
Markaki, 2018[95] HUNT2 Cohort Fair	Yes	No	No. Entire county was sampled. 70% response rate	Yes	Yes, max followup 16 yrs. Two models estimated – 6 year and 16 year.	Yes, probably (although some uncertainty about validity and reliability of registry and ICD codes)	Yes
Tammemagi, 2013[85] PLCOm2012 Good	Yes	No	Yes	Yes	Yes	Yes	Yes
Tammemagi, 2014[87] NLST, PLCO Good	Yes	No	Yes	Yes	Yes	Yes	Yes
ten Haaf, 2017[83] NA Good	Yes	No	Yes	Yes	Yes	Yes	Yes

Appendix D Table 5. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 1

First Author, Year Model Name Quality Rating	Does study sample adequately capture the population of interest?	Was there selective inclusion of participants in the model based on data availability?	Enrolled consecutive patients or a random sample?	Selection criteria clearly described?	Was followup duration for the cohort the same as the time horizon of the prediction reported?	Is a valid and reliable definition and method for measurement of the outcomes reported?	Was the same outcome definition (and method for measurement) used in all patients?
Weber, 2017[86] PLCOm2012 Good	Yes	Some	Yes	Yes	Yes	Yes	Yes

Abbreviations: COPD=Chronic Obstructive Pulmonary Disease; COPD-LUCSS=COPD-Lung Cancer Screening Score; EPIC=European Prospective Investigation of Cancer and Nutrition; KQ=key question; NA=not applicable; NHIS=National Health Interview Survey; NLST=National Lung Screening Trial; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial

Appendix D Table 6. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 2

First Author, Year Model Name Quality Rating	Were the outcomes assessed without knowledge of the candidate predictors?	Are valid and reliable definitions and methods for measurement and classification of candidate predictor(s) reported?	Was the same predictor definition and method of measurement used in all patients?	Were all relevant predictors included?	Were predictors assessed blinded for the outcome, and for each other (if relevant)?	How were the predictors handled in the modelling?
De-Torres, 2015[88] COPD-LUCSS Fair	Yes	Yes	Yes	Yes	Yes	Categorized/dichotomized
Katki, 2016[84] PLCO, NLST, NHIS Good	Yes	Yes	Yes	Yes	Yes	Depends on predictor
Kovalckik, 2013[56] NLST Good	Yes	Yes for most (all historical/questionnaire) Unclear how NLST defined COPD/emphysema	Yes	Yes	Yes	Continuous for age, categorical for race/ethnicity, count for years since smoking cessation, first degree relatives with lung cancer, binary for sex, emphysema, and nonlinear for BMI
Landy, 2019[89] NHIS Fair	NA – modeling study	NR	NR	Yes, based on development papers[84, 85]	NA – modeling study	Refer to development papers[84, 85]
Li, 2015[394] EPIC Cohort Poor	NR	Yes	Yes	No (in this external validation, only for the Bach model were all predictors included)	Yes	Varies by model and predictor
Markaki, 2018[95] HUNT2 Cohort Fair	Probably yes (linkage to registry data on outcomes)	Probably yes (survey questions, although uncertain validity of that approach for hours of daily indoor exposure to smoke, which was in their final model)	Yes	Yes	Yes – prospective	Multiple ways (continuous cigarettes/day; log transformation – pack-years, years since quit, BMI, smoke exposure; p-spline transformation – age)

Appendix D Table 6. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 2

First Author, Year Model Name Quality Rating	Were the outcomes assessed without knowledge of the candidate predictors?	Are valid and reliable definitions and methods for measurement and classification of candidate predictor(s) reported?	Was the same predictor definition and method of measurement used in all patients?	Were all relevant predictors included?	Were predictors assessed blinded for the outcome, and for each other (if relevant)?	How were the predictors handled in the modelling?
Tammemagi, 2013[85] PLCOm2012 Good	Yes	Yes/No Self-reported demo, smoking	Yes/Unclear - most predictors are self-reported. - Unclear how COPD defined for NLST and PLCO (primary papers reviewed and no information - Oken and Aberle)	Yes	Yes	Continuous for age, BMI, education, duration smoking, smoking quit time, categorized for race/ethnicity, COPD, cancer history, family history cancer, smoking status, nonlinear transformation for smoking intensity
Tammemagi, 2014[87] NLST, PLCO Good	Yes	Yes	Yes	Yes	Yes	Continuous for age, BMI, education, duration smoking, smoking quit time, categorized for race/ethnicity, COPD, cancer history, family history cancer, smoking status, nonlinear transformation for smoking intensity
ten Haaf, 2017[83] NA Good	Yes	Yes	Probably- "data on predictor variables in each trial were collected through epidemiologic questionnaires administered at study entry and harmonized across both trials"	Yes	Yes	Nine models were considered. Refer to primary papers. (pull refs)
Weber, 2017[86] PLCOm2012 Good	Yes	Yes	Yes	Yes	Yes	Varies

Abbreviations: BMI=Body Mass Index; COPD=chronic obstructive pulmonary disease; COPD-LUCSS=COPD-Lung Cancer Screening Score; EPIC=European Prospective Investigation of Cancer and Nutrition; KQ=key question; NA=not applicable; NHIS=National Health Interview Survey; NLST=National Lung Screening Trial; NR=Not reported; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial

Appendix D Table 7. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 3

First Author, Year Model Name Quality Rating	Number (%) participants with missing data	Did the study have high attrition (>10%), raising concerns for bias?	How was missing data handled?	Modeling assumptions satisfied?	Describe the method for selection of predictors for inclusion in multivariable modelling	Describe the method for selection of predictors during multivariable modelling and criteria used
De-Torres, 2015[88] COPD-LUCSS Fair	Low	No	Imputation or assumption	NR	All	Significance in multivariable model, backwards selection
Katki, 2016[84] PLCO, NLST, NHIS Good	Less than 2%	No	Imputation or assumption	Yes	Previous models	Akaike and other
Kovalckik, 2013[56] NLST Good	From NLST parent paper < 1%	No	NR	Not reported	Based on prior studies	Lasso regression
Landy, 2019[89] NHIS Fair	1.8% for race/ethnicity, 0.4% for education, 2.9% for body mass index, 0.4% for number of years since quitting, 7.3% for number of cigarettes smoked per day, 0.3% for number of years of smoking, 0.2% for presence of emphysema, and 12.1% for family history of lung cancer	NA – modeling study	Multiple imputation	NR	Refer to development papers[84, 85]	Refer to development papers[84, 85]

Appendix D Table 7. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 3

First Author, Year Model Name Quality Rating	Number (%) participants with missing data	Did the study have high attrition (>10%), raising concerns for bias?	How was missing data handled?	Modeling assumptions satisfied?	Describe the method for selection of predictors for inclusion in multivariable modelling	Describe the method for selection of predictors during multivariable modelling and criteria used
Li, 2015[394] EPIC Cohort Poor	NR, although less than half of the EPIC cohort were included (20,700/53,088)	NR	Not reported for the outcomes; for predictors, they only included people with data for predictors and for the predictors that they had no data for in their cohort (e.g., COPD, pneumonia, emphysema, dust exposure, family history of lung cancer) they assumed that risk factors were absent	Not applicable - external validation only	Not applicable - external validation only (although see entry for missing data regarding how they didn't include all predictors from the original models)	Not applicable - external validation only
Markaki, 2018[95] HUNT2 Cohort Fair	9.35% total for all predictors	NR	Multiple imputation	NR	Authors selected risk factors for lung cancer and other smoking-related behaviors	Backwards selection; criteria not reported
Tammemagi, 2013[85] PLCOm2012 Good	PLCO < 5% for all predictors NLST < 1% for all predictors	No	NR; presumably complete case	Yes	Predictor selection guided by predictive performance, not based on univariate association p value	Predictor selection guided by predictive performance, not based on univariate association p value
Tammemagi, 2014[87] NLST, PLCO Good	< 5% missing per Oken 2011 and Kovalchik supplement (32)	Not reported, but per Oken 2011, overall adherence was high 91.2% of participants had undergone at least 1 CXR screen,	NR	Yes	Predictor selection guided by predictive performance, not based on univariate association p value	Predictor selection guided by predictive performance, not based on univariate association p value

Appendix D Table 7. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 3

First Author, Year Model Name Quality Rating	Number (%) participants with missing data	Did the study have high attrition (>10%), raising concerns for bias?	How was missing data handled?	Modeling assumptions satisfied?	Describe the method for selection of predictors for inclusion in multivariable modelling	Describe the method for selection of predictors during multivariable modelling and criteria used
ten Haaf, 2017[83] NA Good	<7% across all predictors	Probably No Reviewing primary studies: Aberle and Oken NLST <10% both arm PLCO intervention arm 16.5% PLCO control arm 8.8%	Multiple imputation	NR	NA - Model validation only	NA - Model validation only
Weber, 2017[86] PLCOm2012 Good	Low	No	Imputation or assumption	Yes	NA – Model validation only	NA – Model validation only

Abbreviations: COPD=chronic obstructive pulmonary disease; COPD-LUCSS=COPD-Lung Cancer Screening Score; CXR=chest X-ray; EPIC=European Prospective Investigation of Cancer and Nutrition; KQ=key question; NA=not applicable; NHIS=National Health Interview Survey; NLST=National Lung Screening Trial; NR=not reported; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial.

Appendix D Table 8. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 4

First Author, Year Study Name Quality Rating	Were a priori cut points used for classification measures?	Method used for testing model performance: development dataset only or separate external validation?	Were coefficients of final model published?	In case of poor validation, was the model adjusted or updated?	Was there comparison of the distribution of predictors for development and validation datasets?	Overall Rating	Comments for Poor Quality Studies
De-Torres, 2015[88] NLST Fair	Some	Separate, external	Yes	NA	Unclear	Fair	NA
Katki, 2016[84] PLCO, NLST, NHIS Good	Yes	Separate, external	Yes	NA	Yes	Good	NA
Kovalckik, 2013[56] NLST Good	NA	Development cohort: NLST CXR arm Validation cohort: PLCO CXR arm	No	NA	No	Good	NA
Landy, 2019[89] NHIS Fair	Yes	NA	Refer to development papers[84, 85]	NA	NA	Fair	NA
Li, 2015[394] EPIC Cohort Poor	No	Separate external validation	No	NA	NA	Poor	Concerns with missing data, missing predictor variables, selection of the sample, and changing the original models for analyses. Limited to ever smokers from among the larger cohort, introducing risk for bias.
Markaki, 2018[95] HUNT2 Cohort Fair	Yes	External validation	Yes	NA	NR	Fair	NA
Tammemagi, 2013[85] PLCOm2012 Good	No	External Validation	Yes	NA	Yes	Good	NA
Tammemagi, 2014[87] NLST, PLCO Good	No	External Validation	Yes	NA	Yes	Good	NA

Appendix D Table 8. Risk of Bias and Overall Quality Assessment Ratings for Risk Prediction Model (KQ 2) Studies: Part 4

First Author, Year Study Name Quality Rating	Were a priori cut points used for classification measures?	Method used for testing model performance: development dataset only or separate external validation?	Were coefficients of final model published?	In case of poor validation, was the model adjusted or updated?	Was there comparison of the distribution of predictors for development and validation datasets?	Overall Rating	Comments for Poor Quality Studies
ten Haaf, 2017[83] NA Good	No	External Validation	Review primary studies. PLCOm2012 has published coefficients	NA	Yes	Good	NA
Weber, 2017[86] PLCO, 2012 Good	Yes	Separate, external	Yes	NA	Unclear	Good	NA

Abbreviations: COPD=chronic obstructive pulmonary disease; COPD-LUCSS=COPD-Lung Cancer Screening Score; CXR=chest X-ray; EPIC=European Prospective Investigation of Cancer and Nutrition; KQ=key question; NA=not applicable; LC=lung cancer; LLP=Liverpool Lung Project; NHIS=National Health Interview Survey; NLST=National Lung Screening Trial; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; USPSTF=United States Preventive Services Task Force.

Appendix D Table 9. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 1

First Author, Year Study Name Quality Rating	Was a consecutive or random sample of patients used?	Was a case control design avoided?	Did the study avoid inappropriate exclusions?	Bias due to patient selection?	Were the test and reference standard results interpreted independently (blinded)?	If a threshold was used, was it pre-specified?	Were the tests adequately described (or referenced)?	Were methods for calculating accuracy clearly reported and valid?	Bias due to index test (LDCT)?
Aberle, 2011[32] NLST Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	NA	Low
Aberle, 2011[58] NLST Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Becker, 2012[60] LUSI Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	NA	Low
Becker, 2015[59] LUSI Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	NA	Low
Chung, 2017[132] NLST Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Church, 2013[57] NLST Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Croswell, 2010[119] NA Fair	Yes	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low
Crucitti, 2015[111] “Un repiro per la vita” Fair/Poor	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes for false-positive screens	Low
De Koning, 2020[76]	Yes	Yes	Yes	Low	Yes	Yes	Yes	No	High
Field, 2016[97] UKLS Fair	Random	Yes	Yes	High	Unclear	Yes	Yes	Yes	Low
Field, 2016[117] UKLS Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Gierada, 2017[110] NLST Fair	Yes (in parent trial)	No	Yes	Low	Not completely	Yes	Yes	Yes	Low

Appendix D Table 9. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 1

First Author, Year Study Name Quality Rating	Was a consecutive or random sample of patients used?	Was a case control design avoided?	Did the study avoid inappropriate exclusions?	Bias due to patient selection?	Were the test and reference standard results interpreted independently (blinded)?	If a threshold was used, was it pre-specified?	Were the tests adequately described (or referenced)?	Were methods for calculating accuracy clearly reported and valid?	Bias due to index test (LDCT)?
Gohagan, 2004[70] LSS Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Henschke, 2004[131] I-ELCAP Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Henschke, 2006[128] I-ELCAP Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Henschke, 2006[129] I-ELCAP Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Henschke, 2013[107] I-ELCAP Fair	Yes	Yes	Unclear	Low	Unclear	Multiple thresholds used	Yes	Yes	Low
Henschke, 2016[106] I-ELCAP Fair	Probably	Yes	Yes	Low	Yes	Yes	Yes	NA	Low
Heuvelmans, 2015[325] NELSON Poor	Random	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Unclear
Heuvelmans, 2013[114] NELSON Fair	Yes	Yes	Yes	Low	Yes	No	Yes	Yes	Low
Horeweg, 2013[98] NELSON Fair	Random	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low

Appendix D Table 9. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 1

First Author, Year Study Name Quality Rating	Was a consecutive or random sample of patients used?	Was a case control design avoided?	Did the study avoid inappropriate exclusions?	Bias due to patient selection?	Were the test and reference standard results interpreted independently (blinded)?	If a threshold was used, was it pre-specified?	Were the tests adequately described (or referenced)?	Were methods for calculating accuracy clearly reported and valid?	Bias due to index test (LDCT)?
Horeweg, 2014[33] NELSON Fair	Random	Yes	No	Low	Unclear	Yes	No	Yes	High
Infante, 2009[71] DANTE Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Infante, 2015[61] DANTE Fair	Random	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low
Kinsinger, 2017[38] LCSDP Fair	No	Yes	NA	Unclear	NR	NR	Yes	Yes	Low
Lopes Penga, 2009[125] ITALUNG Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
McKee, 2015[395] NA Poor	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
McWilliams, 2013[116] PanCan, BCCA Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Menezes, 2010[121] NA Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Paci, 2017[62] ITALUNG Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Pedersen, 2009[122] DLCST Good	Yes	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low

Appendix D Table 9. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 1

First Author, Year Study Name Quality Rating	Was a consecutive or random sample of patients used?	Was a case control design avoided?	Did the study avoid inappropriate exclusions?	Bias due to patient selection?	Were the test and reference standard results interpreted independently (blinded)?	If a threshold was used, was it pre-specified?	Were the tests adequately described (or referenced)?	Were methods for calculating accuracy clearly reported and valid?	Bias due to index test (LDCT)?
Pinsky, 2015[100] NLST Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Pinsky, 2015[64] NLST Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Pinsky, 2015[101] NLST Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Pinsky, 2015[102] NLST Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Scholten, 2013[103] NA Good	Yes	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low
Sverzellati, 2016[82] MILD Fair	Yes	Yes	Yes	Low	NR	Yes	Yes	No	Unclear
Swensen, 2005[130] NA Fair	Yes	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low
Tammemagi, 2017[115] PanCan Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Toyoda, 2008[126] NA Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	NR	Yes	Unclear
Tsushima, 2008[123] NA Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low

Appendix D Table 9. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 1

First Author, Year Study Name Quality Rating	Was a consecutive or random sample of patients used?	Was a case control design avoided?	Did the study avoid inappropriate exclusions?	Bias due to patient selection?	Were the test and reference standard results interpreted independently (blinded)?	If a threshold was used, was it pre-specified?	Were the tests adequately described (or referenced)?	Were methods for calculating accuracy clearly reported and valid?	Bias due to index test (LDCT)?
van Klaveren, 2009[120] NELSON Good	Yes	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low
Van Riel, 2015[113] NELSON Good	Yes	NA	NA	Unclear	Yes	NA	Yes	Yes	Low
Veronesi, 2008[124] COSMOS Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Veronesi, 2008[127] COSMOS Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Wagnetz, 2012[118] NA Fair	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Low
Walter, 2016[78] NELSON Good	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Wang, 2012[112] NELSON Fair	Yes	Yes	No	High	Yes	Yes	Yes	Yes	Low
Wille, 2014[108] DLCST Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	NA	Low
Xu, 2006[79] NELSON Fair	Yes	Yes	Yes	Low	Unclear	Yes	Yes	Yes	Low
Yankelevitz, 2015[105] I-ELCAP Fair	Unknown	Yes	Yes	Unclear	Yes	Yes	Yes	NA	Low

Appendix D Table 9. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 1

First Author, Year Study Name Quality Rating	Was a consecutive or random sample of patients used?	Was a case control design avoided?	Did the study avoid inappropriate exclusions?	Bias due to patient selection?	Were the test and reference standard results interpreted independently (blinded)?	If a threshold was used, was it pre-specified?	Were the tests adequately described (or referenced)?	Were methods for calculating accuracy clearly reported and valid?	Bias due to index test (LDCT)?
Yip, 2014[104] NLST, I-ELCAP Fair	Yes	Yes	No	Unclear	Yes	Yes	Yes	NA	Low
Yousaf-Khan, 2017[389] NELSON Poor	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear
Zhao, 2011[77] NELSON Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low
Zhao, 2014[109] NELSON Fair	Yes	Yes	Yes	Low	Yes	Yes	Yes	Yes	Low

Abbreviations: BCCA=British Columbia Cancer Agency; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology Trial; DLCST=Danish Lung Cancer Screening Trial; I-ELCAP=International Early Lung Cancer Action Project; ITALUNG=The Italian Lung Study; KQ=Key Question; LCSDP=Lung Cancer Screening Demonstration Project; LDCT=Low-Dose Computed Tomography; LUSI=German Lung Cancer Screening Intervention Trial; MILD=Multicentric Italian Lung Detection Trial; NA=not applicable; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial; NLST=National Lung Screening Trial; NR=Not reported; PanCan=Pan-Canadian Early Detection of Lung Cancer Study; UKLS=UK Lung Cancer Screening Trial.

Appendix D Table 10. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 2

First Author, Year Study Name Quality Rating	Reference Standard Used	Comments about Reference Standard	Is the reference standard likely to correctly classify the target condition?	Were the reference standard results interpreted without knowledge of the results of the index test (blinded)?	Did patients receive the reference test regardless of screening test results?	Bias due to reference standard?
Aberle, 2011[32] NLST Good	Subsequent diagnosis of LC within 1 yr	Lung cancer diagnosis was ascertained from patient questionnaires, certified by medical record abstraction, augmented by search from the NDI	Yes	Yes	Yes	Low
Aberle, 2011[58] NLST Good	Subsequent diagnosis of LC within 1 yr	Lung cancer diagnosis was ascertained from patient questionnaires, certified by medical record abstraction, augmented by search from the NDI	Yes	Yes	No	Low
Becker, 2012[60] LUSI Good	Subsequent diagnosis of LC within 1 yr	No comments	Yes	NR	Yes	Low
Becker, 2015[59] LUSI Good	Subsequent diagnosis of LC within 1 yr	No comments	Yes	NR	Yes	Low
Chung, 2017[132] NLST Good	Subsequent diagnosis of LC within 1 yr	Lung cancer diagnosis was ascertained from patient questionnaires, certified by medical record abstraction, augmented by search from the NDI	Yes	Yes	Yes	Low
Church, 2013[57] NLST Good	Subsequent diagnosis of LC within 1 yr	Lung cancer diagnosis was ascertained from patient questionnaires, certified by medical record abstraction, augmented by search from the NDI	Yes	Yes	No	Low
Croswell, 2010[119] NA Fair	Multiple	Biopsy/surgical	Yes	Unclear	No	Low
Crucitti, 2015[111] “Un repiro per la vita” Fair/Poor	Multiple	Multiple; they had protocol for workup of initial positive screen (most went on to additional imaging, some had biopsies). For sensitivity (false negatives), the reference standard is unclear and they were not really aiming to determine sensitivity	Yes, for false-positive screens/ specificity Unclear, for sensitivity	No	No	Low for false-positive screens High for sensitivity/false-negative screens
De Koning, 2020[76]	Multiple	Subsequent imaging and evaluation, diagnosis of lung cancer, registry determined lung cancer death	Yes	Yes	No	Low
Field, 2016[97] UKLS Fair	Biopsy	Diagnosis appeared to be made by lung resection or biopsy, 1 was made radiographically	Yes	Unclear	No	Low

Appendix D Table 10. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 2

First Author, Year Study Name Quality Rating	Reference Standard Used	Comments about Reference Standard	Is the reference standard likely to correctly classify the target condition?	Were the reference standard results interpreted without knowledge of the results of the index test (blinded)?	Did patients receive the reference test regardless of screening test results?	Bias due to reference standard?
Field, 2016[117] UKLS Fair	Other	Lung cancer diagnosis ascertained from biopsy and search of the following databases: the Office for National Statistics the Hospital Episode Statistics database and the National Cancer Registration Service. However, timing of followup to determine lung cancer is unclear and authors are clear that lung cancer incidence will only be studied after data is pooled with other European studies.	Yes	Yes	Yes	Low
Gierada, 2017[110] NLST Fair	Subsequent diagnosis of LC within 1 yr	Prior reading of same LDCT scan along with clinical knowledge of progression to lung cancer	Yes	Yes	Yes	Unclear
Gohagan, 2004[70] LSS Fair	Multiple	No algorithm for this protocol; abstracted histology	Yes	Unclear	No	Low
Henschke, 2004[131] I-ELCAP Fair	Biopsy	No comments	Yes	Unclear	No	Low
Henschke, 2006[128] I-ELCAP Fair	Biopsy	No comments	Yes	Unclear	No	Low
Henschke, 2006[129] I-ELCAP Fair	Multiple	Biopsy/surgical resection	Yes	Unclear	No	Low
Henschke, 2013[107] I-ELCAP Fair	Subsequent diagnosis of LC within 1 yr	No comments	Yes	Unclear	Unclear	Unclear
Henschke, 2016[106] I-ELCAP Fair	Biopsy	Diagnosis defined on cytology from nonsurgical biopsy and path from resection	Unclear	No	Yes	Unclear

Appendix D Table 10. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 2

First Author, Year Study Name Quality Rating	Reference Standard Used	Comments about Reference Standard	Is the reference standard likely to correctly classify the target condition?	Were the reference standard results interpreted without knowledge of the results of the index test (blinded)?	Did patients receive the reference test regardless of screening test results?	Bias due to reference standard?
Heuvelmans, 2015[325] NELSON Poor	Other	Histology was the reference	Yes	Unclear	No	High
Heuvelmans, 2013[114] NELSON Fair	Biopsy	Median followup was 4.4 yrs	Yes	Yes	No	Low
Horeweg, 2013[98] NELSON Fair	Other	Histology	Yes	Unclear	No	Unclear
Horeweg, 2014[33] NELSON Fair	Biopsy	No comments	Yes	Unclear	No	High
Infante, 2009[71] DANTE Fair	Biopsy	No comments	Yes	Unclear	No	Low
Infante, 2015[61] DANTE Fair	Other	Reference standard was histology	Yes	Unclear	No	Unclear
Kinsinger, 2017[38] LCSDP Fair	Multiple	Reference standard is LC diagnosis made by clinical teams, date are extracted from VA system central data system and probably other sources since these screened patients were tracked in a registry	Yes	No	Yes	Low
Lopes Penga, 2009[125] ITALUNG Fair	Biopsy	No comments	Yes	Unclear	No	Low
McKee, 2015[395] NA Poor	Subsequent diagnosis of LC within 1 yr	1) Diagnosed lung cancer=biopsy proven + positive PET for patients that could not undergo biopsy 2) Biopsy-prove lung cancer	Yes	No	No	Unclear
McWilliams, 2013[116] PanCan, BCCA Fair	Biopsy	1) Histopathological exam of resected surgical specimens 2) Cytopathology from needle-aspiration biopsy samples	Yes	No	No	Unclear

Appendix D Table 10. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 2

First Author, Year Study Name Quality Rating	Reference Standard Used	Comments about Reference Standard	Is the reference standard likely to correctly classify the target condition?	Were the reference standard results interpreted without knowledge of the results of the index test (blinded)?	Did patients receive the reference test regardless of screening test results?	Bias due to reference standard?
Menezes, 2010[121] NA Fair	Biopsy	No comments	Yes	Unclear	No	Low
Paci, 2017[62] ITALUNG Good	Multiple	Biopsy reports, telephone followup, death registry	Yes	Yes	Yes	Low
Pedersen, 2009[122] DLCST Good	Biopsy	No comments	Yes	Unclear	No	Low
Pinsky, 2015[100] NLST Fair	Subsequent diagnosis of LC within 1 yr	No comments	Yes	Yes	Yes	Low
Pinsky, 2015[64] NLST Good	Subsequent diagnosis of LC within 1 yr	No comments	Yes	Yes	Yes	Low
Pinsky, 2015[101] NLST Fair	Subsequent diagnosis of LC within 1 yr	No comments	Yes	Unclear	Yes	Low
Pinsky, 2015[102] NLST Fair	Subsequent diagnosis of LC within 1 yr	No comments	Yes	Unclear	Yes	Low
Scholten, 2013[103] NA Good	Biopsy	No comments	Yes	Unclear	No	Low
Sverzellati, 2016[82] MILD Fair	Subsequent diagnosis of LC within 1 yr	No comments	Yes	Unclear	Unclear	Unclear
Swensen, 2005[130] NA Fair	Multiple	Determined by an individual's provider	Unclear	Unclear	No	High

Appendix D Table 10. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 2

First Author, Year Study Name Quality Rating	Reference Standard Used	Comments about Reference Standard	Is the reference standard likely to correctly classify the target condition?	Were the reference standard results interpreted without knowledge of the results of the index test (blinded)?	Did patients receive the reference test regardless of screening test results?	Bias due to reference standard?
Tammemagi, 2017[115] PanCan Fair	Subsequent diagnosis of LC within 2 yrs	Any of the following 1) histopathological exam of resected surgical specimens 2) cytopathology from FNA 3) nodules stable, nodules not visible, benign calcification developed	Yes	No	No	Low
Toyoda, 2008[126] NA Fair	Other	Histology used, but procedures unclear	Yes	Unclear	No	Low
Tsushima, 2008[123] NA Fair	Multiple	Biopsy/surgical	Yes	Unclear	No	Low
van Klaveren, 2009[120] NELSON Good	Biopsy	No comments	Yes	Unclear	No	Low
Van Riel, 2015[113] NELSON Good	Other	This is study only looked at inter observer agreement, and its potential effect on subsequent testing. As such there was no clear reference standard in sensitivity and specificity were not calculated. In other words, this was the study of reliability.	NA	NA	NA	Unclear
Veronesi, 2008[124] COSMOS Fair	Biopsy	No comments	Yes	Unclear	No	Low
Veronesi, 2008[127] COSMOS Fair	Biopsy	No comments	Yes	Unclear	No	Low
Wagnetz, 2012[118] NA Fair	Multiple	Biopsy/VATS	Yes	Unclear	No	Low
Walter, 2016[78] NELSON Good	Multiple	LC diagnosis based on histology; benignity based on histology or stable size for at least 2 yrs	Yes	Unclear	Yes	Low

Appendix D Table 10. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 2

First Author, Year Study Name Quality Rating	Reference Standard Used	Comments about Reference Standard	Is the reference standard likely to correctly classify the target condition?	Were the reference standard results interpreted without knowledge of the results of the index test (blinded)?	Did patients receive the reference test regardless of screening test results?	Bias due to reference standard?
Wang, 2012[112] NELSON Fair	Multiple	Pathology or no cancers diagnosed in 2 yr followup	Yes	No	No	Unclear
Wille, 2014[108] DLCST Fair	Subsequent imaging	Last annual CT scan	Unclear	Yes	Yes	Unclear
Xu, 2006[79] NELSON Fair	Multiple	Brushings, biopsy, VATS, resection	Yes	Unclear	Not planned	Low
Yankelevitz, 2015[105] I-ELCAP Fair	Biopsy	Diagnosis defined on cytology from nonsurgical biopsy and path from resection -- for nonsolid nodules, FNAs can be operator dependent and not useful (according to authors in introduction)	Yes	No	No	High
Yip, 2014[104] NLST, I-ELCAP Fair	Biopsy	Outcome is lung cancer incidence, relies on biopsy.	Yes	No	No	High
Yousaf-Khan, 2017[389] NELSON Poor	Multiple	LC diagnosis based on histology; benignity based on histology or stable size for at least 2 yrs	Yes	Yes	Yes	Low
Zhao, 2011[77] NELSON Fair	Subsequent diagnosis of LC within 1 yr	Subsequent diagnosis of LC within various time intervals, according to NELSON management protocol. Intervals could be 3 mos, 1 yr, or 2 yrs.	Yes	Yes	Unclear	Low
Zhao, 2014[109] NELSON Fair	Multiple	Nodules were classified as benign or malignant based on histologic examination or as benign based on stable volume for more than 2 yrs after baseline.	Yes	Unclear	No, but they were subject to the same multicomponent reference standard	Unclear

Abbreviations: BCCA=British Columbia Cancer Agency; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology Trial; DLCST=Danish Lung Cancer Screening Trial; I-ELCAP=International Early Lung Cancer Action Project; ITALUNG=The Italian Lung Study; KQ=Key Question; LC=lung cancer; LCSDP=Lung Cancer Screening Demonstration Project; LUSI=German Lung Cancer Screening Intervention Trial; MILD=Multicentric Italian Lung Detection Trial; NA=not applicable; NDI=National Death Index; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial; NLST=National Lung Screening Trial; NR=Not reported; PanCan=Pan-Canadian Early Detection of Lung Cancer Study; UKLS=UK Lung Cancer Screening Trial.

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Aberle, 2011[32] NLST Good	Yes	Only patients with positive screen underwent diagnostic evaluation, but all received questionnaire and NDI search	Yes	No	Yes	Low	Good	NA
Aberle, 2011[58] NLST Good	Yes	Only patients with positive screen underwent diagnostic evaluation, but all received questionnaire and NDI Search	Yes	No	Yes	Low	Good	NA
Becker, 2012[60] LUSI Good	Yes	Whole sample - LC diagnosis by biopsy or followup	Yes	No	NR	Low	Good	NA
Becker, 2015[59] LUSI Good	Yes	Whole sample - LC diagnosis by biopsy or followup	Yes	No	Yes	Low	Good	NA
Chung, 2017[132] NLST Good	Yes	Only patients with positive screen underwent diagnostic evaluation, but all received questionnaire and NDI Search	Yes	No	Yes	Low	Good	NA

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Church, 2013[57] NLST Good	Yes	Only patients with positive screen underwent diagnostic evaluation, but all received questionnaire and NDI Search	Yes	No	Yes	Low	Good	NA
Croswell, 2010[119] NA Fair	Yes	No	Yes	Yes	NR	High	Fair	NA
Crucitti, 2015[111] "Un repiro per la vita" Fair/Poor	Yes, for specificity and false-positive screens; Unclear, for sensitivity	No	No	No	NR	Low for false-positive screens High for sensitivity/ false-negative screens	Fair for false-positive screens Poor for sensitivity and false-negative screens	Poor quality rating for sensitivity and false- negative outcomes is due to high risk of ascertainment bias; unreported length of followup or ascertainment approach (e.g., medical record review or endpoint verification); number of patients lost to followup; and methods of handling missing data
De Koning, 2020[76]	Yes	Yes	Yes	No	Yes	Low	Fair	NA
Field, 2016[97] UKLS Fair	Unclear how long after LDCT patients had biopsy	No	No	No	Unclear	Unclear	Fair	NA
Field, 2016[117] UKLS Fair	Unclear	Yes , if composite reference test of biopsy/imaging	Yes	No	NR (but unlikely)	Low	Fair	NA
Gierada, 2017[110] NLST Fair	No - it is possible that interval cancer developed	Yes	No	No	NA	Low	Fair	NA

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Gohagan, 2004[70] LSS Fair	Unclear	No	Unclear	No	NR	Low	Fair	NA
Henschke, 2004[131] I-ELCAP Fair	Yes	No	Yes	No	NR	Low	Fair	NA
Henschke, 2006[128] I-ELCAP Fair	Yes	No	Yes	Yes (>10%)	NR	Low	Fair	NA
Henschke, 2006[129] I-ELCAP Fair	Yes	No	Yes	No	NR	Low	Fair	NA
Henschke, 2013[107] I-ELCAP Fair	Yes	Unclear	No	Unclear	Unclear	Unclear	Fair	NA
Henschke, 2016[106] I-ELCAP Fair	Yes	Selection	Yes	NR	NR	Unclear	Fair	NA
Heuvelmans, 2015[325] NELSON Poor	Unclear	No	Yes	No	Unclear	High	Poor	Poor quality rating is due to several unclear and high categories, including unclear independence of test and reference standard interpretation, unclear bias due to index test
Heuvelmans, 2013[114] NELSON Fair	NA	No	Yes	No	NA	Low	Fair	NA

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Horeweg, 2013[98] NELSON Fair	Unclear	No	Yes	No	Yes	Low	Fair	NA
Horeweg, 2014[33] NELSON Fair	Unclear	No	Yes	No	Yes	Low	Fair	NA
Infante, 2009[71] DANTE Fair	Yes	No	Yes	No	NR	Low	Fair	NA
Infante, 2015[61] DANTE Fair	Unclear	No	Yes	No	Unclear	Unclear	Fair	NA
Kinsinger, 2017[38] LCSDP Fair	NR	Yes	Yes	NR	NR	Unclear	Fair	NA
Lopes Penga, 2009[125] ITALUNG Fair	Yes	No	Yes	Yes	NR	Low	Fair	NA
McKee, 2015[395] NA Poor	Yes	Yes	Yes	Yes	Unclear	High	Poor	Poor rating is due to the lack of clinical followup and inclusion of 26% of the sample in analysis. Given the small number of cases reclassified, results could change if data from missing participants had been available.
McWilliams, 2013[116] PanCan, BCCA Fair	Unclear	Biopsy	Yes	No	Yes	Unclear	Fair	NA

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Menezes, 2010[121] NA Fair	Yes	No	Yes	Yes	NR	Unclear	Fair	NA
Paci, 2017[62] ITALUNG Good	Yes	All received the same outcome assessment process	Not all received biopsy	No	Yes	Low	Good	NA
Pedersen, 2009[122] DLCST Good	Yes	No	Yes	No	NR	Low	Good	NA
Pinsky, 2015[100] NLST Fair	Yes	All received the same outcome assessment process	Not all received biopsy	No	Yes	Low	Fair	NA
Pinsky, 2015[64] NLST Good	Yes	All received the same outcome assessment process	Not all received biopsy	No	Yes	Low	Good	NA
Pinsky, 2015[101] NLST Fair	Yes	All received the same outcome assessment process	Not all received biopsy	No	Yes	Low	Fair	NA
Pinsky, 2015[102] NLST Fair	Yes	All received the same outcome assessment process	Not all received biopsy	No	Yes	Low	Fair	NA
Scholten, 2013[103] NA Good	Yes	No	Yes	No	NR	Low	Good	NA
Sverzellati, 2016[82] MILD Fair	Yes	Unclear	Not all received biopsy	Unclear	Unclear	Unclear	Fair	NA

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Swensen, 2005[130] NA Fair	Yes	No	Yes	Yes, for fourth annual (20%)	NR	High	Fair	NA
Tammemagi, 2017[115] PanCan Fair	Yes	Yes - if composite reference test of biopsy/imaging.	Yes	Yes	Unclear	High	Fair	NA
Toyoda, 2008[126] NA Fair	Yes	No	Yes	No	NR	Low	Fair	NA
Tsushima, 2008[123] NA Fair	Yes	No	Yes	No	NR	Low	Fair	NA
van Klaveren, 2009[120] NELSON Good	Yes	No	Yes	No	NR	Low	Good	NA
Van Riel, 2015[113] NELSON Good	NA	NA	NA	NA	NA	Low	Good	NA
Veronesi, 2008[124] COSMOS Fair	Yes	No	Yes	No	NR	Low	Fair	NA
Veronesi, 2008[127] COSMOS Fair	Yes	No	Yes	No	NR	Low	Fair	NA
Wagnetz, 2012[118] NA Fair	Yes	No	Yes	No	NR	Low	Fair	NA

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Walter, 2016[78] NELSON Good	Yes	Yes	Same protocol for all	No	NA	Low	Good	NA
Wang, 2012[112] NELSON Fair	Yes	All	Yes	NR	NR	Unclear	Fair	NA
Wille, 2014[108] DLCST Fair	Yes	Intervention arm	Yes	No	NR	Low	Fair	NA
Xu, 2006[79] NELSON Fair	NR	Not planned	Likely planned, but unclear	No data	No data	Unclear	Fair	NA
Yankelevitz, 2015[105] I-ELCAP Fair	Yes	Selection	Yes	For the sample of nonsolid lesions, none.	NR	Unclear	Fair	NA
Yip, 2014[104] NLST, I-ELCAP Fair	Yes	Selection	Yes	No	Yes	Low	Fair	NA
Yousaf-Khan, 2017[389] NELSON Poor	Yes	Yes	Same protocol for all	Yes	None	High	Poor	Poor quality assessment is due to a number of unclear bias ratings, including the length of time (2 yrs) between index and reference test, and the participation rate (which was optional in the fourth round of screening).
Zhao, 2011[77] NELSON Fair	Yes	All received the same outcome assessment process	Not all received biopsy	Unclear based on this paper	Unclear	Unclear	Fair	NA

Appendix D Table 11. Risk of Bias and Overall Quality Assessment Ratings for Accuracy (KQ 3) Studies: Part 3

First Author, Year Study Name Quality Rating	Is the time period between the test and reference test short enough ?	Did the whole or a random selection of the patients receive the reference test?	Did patients receive the same reference standard for the outcome specified?	Did the study have high attrition raising concern for bias?	Was an appropriate method used to handle missing data?	Bias due to flow and timing?	Quality Rating	Comments any Study With Poor Quality
Zhao, 2014[109] NELSON Fair	Unclear	No	No	Unclear	Unclear	Unclear	Fair	NA

Abbreviations: BCCA=British Columbia Cancer Agency; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology Trial; DLCST=Danish Lung Cancer Screening Trial; I-ELCAP=International Early Lung Cancer Action Project; ITALUNG=The Italian Lung Study; KQ=key question; LC=lung cancer; LCSDP=Lung Cancer Screening Demonstration Project; LUSI=German Lung Cancer Screening Intervention Trial; MILD=Multicentric Italian Lung Detection Trial; NA=not applicable; NDI=National Death Index; NELSON=Dutch-Belgian Randomized Lung Cancer Screening Trial; NLST=National Lung Screening Trial; NR=not reported; PanCan=Pan-Canadian Early Detection of Lung Cancer Study; UKLS=UK Lung Cancer Screening Trial.

Appendix E Table 1. Screening Details of Included Trials, KQ 1

Trial	Inclusion Criteria	Exclusion Criteria	Description of Screening Method	Positive Screen and Evaluation Strategy
DANTE[61]	Male ages 60-74 who are current or former smokers, of at least 20 pack-years who quit less than 10 years ago	Severe comorbid conditions, life expectancy of less than 5 years, inability to comply with followup protocol, history of a previous malignancy within 10 years prior to enrollment in study	LDCT, contiguous 5 mm increments and 1.25 pitch with high-resolution bone algorithm (width 1700, level -600). Single-slice scanner with low-dose setting (140 kvp, 40 mA)	Noncalcified pulmonary nodules, hilar masses, FGG lesions, major atelectasis, endobronchial lesions, mediastinal adenopathy, pleural effusion, or pleural masses. Solid lesions, smooth and 10 mm or less: LDCT at 3, 6, and 12 months. If no change, followup 1 year. Solid lesions, nonsmooth and 5 mm or less: LDCT at 3-6 and 12 months. If no change, followup 1 year. Solid lesions, 6 mm to <10 mm: Commonly oral antibiotics. New HRCT after 6-8 weeks. Solid lesions, 10 mm to 20 mm: Oral antibiotics and new HRCT after 6-8 weeks. If no regression, PET-scan. If PET positive, tissue dx. PET-negative, close followup. Solid lesions, 20 mm or larger: Discretional antibiotics and repeat LDCT or contrast-enhanced CT and PET Subsolid (FGG) <10 mm: Oral antibiotics and new HRCT 6-8 weeks. If no regression, followup 6 months Subsolid (FGG) >10 mm: antibiotics and new HRCT 6-8 weeks. If no regression, evaluate case by case
DLCST[67]	Adult ages 50-70 who are current or former smokers with at least 20 pack-years of smoking. Former smokers should have quit after age 50 and abstinent for <10 years. Ability to climb 2 flights of stairs without pause and lung function by spirometry FEV1 of at least 30% of predicted volume	Weight of > 130 kg, history of cancer diagnosis and treatment, lung tuberculosis, illness that could shorten life expectancy to less than 10 years, chest CT in the last year for any reason	LDCT (120 kV and 40 mA)	Nodules were classified into 5 categories: 1=nodules up to 15 mm with benign characteristics; 2=no nodules or nodules <5 mm; 3=5-15 mm without benign characteristics; 4 ≥15 mm; 5=rapid-growing nodules (>25% increase in volume). Categories 1 and 2 were considered negative screening results. Category 3 were rescanned in 3 months. Categories 4 and 5 were referred to chest physicians for diagnostic workup.

Appendix E Table 1. Screening Details of Included Trials, KQ 1

Trial	Inclusion Criteria	Exclusion Criteria	Description of Screening Method	Positive Screen and Evaluation Strategy
ITALUNG[62]	55-69 years old with a smoking history at least 20 pack-years in the last 10 years or quit within the last 10 years	History of previous cancer other than nonmelanoma skin cancer and general conditions precluding thoracic surgery	LDCT, 120 to 140 kV, 20 to 43 mAs, pitch 1-2	At least one calcified solid or part solid with solid part at least 5 mm. Noncalcified, nonsolid at least 10 mm (Management of positive screens fundamentally derived from I-ELCAP)
LUSI[59, 60, 73]	Adults ages 50-69 years with a history of at least 25 years of smoking of at least 15 cigarettes per day or at least 30 years of smoking at least 10 cigarettes per day; including ex-smokers who stopped at most 10 years ago	History of cancer in the last 5 years, medical condition preventing surgical treatment and having a serious illness that shortens life expectancy to less than 10 years	LDCT (1.6-2 mSv, 1 mm slice thickness, reconstruction interval 0.8 mm and 0.7 mm, respectively)	Early recall for repeat CT depending on largest nodule size: 6 months for 5-7 diameter nodules, 3 months for 8-10 diameter and immediate pulmonology referral for >10 mm nodule. VDT calculated for known nodules and VDT above 600 days was considered negative while VDT < 600 days was positive and subject to early recall with timing to screening depending on size of nodule
LSS[69, 75]	Men and women ages 55 to 74 years with ≥30 pack-year smoking history and quit within 10 years	History of a spiral CT exam of the lungs or thorax in the previous 24 months, history of lung cancer, current treatment for any cancer other than nonmelanoma skin cancer, removal of a portion of or an entire lung, and participation in another cancer screening trial or a cancer primary prevention trial other than a smoking cessation study.	120-140 kVp, 60 mA, scan time of one second, 5 mm collimation, pitch of 2 or equivalent (depending on the model and type of scanner), and contiguous reconstructions	Noncalcified nodules ≥4 mm and several other specific findings (even with nodules <4 mm). At the 1-year examination, any noncalcified nodule ≥4 mm was considered a positive screen, and other abnormalities could be considered suspicious for lung cancer at the discretion of the radiologist
NELSON[33, 76-79, 81]	Men and women ages 50 to 74 years who smoked >15 cigarettes/day for >25 years or >10 cigarettes/day for >30 years; current smokers or those who quit ≤10 years ago	Moderate or severe health problems and an inability to climb 2 flights of stairs; weight >140 kg; current or past renal cancer, melanoma, or breast cancer; a diagnosis of lung cancer or treatment related to lung cancer within the past 5 years; or a chest CT scan within the past year	LDCT, using volumetric approach and volume doubling time (VDT); 80-140 kV, 40-80 mAs	Volume of solid nodule >500 mm^3; pleural-based solid nodule with a minimal diameter of >10 mm; solid component in a partial solid nodule with a volume of >500 mm^3; or an indeterminate baseline screen (e.g., solid nodule 50-500 mm^3) with VDT<400 days on 3-month repeat

Appendix E Table 1. Screening Details of Included Trials, KQ 1

Trial	Inclusion Criteria	Exclusion Criteria	Description of Screening Method	Positive Screen and Evaluation Strategy
NLST[32, 63, 74]	Ages 55-74 with 30 or more pack-year history of smoking and currently smoking or quit within the past 15 years	Previous history of lung cancer, history of chest CT within 18 months before enrollment, history of hemoptysis or unexplained weight loss of more than 15 lb in preceding year	LDCT with average effective dose of 1.5 mSv	≥1 noncalcified nodule measuring at least 4 mm in long-axis diameter, mediastinal masses, pleural disease or atelectasis of more than one segment. Interpreting radiologist judgment regarding whether results were positive on the basis of findings such as noncalcified hilar or mediastinal adenopathy, atelectasis, and pleural disease. Results and recommendations were sent to the participant and his/her health provider.

Abbreviations: CT= computed tomography; DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology trial; DLCST=Danish Lung Cancer Screening Trial; dx=diagnosis; FEV=forced expiratory volume; FGG=focal ground glass; HRCT=high-resolution computed tomography; I-ELCAP=International Early Lung Cancer Action Project; ITALUNG=The Italian Lung Study; KQ=key question; LDCT=low-dose computed tomography; LSS=The Lung Screening Study; LUSI=German Lung Cancer Screening Intervention Trial; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial; PET=positron emission tomography; VDT=volume doubling time.

Appendix E Table 2. Types and Stages of Incident Lung Cancer, KQ 1

Study	Cumulative Incidence	Type of Incident Lung Cancer	Stages of Incident Lung Cancer
DANTE[61]	LDCT: 106 (8.2%) Control: 73 (5.2%)	**LDCT** Adenocarcinoma=44 (42%) Squamous 25=(24%) Non-small cell NOS=7 (6.7%) Other=7 (6.7%) Small cell=9 (8.7%) Missing=12 (11.5%) **Control** Adenocarcinoma=19 (26%) Squamous=17 (23.6%) Non-small cell NOS=8 (11.1%) Other=6 (8.3%) Small cell=6 (8.3%) Missing=16 (22.2%)	**LDCT** Stage IA=31 (29.8%) Stage IB=16 (15.4%) Stage II=7 (6.7%) Stage IIIA=9 (8.7%) Stage IIIB=8 (7.7%) Stage IV=26 (25%) Missing=7 (6.7%) **Control** Stage IA=6 (8.3%) Stage IB=10 (13.9%) Stage II=5 (6.9%) Stage IIIA=6 (8.3%) Stage IIIB=6 (8.3%) Stage IV=33 (45.8 %) Missing=6 (8.3%)

Appendix E Table 2. Types and Stages of Incident Lung Cancer, KQ 1

Study	Cumulative Incidence	Type of Incident Lung Cancer	Stages of Incident Lung Cancer
DLSCT[67]	LDCT: 100 (4.9%) Control : 53 (2.6%)	**LDCT** Adenocarcinoma=40 (40%) Adenocarcinoma + broncho-alveolar carcinoma=17 (17%) Adenocarcinoma + squamous cell carcinoma=1 (1%) Squamous cell carcinoma =14 (14%) Broncho-alveolar carcinoma=1 (1%) Non-small cell lung cancer=14 (14%), Non-small cell lung cancer + broncho-alveolar carcinoma=0 Small cell lung cancer + non-small cell lung cancer=0 Small cell lung cancer=11 (11%) Large cell neuroendocrine carcinoma=1(1%) Carcinoid=0 Unknown histology 1 (1%) **Control:** Adenocarcinoma=18 (34%) Adenocarcinoma + broncho-alveolar carcinoma=0 Adenocarcinoma + squamous cell carcinoma=0 Broncho-alveolar carcinoma=0 Squamous cell carcinoma=9 (17%) Non-small cell lung cancer=9 (17%) Non-small cell lung cancer + broncho-alveolar carcinoma=1 (1.9%) Small cell lung cancer + non-small cell lung cancer=3 (5.7%) Small cell lung cancer=11 (21%) Large cell neuroendocrine carcinoma=0 Unknown histology=1 (1.9%)	**LDCT** Stage I=50 (50%) Stage II=4 (4%) Stage IIIA=15 (15%) Stage IIIB=8 (8%) Stage IV=23 (23%) Unknown stage=0 **Control:** Stage I=8 (15.1%) Stage II=2 (3.8%) Stage IIIA=3 (5.7%) Stage IIIB=6 (11.3%) Stage IV=32 (60.4%) Unknown stage=2 (3.8%)

Appendix E Table 2. Types and Stages of Incident Lung Cancer, KQ 1

Study	Cumulative Incidence	Type of Incident Lung Cancer	Stages of Incident Lung Cancer
ITALUNG[62]	LDCT: 67 (4.1%) Control: 71 (4.5%)	**LDCT** Adenocarcinoma=29 (43%) Squamous cell carcinoma=14 (21%) Small cell lung cancers=10 (15%) Carcinoid=2 (3%) Non-small cell carcinoma=3 (4%) Unclassified=9 (13%) **Control** Adenocarcinoma=21 (30%) Squamous cell carcinoma=17 (24%) Small cell lung cancers=11 (15%) Carcinoid=0 (0%) Non-small cell carcinoma=5 (7%) Unclassified=17 (24%)	**LDCT** Stage 1=24 (36%) Stage II=5 (7%) Stage III=9 (13%) Stage IV =24 (36%) Unknown =5 (7%) **Control** Stage 1=8 (11%) Stage II=5 (7%) Stage III=8 (11%) Stage IV=35 (49%) Unknown=15 (21%) p=0.005
LUSI[59, 60, 73]	Reported for years 0-5 LDCT: 63 (3.1%) Control: 36 (1.8%) Reported at any time, with followup to a median of 8.8 years LDCT: 85 (4.2%) Control: 67 (3.3%)	Data limited to the first 5 years (99 cancers) **LDCT:** Small cell carcinoma=5 (8%) Squamous cell=10 (16%) Adenocarcinoma=43 (68%) Large cell carcinoma=1 (2%) Carcinoid=2 (3%) Carcinoma unspecified=2 (3%) **Control** Small cell carcinoma=9 (25%) Squamous cell carcinoma=6 (17%) Adenocarcinoma=18 (50%) Large cell carcinoma=1 (3%) Carcinoid=0 (0%) Carcinoma unspecified=2 (6%)	Data provided for followup to a median of 8.8 years (152 cancers) **LDCT** Stage IA=37 (44%) Stage IB=11 (13%) Stage IIA=3 (4%) Stage IIB=4 (5%) Stage IIIA=10 (12%) Stage IIIB=2 (2%) Stage IV=17 (20%) Unknown=1 (1%) **Control** Stage IA=2 (3%) Stage IB=4 (6%) Stage IIA=5 (7%) Stage IIB=4 (6%) Stage IIIA=16 (24%) Stage IIIB=5 (7%) Stage IV=30 (45%) Unknown=1 (1%)

Appendix E Table 2. Types and Stages of Incident Lung Cancer, KQ 1

Study	Cumulative Incidence	Type of Incident Lung Cancer	Stages of Incident Lung Cancer
LSS[69]	LDCT: 40 (2.4%) Control: 20 (1.5%)	**LDCT** Adenocarcinoma=24 (60%) Squamous cell carcinoma=5 (13%) Small cell carcinoma=4 (10%) Large cell carcinoma=4 (10%) Non-small cell carcinoma NOS=3 (8%) Carcinoid tumor=NR Unknown=NR **Control** Adenocarcinoma=9 (45%) Squamous cell carcinoma=6 (30%) Small cell Carcinoma=2 (10%) Large cell carcinoma=1 (5%) Non-small cell carcinoma NOS=0 Carcinoid tumor=1 (5%) Unknown=1 (5%)	**LDCT** Stage I =19 (48%) Stage II=3 (8%) Stage III=11 (28%) Stage IV=5 (13%) Unknown=2 (5%) **Control** Stage I=8 (40%) Stage II=1 (5%) Stage III=5 (25%) Stage IV=4 (20%) Unknown=2 (10%)
NELSON[33, 76-79]	Data reported for male participants only LDCT: 344 (5.2%) Control: 304 (4.6%)	**LDCT** Adenocarcinoma=179 (52%) Squamous cell carcinoma=77 (22%) Small cell carcinoma=40 (12%) Non-small cell carcinoma NOS=16 (5%) Other=32 (9%) **Control** Adenocarcinoma=133 (44%) Squamous cell carcinoma= 94 (31%) Small cell carcinoma=46 (15%) Non-small cell carcinoma NOS=13 (4%) Other=18 (6%)	**LDCT** Stage IA=105 (31%) Stage IB=34 (10%) Stage IIA=12 (4%) Stage IIB=17 (5%) Stage IIIA=34 (10%) Stage IIIB=27 (8%) Stage IV=92 (27%) Unknown=23 (7%) **Control** Stage IA=21 (7%) Stage IB=20 (7%) Stage IIA=13 (4%) Stage IIB=17 (6%) Stage IIIA=43 (14%) Stage IIIB=34 (11%) Stage IV=139 (46%) Unknown=17 (6%)

Appendix E Table 2. Types and Stages of Incident Lung Cancer, KQ 1

Study	Cumulative Incidence	Type of Incident Lung Cancer	Stages of Incident Lung Cancer
NLST[32, 63]	Median followup of 6.5 years LDCT: 1,089 (4.1%) Control: 969 (3.6%) Post-trial followup to a median of 11.3 years LDCT: 1701 (6.4%) Control: 1681 (6.3%)	Median followup of 6.5 years **LDCT** Bronchioloalveolar carcinoma=111 (10%) Adenocarcinoma=389 (35%) Squamous cell=249 (22%) Large cell carcinoma=40 (4%) Non-small cell or other=137 (12%) Small cell carcinoma=143 (13%) Carcinoid=6 (0.5%) Unknown=34 (3%) **Control** Bronchioloalveolar carcinoma=36 (4%) Adenocarcinoma=337 (34%) Squamous cell=214 (22%) Large cell carcinoma=44 (4%) Non-small cell or other=162 (16%) Small cell carcinoma=163 (16%) Carcinoid=3 (0.3%) Unknown=34 (3%) Median followup of 11.3 years **LDCT** Bronchioloalveolar carcinoma=121 (7%) Adenocarcinoma=608 (36%) Squamous cell=416 (25%) Large cell carcinoma=56 (3%) Other non-small cell=196 (12%) Small cell carcinoma=245 (14%) Carcinoid=12 (0.7%) Unknown=47 (3%) **Control** Bronchioloalveolar carcinoma=46 (3%) Adenocarcinoma=598 (36%) Squamous cell=395 (24%) Large cell carcinoma=53 (3%) Other non-small cell=251 (15%) Small cell carcinoma=291 (17%) Carcinoid=7 (0.4%) Unknown=40 (2%)	Median followup of 6.5 years **LDCT** Stage 1A 416 (40%) Stage 1B =104 (10%) Stage IIA= 35 (3.4%) Stage IIB=38 (3.7%) Stage IIIA=99 (9.5%) Stage IIIB=122 (11.7%) Stage IV=226 (21.7%) **Control** Stage 1A=196 (21.1%) Stage 1B=93 (10%) Stage IIA=32 (3.4%) Stage IIB=42 (4.5%) Stage IIIA=109 (11.7%) Stage IIIB=122 (13.1%) Stage IV=335 (36.1%) Median followup of 11.3 years **LDCT** Stage 1A=523 (31%) Stage 1B=148 (9%) Stage IIA=91 (5%) Stage IIB=43 (3%) Stage IIIA=204 (12%) Stage IIIB=84 (5%) Stage IV=468 (28%) Occult=5 Unknown=112 (7%) **Control** Stage 1A=326 (19%) Stage 1B=134 (8%) Stage IIA=80 (5%) Stage IIB=66 (4%) Stage IIIA=216 (13%) Stage IIIB=94 (6%) Stage IV=597 (36%) Occult=4 Unknown=143 (9%)

Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology trial; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=The Italian Lung Study; KQ=key question; LDCT=low-dose computed tomography; LSS=The Lung Screening Study; LUSI=German Lung Cancer Screening Intervention Trial; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial; NOS=not otherwise specified; NR=not reported.

Appendix E Table 3. Incidental Findings From KQ 4 Studies

Author, Year	Study Name	Sample Size	Incidental Findings Reported
Field, 2016[117]	UKLS	4,055	Thoracic incidental findings for which supplementary radiology report was submitted: 115 Thoracic incidental findings included: Aortic dilatation: 4 Severe aortic valve calcification: 5 Mediastinal mass: 4 Mediastinal or hilar lymphadenopathy: 6 Pneumonia: 41 Bronchiectasis: 5 Pleural thickening: 8 Smoking related interstitial lung disease: 7 Severe emphysema: 9 Interstitial fibrosing lung disease (unspecified): 6 Non-specific interstitial pneumonia: 2 Usual interstitial pneumonia: 12 Sarcoidosis: 1 Oesophageal thickening or dilatation: 2 Breast mass: 1 Lobar collapse: 2 Extrathoracic incidental findings for which supplementary radiology report was submitted: 13 Extrathoracic incidental findings included: Biliary dilatation: 1 Adrenal mass: 3 Cirrhosis: 1 Hydronephrosis: 1 Liver mass: 1 Pancreatic cysts: 1 Renal mass: 3 Splenomegaly: 1 Thyroid mass: 1

Appendix E Table 3. Incidental Findings From KQ 4 Studies

Author, Year	Study Name	Sample Size	Incidental Findings Reported
Kinsinger, 2017[38]	LCSDP	2,106	Patients with ≥1 incidental finding reported: 857 (40.7%) Total N of incidental findings: 1,044 Findings included: Abdominal abnormalities and masses: 146 (14%) Aortic dilation or aneurysm: 87 (8.3%) Infectious, inflammatory, or interstitial processes: 265 (25.4%) Thyroid nodules: 25 (2.4%) Other (including CAC and emphysema): 521 (49.9%) Patients with incidental (nonnodule) findings, by demonstration site: Site 1: 211 (47.7%) Site 2: 106 (46.5%) Site 3: 135 (63.4%) Site 4: 89 (20.0%) Site 5: 149 (60.3%) Site 6: 54 (40.0%) Site 7: 81 (31.4%) Site 8: 32 (23.0%)

Appendix E Table 3. Incidental Findings From KQ 4 Studies

Author, Year	Study Name	Sample Size	Incidental Findings Reported
Morgan, 2017[167]	NA	320	Incidental findings resulting in further evaluation: 15% Findings included: Respiratory Total respiratory: 223 (69.6%) Emphysema: 162 (50.6%) Bronchial wall thickening: 126 (39.4%) Atelectasis: 52 (16.3) Ground-glass opacity: 26 (8.1%) Bronchiectasis: 14 (4.4%) Cardiovascular: Total cardiovascular: 216 (67.5%) CAC: 182 (56.0%) Aortic calcification: 66 (20.6%) Aortic dilation: 26 (8.1%) Endocrinological Total endocrinological: 23 (7.2%) Adrenal nodule 12 (3.8%) Thyroid nodule 11 (3.4%) Gastrointestinal Total gastrointestinal: 79 (24.7%) Hiatal hernia: 30 (9.4%) Liver cyst: 22 (6.8%) Dilated esophagus: 7 (2.2%) Gallstone: 6 (1.9%) Diaphragmatic hernia: 5 (1.6%) Other: 9 (2.8%) Genitourinary Total genitourinary: 14 (4.4%) Renal cyst: 8 (2.5%) Renal stone: 4 (1.3%) Renal mass: 2 (0.6%) Other Systems Total other: 78 (24.4%) Degenerative joint disease: 74 (23.1%) Compression fracture: 3 (0.9%) Breast nodule: 1 (0.3%) Splenic lesion: 1 (0.3%)

Appendix E Table 3. Incidental Findings From KQ 4 Studies

Author, Year	Study Name	Sample Size	Incidental Findings Reported
Nguyen, 2017[166]	NLST	17,309	Extrapulmonary findings (≥1 finding): 10,166 (58.7%) Potentially significant findings: 3,398 (19.6%) Minor findings 9,152 (52.9%) Significant cardiovascular findings: 1,378 (8.0%) Significant above diaphragm: 1,255 (7.3%) Significant below diaphragm: 1,311 (7.6%) Extrapulmonary malignancies: Thyroid: 14 (0.08%, 1 malignancy for every 14 found incidentally) Adrenal: 0 (0%) Kidney: 45 (0.26%, 1:37 renal abnormalities to find a malignancy) Liver: 8 (0.05%, none had significant findings on screening)
O'Grady, 2015[169]	NLST, PLCO	195,642 (53,248 from NLST 142,394 from PLCO)	Incidental thyroid cancer findings: NLST Control: 23 Intervention: 37 PLCO Control: 130 Intervention: 104
Pinsky, 2014[64]	NLST	26,722 NLST patients from LDCT arm 19,612 in <65 age cohort 7,110 in 65+ age cohort	This study reports emphysema, significant cardiovascular abnormality, abnormalities above the diaphragm, and abnormalities below the diaphragm. However, it is NR which of those are incidental. Aggregate frequencies of reported abnormal findings on screening: <65 age cohort: 6.9% 65+ age cohort: 9.2% p <0.001

Appendix E Table 3. Incidental Findings From KQ 4 Studies

Author, Year	Study Name	Sample Size	Incidental Findings Reported
Swensen, 2002[168]	NA	1,520	Patients with nonpulmonary incidental findings of significance: 210 (14%) Findings included: Renal cell cancer: 4 Indeterminate renal mass: 33 Renal calculi: 24 Bronchial carcinoid: 2 Tracheal nodule: 7 Lobar collapse: 2 Bronchiectasis: 11 Breast cancer: 3 Breast nodule: 17 Atrial myxoma: 1 Abdominal aortic aneurysm: 51 Pericardial effusion: 9 Pleural effusion: 4 Pulmonary artery calcification: 1 Lymphoma: 2 Spine metastasis: 1 Adrenal mass: 35 Pheochromocytoma: 1 Gastric tumor: 2
Wilson, 2008[137]	PLuSS	3,642	Number of screenings due to significant incidental finding: Initial screening: 82/3,642 (2.3%) Imaging studies: 19/3,642 (0.5%) Repeat screening: 50/3,423 (1.5%)

Abbreviations: CAC=coronary artery calcification; KQ=key question; LCSDP=Lung Cancer Screening Demonstration Project; NA=not applicable; NLST=National Lung Screening Trial; NR=not reported; PLCO=Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; PLuSS=Pittsburgh Lung Screening Study; UKLS=UK Lung Cancer Screening Trial.

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Allibhai, 2013[259] SBRT/SABR N=185 KQ 7 Fair	NA Canada 2004-2010 Patients with T1-2N0M0 NSCLC deemed medically inoperable by an experienced thoracic surgeon Followup, median (range) 15.2 mos Funding source University, private, other unspecified	Age, median 74.8 yrs Male, N (%) 93 (*50.3*) Race/ethnicity NR Comorbidities NR	Stage, N (%) T1: 133 (72) T2: 52 (28) TNM edition(s) NR Histology, N (%) NR Tumor diameter, mean (range) 2.2 cm (0.6 to 5.7 cm)	SBRT patients, N (%) 185 (100) SBRT dosing NR, but dosage options included 48 Gy x 4 fx, 54 to 60 Gy x 3 fx, 60 Gy x 8 fx, and 50 Gy x 10 fx, depending on tumor location and size
Arnold, 2017[199] SBRT/SABR N=75 KQ 6 Fair	NCDB U.S. 2004-2012 Patients diagnosed with c-stage I NSCLC with tumors ≤4 cm who were ≥90 years old at the time of diagnosis, had no other cancer, and had no history of radiation therapy or nonstandard therapy Followup, median (range) NR Funding source NR	Age NR Male, N (%) NR Race/ethnicity NR Charlson Comorbidity Index, N (%) NR	Stage, N (%) c-stage 1: 75 (100) TNM edition(s) NR Histology, N (%) NR Tumor size, N (%) NR	SBRT patients, N (%) 75 (100) SBRT dosing 100-200 Gy x 3-5 fx: 75 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Badellino, 2017[270] SBRT/SABR N=148 KQ 7 Fair	NA Italy 2004-2014 Patients with Stage I NSCLC and contraindication to surgery after multidisciplinary evaluation; ECOG performance status ≤2; accurate staging with PET and brain CT scan; prior thoracic radiation therapy Followup, median 20.5 mos Funding source NR	Age, mean (range) SBRT 3D-CRT: 75 yrs (53 to 89 yrs) SBRT VMAT: 76 yrs (52 to 88 yrs) Male, N (%) SBRT 3D-CRT: 77 (81) SBRT VMAT: 40 (75.5) Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) Clinical T1a SBRT 3D-CRT: 78 (82.1) SBRT VMAT: 30 (56.6) Clinical T1b SBRT 3D-CRT: 17 (17.9) SBRT VMAT: 23 (43.4) TNM edition(s) NR Histology, N (%) Adenocarcinoma SBRT 3D-CRT: 19 (20) SBRT VMAT: 16 (30.2) Squamous cell carcinoma SBRT 3D-CRT: 16 (16.8) SBRT VMAT: 9 (17) Other SBRT 3D-CRT: 12 (12.7) SBRT VMAT: 4 (7.5) Unknown SBRT 3D-CRT: 48 (50.5) SBRT VMAT: 24 (45.3) Tumor diameter, mean (range) SBRT 3D-CRT: 2.5 cm (1 to 5 cm) SBRT VMAT: 3 cm (1.3 to 5 cm)	SBRT patients, N (%) 148 (100) SBRT dosing, N (%) Total dose in Gy, mean (range) SBRT 3D-CRT: 110.8 (100-120) SBRT VMAT: 110.5 (100-120) 15 Gy x 3 fx SBRT 3D-CRT: 82 (86) SBRT VMAT: 9 (16) 14 Gy x 3 fx SBRT 3D-CRT: 12 (13) SBRT VMAT: 2 (3) 11 Gy x 5 fx SBRT 3D-CRT: 1 (1) SBRT VMAT: 21 (39) 7.5 Gy x 8 fx SBRT 3D-CRT: 0 (0) SBRT VMAT: 21 (39)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Bibault, 2015[254] SBRT/SABR Total N=205 Monte Carlo N=88 Type A N=117 KQ 7 Fair	NA France 2007-2013 Inoperable patients with stage NSCLC, T1 or T2 tumors >15 mm without lymph node or distant metastasis, and performance status ≤2 treated with SBRT Followup, median (range) Monte Carlo protocol: 15 mos (3 to 40 mos) Type A algorithm: 24 mos (3 to 55 mos) Private funding (Accuray, Oscar Lambret Comprehensive Cancer Center)	Age, median (range) Monte Carlo: 70.5 yrs (46 to 87 yrs) Type A: 69 yrs (49 to 92 yrs) Male, N (%) Total: *173* (*84.4*) Monte Carlo: 72 (81.8) Type A: 101 (86.3) Race/ethnicity NR Comorbidities, N (%) <u>Respiratory failure</u> Monte Carlo: 67 (76.1) Type A: 96 (82.1)	Stage, N (%) <u>Monte Carlo</u> T1a: 36 (38.7) T1b: 31 (33.3) T2a: 24 (25.8) T2b: 2 (2.2) <u>Type A</u> T1a: 50 (42.0) T1b: 36 (30.3) T2a: 30 (25.2) T2b: 3 (2.5) TNM edition(s) NR Histology, N (%) NR Tumor diameter, median (range) 22 mm (15 to 60 mm)	SBRT patients, N (%) 205 (100) SBRT dosing 60 Gy x 3 fx: NR 60 Gy x 5 fx: NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Brooks, 2017[204] SBRT/SABR N=772 KQs 6, 7 Fair	NA U.S. 2004-2014 Patients with c-stage 1-2 (T1-3N0M0) NSCLC not involving the bronchial tree or blocking the airway, with or without a lung cancer history (but no evidence of previous disease), and treated with SBRT; current cancer must have been outside the previously irradiated field, if patients had received previous radiation therapy for NSCLC Followup, median Age <75 yrs: 54.6 mos Age ≥75 yrs: 55.2 mos Funding source University, other unspecified source(s)	Age, median (range) Mean (range): *73.9 yrs* (46 to 91.8 yrs) Median: NR Male, N (%) *385 (49.9)* Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) Stage T1: *642 (83.2)* Stage T2: *120 (15.5)* Stage T3 (and Stage 2 NSCLC): *10 (1.3)* TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: *405 (52.5)* Squamous cell: *268 (34.7)* Other: *19 (2.5)* NSCLC NOS: *72 (9.3)* No pathologic features: *8 (1.0)* Tumor size, mean (SD) NR	SBRT patients, N (%) 772 (100) SBRT dosing, N (%) 50 Gy x 4 fx (BED 112.5 Gy): *636 (82.4)* 70 Gy x 10 fx (BED 119 Gy): *99 (12.8)* Other (75-149.6 Gy): *37 (4.8)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Brunelli, 2015[181] Surgery N=1,370 KQ 6 Good	NA U.S., Italy, Spain 2000-2011 Patients with p-stage 1 NSCLC with predicted postoperative FEV1 and DLCO <30% in association with peak oxygen consumption <10 mL/(kg-x-min) and deemed in stable cardiac condition and, if unstable hemodynamic conditions were present, receiving optimized cardiologic treatment prior to complete resection (but no induction chemotherapy) Followup, median 77 mos Funding source NR	Age, mean (SD) 66.1 yrs (10.2 yrs) Male, N (%) 1,014 (74) Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) p-stage 1: 1,370 (100) Stage pT1: 533 (39) TNM edition(s) 7th edition Histology, N (%) NR Tumor size, mean (SD) NR	Surgical approach, N (%) L/Bi-L: *1,304 (95.2)* P: 66 (4.8)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Bryant, 2018[196] Surgery & SBRT/SABR N=4,069 KQs 6, 7 Fair	VA U.S. 2006-2015 Patients with biopsy-proven c-stage 1 NSCLC (i.e., T1 or T2a [<5 cm in greatest dimension], N0, M0) who were treated definitively with either first-line surgery or SBRT (BED ≥100 Gy) within 6 mos of diagnosis and received pre-treatment pulmonary function tests, but no history of prior malignancy, other active cancer at diagnosis, unknown cause of death, or missing data needed to confirm eligibility Followup, median Total: *2.3 yrs* L: 2.9 yrs SLR: 2.6 yrs SBRT: 1.5 yrs Funding source Government	Age, mean (SD) Total: 67 yrs (8.2 yrs) L: 66 yrs (7.8 yrs) SLR: 69 yrs (8.5 yrs) SBRT: 71 yrs (8.6 yrs) Male, N (%) Total: 3,905 (96) L: 2,860 (96) SLR: 608 (96) SBRT: 437 (97) White, N (%) Total: 3,433 (84) L: 2,519 (84) SLR: 535 (84) SBRT: 379 (84) Comorbidities, N (%) Smoking status <u>Current</u> Total: 2,052 (50) L: 1,522 (51) SLR: 311 (49) SBRT: 219 (49) <u>Past</u> Total: 1,805 (44) L: 1,303 (44) SLR: 285 (45) SBRT: 217 (48) <u>Never</u> Total: 124 (3) L: 100 (3) SLR: 18 (3) SBRT: 6 (1)	Stage, N (%) Clinical T status <u>T1a (<2 cm)</u> Total: 1,911 (47) L: 1,329 (45) SLR: 395 (62) SBRT: 187 (42) <u>T1b (2 to 3 cm)</u> Total: 1,193 (29) L: 849 (28) SLR: 168 (26) SBRT: 176 (39) <u>T2a (3 to 5 cm)</u> Total: 965 (24) L: 808 (27) SLR: 71 (11) SBRT: 86 (19) TNM edition(s) NR Histology, N (%) <u>Adenocarcinoma</u> Total: 2,244 (55) L: 1,699 (57) SLR: 369 (58) SBRT: 176 (39) <u>Squamous cell carcinoma</u> Total: 1,375 (34) L: 964 (32) SLR: 209 (33) SBRT: 202 (45) <u>Other/unknown</u> Total: 450 (11) L: 323 (11) SLR: 56 (9) SBRT: 71 (16)	Surgical approach, N (%) L: 2,986 (73) SLR: 634 *(15.6)* <u>SLR subtypes</u> W: 414 *(65.3)* Segmental resection (SLR subtype): 220 *(34.7)* SBRT patients, N (%) 449 (11) SBRT dosing, mean dose (SD) (range) 124 (27) (100 to 216) Gy x 1-5 daily fx

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Bryant, 2018[196] (continued)		Unknown Total: 88 (2) L: 61 (2) SLR: 20 (3) SBRT: 7 (2)	Tumor size, mean (SD) NR	
Chang, 2007[192] Surgery N=10,761 KQ 6 Fair	SEER U.S. 1988-1997 Patients with diagnostic confirmation of T1N0M0 NSCLC with tumors ≤3.0 cm, but without VPI or within 2 cm of the carina, who underwent surgical resection Followup, median NR Funding source NR	Age, median 67 yrs Age, N (%) <67 yrs: 4,936 *(45.7)* ≥67 yrs: 5,825 *(54.1)* Male, N (%) 5,441 (50.6) Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) Stage 1A: 10,761 (100) TNM edition(s) NR Histology, N (%) Adenocarcinoma: *4,520* (42) SCC: *2,690* (25) Tumor size, N (%) 0.1 to 2.0 cm: 6,161 *(57.3)* 2.1 to 2.9 cm: 4,600 *(42.7)*	Surgical approach, N (%) L: 8,527 *(79.2)* SLR: 2,234 *(20.8)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Cox, 2017[186] Surgery N=1,544 1,991 KQ 6 Fair	NCDB U.S. 2003-2006 Patients with cT1-T2N0M0 lepidic adenocarcinoma treated with lobectomy or SLR, but not induction chemotherapy, radiotherapy, local excision, or pneumonectomy Followup, median NR Funding source Government	Age, median (range) Total: NR L: 69 yrs (61.0 to 75.0 yrs) SLR: 70 yrs (62.0 to 77.0 yrs) Male, N (%) Total: *711 (35.7)* L: 572 (37.0) SLR: 139 (31.1) White, N (%) Total: *1,803 (90.6)* L: 1,391 (90.1) SLR: 412 (92.2) Charlson Comorbidity Index, N (%) Score=0, n (%) Total: *1,217 (61.1)* L: 982 (63.6) SLR: 235 (52.6) Score=1, n (%) Total: *571 (28.7)* L: 424 (27.5) SLR: 147 (32.9) Score=2, n (%) Total: *203 (10.2)* L: 138 (8.9) SLR: 65 (14.5) Score >1, n (%) Total: *774 (38.9)* L: *562* (36.4) SLR: *212* (47.4)	Stage, N (%) Clinical T1 Total: *1,403 (70.5)* L: 1,043 (67.6) SLR: 360 (80.5) Clinical T2 Total: *588 (29.5)* L: 501 (32.4) SLR: 87 (19.5)	Surgical approach, N (%) L: 1,544 (77.5) SLR: 447 (22.5)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Cox, 2017[186] (continued)			TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: 1,991 (100) Tumor diameter, median (IQR) Total: NR L: 2.4 cm (1.7 to 3.4 cm) SLR: 1.6 cm (1.1 to 2.4 cm)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Crabtree, 2013[265] Timmerman, 2010[272] SBRT/SABR N=55 KQ 7 Fair	RTOG 0236 Canada, U.S. 2004-2006 Medically inoperable, nonpregnant, nonlactating patients aged ≥18 with Zubrod performance status score of 0-2 and cytologically or histologically proven, NSCLC, staged as T1-T2N0M0, with no active systemic, pulmonary, or pericardial infection, no history of nonsynchronous malignancy within 2 years of study entry, radiotherapy to thorax, and no plans to receive conventional radiotherapy, chemotherapy, biological therapy, vaccine therapy, or surgery as treatment (except at disease progression) Followup, median 34.4 mos Funding source Government, academic	Age, median (range) 72 yrs (48 to 89 yrs) Age >75 yrs, N (%) 21 (38.9) Male, N (%) 21 (38) White, N (%) 51 (93) Comorbidities, N (%) NR	Stage, N (%) Stage 1A: 44 (80) Stage 1B: 11 (20) TNM edition(s) NR Histology, N (%) Squamous cell carcinoma: 17 (31) Adenocarcinoma: 19 (35) Large cell undifferentiated: 3 (5) NSCLC NOS: 16 (29) Tumor size, mean (SD) NR	SBRT patients, N (%) 55 (100) SBRT dosing, N (%) 20 Gy x 3 fx: 55 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Eba, 2016[201] SBRT/SABR N=40 KQ 6 Fair	NA Japan 2002-2007 Patients with histologically or cytologically proven adenocarcinoma at c-stage IA (i.e., T1N0M0) and being operable (i.e., judged able to undergo lobectomy or larger lung resection prior to registration in the JCOG0403 OR JCOG0201 trials) Followup, median NR Funding source Government	Age, median (IQR) 79 yrs (74.5 to 83.5 yrs) Male, N (%) 20 (50) Race/ethnicity NR Comorbidities, N (%) NR	c-stage, N (%) 1A: 40 (100) TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: 40 (100) Tumor size, median (IQR) 2.4 cm (1.9 to 2.6 cm)	SBRT patients, N (%) 40 (100) SBRT dosing, N (%) 48 Gy x 4 fx: 40 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Fernandez, 2012[188] Surgery N=657 KQ 6 Fair	SEER U.S. 1998-2005 Patients ≥66 with c-stage 1A NSCLC treated with SLR, but no other therapies within 1 yr before diagnosis or lymph node sampling at time of surgery Followup, median 34.1 mos Funding source NR	Age, mean (SD) 75.5 yrs (5.7 yrs) Age, N (%) 66-70 yrs: 133 (20.2) 71-75 yrs: 219 (33.3) 76-80 yrs: 177 (26.9) 81-85 yrs: 92 (14.0) 86+ yrs: 36 (5.5) Male, N (%) 305 (46.4) White, N (%) 601 (91.5) Klabunde-modified Charlson Comorbidity Scores, N (%) 0: 181 (28.1) 1: 243 (37.7) 2: 104 (16.2) 3+: 116 (18.0)	Stage, N (%) c-stage 1A: 657 (100) TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: 324 (49.3) Large cell: 24 (3.7) Squamous cell: 199 (30.3) NSCLC NOS: 110 (16.7) Tumor size, mean (SD) 17.9 mm (6.3 mm) Tumor size, N (%) ≤10 mm: 98 (14.9) 11-20 mm: 362 (55.1) 21-30 mm: 197 (30.0)	Surgical approach, N (%) W: 547 (83.3) S: 92 (14.0) SLR NOS: 18 (2.7)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Ferrero, 2015[262] SBRT/SABR N=30 KQ 7 Fair	NA Italy 2012-2013 Patients with inoperable stage 1 NSCLC diagnosis and eligible for SBRT due to medical contraindications to surgery after multidisciplinary evaluation, ECOG performance status ≤2, complete staging including 18FDG-PET and CT scan, and no prior radiation therapy to site of SBRT Followup, median 14 mos Funding source NR	Age, mean (range) 77 yrs (61 to 84 yrs) Male, N (%) 23 (76.7) Race/ethnicity NR Age-adjusted Charlson Comorbidity Index, mean (range) 6.9 (3 to 14) Age-adjusted Charlson Comorbidity Index, N (%) Score <7: 16 (53.3) Score ≥7: 14 (46.7) Comorbidities <u>Smoking status, N (%)</u> Former: 19 (63.3) Current: 8 (26.7) Never: 3 (10)	Stage, N (%) 1A: 17 (56.7) 1B: 13 (43.3) TNM edition(s) NR Histology, N (%) Adenocarcinoma: 9 (30) Squamous cell: 8 (26.7) NSCLC NOS: 4 (13.3) Unknown: 9 (30) Tumor max diameter, mean (range) 25.5 mm (12 to 55 mm)	SBRT patients, N (%) 30 (100) SBRT dosing, N (%) 45 to 54 Gy x 3 fx: 9 (30) 55 Gy x 5 fx: 11 (37) 60 Gy x 8 fx: 10 (33)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Goya, 2005[195] Surgery N=*3,965* eligible (of 6,644 analyzed) KQ 6 Fair	NA Japan 1994-2001 Patients with primary histological NSCLC (adenocarcinoma, SCC, large-cell carcinoma, and adenosquamous carcinoma) resected at time of thoracotomy in 1994 at certified teaching hospitals and with complete data Followup, median NR, but ≥5 yrs Funding source NR	Age, mean (range) NR Male, N (%) NR Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) c-stage IA: 2423 (36.5) IB: 1542 (23.2) IIA: 150 (2.3) IIB: 746 (11.2) IIIA: 1270 (19.1) IIIB 366 (5.5) IV: 147 (2.2) TNM edition(s) 5th edition Histology, N (%) NR Tumor size, mean (SD) NR	Surgical approach, N (%) NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Grills, 2012[256] SBRT/SABR N=483 (505 tumors) KQs 6, 7 Fair	NA U.S. 1998-2010 Patients diagnosed with c-stage IA-IIB (T1-T3 N0 M0; peripheral T3 including chest-wall invasion only) or locally recurrent (after prior wedge resection) NSCLC Followup, median; mean 1.3 yrs; 1.6 yrs William Beaumont Hospital, Royal Oak, Michigan; University of Wuerzburg, Wuerzburg, Germany; Netherlands Cancer Institute, Amsterdam, The Netherlands; Princess Margaret Hospital, University of Toronto, Toronto, Ontario, Canada; and Thomas Jefferson University Hospital, Philadelphia, PA; Elekta	Age, median (range) 74 yrs (42 to 94 yrs) Male, N (%) *251* (52) Race/ethnicity NR Comorbidities NR	Clinical Stage, N (%) IA (T1N0): *318* (63) IB (T2N0): *167* (33) IIA (T3N0): *10* (2) Local recurrence: *5* (1) TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: *237* (47) Squamous cell carcinoma: *162* (32) Large cell/NOS/mixed: *111* (22) Tumor size, N (%) NR	SBRT patients, N (%) 483 (100) SBRT dosing <u>William Beaumont Hospital (N=108)</u> 12 Gy x 4 fx: 69 (*63.9*) 12 Gy x 5 fx: 34 (*31.5*) <u>Netherlands Cancer Institute (N=187)</u> 18 Gy x 3 fx: 182 (*97.3*) <u>Thomas Jefferson University (N=21)</u> 10 Gy x 5 fx: 10 (*47.6*) <u>Princess Margaret Hospital (N=129)</u> 7.5 Gy x 8 fx: 13 (*10.1*) 12 Gy x 4 fx: 59 (*45.7*) 18 Gy x 3 fx: 27 (*20.9*) 20 Gy x 3 fx: 20 (*15.5*) <u>University of Wuerzburg (N=60)</u> 12.5 Gy x 3 fx: 35 (*58.3*)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Guerrera, 2015[171] Surgery N=848 KQ 6 Fair	NA Italy 2004-2012 Consecutive patients receiving surgical resection, but no preoperative treatment regimen, for Stage 1A and 1B NSCLC of any histology except a neuroendocrine subtype Followup, mean 48 mos Funding source NR	Age, median (IQR) 67 yrs (62 to 73 yrs) >75 yrs, N (%): 135 (14) Male, N (%) 610 (72) Race/ethnicity NR Comorbidities ≥1 comorbidity, N (%) 563 (77) "Smoking habit," N (%) 727 (86)	Stage, N (%) pT status pT1a: 249 (29) pT1b: 190 (23) pT2a: 409 (48) TNM edition(s) NR Histology, N (%) Adenocarcinoma: 551 (65) Bronchioalveolar carcinoma: 25 (3) Squamous cell carcinoma: 247 (29) Large-cell carcinoma: 25 (3) Tumor size, median (IQR) 2.5 cm (1.8 to 3.5 cm)	Surgical approach, N (%) W: 85 (10) S: 81 (10) L: 651 (77) Sleeve resection: 3 (0.5) Bi-L: 12 (1) P: 16 (1.5)
Haidar, 2014[257] SBRT/SABR N=55 KQ 7 Fair	NA U.S. 2002-2012 Patients treated with SBRT for early stage lung cancer Followup, median (range) NPC: 24.2 mos (1.9 to 64.6 mos) PC: 25.8 mos (4.3 to 53.4 mos) Funding source Government	Age, mean (range) NPC: 78 yrs (63 to 89 yrs) PC: 78.2 yrs (60 to 88 yrs) Male, N (%) Total: *35* (*63.64*) NPC: 17 (74) PC: 18 (56) Race/ethnicity NR Comorbidities Smokers Total: *53* (*96.36*) NPC: 22 (96) PC: 31 (97)	Stage, N (%) NPC: T1aN0M0, IA: 11 (46) T1bN0M0, IA: 7 (29) T2aN0M0, IB: 5 (21) T2bN0M0, IIA: 0 (0) T2bN0M0, IIB: 0 (0) T3aN0M0, IIB: 1 (4) TNM edition(s) 7th edition Histology, N (%) NR Tumor size, N (%) Mean (SD) NPC: 2.5 (1.1) PC: 2.7 (1.25)	SBRT patients, N (%) 55 (100) SBRT dosing, median (range) NPC: 50 Gy (48 to 56 Gy)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Husain, 2015[239] Surgery N=112,216 KQ 7 Fair	NCDB U.S. 2003-2011 Adult patients with c-stage I NSCLC Followup, median (range) NR Funding source NR	Age, median 68 yrs Age, N (%) <65 yrs: 24,535 (34.5) 65-74.99 yrs: 27,557 (42.3) ≥75 yrs: 19,083 (23.3) Male, N (%) 33,168 (46.6) White, N (%) 63,095 (88.6) Charlson-Deyo Comorbidity Index, N (%) 0: 34,750 (48.8) 1: 26,186 (36.8) 2: 10,239 (14.4)	Clinical Stage, N (%) T1N0: 48,294 (67.9) T2N0: 22,881 (32.1) TNM edition(s) 6th or 7th editions Histology, N (%) Large cell: 2278 (3.2) Squamous cell: 20,243 (28.4) Adenocarcinoma: 43,699 (61.4) Other: 4955 (7.0) Tumor size, median 2.4 cm Tumor size, N (%) ≤2 cm: 29,851 (41.9) 2.1-3 cm: 19,919 (28.0) 3.1-5 cm: 15,749 (22.1) >5 cm: 5,006 (7.0) Unknown: 650 (0.9)	Surgical approach, N (%) L: 57,569 (80.9) SLR: 13,606 (19.1)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Jeon, 2018[268] SBRT/SABR N=53 KQ 7 Fair	NA South Korea 2006-2015 Patients with Stage 1 NSCLC tumor size <5 cm, and peripheral tumor location ≥2 cm away from bronchial tree and treated with SBRT, regardless of medical operability Followup, median 37.1 mos Funding source Government	Age, median (range) 74 yrs (54 to 87 yrs) Age, N (%) ≤75 yrs: 32 (60.3) >75 yrs: 21 (39.7) Male, N (%) 40 (75.5) Race/ethnicity NR Comorbidities, N (%) Medically inoperable (i.e., significant comorbidities): 40 (75.5)	Stage, N (%) Clinical T1: 33 *(62.3)* Clinical T2: 20 *(37.7)* TNM edition(s) NR Histology, N (%) Adenocarcinoma: 22 (41.5) Squamous cell: 24 (45.3) Others: 5 (9.4) Unproven: 2 (3.8) Maximum tumor diameter range 1.5 to 4.9 cm Maximum tumor diameter, N (%) ≤2 cm: 3 (5.7) >2 to ≤3 cm: 30 (56.6) >3 cm: 20 (37.7)	SBRT patients, N (%) 53 (100) SBRT dosing, N (%) 5 Gy x 8 fx (40 Gy): 1 (1.9) 6 Gy x 7 fx (42 Gy): 2 (3.8): 6 Gy x 8 fx (48 Gy): 1 (1.9): 7 Gy x 7 fx (49 Gy): 4 (7.6) 7 Gy x 8 fx (56 Gy): 1 (1.9) 9 Gy x 5 fx (45 Gy): 2 (3.8) 10 Gy x 5 fx (50 Gy): 10 (18.8) 11.6 Gy x 5 fx (58 Gy): 1 (1.9) 12 Gy x 4 fx (48 Gy): 10 (18.8) 15 Gy x 3 fx (45 Gy): 2 (3.8) 16 Gy x 3 fx (48 Gy): 3 (5.7) 18 Gy x 3 fx (54 Gy): 16 (30.1)
Jeppesen, 2018[203] SBRT/SABR N=136 KQs 6, 7 Fair	NA Denmark 2007-2013 Patients with histologically or cytologically proven, localized T1-2N0M0 NSCLC with a maximum tumor diameter of 5 cm Followup, median 70.1 mos Funding source Private	Age, mean (range) 72.5 yrs (49 to 90 yrs) Male, N (%) 61 (45) Race/ethnicity NR Comorbidities, N (%) <u>Charlson Comorbidity Index, N (%)</u> Score 0-1: 71 (53) Score 2-3: 38 (28) Score 4+: 26 (19) <u>Smoking history, mean/median (NR which was used) (range)</u> 41 (0-130)	Stage, N (%) NR TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: 77 (57) Squamous cell: 38 (28) Other: 21 (15) Tumor diameter, mean (range) 3.1 cm (1.2 to 5.0 cm)	SBRT patients, N (%) 136 (100) SBRT dosing, N (%) <u>Total central dose to gross tumor volume (GTV)</u> 45 Gy x 3 fx (BED 112 Gy): NR (prior to October 2008) 66 Gy x 3 fx (BED 211 Gy): NR (after October 2008) <u>Total central dose to PTV</u> 30 Gy x 3 fx (BED was NR): NR (prior to October 2008) 45 Gy x 3 fx (BED 112 Gy): NR (after October 2008)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Katoh, 2017[255] SBRT/SABR N=283 (286 tumors) KQs 6, 7 Fair	NA Japan 2000-2012 Patients diagnosed with histologically proven NSCLC and peripherally located c-stage I and IIA and treated with SBRT, but not thoracic radiation therapy for simultaneous malignant tumors within three months before or after starting SBRT Followup, median (range) 28 mos (0 to 127 mos) Japan Society for the Promotion of Science; Hokkaido University	Age, median (range) 78 yrs (52 to 90 yrs) Male, N (%) 215 (*75.6*) Race/ethnicity NR Comorbidities NR	Stage, N (%) 1a and 1b: 195 (*68.2*) 2a and 2b: 91 (*31.8*) TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 185 (*65.4*) Squamous cell carcinoma: 80 (*28.3*) Maximum tumor diameter, median (range) 1.9 cm (0.7 to 4.0 cm)	SBRT patients, N (%) 283 (100) SBRT dosing, N (%) 40 Gy x 4 fx: 94 (32.9) 48 Gy x 4 fx: 149 (52.1) 50 Gy x 5 fx: 19 (6.6)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Khullar, 2015[178] Surgery N= 54,350 (of 92,929 total) KQ 6 Fair	NCDB U.S. 2003-2006 Patients who underwent pulmonary resection for a first or single invasive cancer, who were treated (not with palliative care) at the reporting facility, and for whom data about laterality and survival were available Followup, median NR Funding source Government, university	Age, mean (SD) 66.0 yrs (10.3 yrs) Male, N (%) NR Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) Analytic stage 1: 54,350 (62.9) Analytic stage 2: 14,137 (16.4) Analytic stage 3: 13,830 (16.0) Analytic stage 4: 4,023 (4.7) TNM edition(s) NR Histology, N (%) NR Tumor size, mean (SD) NR	Surgical approach, N (%) W: 54,350 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Khullar, 2015[189] Surgery N=28,241 KQs 6, 7 Fair	NCDB U.S. 2003-2011 Patients undergoing surgical resection, but not neoadjuvant radiation or palliative care, at the same facility providing diagnosis for preoperative clinical T1a N0 NSCLC with known laterality as their first or only lifetime cancer from 2003 to 2011 (OS measures limited to patients treated from 2003-2006) Followup, median NR Funding source Government, university	Age, mean (SD) L: 65.8 yrs (9.9 yrs) W: 68.9 yrs (9.8 yrs) S: 68.7 yrs (9.4 yrs) Male, N (%) Total: *11,382 (40.3)* L: 8001 (40.6) W: 2937 (40.3) S: 444 (36.2) White, N (%) Total: *25,136 (89.0)* L: 17,464 (89.4) W: 6570 (90.9) S: 1102 (91.1) Charlson Comorbidity Index, N (%) <u>Score of 0</u> Total: *13,366 (47.3)* L: 9849 (50.0) W: 3017 (41.4) S: 500 (40.8) <u>Score of 1</u> Total: *10,783 (38.2)* L: 7293 (37.0) W: 2976 (40.8) S: 514 (41.9) <u>Score of 2+</u> Total: *4,092 (14.5)* L: 2576 (13.1) W: 1304 (17.9) S: 212 (17.3)	Stage, N (%) c-stage T1A N0 NSCLC: 28,241 (100) TNM edition(s) NR Histology, N (%) <u>Adenocarcinoma</u> Total: *18,193 (64.4)* L: 13,097 (66.4) W: 4336 (59.4) S: 760 (62.0) <u>Squamous cell carcinomas</u> Total: *6,041 (21.4)* L: 3957 (20.1) W: 1795 (24.6) S: 289 (23.6) <u>Unknown histology</u> Total: *913 (3.2)* L: 596 (3.0) W: 278 (3.8) S: 39 (3.2) Tumor size, mean (SD) L: 1.52 cm (0.39 cm) W: 1.4 cm (0.42 cm) S: 1.46 cm (0.40 cm)	Surgical approach, N (%) L: 19,718 *(69.8)* W: 7,297 *(25.8)* S: 1,226 *(4.3)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Koshy, 2015[200] SBRT/SABR N=498 KQ 6 Fair	NCDB U.S. 2003-2006 Patients with histologically confirmed first primary Stage 1 NSCLC who received all or part of their first course of treatment at Commission on Cancer-accredited facilities and SBRT at a calculated BED of ≥70 Gy in 1 to 10 fx Followup, median 68 mos Funding source NR	Age, N (%) 18-59 years: *40* (8.0) 60-69 years: *91* (18.3) 70-79 years: *231* (46.4) 80+ years: *136* (27.3) Male, N (%) *219* (44.0) White, N (%) *444* (89.2) Charlson Comorbidity Index, N (%) Score=0: *327* (65.7) Score=1: *125* (25.1) Score=2+: *46* (9.2)	Stage, N (%) T1: *334* (67.1) T2: *164* (32.9) TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: *180* (36.1) NSCLC NOS: *155* (31.1) Squamous cell: *146* (29.3) Large cell: *17* (3.4) Tumor size, median (IQR) T1 tumors: 2 cm (1.6 to 2.5 cm) T2 tumors: 3.7 cm (3.2 to 4.5 cm)	SBRT patients, N (%) 498 (100) SBRT dosing 20 Gy x 3 fx: *169* (34) 12 Gy x 4 fx: *80* (16) 18 Gy x 3 fx: *50* (10) 15 Gy x 3 fx: *50* (10) 16 Gy x 3 fx: *20* (4) Other dose & fx schedules: *129* (*26*)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Lakha, 2014[175] Surgery N=16,315 KQ 6 Fair	SEER U.S. 2004-2010 Patients with incident, histologically confirmed NSCLC diagnosed with tumors <7 cm, without lymph node involvement (N0) or distant metastasis (M0), who were experiencing their first and only malignancy, and who underwent lobectomy but not preoperative radiotherapy Followup, median NR Funding source NR	Age, N (%) <50 yrs: *942* (*5.8*) 50-60 yrs: *2,985* (*18.3*) >60 yrs: *12,388* (*75.9*) Male, N (%) *7,707* (*47.2*) White, N (%) *13,077* (*80.2*) Comorbidities, N (%) NR	Stage, N (%) NR TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: *9,784 (60.0*) Squamous cell carcinoma: *4,273 (26.2*) Large-cell carcinoma: *598 (3.7*) Other: *257 (1.6)* Tumor size, N (%) <2 cm: *6,048 (37.1*) 2-3 cm: *4,674 (28.6*) >3-5 cm: *4,345 (26.6*) >5-7 cm: *1,248 (7.6*)	Surgical approach, N (%) L: 16,315 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Lam, 2018[202] SBRT/SABR N=4,454 KQs 6, 7 Fair	NCDB U.S. 2004-2014 Patients with T1a-1bN0M0 NSCLC tumors ≤3 cm and histology classifications of adenocarcinoma, squamous cell carcinoma, large cell carcinoma, or NSCLC NOS (but no nodal or extrapulmonary disease) who were treated at high-volume centers without chemotherapy, immunotherapy, or hormone therapy, had available survival data, and were not lost to followup Followup, median 50.2 mos Funding source NR	Age, median (range) NR Male, N (%) NR Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) NR TNM edition(s) 7th edition Histology, N (%) NR Tumor size, mean (SD) NR	SBRT patients, N (%) 4,454 (100) SBRT dosing, N (%) NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Landreneau, 2014[176] Surgery N=614 KQs 6, 7 Fair	NA U.S. NR Patients with c-stage 1 NSCLC >5 cm with data available from the Lung Cancer Database of the University of Pittsburgh Followup, median 5.4 yrs Funding source Government, private (Thoracic Surgery Foundation for Research and Education)	Age, mean (SD) Total: 68.5 yrs (NR) S: 68.5 yrs (9.2 yrs) L: 68.4 yrs (9.2 yrs) Male, N (%) Total: *283 (45.4)* S: 139 *(44.6)* L: 144 *(46.2)* Race/ethnicity NR Comorbidities, N (%) <u>COPD, N (%)</u> Total: *208 (33.3)* S: 103 (33.0) L: 105 (33.7) <u>Smoking status, N (%)</u> Ever Total: *480* (92.9) S: 290 (92.9) L: 290 (92.9) Never Total: *44 (7.1)* S: 22 (7.1) L: 22 (7.1)	Stage, N (%) <u>c-stage 1A</u> Total: *487 (78.0)* S: 248 *(79.5)* L: 239 *(76.6)* <u>c-stage 1B</u> Total: *137 (22.0)* S: 64 *(20.5)* L: 73 *(23.4)* TNM edition(s) 7th edition Histology, N (%) <u>Adenocarcinoma</u> Total: *360 (57.7)* S: 177 (56.7) L: 183 (58.7) <u>Squamous cell</u> Total: *186 (29.8)* S: 89 (28.5) L: 97 (31.1) Tumor size, mean (SD) Total: 2.2 cm (NR) S: 2.2 cm (1.0 cm) L: 2.2 cm (1.1 cm)	Surgical approach, N (%) S: 312 (50) L: 312 (50)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Licht, 2013[249] Surgery N=1,513 KQ 7 Fair	Danish Lung Cancer Registry The Netherlands 2007-2011 Patients undergoing standard anatomic lobectomy for c-stage 1 NSCLC Followup, median 28 mos Funding source NR	Age, N (%) <50 yrs: 51 *(3.4)* 50-59 yrs: 257 *(17.0)* 60-69 yrs: 613 *(40.5)* 70-79 yrs: 515 *(34.0)* >80 yrs: 77 *(5.1)* Male, N (%) Total: 742 (49) VATS L: *319 (44.5)* Open L: *423 (53.1)* Race/ethnicity NR Charlson Comorbidity Index <u>Median score; mean score (95% CI)</u> VATS L: 1; 1.1 (1.0 to 1.2) Open L: 0; 1.0 (0.9 to 1.1) <u>Specific scores, n (%)</u> Score=0: 762 *(50.4)* Score=1: 343 *(22.7)* Score=2: 207 *(13.7)* Score=3: 106 *(7.0)* Score=4: 37 *(2.4)* Score=5: 28 *(1.9)* Score ≥6: 30 *(2.0)*	Stage, N (%) c-stage T1: 787 *(52.0)* c-stage T2: 726 *(48.0)* TNM edition(s) NR Histology, N (%) <u>Adenocarcinoma</u> Total: *745 (49.2)* VATS L: 390 (54.4) Open L: 355 (44.6) <u>Squamous cell</u> Total: *398 (26.3)* VATS L: 145 (20.2) Open L: 253 (31.8) <u>Adenosquamous cell</u> Total: *14 (0.9)* VATS L: 8 (1.1) Open L: 6 (0.8) <u>Mixed tumor</u> Total: *246 (16.3)* VATS L: 124 (17.3) Open L: 122 (15.3)	Surgical approach, N (%) VATS L: 71 (47) Open L: 796 (53)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Licht, 2013[249] (continued)			Bronchioloalveolar carcinoma Total: *8 (0.5)* VATS L: 5 (0.7) Open L: 3 (0.4) Large-cell carcinoma Total: *60 (4.0)* VATS L: 23 (3.2) Open L: 37 (4.6) Sarcomatoid carcinoma Total: *9 (0.6)* VATS L: 4 (0.6) Open L: 5 (0.6) Salivary gland-like carcinoma Total: *1 (0.1)* VATS L: 0 (0) Open L: 1 (0.1) Non-specified NSCLC Total: *32 (2.1)* VATS L: 18 (2.5) Open L: 14 (1.8) Tumor size, mean (SD) NR	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Lindberg, 2015[207] SBRT/SABR N=57 KQs 6, 7 Fair	NA Sweden, Norway, Denmark 2003-2005 Patients with Stage 1 T1-2N0M0 peripherally located NSCLC with no central tumor growth adjacent to trachea, main bronchus, or esophagus who were medically inoperable or refused surgery and received SBRT at the prescribed dose of 15 Gy x 3 fx; life expectancy of ≥12 mos; Karnofsky performance score ≥70; no prior malignancy within last 5 yrs Followup, median 41.5 mos Funding source Government, private	Age, mean (range) 75.2 yrs (58.9 to 86.8 yrs) Male, N (%) 26 (46) Race/ethnicity NR Comorbidities, N (%) COPD: 37 (65)	Stage, N (%) Stage T1a: 10 (18) Stage T1b: 31 (54) Stage T2a: 16 (28) TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 19 (33) Squamous cell: 8 (14) Large cell carcinoma: 1 (2) NSCLC NOS: 10 (18) Not analyzed: 19 (33) Tumor volume, median (range) 16 mL (1 to 51 mL) Tumor diameter, median (range) 25 mm (6 to 50 mm)	SBRT patients, N (%) 57 (100) SBRT dosing, N (%) 15 Gy x 3 fx: 57 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Louie, 2016[238] Surgery *13,598* KQ 7 Fair	STS-GTS Database (Society of Thoracic Surgeons Database) U.S. 2009-2013 Patients with c-stage 1-2 NSCLC undergoing primary lobectomy performed using VATS or robotic approach, but not converted to open procedures or combined with chemotherapy or radiation therapy, at high-volume centers Followup, median (range) NR Funding source NR	Age, median (IQR) Total: 68.0 yrs (61.0-75.0 yrs) Robotic L: 69.0 yrs (61.0-75.0 yrs) VATS L: 68.0 yrs (61.0-75.0 yrs) Male, N (%) Total: 5,857 (43.1) Robotic L: 527 (43.2) VATS L: 5,330 (43.1) Race/ethnicity NR Comorbidities COPD Total: 4,497 (33.1) Robotic L: 425 (34.8) VATS L: 4,072 (32.9) Ever smoker Total: 11,339 (83.4) Robotic L: 985 (80.7) VATS L: 10,354 (83.6) ASA risk class 1, N (%) Total: 57 (0.4) Robotic L: 7 (0.6) VATS L: 50 (0.4) ASA risk class 2, N (%) Total: 2,528 (18.6) Robotic L: 197 (16.1) VATS L: 2,331 (18.8)	Stage, N (%) cT1aN0 Total: 6,095 (44.8) Robotic L: 515 (42.2) VATS L: 5,580 (45.1) cT1bN0 Total: 3,481 (25.6) Robotic L: 328 (26.9) VATS L: 3,153 (25.5) cT2aN0 Total: 2,655 (19.5) Robotic L: 269 (22.0) VATS L: 2,386 (19.3) cT2bN0 Total: 636 (4.7) Robotic L: 51 (4.2) VATS L: 585 (4.7) cT1aN1 Total: 196 (1.4) Robotic L: 16 (1.3) VATS L: 180 (1.5) cT1bN1 Total: 196 (1.4) Robotic L: 15 (1.2) VATS L: 181 (1.5) cT2aN1 Total: 240 (1.8) Robotic L: 18 (1.5) VATS L: 222 (1.8) cT2bN1 Total: 99 (0.7) Robotic L: 8 (0.7) VATS L: 91 (0.7)	Surgical approach, N (%) Robotic L: 1,220 (*9.0*) VATS L: 12,378 (*91.0*)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Louie, 2016[238] (continued)		ASA risk class 3, N (%) Total: 10,037 (73.8) Robotic L: 932 (76.4) VATS L: 9,105 (73.6) ASA risk class 4, N (%) Total: 969 (7.1) Robotic L: 84 (6.9) VATS L: 885 (7.1) ASA risk class 5, N (%) Total: 3 (0.0) Robotic L: 0 (0) VATS L: 3 (0.0)	TNM edition(s) NR Histology, N (%) NR Tumor size, N (%) NR	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Ma, 2017[269] SBRT/SABR N=155 patients (159 tumors) KQ 7 Fair	RPCI database U.S. 2007-2015 Patients receiving definitive single-fx or triple-fx SBRT for peripheral NSCLC, but not participating in the RTOG 0915 clinical trial Followup, median 22.2 mos Funding source Private	Age, median (IQR) Total: 76.3 yrs (70.5 to 82.3 yrs) Single-fx SBRT: 76.4 yrs (70.6 to 82.5 yrs) Triple-fx SBRT: 76.2 yrs (70.1 to 82.0 yrs) Male, N (%) Total: *77 (48.4)* Single-fx SBRT: 30 (46) Triple-fx SBRT: 47 (50) Race/ethnicity NR Comorbidities Medically operable, n (%) Total: *42 (26.4)* Single-fx SBRT: 21 (32) Triple-fx SBRT: 21 (22) Medical inoperable, n (%) Total: *117 (73.6)* Single-fx SBRT: 44 (68) Triple-fx SBRT: 73 (78) Smoking history Median pack-years (IQR): 50 (40-75) <50 pack-years, n (%) Total: 57 *(35.8)* Single-fx SBRT: 27 (42) Triple-fx SBRT: 30 (32)	Stage, N (%) Stage 1A Total: *120 (75.5)* Single-fx SBRT: 54 (83) Triple-fx SBRT: 66 (70) Stage 1B Total: *35 (22.0)* Single-fx SBRT: 10 (15) Triple-fx SBRT: 25 (27) Stage T2a Total: *24 (15.1)* Single-fx SBRT: 1 (2) Triple-fx SBRT: 1 (1) Stage T2b Total: *2 (1.3)* Single-fx SBRT: 0 (0) Triple-fx SBRT: 2 (2) TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma Total: *69 (43.4)* Single-fx SBRT: 34 (52) Triple-fx SBRT: 35 (37) Squamous cell Total: *64 (40.3)* Single-fx SBRT: 25 (38) Triple-fx SBRT: 39 (41) Other Total: *6 (3.8)* Single-fx SBRT: 1 (2) Triple-fx SBRT: 5 (5)	SBRT patients, N (%) 155 (100) SBRT dosing, N (%) 30 Gy x 1 fx (median dose of 30 Gy): 65 *(40.9)* 48-60 Gy x 3 fx (median dose of 60 Gy): 94 *(59.1)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Ma, 2017[269] (continued)		≥50 pack-years, n (%) Total: 96 *(60.4)* Single-fx SBRT: 34 (52) Triple-fx SBRT: 62 (66) NA Total: 6 *(3.8)* Single-fx SBRT: 4 (6) Triple-fx SBRT: 2 (2)	NA Total: *20 (12.6)* Single-fx SBRT: 5 (8) Triple-fx SBRT: 15 (16) Tumor size, median (IQR) Total: 2.1 cm (1.5 to 3 cm) Single-fx SBRT: 2 cm (1.5 to 3 cm) Triple-fx SBRT: 2.2 cm (1.5 to 3 cm)	
Maeda, 2010[191] Surgery N=734 KQ 6 Fair	NA Japan 1994-2003 Patients with p-stage I NSCLC with tumors up to 3 cm in maximum dimension and who underwent complete resection, but no pre- or post-operative chemotherapy or radiotherapy Followup, median NR Funding source Government, university	Age, median (range) Age <65 yrs: 371 *(52.0)* Age ≥65 yrs: 342 *(48.0)* Male, N (%) 385 *(54)* Race/ethnicity NR Comorbidities, N (%) Smoking status Nonsmoker: 318 *(44.6)* Current or former smoker: 395 *(55.4)*	Stage, N (%) Overall with Stage 1: 605 *(84.9)* Stage 1A: *357 (50.1)* Stage 1B: *248 (34.8)* TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 569 *(79.8)* Squamous cell carcinoma: 104 *(14.6)* Large cell carcinoma: 27 *(3.8)* Adenosquamous carcinoma: 9 *(1.3)* Pleomorphic carcinoma: 4 *(0.56)* Tumor size, N (%) ≤20 mm: 393 *(55.1)* >20 mm: 320 *(44.9)*	Surgical approach, N (%) L: 616 *(86.4)* S or W: 97 *(13.6)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Maeda, 2012[184] Surgery N=1,074 KQ 6 Fair	NA Japan 1992-2007 Consecutive patients receiving complete surgical resection by lobectomy or systematic lymph node dissection for c-stage 1A NSCLC adenocarcinoma Followup, median 57 mos Funding source Government, other not disclosed	Age, N (%) <65 yrs: 562 (53) >65 yrs: 508 (47) Male, N (%) 499 (47) Race/ethnicity NR Comorbidities, N (%) <u>Smoking status</u> Never: 528 *(49.3)* Ever: *543 (50.7)* <u>Smoking history</u> No pack-years: 528 *(49.3)* 0 ≤ pack-years ≤ 10: 75 *(7.0)* 10 < pack-years ≤ 20: 74 *(6.9)* 0 ≤ pack-years ≤ 20: 677 (63) 20 < pack-years ≤ 40: 182 *(17.0)* 40 < pack-years ≤ 60: 126 *(11.8)* Pack-years >60: 85 *(7.9)* Pack-years >20: 393 (37)	Stage, N (%) c-stage 1A: 1,070 (100) TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 1,074 (100) Well-differentiated histology: 456 (43) Moderately/poorly differentiated histology: 614 (57) Tumor size, N (%) <2.0 cm (T1a): 703 (66) 2.1 to 3.0 cm (T1b): 367 (34)	Surgical approach, N (%) L: 1,074 (!00)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Mathieu, 2015[260] SBRT/SABR N=45 KQ 7 Fair	NA Canada 2010-2013 Patients with biopsy-confirmed stage 1 NSCLC (T1-T2aN0M0), Karnofsky performance status ≥60, and medical inoperability because of poor pulmonary function, medical comorbidities, or surgery refusal, but no prior thoracic radiation or cancer in last 5 yrs Followup, median 41 mos Funding source NR	Age, median (range) 77 yrs (60 to 94 yrs) Male, N (%) 17 (38) Race/ethnicity NR Comorbidities, N (%) Charlson Comorbidity Index Score=0-2: 4 (9) Score=3-4: 24 (53) Score >4: 17 (38) Smoking pack-years, median (range) 45 (0-100)	Stage, N (%) T1a: 19 (42) T1b: 17 (38) T2a: 9 (20) TNM edition(s) NR Histology, N (%) Adenocarcinoma: 25 (56) Other: 4 (9) Squamous cell: 14 (31) Large cell: 2 (4) Gross tumor volume, median (range) 7.9 mL (0.5 to 35.9 mL)	SBRT patients, N (%) 45 (100) SBRT dosing 60 Gy x 3 fx: 32 (71) 50 Gy x 4 fx: 7 (16) 50 Gy x 5 fx: 6 (13)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Matsuo, 2014[198] SBRT/SABR N=115 KQs 6, 7 Fair	Databases maintained by Departments of Radiation Oncology & Thoracic Surgery of Kyoto University Hospital Japan 2003-2009 Consecutive patients with histological confirmation of c-Stage I NSCLC ≤50 mm who underwent SBRT because of medical comorbidities Followup, median 6.7 yrs Japan Society for the Promotion of Science	Age, median (range) 77 yrs (56 to 88 yrs) Male, N (%) 83 (72.17) Charlson Comorbidity Index score, median (range) 2 (0 to 8) Race/ethnicity NR	Stage, N (%) c-stage I: 115 (100) TNM edition(s) NR Histology, N (%) Adenocarcinoma: 58 (*50.43*) Squamous cell carcinoma: 41 (*35.65*) Large cell carcinoma: 4 (*3.48*) Others: 12 (*10.43*) Tumor diameter, median (range) 25 mm (10 mm to 45 mm)	SBRT patients, N (%) 115 (*63.89*) SBRT dosing, N (%) 48 Gy x 4 fx: *108* (*93.91*) 60 Gy x 8 fx: 5 (*4.35*) 56 Gy x 4 fx: 1 (*0.09*) 60 Gy x 4 fx: 1 (*0.09*)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Mediratta, 2014[177] Surgery N=540 KQs 6, 7 Good	NA U.K. 2001-2012 Patients with Stage 1 adenocarcinoma or squamous carcinoma who had undergone a potentially curative wedge resection Followup, median 1,012 days Funding source NR	Age, median (IQR) 72 yrs (64 to 77 yrs) Male, N (%) *274 (51)* Race/ethnicity NR Comorbidities COPD, N (%) 114 (21) Emphysema, N (%) 21 (4) Smoking status, N (%) Current: 128 (24) Former: 305 (57) Never: 107 (19) Pack-year history, median (IQR) 25 (23.2 to 26.7)	Stage, N (%) T stage 1: 411 (76) T stage 2: 129 (24) N stage 0: 540 (100) TNM edition(s) NR Histology, N (%) Adenocarcinoma: 400 (74) Squamous carcinoma: 140 (26) Tumor diameter, median (IQR) 20.5 mm (15 to 25 mm)	Surgical approach, N (%) W: 540 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Melvan, 2015[243] Surgery N=127,366 (of 215,645 total) KQ 7 Fair	NCDB U.S. 2003-2011 Patients with one lifetime NSCLC diagnosis that underwent surgical resection, or such cases where the reported tumor was the first of multiple diagnoses Followup NR Funding source Government, university	Age, mean (SD) NR Age, N (%) NR Male, N (%) NR Race/ethnicity NR Comorbidities NR	Analytic stage, N (%)† 0 to 1: 127,366 (62.7) II: 35,679 (17.6) III: 31,090 (15.3) IV: 8,938 (4.4) Missing: 12,572 (5.83) TNM edition(s) NR Histology, N (%) NR Tumor size NR	Surgical approach, N (%) W, <1 lobe: NR S: NR L: NR P: NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Nagata, 2015[205] SBRT/SABR N=169 KQs 6, 7 Fair	JCOG Japan 2004-2008 Histologically or cytologically proven NSCLC (clinical T1N0M0) staged by at least bronchoscopy and CT; ECOG performance status 0 to 2; age ≥20 years; PaO2 ≥60 torr (under room air); FEV 1.0 ≥700 mL; no history of radiation therapy, chemotherapy, or continuous systemic steroid therapy; classified as either operable or inoperable by surgeons, study coordinator, and group coordinator; dose constraints of all organs at risk expected to be fulfilled; no apparent or active pneumonitis, pulmonary fibrosis, infectious disease, severe psychological disorder, or synchronous or metachronous cancer within last 5 yrs Followup, median NR Funding source Government, private (nonprofit organization)	Age, N (%) <75 yrs: *59 (34.9)* 76-80 yrs: *61 (36.1)* 81 yrs: *49 (29)* Male, N (%) *122 (72.2)* White, N (%) 0 (0) Comorbidities, N (%) Smoking history (no further details provided): *130 (76.9)*	Stage, N (%) NR TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: *90 (53.3)* Squamous cell carcinoma: *61 (36.1)* Other: *18 (10.7)* Tumor size, median (range) 21 mm (9 to 30 mm)	SBRT patients, N (%) 169 (100) SBRT dosing, N (%) Prescribed dose of 48 Gy x 4 fx: NR Planned dose constraint for lung of 40 Gy x 4 fx: NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Nakamura, 2015[173] Surgery N=1,336 KQ 6 Fair	NA Japan 1983-2012 Patients undergoing resection of lung cancer in the hospital Followup, mean (SD) (range) 37 mos (34 mos) (1 to 219 mos) Funding source NR	Age, N (%) <69: 553 (*54.4*) ≥69: 463 (*45.6*) Male, N (%) 640 (*63.0*) Race/ethnicity NR Comorbidities NR	Stage, N (%) (for N analyzed=1016) p-stage 1A: 402 (39.6) p-stage 1B: 220 (21.7) p-stage 2A: 92 (9.1) p-stage 2B: 71 (6.99) p-stage 3A: 192 (18.9) p-stage 3B: 10 (0.98) p-stage 4: 29 (2.9) TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 660 (*67.0*) Nonadenocarcinoma: 356 (*35.0*) Tumor size, N (%) NR	Surgical approach, N (%) L: 1,016 (*76.0*) SLR: 174 (*13.0*) P: 106 *(8.0)* Combined resection: 40 (*3.0*)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Nyman, 2016[267] SBRT/SABR N=49 KQ 7 Fair	SPACE Norway, Sweden 2007-2011 Patients with Stage 1 T1-2N0M0 NSCLC (max tumor diameter ≤6 cm and no central tumor growth adjacent to trachea, main bronchus, or esophagus) who were medically inoperable or refused surgery and had WHO performance status score 0-2, but no prior malignancy in last 5 yrs, history of thoracic radiotherapy, or current neoadjuvant or adjuvant chemotherapy or targeted drugs Followup, median 37 mos Funding source Private	Age, mean (range) 73 yrs (57 to 86 yrs) Male, N (%) 22 (45) Race/ethnicity NR Comorbidities, N (%) COPD: 35 (71)	Stage, N (%) Clinical T1: 26 (53) Clinical T2: 23 (47) TNM edition(s) 6th edition Histology, N (%) Adenocarcinoma: 16 (33) Squamous cell: 9 (18) NSCLC NOS: 5 (10) Not performed: 18 (37) Missing: 1 (2) Tumor size, mean (SD) NR	SBRT patients, N (%) 49 (100) SBRT dosing, N (%) 66 Gy x 3 fx: 49 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Okada, 2006[193] Surgery N=567 KQ 6 Fair	NA Japan 1992-2001 Patients with a clinical T1N0M0 peripheral lung tumor of 2 cm or less in every dimension, located in the outer one third of the lung on CT scan, and able to tolerate a lobectomy as evaluated by cardiopulmonary functional tests, no history of previously treated cancer Followup, median (range) Total: 72 mos (22 to 158 mos) L: 71 mos (22 to 158 mos) SLR: 72 mos (29 to 155 mos) Funding source NR	Age, mean (range) SLR: 63.2 yrs (35 to 82 yrs) L: 64.0 yrs (38 to 84 yrs) Male, N (%) *313 (55.2)* Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) c-stage T1N0M0: 567 (100) TNM edition(s) NR Histology, N (%) Adenocarcinoma: *505 (89)* SCC: *57 (10.1)* Adenosquamous: *5 (0.9)* Tumor size, mean (range) SLR: 15.7 mm (5 to 20 mm) L: 16.2 mm (8 to 20 mm) Tumor size, N (%) 0 to 10 mm: *57 (10.1)* 11 to 20 mm: *510 (89.9)* Tumor size, mean (range) SLR: 15.7 mm (5 to 20 mm) L: 16.2 mm (8 to 20 mm) Tumor size, N (%) 0 to 10 mm: *57 (10.1)* 11 to 20 mm: *510 (89.9)*	Surgical approach, N (%) Assigned L: 262 (46.2) SLR: 305 (53.8) Actual S: 230 *(40.6)* W: *32 (5.6)* L: *303 (48.9)* T: 2 *(0.4)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Puri, 2014[242] Surgery N=1,066 KQs 6, 7 Fair	ACOSOG z4032, z4033 U.S. 2000-2010 Patients with c-stage 1 NSCLC Followup NR Funding source NR	Age NR Male, N (%) NR Race/ethnicity NR Comorbidities NR	Stage, N (%) NR TNM edition(s) NR Histology, N (%) NR Tumor size, N (%) NR	Surgical approach, N (%) L: *782 (73.4)* SLR or other resection: *282 (26.5)* VATS approach: *328 (30.8)* Open approach: *738 (69.2)*
Puri, 2015[252] Surgery N=111,731 KQ 7 Fair	NCDB U.S. 1998-2010 Patients with c-stage I NSCLC (tumor size ≤5 cm) who received treatment with either surgical resection or SBRT, but not neoadjuvant therapy or palliative treatment Followup, mean 36.5 mos Funding source Government	Age, mean (SD) Surgical resection (full set): 67.9 yrs (9.9 yrs) SLR (full set): 70.1 yrs (9.3 yrs) Male, N (%) Surgical resection (full set): *52,393 (46.9)* SLR (full set): *11,622 (44.2)* White, N (%) Surgical resection (full set): 110,560 (90)	Stage, N (%) <u>Clinical T1</u> Surgical resection (full set): 80,184 (71.8) SLR (full set): NR <u>Clinical T2</u> Surgical resection (full set): 31,547 (28.2) SLR (full set): NR TNM edition(s) NR Histology, N (%) NR	Surgical approach, N (%) L: 82,749 *(74.1)* W: 22,010 *(19.7)* S: 4,282 *(3.8)* P: 2,690 *(2.4)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Puri, 2015[252] (continued)		SLR (full set): 24,016 (91.3) Charlson/Deyo Comorbidity Score, N (%) <u>Score=0</u> Surgical resection (full set): 42,761 *(50.6)* SLR (full set): 9,087 *(45.5)* <u>Score=1</u> Surgical resection (full set): 30,401 *(36)* SLR (full set): 7,662 *(38.4* <u>Score=2</u> Surgical resection (full set): 11,342 *(13.4)* SLR (full set): 3,211 *(12.2))*	Tumor size, mean (SD) Surgical resection (full set): 24.1 mm (10.7 mm) SLR (full set): 19.3 mm (9.0 mm)	
Razi, 2016[180] Surgery N=1,640 KQ 6 Fair	SEER U.S. 1998-2007 Patients aged ≥75 y who underwent lobectomy or SLR (W or S), but not chemotherapy or radiotherapy, for Stage IA (T1a/b, N0, M0) NSCLC, restricted by histology to either squamous cell or adenocarcinoma Followup, median NR Funding source NR	Age, median 78 yrs Age, mean (SE) L/Bi-L: 78.7 yrs (0.10 yrs) S: 79.4 yrs (0.35 yrs) W: 79.7 yrs (0.17 yrs) Male, N (%) L/Bi-L: *502* (47.8) S: *48* (40.3) W: *222* (47.2) White, N (%) L/Bi-L: 951 (90.5) S: 108 (90.8) W: 427 (90.9) Comorbidities, N (%) NR	Stage, N (%) c-stage 1A: 1,640 (100) TNM edition(s) 7th edition Histology, N (%) <u>Adenocarcinoma</u> L/Bi-L: 657 (62.5) S: 71 (59.7) W: 254 (54) <u>Squamous cell carcinoma</u> L/Bi-L: 394 (37.5) S: 48 (40.3) W: 216 (46)	Surgical approach, N (%) L/Bi-L: 1,051 *(64.1)* S: 119 *(7.3)* W: 470 *(28.6)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Razi, 2016[180] (continued)			Tumor size, mean (SE) L/Bi-L: 2.2 cm (0.02 cm) S: 1.9 cm (0.06 cm) W: 1.9 cm (0.03 cm)	
Robinson, 2013[266] SBRT/SABR N=78 KQ 7 Fair	NA U.S. 2004-2008 Patients with pathologically confirmed Stage 1 NSCLC and receiving SBRT with BED ≥100 Gy Followup, median 50.3 mos Funding source NR	Age, median (range) 76 yrs (31 to 93 yrs) Male, N (%) *44 (56.4)* White, N (%) 68 (87.2) Charlson Comorbidity Index, median (range) Raw score: 4 (2 to 10) Age-adjusted score: 7 (3 to 12) ACE-27 Comorbidity Index, median (range) 2 (0 to 3)	Clinical Stage, N (%) T1a: 36 (46.2) T1b: 20 (25.6) T2a: 19 (24.4) T2b: 3 (3.8) T3: 0 (0) TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 36 (46.2) Squamous cell: 25 (32.1) NSCLC NOS: 16 (20.5) Other/unknown: 1 (1.3) Maximal tumor size, median (range) 2 cm (1.1 to 6 cm)	SBRT patients, N (%) 78 (100) SBRT dosing, N (%) 54 Gy x 3 fx: 68 (87.2) 50 Gy x 5 fx: 4 (5.1) 45 Gy x 3 fx: 6 (7.7)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2014[258] SBRT/SABR N=79 KQ 7 Fair	NA U.S. 2005-2010 Patients with biopsy-proven or clinically diagnosed T1-2N0M0 NSCLC and treated with TomoTherapy helical SBRT Followup, median 27 mos Funding source NR	Age, median (range) 73 (27 to 92) Male, N (%) 33 (42) Race/ethnicity NR Comorbidities NR	Stage, N (%) T1a: 59 (75) T1b: 20 (25) TNM edition(s) NR Histology, N (%) Adenocarcinoma: 22 (28) Squamous cell: 18 (23) NSCLC NOS: 22 (28) No histology: 17 (21) Tumor diameter, mean (range) 2.3 cm (0.5 to 6.0 cm)	SBRT patients, N (%) 79 (100) SBRT dosing, N (%) 12 Gy x 4 fx: 20 (*25.3*) 12 Gy x 5 fx: 59 (*74.7*)
Rosen, 2014[244] Surgery N=66,283 (of 119,146 total) KQ 7 Fair	NCDB U.S. 2004-2009 All patients over the age of 19 years diagnosed with NSCLC and undergoing surgical resection (W, S, L/Bi-L, extended L/Bi-L, P) Followup, median (range) NR Funding source University	Age, median (range) NR Male, N (%) NR Race/ethnicity NR Comorbidities NR	Stage, N (%) p-stage 1: 66,283 (*55.6*) p-stage 2: 17,434 (*14.6*) p-stage 3: 15,610 (*13.1*) p-stage 4: 4,196 (*3.5*) Unknown: 15,623 (*13.1*) TNM edition(s) NR Histology, N (%) NR Tumor size, N (%) NR	Surgical approach, N (%) W: NR S: NR L/Bi-L: NR Extended L/Bi-L: NR P: NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2016[185] Surgery & SBRT/SABR Total N=15,433 PSM subset N=3,562 <u>Primary analyses (i.e., patients with Charlson-Deyo score=0)</u> Total: 15,433 L (full selected set): 13,652 L (PSM subset): 1,781 SBRT: 1,781 <u>Secondary analyses (i.e., patients unselected based on Charlson-Deyo score)</u> Total: 29,267 L (unselected): 29,032 L (unselected PSM subset) 235 SBRT (unselected PSM subset): 235 KQs 6, 7 Good	NCDB U.S. 2008-2012 <u>Primary analysis</u> Patients aged >20 years, diagnosed with invasive c-stage I NSCLC and free of comorbidities (i.e., AJCC overall stage group of I, IA, or IB, and T stage of T1, T1a, T1b, or T2a, tumor size ≤5 cm, N stage of 0, and M stage of 0) and treated with lobectomy or SBRT, but not chemotherapy or radiotherapy <u>Secondary analysis</u> Patients aged >20 years diagnosed with invasive c-stage I NSCLC, as diagnosed for the primary analysis, with or without comorbidities who underwent SBRT after refusing surgery, but not chemotherapy or radiotherapy Followup, median Total: *30.1 mos* Lobectomy: 31.6 mos SBRT: 28.6 mos Funding source University	Age, median (range) <u>Primary analysis</u> Unmatched cohort <u>Mean (SD)</u> L: 66.6 (10.2) SBRT: 75.5 (9.1) Propensity-matched subset <u>Mean (SD)</u> L (PSM subset): 74.8 (7.8) SBRT: 75.5 (9.1) <u>Secondary analysis</u> Unmatched cohort <u>Mean (SD)</u> L (unselected): 66.9 (9.7) SBRT (unselected PSM subset): 75.3 (8.9) Propensity-matched subset <u>Mean (SD)</u> L (unselected PSM subset) 75.0 (8.2) SBRT (unselected PSM subset): 75.3 (8.9) Male, N (%) <u>Primary analysis</u> Unmatched cohort L: 6,111 (45) SBRT: 767 (43)	Stage, N (%) <u>Primary analysis</u> Unmatched cohort <u>Clinical T1</u> L: 9,543 (70) SBRT: 1,371 (77) <u>Clinical T2</u> L: 4,109 (30) SBRT: 410 (23) Propensity-matched subset	Surgical approach, N (%) Primary analysis <u>Unmatched cohort</u> L: 13,652 *(88.5)* <u>Propensity-matched subset</u> L: 1,781 *(50)* Secondary analysis <u>Unmatched cohort</u> L: 29,032 *(99.2)* <u>Propensity-matched subset</u> L: 235 *(0.8)* SBRT patients, N (%) Primary analysis <u>Unmatched cohort</u> 1,781 *(11.5)* <u>Propensity-matched subset</u> 1,7812 *(50)* Secondary analysis <u>Unmatched cohort</u> SBRT: 235 (100) <u>Propensity-matched subset</u> SBRT: 235 (100) SBRT dosing, N (%) 100-200 Gy x 3-5 fx: 1,781 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2016[185] (continued)		Propensity-matched cohort L (PSM subset): 777 (44) SBRT: 767 (43) Secondary analysis Unmatched cohort L (unselected): 13,713 (47) SBRT (unselected PSM subset): 95 (40) Propensity-matched cohort L (unselected PSM subset) 84 (36) SBRT (unselected PSM subset): 95 (40) White, N (%) Primary analysis Unmatched cohort L: 11,938 (87) SBRT: 1,616 (91) Propensity-matched cohort L (PSM subset): 1,610 (90) SBRT: 1,616 (91) Secondary analysis Unmatched cohort L (unselected): 25,573 (88) SBRT (unselected PSM subset): 208 (89)	Clinical T1 L (PSM subset): 1,374 (77) SBRT: 1,371 (77) Clinical T2 L (PSM subset): 407 (23) SBRT: 410 (23) Secondary analysis Unmatched cohort	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2016[185] (continued)		Propensity-matched cohort L (unselected PSM subset) 212 (90) SBRT (unselected PSM subset): 208 (89) Comorbidities, N (%) Primary analysis Charlson-Deyo score: 0 (0) for all patients in the unmatched and propensity-matched cohorts Secondary analysis, N (%) Unmatched cohort Charlson-Deyo score=0 L (unselected): 13,652 (47) SBRT (unselected PSM subset): 157 (67) Charlson-Deyo score=1 L (unselected): 10,877 (37) SBRT (unselected PSM subset): 50 (21) Charlson-Deyo score=2+ L (unselected): 4,503 (16) SBRT (unselected PSM subset): 28 (12) Propensity-matched subset Charlson-Deyo score=0 L (unselected PSM subset) 156 (66) SBRT (unselected PSM subset): 157 (67)	Clinical T1 L (unselected): 20,555 (71) SBRT (unselected PSM subset): 174 (74) Clinical T2 L (unselected): 8,477 (29) SBRT (unselected PSM subset): 61 (26) Propensity-matched cohort Clinical T1 L (unselected PSM subset) 175 (74) SBRT (unselected PSM subset): 174 (74) Clinical T2 L (unselected PSM subset) 60 (26) SBRT (unselected PSM subset): 61 (26)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2016[185] (continued)		Charlson-Deyo score=1 L (unselected PSM subset) 52 (22) SBRT (unselected PSM subset): 50 (21) Charlson-Deyo score=2+ L (unselected PSM subset) 27 (11) SBRT (unselected PSM subset): 28 (12)	TNM edition(s) 6th & 7th editions Histology, N (%) Primary analysis, N (%) Unmatched cohort Adenocarcinoma L: 9,379 (69) SBRT: 850 (48) Squamous cell carcinoma L: 3,502 (26) SBRT: 583 (33) Large cell carcinoma L: 317 (2) SBRT: 17 (1)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2016[185] (continued)			Other L: 454 (3) SBRT: 331 (19) Propensity-matched cohort Adenocarcinoma L: 886 (50) SBRT: 850 (48) Squamous cell carcinoma L: 646 (36) SBRT: 583 (33) Large cell carcinoma L: 21 (1) SBRT: 17 (1) Other L: 228 (13) SBRT: 331 (19) Secondary analysis, N (%) Unmatched cohort Adenocarcinoma L (unselected): 18,200 (63) SBRT (unselected PSM subset): 125 (53) Squamous cell carcinoma L (unselected): 9,130 (31) SBRT (unselected PSM subset): 69 (29) Large cell carcinoma L (unselected): 797 (3) SBRT (unselected PSM subset): *2 (0.9)*	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2016[185] (continued)			Other L (unselected): 905 (3) SBRT (unselected PSM subset): 39 (17) Propensity-matched cohort Adenocarcinoma L (unselected PSM subset) 125 (53) SBRT (unselected PSM subset): 125 (53) Squamous cell carcinoma L (unselected PSM subset) 61 (26) SBRT (unselected PSM subset): 69 (29) Large cell carcinoma L (unselected PSM subset) *4 (1.7)* SBRT (unselected PSM subset): *2 (0.9)* Other L (unselected PSM subset) 45 (19) SBRT (unselected PSM subset): 39 (17)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Rosen, 2016[185] (continued)			Tumor size, mean (SD) <u>Primary analysis</u> Unmatched cohort L: 25.4 mm (10.5 mm) SBRT: 23.8 mm (9.3 mm) <u>Propensity-matched subset</u> L: 23.7 mm (10.0 mm) SBRT: 23.8 mm (9.3 mm) <u>Secondary analysis</u> <u>Unmatched cohort</u> L (unselected): 25.1 mm (10.5 mm) SBRT (unselected PSM subset): 24.0 mm (9.3 mm) <u>Propensity-matched subset</u> L (unselected PSM subset) 23.6 mm (9.9 mm) SBRT (unselected PSM subset): 24.0 mm (9.3 mm)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Samson, 2015[240] Surgery N=55,653 KQs 6, 7 Fair	NCDB U.S. 2000-2012 Overall and PSM samples: Patients diagnosed with c-stage I NSCLC undergoing surgical resection Single-center sample: Patients diagnosed with c-stage I NSCLC undergoing surgical resection Followup, median (range) NR Funding source Government	Age, median (range) PSM analysis Early surgery: 68.7 (9.8) Delayed surgery: 68.8 (9.7) Single-center analysis Early surgery: 66.0 (10.1) Delayed surgery: 66.9 (9.7) Male, N (%) PSM analysis Male Early surgery: 6,505 (48.1) Delayed surgery: 6,564 (48.6) Single-center analysis Female Early surgery: 276 (53) Delayed surgery: 232 (52) White, N (%) PSM analysis Early surgery: 11,765 (87.1) Delayed surgery: 11,787 (87.2) Single-center analysis Early surgery: 466 (89) Delayed surgery: 368 (82)	Stage, N (%) PSM analysis AJCC clinical T1 Early surgery: 8,608 (63.7) Delayed surgery: 8,656 (64.1) AJCC clinical T2 Early surgery: 4,903 (36.3) Delayed surgery: 4,855 (35.9) Single-center analysis AJCC clinical T1 Early surgery: 338 (65) Delayed surgery: 342 (76) TNM edition(s) NR Histology, N (%) Malignant cytologic diagnosis: 568 (1.0)	Surgical approach, N (%) PSM analysis Total: 27,022 Early surgery: 13,511 Delayed surgery: 13,511 Single-center analysis Total: 971 Early surgery: 522 Delayed surgery: 449

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Samson, 2015[240] (continued)		Charlson Comorbidity Index, N (%) PSM analysis Score=0 Early surgery: 6,459 (47.8) Delayed surgery: 6,490 (48.0) Score=1 Early surgery: 5,011 (37.1) Delayed surgery: 4,895 (36.2) Score=2+ Early surgery: 2,041 (15.1) Delayed surgery: 2,126 (15.7) Adult Comorbidity Evaluation, N (%) Single-center analysis Score=0 Early surgery: 83 (16) Delayed surgery: 37 (8) Score=1 Early surgery: 211 (40) Delayed surgery: 156 (35) Score=2	Tumor size in mm, mean (SD) PSM analysis Size Early surgery: 30.1 (22.6) Delayed surgery: 30.5 (21.3) Single-center analysis NR	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Samson, 2015[240] (continued)		Early surgery: 125 (24) Delayed surgery: 125 (28) Score=3 Early surgery: 63 (12) Delayed surgery: 79 (18) Pulmonary hypertension Single-center analysis, N (%) Early surgery: 3 (0.6) Delayed surgery: 7 (1.6) Smoking status Single-center analysis, N (%) Current smokers Early surgery: 170 (33) Delayed surgery: 164 (37) Former smokers Early surgery: 302 (58) Delayed surgery: 244 (54) Never smokers Early surgery: 50 (10) Delayed surgery: 41 (9)		

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Samson, 2017[245] Surgery N=146,908 KQ 7 Fair	NCDB U.S. 2004-2013 c-stage I NSCLC patients who underwent operation within 1 yr of diagnosis but no preoperative chemotherapy or radiotherapy Followup, median NR Funding source Government	Age, mean Nonanatomical vs. anatomical resection (total sample) *68.75* yrs Early vs. delayed resection *68.3* yrs R0 vs. ≥R1 resection *68.5* yrs <10 vs. ≥10 lymph nodes *67.9* yrs Male, N (%) Nonanatomical vs. anatomical resection (total sample) *67,453 (45.9)* Early vs. delayed resection *66,604 (45.9)* R0 vs. ≥R1 resection *66,486 (45.9)* <10 vs. ≥10 lymph nodes *62,578 (45.8)* White, N (%) Nonanatomical vs. anatomical resection (total sample) *130,697 (89)* Early vs. delayed resection *129,131 (89)* R0 vs. ≥R1 resection *128,929 (89)* <10 vs. ≥10 lymph nodes *121,413 (88.9)*	Clinical Stage 1B, N (%) Nonanatomical vs. anatomical resection (total sample) *41,546 (28.3)* Early vs. delayed resection *40,974 (28.2)* R0 vs. ≥R1 resection *40,894 (28.2)* <10 vs. ≥10 lymph nodes *38,373 (28.1)* TNM edition(s) NR Histology, N (%) NR Tumor size, mean Nonanatomical vs. anatomical resection (total sample) *23.5 mm* Early vs. delayed resection *26.25 mm*	Surgical approach, N (%) Overall W: 29,649 (20.2) S: 6,212 (4.2) Lobectomy: 107,687 (73.3) Pneumonectomy: 3,360 (2.3) Nonanatomical vs. anatomical resection W: 29,649 (20.2) S: 6,212 (4.2) Lobectomy: 107,687 (73.3) Pneumonectomy: 3,360 (2.3) Early vs. delayed resection W: *29,367 (20.2)* S: *6,125 (4.2)* Lobectomy: *106,291 (73.3)* Pneumonectomy: *3,307 (2.3)* R0 vs. ≥R1 resection W: *28,908 (19.9)* S: *6,132 (4.2)* Lobectomy: *106,610 (73.6)* Pneumonectomy: *3,271 (2.6)* <10 vs. ≥10 lymph nodes W: *28,161 (20.6)* S: *5,750 (4.2)* Lobectomy: *99,622 (72.9)* Pneumonectomy: *3,079 (2.3)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Samson, 2017[245] (continued)		Charlson/Deyo comorbidity score, N (%) Nonanatomical vs. anatomical resection (total sample) Charlson/Deyo score ≥2: *20,940 (13.9)* Early vs. delayed resection (N analyzed=145,090) Charlson/Deyo score ≥2: *20,302 (14)* R0 vs. ≥R1 resection Charlson/Deyo score ≥2 (N analyzed=144,921): *20,245 (14)* <10 vs. ≥10 lymph nodes (N analyzed=136,612) Charlson/Deyo score ≥2: *19,167 (14)*	R0 vs. ≥R1 resection *28.35 mm* <10 vs. ≥10 lymph nodes *26.4 mm* Tumor size, N (%) <2 cm: 3,675 (59.2)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Sawabata, 2011[190] Surgery N=9,083 eligible (of 11,663 total) KQ 6 Fair	Japanese Joint Committee of Lung Cancer Registry (JJCLCR) Japan 2004-2010 Pathological diagnosis of any type of lung cancer at a participating institution, diagnosis obtained in 2004, and treated by surgery Followup, median 2 to 78 mos Funding source NR	Age, median (range) NR Male, N (%) NR Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) c-stage 1A: 6,295 (54) c-stage 1B: 2,788 (23.9) p-stage 1A: 5,611 (48.1) p-stage 1B: 2,398 (20.4) TNM edition(s) 6th & 7th editions Histology, N (%) NR Tumor size, mean (SD) NR	Surgical approach, N (%) NR
Scheel, 2015[170] Surgery N=800 KQs 6, 7 Fair	NR U.S. 2000-2012 Patients who underwent initial resection by lobectomy or SLR of p-stage I NSCLC between January 2000 and December 2012 at Washington University School of Medicine Followup, median (range) NR Funding source Government	Age, mean (SD) NR for overall sample, but range from 64.3-65.5 across surg exp groups Male, N (%) *361 (45.1)* White, N (%) *690 (86.3)* Smoking status, N (%) Never: *96 (12.0)* Past: *421 (52.6)* Current: *283 (35.4)*	Stage, N (%) p-stage I: 800 (100) TNM edition(s) NR Histology, N (%) NR Tumor size, N (%) NR	Surgical approach, N (%) All Resections: 800 L: 638 (79.8) SLR: 162 (20.2)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Schuchert, 2012[248] Surgery N=899 KQ 7 Fair	NA U.S. 1999-2010 Patients with p-stage 1 NSCLC without multicentric disease and undergoing complete anatomic segmentectomy or lobectomy, but not preoperative radiotherapy or chemotherapy Followup, median 37 mos Funding source NR	Age, mean (SD) (range) Total: 69.2 yrs (NR) (22-91 yrs) Anatomic S: 70.0 yrs (8.6 yrs) (40 to 91 yrs) L: 68.4 yrs (10.1 yrs) (22 to 90 yrs) Male, N (%) Total: 427 *(47.5)* Anatomic S: 145 *(47.5)* L: 282 *(47.5)* Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) <u>p-stage 1A</u> Total: 477 *(53.1)* Anatomic S: 187 *(61.3)* L: 290 *(57.5)* <u>p-stage 1B</u> Total: 422 *(46.9)* Anatomic S: 118 *(38.7)* L: 304 *(60.3)* TNM edition(s) 6th edition Histology, N (%) <u>Adenocarcinoma</u> Overall: *487 (54.2)* Anatomic S: 161 (52.8) L: 326 (54.9) <u>Squamous cell</u> Overall: *295 (32.8)* Anatomic S: 96 (31.5) L: 199 (33.5) <u>Other NSCLC</u> Overall: *117 (13.0)* Anatomic S: 48 (15.7) L: 69 (11.6) Tumor size, median (IQR) (range) Overall: NR Anatomic S: 2.0 cm (1.5 to 2.8 cm) (0.2 to 5.0 cm) L: 2.5 cm (1.8 to 4.0 cm) (0.2 to 12 cm)	Surgical approach, N (%) Anatomic S: 305 (33.9) L: 594 (66.1) <u>Open procedure</u> Total: *489 (54.4)* Anatomic S: 120 (39.3) L: 369 (62.1) <u>VATS approach</u> Total: *410 (45.6)* Anatomic S: 185 (60.7) L: 225 (37.9)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Shapiro, 2012[247] Surgery N=4,975 KQ 7 Fair	SEER U.S. 1992-2002 Patients with Stage I NSCLC aged ≥65 years who underwent lobectomy, but no pre-operative chemotherapy or radiotherapy Followup, median NR Funding source Government	Age, N (%) 65-69 yrs: *1,421 (28.6)* 70-74 yrs: *1,662 (33.4)* 75-79 yrs: *1,244 (25)* ≥80 yrs: *648 (13)* Male, N (%) *2,565 (51.6)* White, N (%) *4,348 (87.4)* Comorbidities, N (%) Charlson/Deyo score 0-1, N (%): *4,238 (85.2)* Charlson/Deyo score 2-3, N (%): *479 (9.6)* Charlson/Deyo score ≥4, N (%): *258 (5.2)*	Stage, N (%) NR TNM edition(s) 5th edition Histology, N (%) Adenocarcinoma: *2,205 (44.3)* Bronchioalveolar carcinoma: *219 (4.4)* Squamous carcinoma: *1,631 (32.8)* Large cell carcinoma: *267 (5.4)* Other: *653 (13.1)* Tumor size, N (%) ≤20 mm: *1,473 (29.6)* 21-30 mm: *1,526 (30.7)* 31-50 mm: *1,409 (28.3)* 51-70 mm: *403 (8.1)* ≥71 mm: *164 (3.3)*	Surgical approach, N (%) L: 4,975 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Shirvani, 2012[237] Surgery & SBRT/SABR N=10,923 KQ 7 Fair	SEER-Medicare database U.S. 2001-2007 Patients aged >66 years diagnosed with early-stage (IA-IB) NSCLC without prior or future malignancy within 120 days of index cancer and who were treated with SABR, but not nonstandard therapies (e.g., chemotherapy), reported in the SEER-Medicare cohort demographic Followup, median 3.2 yrs Cancer Prevention & Research Institute of Texas; NCI; and Varian Medical Systems	Age, median 75 yrs <u>Age 66-69, N (%)</u> SLR: 234 (18) SABR: 11 (9) L: 1,408 (22) <u>Age 70-74, N (%)</u> SLR: 362 (28) SABR: 20 (16) L: 2,055 (31) <u>Age 75-79, N (%)</u> SLR: 392 (31) SABR: 29 (23) L: 1,907 (29) <u>Age ≥80, N (%)</u> SLR: 289 (23) SABR: 64 (52) L: 1,161 (18) Male, N (%) SLR: 571 (45) SABR: 49 (40) L: 3,011 (46) White, N (%) SLR: 1,184 (93) SABR: >11 (>90) L: 5,927 (91)	Stage, N (%) NR TNM edition(s) NR Histology, N (%) <u>NSCLC, NOS</u> SLR: 84 (7) SABR: 34 (27) L: 373 (6) <u>Adenocarcinoma</u> SLR: 749 (59) SABR: 53 (43) L: 3,931 (60) <u>Squamous cell carcinoma</u> SLR: 389 (30) SABR: 36 (29) L: 1,982 (30)	Surgical approach, N (%) SLR: 1,277 (11.7) L: 6,531 (58.9) SABR patients, N (%) 124 (1.1) SABR dosing NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Shirvani, 2012[237] (continued)		Charlson Comorbidity Index, N (%) Score=0 SLR: 339 (27) SABR: 28 (23) L: 2,814 (43) Score=1 SLR: 447 (35) SABR: 42 (34) L: 2,042 (31) Score ≥2 SLR: 457 (36) SABR: 54 (44) L: 1,495 (23) Missing Total: 366 (3)	Tumor size, N (%) ≤2.0 cm SLR: 820 (64) SABR: 48 (39) L: 2,723 (42) 2.1-3.0 cm SLR: 316 (25) SABR: 48 (39) L: 2,188 (34) 3.1-5.0 cm SLR: 141 (11) SABR: 28 (23) L: 1,620 (25)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Shirvani, 2014[241] Surgery & SBRT/SABR N=9,093 KQ 7 Fair	SEER-Medicare U.S. 2003-2009 Patients with early-stage, node-negative, pathologically confirmed NSCLC who underwent lobectomy, SLR, or SABR without undergoing any nonstandard therapies Followup, median (range) NR Funding source Government	Age, N (%) <u>66 to 69 yrs</u> L: 1515 (21.0) SLR: 235 (15.7) SABR: 39 (10.2) <u>70 to 74 yrs</u> L: 2182 (30.2) SLR: 415 (27.7) SABR: 71 (18.6) <u>75 to 79 yrs</u> L: 2069 (28.7) SLR: 435 (29.1) SABR: 94 (24.6) <u>≥80 yrs</u> L: 1449 (20.1) SLR: 411 (27.5) SABR: 178 (46.6) Male, N (%) L: 3365 (46.6) SLR: 693 (46.3) SABR: 143 (37.4) White, N (%) L: 6456 (89.5) SLR: 1360 (90.9) SABR: 340 (89.0) Charlson Comorbidity Index, N (%) <u>0</u> L: 4368 (60.5) SLR: 792 (52.9) SABR: 170 (44.5)	Stage, N (%) NR TNM edition(s) NR Histology, N (%) <u>NSCLC, NOS</u> L: 366 (5.1) SLR: 90 (6.0) SABR: 82 (21.5) <u>Adenocarcinoma</u> L: 4371 (60.6) SLR: 866 (57.9) SABR: 178 (46.6) <u>Squamous cell carcinomas</u> L: 2236 (31.0) SLR: 482 (32.2) SABR: >110 (>25) <u>Large cell cancer</u> L: 242 (3.4) SLR: 58 (3.9) SABR: <11 (<5)	Surgical approach, N (%) L: 7,215 (*79.3*) SLR: 1,496 (*16.5*) SABR patients, N (%) 382 (*4.2*) SABR dosing NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Shirvani, 2014[241] (continued)		1 L: 1700 (23.6) SLR: 379 (25.3) SABR: 108 (28.3) ≥ 2 L: 1147 (15.9) SLR: 325 (21.7) SABR: 104 (27.2) COPD L: 4459 (61.8) SLR: 1136 (75.9) SABR: 296 (77.5)	Tumor size by T stage, N (%) T1a (0.0 to 2.0 cm) L: 3169 (43.9) SLR: 964 (64.4) SABR: 153 (40.1) T1b (2.1 to 3.0 cm) L: 2370 (32.8) SLR: 355 (23.7) SABR: 153 (40.1) T2a (3.1 to 5.0 cm) L: 1676 (23.2) SLR: 177 (11.8) SABR: 76 (19.9)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Speicher, 2016[187] Surgery N=39,403 KQ 6 Fair	NCDB U.S. 2003-2006 Patients with c-stage 1A T1N0M0 NSCLC undergoing a lobectomy or SLR without induction therapy Followup, median 6.3 yrs Funding source Government, other unspecified	Age, mean (SD); Median Total: 67.4 yrs (9.8 yrs); 68.0 yrs L: 66.7 yrs (9.7 yrs); 67.0 yrs SLR: 69.6 yrs (9.5 yrs); 70.0 yrs Male, N (%) Total: 17,112 (43.4) L: 12,970 (43.6) SLR: 4,142 (42.8) White, N (%) Total: 35,266 (89.5) L: 26,491 (89.1) SLR: 8,775 (90.8) Charlson Comorbidity Index, N (%) (for initial sample only, but unclear if the same for survival analysis sample) <u>Score=0</u> Total: 18,438 (46.8) L: 14,615 (49.1) SLR: 3,823 (39.5) <u>Score=1</u> Total: 15,110 (38.3) L: 11,053 (37.2) SLR: 4,057 (42.0) <u>Score ≥2</u> Total: 5,855 (14.9) L: 4,068 (13.7) SLR: 1,787 (18.5)	Stage, N (%) c-stage T1N0M0: 39,403 (100) TNM edition(s) 5th, 6th, and 7th editions Histology, N (%) NR Tumor size, mean (SD) (for initial sample only, but unclear if the same for survival analysis sample) Total: 2.0 cm (0.9 cm) L: 2.0 cm (0.9 cm) SLR: 1.7 cm (0.7 cm)	Surgical approach, N (%) (for initial sample only, but unclear if the same for survival analysis sample) L: 29,736 (75.5) SLR: 9,667 (24.5) <u>SLR subtypes</u> W: 8,192 *(84.7)* S: 1,475 *(15.3)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Stephens, 2014[182] Surgery N=963 KQs 6, 7 Fair	NA U.S. 2002-2011 Consecutive patients with c-stage 1 NSCLC undergoing VATS or open lobectomy, but not other types of lobectomy, preoperative chemotherapy, or radiotherapy Followup, median NR Funding source NR	Age, mean (SD) Total: NR VATS L: 66 yrs (10 yrs) Open L: 67 yrs (10 yrs) Male, N (%) Total: *454 (47.1)* VATS L: 134 (44) Open L: 320 (49) Race/ethnicity NR Comorbidities, N (%) COPD Total: *135 (14.0)* VATS L: 42 (14) Open L: 93 (14)	Stage, N (%) Clinical T1 Total: *613 (63.7)* VATS L: 229 (75) Open L: 384 (58) Clinical T2 Total: *350 (36.3)* VATS L: 78 (25) Open L: 272 (42) TNM edition(s) Clinical: 6th edition Pathologic: 7th edition Histology, N (%) Adenocarcinoma Total: *658 (68.3)* VATS L: 231 (75) Open L: 427 (65) Squamous cell Total: *226 (23.5)* VATS L: 54 (18) Open L: 172 (26) Other NSCLC Total: *79 (8.2)* VATS L: 22 (7) Open L: 57 (9) Tumor diameter, mean (SD) Total: *2.9* cm (NR) VATS L: 2.5 cm (1 cm) Open L: 3.2 cm (2 cm)	Surgical approach, N (%) Planned VATS L: 307 *(31.9)* Open L: 656 *(68.1)* Actual (taking conversion into account) VATS lobectomy: *285 (29.6)* Open lobectomy: *678 (70.4)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Stokes, 2018[251] Surgery & SBRT/SABR N=84,839 KQ 7 Fair	NCDB U.S. 2004-2013 Patients with T1-2N0M0 NSCLC as first primary malignancy and treated with surgery or SBRT at a CoC-accredited facility, without missing treatment or followup timing data Followup, median NR Funding source University, other unspecified source	Age, N (%) <u>≤55 years</u> All surgery: 9,816 (12.8) SBRT: 241 (2.9) <u>56-60 years</u> All surgery: 8,472 (11.1) SBRT: 416 (5.1) <u>61-65 years</u> All surgery: 12,069 (15.8) SBRT: 800 (9.7) <u>66-70 years</u> All surgery: 15,338 (20.0) SBRT: 1,279 (15.6) <u>71-75 years</u> All surgery: 14,030 (18.3) SBRT: 1,556 (18.9) <u>76-80 years</u> All surgery: 10,761 (14.0) SBRT: 1,720 (20.9) <u>≥81 years</u> All surgery: 6,137 (8.0) SBRT: 2,204 (26.8) Male, N (%) All surgery: 34,427 (44.9) SBRT: 3,601 (43.8) White, N (%) All surgery: 67,744 (88.4) SBRT: 7,314 (89.0)	Stage, N (%) <u>T1a</u> All surgery: 32,802 (42.8) SBRT: 3,293 (40.1) <u>T1b</u> All surgery: 19,468 (25.4) SBRT: 2,688 (32.7) <u>T1 NOS</u> All surgery: 2,472 (3.2) SBRT: 154 (1.9) <u>T2a</u> All surgery: 21,881 (28.6) SBRT: 2,081 (25.3) TNM edition(s) 7th edition Histology, N (%) <u>Adenocarcinoma</u> All surgery: 41,110 (53.7) SBRT: 3,511 (42.7) <u>Squamous cell</u> All surgery: 20,031 (26.1) SBRT: 2,831 (34.5) <u>Other</u> All surgery: 15,482 (20.2) SBRT: 1,874 (22.8)	Surgical approach, N (%) All surgery: 76,623 *(90.3)* P: *1,532* (2.0) L: *59,536* (77.7) SLR: *15,555* (20.3) SBRT patients, N (%) 8,216 *(9.7)* SBRT dosing, N (%) 50 Gy x 5 fx: *1,586* (19.3) 60 Gy x 3 fx: *1,454* (17.7) 48 Gy x 4 fx: *1,397* (17.0) 54 Gy x 3 fx: *1,150* (14.0) Other dosage & fx schedules: *2,629 (32.0)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Stokes, 2018[251] (continued)		Charlson Comorbidity Index, N (%) Score=0 All surgery: 37,066 (48.4) SBRT: 4,602 (56.0) Score=1 All surgery: 28,150 (36.7) SBRT: 2,210 (26.9) Score ≥2 All surgery: 11,407 (14.9) SBRT: 1,404 (17.1)	Tumor size, mean (SD) NR	
Strand, 2006[194] Surgery N=1,375 eligible (of 3,211 total) KQ 6 Good	Cancer Registry of Norway Norway 1993-2002 All patients diagnosed with lung cancer in Norway (mandatorily reported to registry) who had a surgical procedure Followup, median 5 yrs Funding source NR	Age, median (range) NR Male, N (%) NR Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) p-stage of N enrolled (n=2,144), N (%) I: 1375 *(64.1)* II: 532 *(24.8)* III: 196 *(9.1)* IV: 41 *(1.9)* p-stage I breakdown, N (% of 1375): IA: 559 *(40.7)* IB: 816 *(59.3)* TNM edition(s) 5th edition Histology, N (%) NR Tumor size, mean (SD) NR	Surgical approach, N (%) L: NR Bi-L: NR P: NR SLR: NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Su, 2014[174] Surgery N=1,023 KQ 6 Fair	Alliance trial ACOSOG Z0030 U.S. NR Patients with a tissue diagnosis of c-stage T1-2 NSCLC, N0 or nonhilar N1, M0 before randomization and ECOG performance status <3 who received surgical resection by means of P, L, Bi-L, or S Followup, median (range) 6.7 yrs Funding source NR	Age, median (range) NR Male, N (%) NR Race/ethnicity NR Comorbidities NR	c-stage, N (%) T1: 578 (57) T2: 440 (43) TNM edition(s) NR Histology, N (%) NR Tumor size, N (%) NR	Surgical approach, N (%) P: NR L: NR Bi-L: NR S: NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Sun, 2017[197] SBRT/SABR N=73 KQs 6, 7 Fair	NA U.S. 2005-2013 Patients with a histologically confirmed, c-stage IA (T1N0M0) or Stage IB (T2aN0M0) NSCLC who underwent SABR due to medical inoperability or if they had operable disease but elected to undergo SABR. Patients with a prior history of lung cancer who were free of lung cancer for >5 years for the same histology or >2 years for a different histology. Followup, median (IQR) 7.2 yrs (4.6 to 8.3 yrs) National Cancer Institute	Age, median (range) 71.8 yrs (54.7 to 91.8 yrs) Male, N (%) 32 (49.2) Race/ethnicity NR Smoking status, N (%) Past or current: 57 (87.7) Never: 8 (12.3)	Stage, N (%) T1a: 38 (58.5) T1b: 24 (36.9) T2 (T2a: ≤ 5 cm, pleural invasion): 3 (4.6) TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 30 (46.2) Squamous: 26 (40.0) NSCC NOS: 9 (13.8) Maximum tumor diameter, median (range) 1.9 cm (0.7 to 4.0 cm)	SABR patients, N (%) 73 (100) SABR dosing, N (%) 50 Gy x 4 fx: 63 (*96.9*) 45 Gy x 4 fx: 1 (*1.5*) 50 Gy X 3 fx: 1 (*1.5*)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Taremi, 2012[261] SBRT/SABR N=46 KQ 7 Fair	NA Canada 2004-2008 Medically inoperable patients with T1-2N0M0 NSCLC treated with 18-20 Gy x 3 fx and with >6 mos followup Followup, median 24.9 mos Funding source Industry, other unspecified	Age, median (range) 72.8 yrs (48.3 to 89.6 yrs) Male, N (%) 22 (*48*) Race/ethnicity NR COPD, N (%) 29 (*63*)	Stage, N (%) All patients had T1-2N0M0 NSCLC TNM edition(s) NR Histology, N (%) NR Tumor size, mean (SD) 2.6 cm (1.2 cm)	SBRT patients, N (%) 46 (100) SBRT dosing, N (%) 18 or 20 Gy x 3 fx: 46 (100)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Taremi, 2012[264] SBRT/SABR N=108 KQ 7 Fair	NA Canada 2004-2008 Medically inoperable patients with synchronous Stage T1-T2N0M0 NSCLC, either biopsy-proven or identified by "suspicious" pulmonary lesions according to evidence of interval progression on ≥2 serial CT imaging studies (minimum of 1 mo apart) and/or increased FDG uptake on PET scan, and ECOG performance status of 0-3 Followup, median 19.1 mos Funding source Government, private	Age, mean (SD) 72.6 yrs (48.3 to 90 yrs) Male, N (%) 53 *(49.1)* Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) T stage 1 (≤3 cm): 86 *(79.6)* T stage 2 (>3 cm): 28 *(20.4)* TNM edition(s) NR Histology, N (%) Adenocarcinoma: 34 *(29.8)* Squamous cell carcinoma: 22 *(19.3)* Large cell carcinoma: 6 *(5.3)* NSCLC, NOS: 19 *(16.7)* No biopsy or nondiagnostic sample: 33 *(28.9)* Tumor size, mean (SD) 2.4 cm (1.1 cm)	SBRT patients, N (%) 108 (100) SBRT dosing, N (%) 60 Gy x 3 fx: 31 *(27.2)* 54 Gy x 3 fx: 20 *(17.5)* 48 Gy x 4 fx: 43 *(37.7)* 60 Gy x 8 fx: 9 *(7.9)* 50 Gy x 10 fx: 11 *(9.6)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Tsutani, 2014[179] Surgery N=618 KQs 6, 7 Good	NA Japan 2005-2010 Patients with clinical T1N0 M0 Stage IA NSCLC adenocarcinoma (no synchronous multiple tumors) who underwent preoperative staging using HRT and FDG-PET/CT and had definitive histopathologic diagnosis, followed by complete curative resection without neoadjuvant chemotherapy or radiotherapy Followup, median 42.9 mos Funding source NR	Age, mean (range) *66 yrs* (31 to 89 yrs) Male, N (%) *272 (44)* Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) Clinical T1a: *354 (57.3)* Clinical T1b: *264 (42.7)* TNM edition(s) 7th edition Histology, N (%) Adenocarcinoma: 618 (100) Adenocarcinoma in situ: *97 (15.7)* Tumor size, mean Whole tumor: 2.0 cm Solid tumor: 1.1 cm	Surgical approach, N (%) L: *383 (62.0)* SLR: *235 (38.0)* S: *98 (15.9)* W: *137 (22.2)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Ubels, 2015[206] SBRT/SABR N=39 KQs 6, 7 Fair	NA The Netherlands 2006-2008 Patients who refused surgery or had inoperable Stage T1-2N0M0 NSCLC with pathological confirmation of diagnosis and no progressive disease 3 weeks after treatment Followup, median 38 mos Funding source NR	Age, median (range) 77 yrs (55 to 87 yrs) Male, N (%) NR Race/ethnicity NR Comorbidities Charlson Comorbidity Index, N (%) Score=0-2: 20 (51) Score=3: 13 (33) Score ≥3: 6 (15) COPD, N (%) 22 (56)	Stage, N (%) Stage T1: 17 (44) Stage T2: 21 (54) Stage T3: 1 (3) TNM edition(s) NR Histology, N (%) Adenocarcinoma: 8 (21) Squamous cell: 14 (36) Large cell carcinoma: 13 (33) Other: 4 (10) Tumor size, mean (SD) NR	SBRT patients, N (%) 39 (100) SBRT dosing, N (%) 60 Gy x 3 fx: 30 *(76.9)* 48-50 Gy x 5-6 fx: 7 *(17.9)* 45 Gy x 3 fx: 2 *(5.1)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers **Author, Year** **Treatment Type(s)** **N Enrolled** **KQs Addressed** **Quality**	**Study Characteristics** **Study or Database Name** **Country** **Study Years** **Eligibility Criteria** **Followup** **Funding Source**	**Baseline Patient Characteristics** **Age** **Gender** **Race/Ethnicity** **Comorbidities**	**NSCLC Characteristics** **Stage** **TNM Edition(s)** **Histology** **Tumor Size**	**Treatment Characteristics** **Surgical Approach** **SBRT/SABR Dosing and Frequency**
Valle, 2016[246] Surgery & SBRT/SABR N=*1,367* KQ 7 Fair	NCCN U.S. 2007-2011 Patients receiving primary thoracic surgery or SBRT at NCCN institution for Stage 1 NSCLC within 120 days of diagnosis, no previous diagnosis within the previous 2 years or another invasive malignancy within the past 5 years, and sufficient followup Followup, median NR Funding source NR	Age, median (range) NR Male, N (%) NR Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) NR TNM edition(s) 6th edition Histology, N (%) NR Tumor size, mean (SD) NR	Surgical approach, N (%) 1,183 *(86.5)* SBRT patients, N (%) 184 *(13.5)* SBRT dosing, N (%) NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Videtic, 2014[271] SBRT/SABR N=80 KQ 7 Fair	NA U.S. 2009-2012 Medically inoperable patients who received treated with single-fx SBRT, including those potentially eligible for the RTOG 0915 or RPCI trials based on tumor size and peripheral location requirements, but who missed eligibility criteria for enrollment (e.g., biopsy result showing proof of malignancy) and received single-fx SBRT up off-protocol Followup, median (range) Single-fx SBRT at 30 Gy: 18.7 mos (1.8 to 43.0 mos) Single-fx SBRT at 34 Gy: 17.8 mos (0.1 to 39.4 mos) Funding source NR	Age, median (range) Single-fx SBRT at 30 Gy: 75 (48 to 91) Single-fx SBRT at 34 Gy: 73 (53 to 84) Male, N (%) Single-fx SBRT at 30 Gy: 36 (65.5) Single-fx SBRT at 34 Gy: 11 (44) Race/ethnicity NR Comorbidities, N (%) Current smoking status Single-fx SBRT at 30 Gy: 10 *(18.2)* Single-fx SBRT at 34 Gy: 8 (32) Pack-year history, median (range) Single-fx SBRT at 30 Gy: 50 (0 to 100) Single-fx SBRT at 34 Gy: 55 (5 to 125)	Stage, N (%) Clinical T1a Single-fx SBRT at 30 Gy: 49 (89.1) Single-fx SBRT at 34 Gy: 24 (96) Clinical T1b Single-fx SBRT at 30 Gy: 6 (10.9) Single-fx SBRT at 34 Gy: 1 (4) TNM edition(s) NR Histology, N (%) Adenocarcinoma Single-fx SBRT at 30 Gy: 12 (32) Single-fx SBRT at 34 Gy: 8 (43) Squamous cell carcinoma Single-fx SBRT at 30 Gy: 14 (37) Single-fx SBRT at 34 Gy: 9 (47) Other Single-fx SBRT at 30 Gy: 4 (10) Single-fx SBRT at 34 Gy: 0 (0) Nondiagnostic Single-fx SBRT at 30 Gy: 8 (21) Single-fx SBRT at 34 Gy: 2 (10) Tumor size, median (range) Single-fx SBRT at 30 Gy: 1.7 cm (0.9 to 4.8 cm) Single-fx SBRT at 34 Gy: 1.7 cm (1.0 to 4.0 cm)	SBRT patients, N (%) 80 (100) SBRT dosing, N (%) 30 Gy x 1 fx: 55 (69) 34 Gy x 1 fx: 25 (31)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Videtic, 2015[263] SBRT/SABR N=84 KQ 7 Fair	RTOG 0915 U.S. 2009-2011 Patients with cytologic or histologic diagnosis of NSCLC >2 cm staged as T1-T2N0M0 and based on CT and PET imaging; Zubrod performance status of 0-2; deemed medically inoperable by thoracic oncology specialist or declining surgery despite being operable; and no prior or planned use of concomitant antineoplastic therapy during SBRT protocol Followup, median 30.2 mos Funding source Government	Age, median (range) SBRT at any dose: 75 yrs (52 to 89 yrs) SBRT 34 Gy x 1 fx: 75 yrs (57 to 89 yrs) SBRT 48 Gy x 4 fx: 75 yrs (52 to 87 yrs) Male, N (%) <u>Male</u> SBRT at any dose: *38 (45.2)* SBRT 34 Gy x 1 fx: 16 (41.0) SBRT 48 Gy x 4 fx: 22 (48.9) Race/ethnicity NR Comorbidities, N (%) NR	Stage, N (%) <u>T1</u> SBRT at any dose: *72 (85.7)* SBRT 34 Gy x 1 fx: 32 (82) SBRT 48 Gy x 4 fx: 40 (88.9) <u>T2</u> SBRT at any dose: *12 (14.3)* SBRT 34 Gy x 1 fx: 7 (18.0) SBRT 48 Gy x 4 fx: 5 (11.1) TNM edition(s) 6th edition Histology, N (%) <u>Adenocarcinoma</u> SBRT at any dose: *49 (58.3)* SBRT 34 Gy x 1 fx: 23 (59.0) SBRT 48 Gy x 4 fx: 26 (57.8) <u>Squamous cell</u> SBRT at any dose: *25 (29.8)* SBRT 34 Gy x 1 fx: 9 (23.1) SBRT 48 Gy x 4 fx: 16 (35.6) <u>NSCLC NOS</u> SBRT at any dose: *10 (11.9)* SBRT 34 Gy x 1 fx: 7 (17.9) SBRT 48 Gy x 4 fx: 3 (6.7) Max tumor diameter, median (range) SBRT at any dose: 2.0 cm (0.8 to 4.98 cm) SBRT 34 Gy x 1 fx: 2.0 cm (1.0 to 4.98 cm) SBRT 48 Gy x 4 fx: 2.0 cm (0.8 to 4.3 cm)	SBRT patients, N (%) 84 (100) SBRT dosing, N (%) 34 Gy x 1 fx: 39 *(46.4)* 48 Gy x 4 fx: 45 *(53.6)*

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Yang, 2016[250] Surgery N=20,191 KQ 7 Fair	NCDB U.S. 2010-2012 Patients diagnosed with clinical T Stage 1-2, N0, M0 NSCLC, undergoing lobectomy, with available data on surgical approach, and no history of unrelated malignancy Followup, median NR Funding source Government, professional association	Age, median (IQR) Open surgery vs. MIS – PMS subset (N=18,780) Open L: 68 yrs (60 to 74 yrs) MIS L: 68 yrs (60 to 74 yrs) VATS vs. robotic L – PMS subset (N=3,876) VATS L: 69 yrs (62 to 74 yrs) Robotic L: 68 yrs (61 to 74 yrs) Male, N (%) Open surgery vs. MIS – PMS subset (N=18,780) Open L: 5,385 (57.3) MIS L: 5,375 (57.2) VATS vs. robotic L – PMS subset (N=3,876) VATS L: 1,079 (55.7) Robotic L: 1,099 (56.7) White, N (%) Open surgery vs. MIS – PMS subset (N=18,780) Open L: 8,336 (88.8) MIS L: 8,263 (88) VATS vs. robotic L – PMS subset (N=3,876) VATS L: 1,721 (88.8) Robotic L: 1,687 (87)	Stage, N (%) Open surgery vs. MIS – PMS subset (N=18,780) Clinical T status T1 Open L: 6,685 (71.2) MIS L: 6,598 (70.3) T2 Open L: 2,705 (28.8) MIS L: 2,792 (29.7) Pathologic T status T0 (in situ) Open L: 7 (0.1) MIS L: 12 (0.1) T1 Open L: 5,398 (59.7) MIS L: 5,259 (57.8) T2 Open L: 3,222 (35.6) MIS L: 3,386 (37.2) T3 Open L: 362 (4.0) MIS L: 393 (4.3) T4 Open L: 56 (0.6) MIS L: 44 (0.5) Pathologic N status N0 Open L: 7,861 (87.8) MIS L: 7,969 (88.5)	Surgical approach, N (%) Open surgery vs. MIS – PMS subset (N=18,780) MIS L: 9,390 (50) VATS L: 9,390 (50) VATS vs. robotic L – PMS subset (N=3,876) Robotic L: 1,938 (50) Open L: 1,938 (50)

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Yang, 2016[250] (continued)		Comorbidities, N (%) Open surgery vs. MIS – PSM subset (N=18,780) Charlson=0 Open L: 4,747 (50.6) MIS L: 4,670 (49.7) Charlson=1 Open L: 3,426 (36.5) MIS L: 3,446 (36.7) Charlson=2+ Open L: 1,217 (13.0) MIS L: 1,274 (13.6) VATS vs. robotic L – PSM subset (N=3,876) Charlson=0 VATS L: 863 (44.5) Robotic L: 889 (45.9) Charlson=1 VATS L: 811 (41.8) Robotic L: 762 (39.3) Charlson=2+ VATS L: 264 (13.6) Robotic L: 287 (14.8)	N1 Open L: 728 (8.1) MIS L: 691 (7.7) N2 Open L: 366 (4.1) MIS L: 338 (3.8) N3 Open L: 1 (0.0) MIS L: 3 (0.0) Pathologic M status M0 Open L: 9,300 (99.8) MIS L: 9,295 (99.7) M1 Open L: 21 (0.2) MIS L: 26 (0.3) VATS vs. robotic L – PMS subset (N=3,876) Clinical T status T1 VATS L: 1,445 (74.6) Robotic L: 1,401 (72.3) T2 VATS L: 493 (25.4) Robotic L: 537 (27.7) Pathologic T status T0 (in situ) VATS L: 5 (0.3) Robotic L: 3 (0.2) T1 VATS L: 1,143 (61.0) Robotic L: 1,112 (59.5)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Yang, 2016[250] (continued)			T2 VATS L: 625 (33.4) Robotic L: 665 (35.6) T3 VATS L: 87 (4.6) Robotic L: 82 (4.4) T4 VATS L: 13 (0.7) Robotic L: 7 (0.4) Pathologic N status N0 VATS L: 1,661 (89.4) Robotic L: 1,652 (89.0) N1 VATS L: 138 (7.4) Robotic L: 136 (7.3) N2 VATS L: 65 (3.5) Robotic L: 67 (3.6) N3 VATS L: 0 (0) Robotic L: 2 (0.1) Pathologic M status M0 VATS L: 1,910 (99.7) Robotic L: 1,910 (99.7) M1 VATS L: 6 (0.3) Robotic L: 6 (0.3) TNM edition(s) 7th edition	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Yang, 2016[250] (continued)			Histology, N (%) Open surgery vs. MIS – PMS subset (N=18,780) Well differentiated Open L: 1,813 (20.5) MIS L: 1,826 (20.5) Moderately differentiated Open L: 4,167 (47.2) MIS L: 4,255 (47.9) Poorly differentiated Open L: 2,758 (31.2) MIS L: 2,722 (30.6) Undifferentiated/anaplastic Open L: 97 (1.1) MIS L: 86 (1) VATS vs. robotic L – PMS subset (N=3,876) Well differentiated VATS L: 359 (19.6) Robotic L: 415 (22.5) Moderately differentiated VATS L: 897 (48.9) Robotic L: 865 (46.9) Poorly differentiated VATS L: 565 (30.8) Robotic L: 551 (29.9) Undifferentiated/anaplastic VATS L: 13 (0.7) Robotic L: 14 (0.8)	

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Yang, 2016[250] (continued)			Tumor size, mean (SD) Open surgery vs. MIS (N=18,780) Pathologic tumor size Open L: 2.7 cm (2.1 cm) MIS L: 2.7 cm (2.1 cm) VATS vs. Robotic L (N=3,876) Pathologic tumor size VATS L: 2.6 cm (1.4 cm) Robotic L: 2.7 cm (2.3 cm)	
Zhai, 2014[172] Surgery N=724 (subset of sample with Stage 1 NSCLC) KQ 6 Fair	NA U.S. 1992-2010 Patients >18 years old with pathologically confirmed newly diagnosed NSCLC (Stages 1-2) and not receiving adjuvant therapy who were consecutively recruited and followed Followup, median 41 mos Funding source Government	Age, mean (SD) NR Male, N (%) NR Race/ethnicity NR Comorbidities *271* (*37.4*)	Stage, N (%) c-stage 1A: 538 (59.6) c-stage 1B: 186 (20.6) TNM edition(s) NR Histology, N (%) NR Tumor size, N (%) NR	Surgical approach, N (%) W: NR L: NR Others: NR

Appendix E Table 4. KQs 6 and 7: Study and Patient Characteristics Table

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Eligibility Criteria Followup Funding Source	Baseline Patient Characteristics Age Gender Race/Ethnicity Comorbidities	NSCLC Characteristics Stage TNM Edition(s) Histology Tumor Size	Treatment Characteristics Surgical Approach SBRT/SABR Dosing and Frequency
Zhao, 2017[183] Surgery N=7,989 KQ 6 Fair	SEER U.S. 2004-2012 Patients with histologically diagnosed Stage 1A lung adenocarcinoma measuring ≥10 but ≤20 mm, not confined to hilus or a primary tumor in main bronchus, and treated with segmentectomy or lobectomy, but not post-operative radiotherapy Followup, median 52.2 mos Funding source Government, university	Age, mean (SD) S: 69.8 yrs (9.2 yrs) L: 67.3 yrs (9.6 yrs) Male, N (%) Female Total: *3,184 (39.9)* S: *202 (35.8)* L: *2,982 (40.2)* White, N (%) Total: *6,834 (85.5)* S: 498 (88.3) L: 6,336 (85.3) Comorbidities, N (%) NR	Stage, N (%) p-stage T1a: 7,989 (100) c-stage T1b: 7,989 (100) TNM edition(s) 8th edition Histology, N (%) Major adenocarcinoma Total: *7,413 (92.8)* S: 506 (89.7) L: 6,907 (93.0) Mucinous adenocarcinoma Total: *348 (4.4)* S: 27 (4.8) L: 321 (4.3) BAC, nonmucinous Total: *228 (2.9)* S: 31 (5.5) L: 197 (2.7) Tumor size, median (SD) Total: NR S: 15.6 mm (2.9 mm) L: 16.2 mm (2.9 mm)	Surgical approach, N (%) S: 564 *(7.1)* L: 7,425 *(92.9)*

***** FEV1 was not available in 13/115 SBRT patients.

† Analytical stage included the AJCC p-stage group if available; otherwise, the c-stage group was used.

Abbreviations: 3D-CRT=three-dimensional conformal radiation therapy; ASA=American Society of Anesthesiologists; BAC=broncholoalveolar carcinoma; Bi-L=bilobectomy; c-stage=clinical stage; cm=centimeter(s); CoC=Commission on Cancer; COPD=chronic obstructive pulmonary disease; DLCO=diffusing capacity of the lungs for carbon monoxide; ECOG=Eastern Cooperative Oncology Group; FEV1=forced expiratory volume in one second; fx=fraction(s); Gy=Gray; IQR=interquartile range; JCOG=Japan Clinical Oncology Group; KQ=Key Question; L=lobectomy; N=number of patients enrolled or analyzed; NA=not applicable; NCDB=National Cancer Database; NCI=National Cancer Institute; NOS=not otherwise specified; NPC=not pathologically confirmed; NR=not reported; NSCLC=non-small cell lung cancer; p-stage=pathologic stage; PC=pathologically confirmed; S=segmentectomy; SBRT/SABR=stereotactic body radiotherapy/stereotactic ablative radiotherapy; SD=standard deviation; SEER=Surveillance, Epidemiology, and End Results Program; SLR=sublobar resection; STS-GTS=Society of Thoracic Surgeons-General Thoracic Surgery Database; surg exp=surgical experience; T=thoracotomy; TNM=tumor-node-metastasis cancer staging system; U.K.=United Kingdom; U.S.=United States; VATS=video-assisted thoracoscopic lobectomy; VMAT=volumetric modulated arc therapy; VPI=visceral pleural invasion; W=wedge resection.

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Brunelli, 2015[181] N=1,370 (1,370) KQs 6, 7 Good	5-yr OS ThRCRI prognostic class A (score 0 to 1) Total: 66 (NR) p-stage T1: 73 (NR) p-stage T2: 61 (NR) ThRCRI prognostic class B (score 1.5 to 2.5) Total: 53 (NR) p-stage T1: 64 (NR) p-stage T2: 48 (NR) ThRCRI prognostic class C (score >2.5) Total: 35 (NR) p-stage T1: 55 (NR) p-stage T2: 32 (NR)	5-yr LCSS ThRCRI prognostic class A (score 0 to 1) Total: 77 (NR) ThRCRI prognostic class B (score 1.5 to 2.5) Total: 75 (NR) ThRCRI prognostic class C (score >2.5) Total: 55 (NR)	30-day mortality 24 (1.8) Postoperative cardiac-related mortality, % ThRCRI prognostic class A (score 0 to 1) Total: 0.03 ThRCRI prognostic class B (score 1.5 to 2.5) Total: 1.4 ThRCRI prognostic class C (score >2.5) Total: 4.1	Major postoperative cardiac events in hospital or within 30 days of surgery (i.e., acute MI, pulmonary edema, ventricular fibrillation or primary cardiac arrest, complete heart block, any cardiac-related death) Total sample 80 (5.8) ThRCRI prognostic class A (score 0 to 1), % Total: 11 ThRCRI prognostic class B (score 1.5 to 2.5), % Total: 19 ThRCRI prognostic class C (score >2.5), % Total: 42 Major postoperative cardiac morbidity, % ThRCRI prognostic class A (score 0 to 1) Total: 4 ThRCRI prognostic class B (score 1.5 to 2.5) Total: 11 ThRCRI prognostic class C (score >2.5) Total: 17 Cardiac event mortality during followup, % ThRCRI prognostic class A (score 0 to 1) Total: 1.5 ThRCRI prognostic class B (score 1.5 to 2.5) Total: 7 ThRCRI prognostic class C (score >2.5) Total: 13

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Bryant, 2018[196] N=*3,620* for surgery (total=*3,620*; L=2,986; SLR=634) KQs 6, 7 Fair	5-yr OS L: 70 (NR) SLR: 56 (NR) 5-yr LC mortality L: 23 (NR) SLR: 32 (NR)	NR	30-day mortality L: *57* (1.9) SLR: *11* (1.7) 90-day mortality L: *107* (3.6) SLR: *16* (2.5)	NR
Chang, 2007[192] N=10,761 (total=10,761; L=8,527; SLR=2,234) KQ 6 Fair	5-yr OS All surg: 57.8 (NR) L: 61.4 (NR) SLR: 44.0 (NR) 5-yr OS after all surgeries and stratified by gender Female: 63.0 (NR) Male: 52.8 (NR) p<0.0001 5-yr OS after all surgeries and stratified by age Age <67: 65.2 (NR) Age ≥67: 51.5 (NR) p<0.0001	NR	NR	NR
Cox, 2017[186] N=1,991 (total=1,991; L=1,544; SLR=447) KQ 6 Fair	5-yr OS Total: NR L: 70.5 (NR) SLR: 67.8 (NR)	NR	NR	NR
Fernandez, 2012[188] N=657 (657) KQ 6 Fair	Unadjusted 5-yr OS 41 (NR) Unadjusted 5-yr DSS 59 (NR)	NR	NR	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Goya, 2005[195] N=*3,965* eligible (total=3,965; c-stage 1A=2,423 and 1B=1,542; p-stage 1A=2,009 and 1B=1,418) KQ 6 Fair	5-yr OS c-stage 1 IA: 72.1 (NR) IB: 49.9 (NR) p-stage 1 IA: 79.5 (NR) IB: 60.1 (NR)	NR	NR	NR
Guerrera, 2015[171] N=848 (848) KQ 6 Fair	5-yr OS 74 (0.71 to 0.77)	NR	NR	NR
Husain, 2015[239] N=112,216 (71,175) KQ 7 Fair	NR	NR	Overall 30-day mortality All surg: *1,566* (2.2) 30-day mortality – subgroup analyses stratified by comorbidities and age, % Charlson-Deyo Comorbidity Score=0 Age <75 yrs All surg: 1.3 L: 1.2	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Husain, 2015[239] (continued)			SLR: 1.5 Age ≥75 yrs All surg: 3.3 L: 3.4 SLR: 3.1 Charlson-Deyo Comorbidity Score=1 Age <75 yrs All surg: 1.6 L: 1.6 SLR: 1.6 Age ≥75 yrs All surg: 4.1 L: 4.5 SLR: 2.7 Charlson-Deyo Comorbidity Score=2 Age <75 yrs All surg: 2.3 L: 2.3 SLR: 2.3 Age ≥75 yrs All surg: 5.8 L: 6.6 SLR: 3.9	
Khullar, 2015[178] N= 54,350 (54,350) KQ 6 Fair	5-yr OS c-stage 1: 57.2 (NR) p-stage 1: 60.5 (NR)	NR	NR	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Khullar, 2015[189] Total N=28,241 (total=28,241; for OS: L=4,857; W=1,891; S=286; for 30-day mortality: L=19,718; W=7,297; S=1,226) KQs 6, 7 Fair	5-yr OS Total: NR L: 70.4 (69.0 to 71.7) W: 54.6 (52.3 to 56.9) S: 59.6 (53.5 to 65.2)	NR	30-day mortality Total: *445 (1.6)* L: *316* (1.6) W: *110* (1.5) S: *19* (1.6)	NR
Lakha, 2014[175] N=16,315 (15,067) KQ 6 Fair	5-yr OS Range: 53 (49 to 57) to 75 (74 to 77) <2 cm without VPI: 75 (74 to 77) <2 cm with VPI: 70 (66 to 75) 2-3 cm without VPI: 68 (65 to 70) 2-3 cm with VPI: 61 (56 to 65) >3-5 cm without VPI: 60 (57 to 62) >3-5 cm with VPI: 53 (49 to 57)	5-yr LCSS Range: 66 (62 to 69) to 88 (86 to 89) <2 cm without VPI: 88 (86 to 89) <2 cm with VPI: 84 (81 to 87) 2-3 cm without VPI: 79 (77 to 81) 2-3 cm with VPI: 71 (67 to 75) >3-5 cm without VPI: 72 (70 to 74) >3-5 cm with VPI: 66 (62 to 69)	NR	NR
Landreneau, 2014[176] N=624 (624) KQs 6, 7 Fair	5-yr OS Total: NR S: 54 (0.47 to 0.61) L: 60 (0.54 to 0.67)	NR	30-day mortality Total: *12 (1.9)* S: *4* (1.2) (95% CI, 0.4-32) L: *8* (2.5) (95% CI, 1.1 to 5.0) 90-day mortality Total: *23 (3.7)* S: *8* (2.6) (95% CI, 1.1-5.0) L: *15* (4.8) (95% CI, 2.7 to 7.8)	Overall morbidity Total: *217 (34.8)* S: *115* (36.9) L: *102* (32.7)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Licht, 2013[249] N=1,513 (total=1,513; VATS L=717; Open L=796) KQ 7 Fair	NR	NR	30-day mortality Total: *31* (2.0) VATS L: *8* (1.1) Open L: *23* (2.9)	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Louie, 2016[238] *13,598 (13,598)* KQ 7 Fair	NR	NR	30-day mortality Total: *106 (0.8)* Robotic L: *7* (0.6) VATS L: *99* (0.8) In-hospital mortality Total: *78 (0.6)* Robotic L: *4* (0.3) VATS L: *74* (0.6)	Air leak >5 days Total: 1,334 (9.8) Robotic L: 122 (10.0) VATS L: 1,212 (9.8) Adult respiratory distress syndrome Total: 61 (0.4) Robotic L: 2 (0.2) VATS L: 59 (0.5) Atelectasis requiring bronchoscopy Total: 391 (2.9) Robotic L: 31 (2.5) VATS L: 360 (2.9) Atrial arrhythmia requiring treatment Total: 1,346 (9.9) Robotic L: 125 (10.2) VATS L: 1,221 (9.9) Bronchopleural fistulas Total: 42 (0.3) Robotic L: 7 (0.6) VATS L: 35 (0.3) Chylothorax requiring medical intervention Total: 64 (0.5) Robotic L: 4 (0.3) VATS L: 60 (0.5) DVT Total: 52 (0.4) Robotic L: 5 (0.4) VATS L: 47 (0.4) Emphysema requiring treatment Total: 50 (0.4) Robotic L: 6 (0.5) VATS L: 44 (0.4) Initial ventilatory support >48 hours Total: 50 (0.4) Robotic L: 6 (0.5) VATS L: 44 (0.4)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Louie, 2016[238] (continued)				Myocardial infarction Total: 42 (0.3) Robotic L: 5 (0.4) VATS L: 37 (0.3) Pneumonia Total: 442 (3.3) Robotic L: 33 (2.7) VATS L: 409 (3.3) Pneumothorax requiring CT reinsertion Total: 474 (3.5) Robotic L: 51 (4.2) VATS L: 423 (3.4) Pulmonary embolus Total: 62 (0.5) Robotic L: 4 (0.3) VATS L: 58 (0.5) Recurrent laryngeal nerve paresis/paralysis Total: 26 (0.2) Robotic L: 2 (0.2) VATS L: 24 (0.2) Reintubation Total: 308 (2.3) Robotic L: 25 (2.0) VATS L: 283 (2.3) Required reoperation for bleeding Total: 65 (0.9) Robotic L: 3 (0.8) VATS L: 62 (0.9) Respiratory failure Total: 119 (1.9) Robotic L: 16 (1.9) VATS L: 103 (1.9) Tracheostomy Total: 99 (0.7) Robotic L: 9 (0.7) VATS L: 90 (0.7)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Maeda, 2010[191] N=734 (713) KQ 6 Fair	5-yr OS 85.8 (NR) 10-yr OS 71.3 (NR)	NR	NR	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Maeda, 2012[184] N=1,074 (1,070 with c-stage 1A; 691 with p-stage 1A NSCLC) KQ 6 Fair	5-yr OS c-stage 1 Total: NR NR by smoking history p-stage 1 Total: NR Smoking history of pack-years ≤20 96.5 (NR) Smoking history of pack-years >20 85.9 (NR) 5-yr OS subgroup analyses Age <65: 83.3 (NR) Age >65: 76.9 (NR) Women: 85.4 (NR) Men: 74.4 (NR) Smoking history of 0 ≤ pack-years ≤ 20 85.5 (NR) Smoking history of no pack-years 85.2 (NR) Smoking history of 0 ≤ pack-years ≤10 89.2 (NR) Smoking history of 10 < pack-years ≤20 84.5 (NR) Smoking history of 20 < pack-years ≤40 73 (NR)	NR	NR	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Maeda, 2012[184] (continued)	Smoking history of 40 < pack-years ≤60 69.7 (NR) Smoking history of pack-years >60 69.3 (NR) Smoking history of pack-years >20 71.1 (NR)			
Mediratta, 2014[177] N=540 (540) KQs 6, 7 Good	5-yr OS 65 (NR)	NR	Overall in-hospital mortality (duration of assessment not specified) *5 (0.9)*	NR
Melvan, 2015[243] N=127,366 (127,366) KQ 7 Fair	NR	NR	30-day mortality 2,989 *(2.4)*	NR
Nakamura, 2015[173] N=1,336 (1,016) KQ 6 Fair	5-yr OS p-stage 1A: 81.7 (NR) p-stage 1B: 62.6 (NR)	NR	NR	Intraoperative blood loss, mean (SD) p-stage 1A: 330 mL (322 mL) p-stage 1B: 415 mL (434 mL)
Okada, 2006[193] N=567 (total=567; SLR=305; L=262) KQ 6 Fair	5-yr OS, N (%) SLR: 173 (89.6) L: 158 (89.1) 5-yr DSS, N (%) SLR: 159 (85.9) L: 149 (83.4)	NR	NR	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Puri, 2014[242] N=1,066 (1,066) KQs 6, 7 Fair	Median OS (used only for descriptive purposes) 8.8 yrs	NR	<u>High-risk vs. normal-risk surgery patients</u> 30-day/hospital mortality High-risk: 2 (1) Normal-risk: 14 (2); p=0.75 Respiratory failure High-risk: 7 (4) Normal-risk: 41 (5); p=0.70 Pneumonia High-risk: 9 (5) Normal-risk: 51 (6); p=0.61 Air leak >5 days High-risk: 16 (8) Normal-risk: 54 (6); p=0.36 Emphysema High-risk: 1 (0.5) Normal-risk: 3 (0.3); p=0.55 Atrial fibrillation High-risk: 25 (13) Normal-risk: 116 (13); p=1.00 Hemorrhage requiring reoperation High-risk: 2 (1) Normal-risk: 8 (1); p=1.00 Pulmonary embolism High-risk: 2 (1) Normal-risk: 3 (0.3); p=0.23 Myocardial infarction High-risk: 0 (0) Normal-risk: 5 (1); p=0.59 Stroke High-risk: 0 (0) Normal-risk: 3 (0.3); p=1.00	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Puri, 2015[252] N=111,731 for surg (all surg=109,485; all surg PSM subset=5,355; all SLR=19,339; SLR PSM subset=4,555) KQ 7 Fair	NR	NR	30-day mortality All surg: 2,596/109,485 (2.4) All surg PSM subset: 136 (2.5) All SLR: 716/19,339 (3.7) SLR PSM subset: 89 (2)	NR
Razi, 2016[180] N=1,640 (1,640) KQ 6 Fair	<u>Overall sample</u> 5-yr OS L/Bi-L: 50.2 (NR) S: 43.8 (NR) W: 38.6 (NR) <u>Subset of patients with T1a tumors</u> 5-yr OS L/Bi-L: 51.8 (NR) S: 45.9 (NR) W: 43.4 (NR)	<u>Overall sample</u> 5-yr LCSS L/Bi-L: 64.5 (NR) S: 59.1 (NR) W: 52.7 (NR) <u>Subset of patients with T1a tumors</u> 5-yr LCSS L/Bi-L: 66.3 (NR) S: 61.7 (NR) W: 59 (NR)	NR	NR
Rosen, 2014[244] N=66,283 (66,283) KQ 7 Fair	NR	NR	30-day mortality *1,790* (2.7)	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Rosen, 2016[185] Primary analyses (i.e., patients selected for Charlson-Deyo score=0) N=13,652 for surg (unmatched: 13,652; PSM subset: 1,781) Secondary analyses (i.e., patients unselected based on Charlson-Deyo score) N=29,032 for surg (unmatched=29,032; PSM subset=235) KQs 6, 7 Good	5-yr OS Primary PSM analysis 59 (NR) Secondary PSM analysis 58 (NR)	NR	30-day mortality Primary unmatched analysis 252 (2) Secondary unmatched analysis 667 (2) 90-day mortality Primary unmatched analysis 449 (3) Secondary unmatched analysis 1,163 (4)	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Samson, 2015[240] N=55,653 (N=55,653 for unmatched analysis; 27,022 for PSM analysis; 971 for single-center analysis) KQs 6, 7 Fair	NR	NR	30-day mortality <u>PSM analysis</u> Early surg: 322 (2.4) Delayed surg: 391 (2.9) <u>Single-center analysis</u> Early surg: 6 (1.1) Delayed surg: 14 (3.1)	<u>Single-center analysis</u> Pneumonia Early surg: 33 (6) Delayed surg: 51 (11) Wound infection Early surg: 4 (1) Delayed surg: 5 (1) Blood transfusion Early surg: 18 (3) Delayed surg: 39 (9) Air leak Early surg: 59 (11) Delayed surg: 43 (10) Respiratory failure Early surg: 27 (5) Delayed surg: 44 (10) Arrhythmia Early surg: 94 (18) Delayed surg: 79 (18) DVT Early surg: 8 (2) Delayed surg: 13 (3) Myocardial infarction Early surg: 5 (1) Delayed surg: 1 (0.2) Reintubation Early surg: 23 (4) Delayed surg: 34 (8) Renal failure Early surg: 9 (2) Delayed surg: 11 (2)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Samson, 2017[245] N=146,908 (total=146,908; nonanatomical vs. anatomical=146,908; early vs. delayed=145,090; R0 vs. ≥R1=144,921; <10 vs. ≥10 LNs=136,612) KQ 7 Fair	NR	NR	30-day mortality Nonanatomical vs. anatomical resection Nonanatomical: 491 (1.8) Anatomical: 2,158 (2.2) Between-group p <0.001 Early vs. delayed resection Early (<8 weeks): 2,000 (2.0) Delayed (≥8 weeks): 619 (2.6) Between-group p <0.001 R0 vs. ≥R1 resection R0: 2,433 (2.0) ≥R1: 163 (3.8) Between-group p <0.001 <10 vs. ≥10 lymph nodes <10 LNs obtained: 1,674 (2.1) ≥10 LNs obtained: 790 (2.3) Between-group p=0.06 90-day mortality Nonanatomical vs. anatomical resection Nonanatomical: 975 (3.6) Anatomical: 3,866 (4.0) Between-group p=0.003 Early vs. delayed resection Early (<8 weeks): 3,633 (3.7) Delayed (≥8 weeks): 1,148 (4.8) Between-group p <0.001 R0 vs. ≥R1 resection R0: 4,434 (3.8) ≥R1: 312 (7.4) Between-group p <0.001 <10 vs. ≥10 LNs <10 LNs obtained: 3,090 (3.9) ≥10 LNs obtained: 1,396 (4.0) Between-group p=0.23	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Sawabata, 2011[190] N=*9,083* eligible (*9,083*) KQ 6 Fair	5-yr OS c-stage 1A: 82 (NR) c-stage 1B: 63.4 (NR) p-stage 1A: 85.9 (NR) p-stage 1B: 69.3 (NR)	NR	NR	NR
Scheel, 2015[170] All surg N=800 L patients N=638 SLR patients N=162 KQs 6, 7 Fair	5-yr OS *71.9* (NR)	NR	30-day hospital mortality – all surg patients *8 (1.0)* 30-day hospital mortality – L patients *7 (0.9)*	Any perioperative morbidity – all surg patients *220 (27.5)* Any perioperative morbidity – L patients *188 (23.5)* Specific AEs – all surg patients Pneumonia *42 (5.3)* Emphysema *3 (0.4)* Blood Transfusion *9 (1.1)* Hemorrhage Requiring Reoperation *6 (0.8)* Bronchopleural Fistula *3 (0.4)* Prolonged Air Leak *54 (6.8)* Respiratory Failure *43 (5.4)* Dysrhythmia *98 (12.3)* DVT *12 (1.5)* Renal Failure *7 (0.9)* Stroke *4 (0.5)*

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Scheel, 2015[170] (continued)				Specific AEs – L patients Pneumonia *37 (4.6)* Emphysema *3 (0.4)* Blood Transfusion *9 (1.1)* Hemorrhage Requiring Reoperation *5 (0.6)* Bronchopleural Fistula *3 (0.4)* Air Leak *43 (5.4)* Respiratory Failure *40 (5.0)* Dysrhythmia *91 (11.4)* DVT *9 (1.1)* Renal Failure *6 (0.8)* Stroke *2 (0.3)*

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Schuchert, 2012[248] Total: N=899 (total=899; S=305; L=594) Aged ≥80 yrs: N=103 (S=39, L=64) Aged 70 to 79 yrs: N=358 (S=132; L=226) Aged <70 yrs: N=439 (S=134; L=305) KQ 7 Fair	NR	NR	30-day mortality Overall: *17 (1.9)* S: *4* (1.3) L: *13* (2.2) 90-day mortality Overall: *37 (4.1)* S: *11* (3.6) L: *26* (4.4)	Overall morbidity <u>Total sample</u> Overall: *380 (42.3)* S: *109* (35.7) L: *271* (45.7) <u>Aged ≥80 yrs</u> Overall: *55 (53.0)* S: *17* (43.6) L: *38* (58.7) <u>Aged 70-79 yrs</u> Overall: *142 (39.6)* S: *48* (36.4) L: *94* (41.4) <u>Aged <70 yrs</u> Overall: *161 (36.7)* S: *45* (33.6) L: *116* (38.1) Major morbidity Overall: *111 (12.3)* S: *28* (9.2) L: *83* (14.0) Pulmonary morbidity Overall: *220 (24.5)* S: *52* (17.0) L: *168* (28.3) Estimated blood loss, median (range) Overall: NR S: 185 mL (10 to 650 mL) L: 291 mL (50 to 800 mL) Operative time, median (range) Overall: NR S: 147 mins (35 to 296 mins) L: 216 mins (40 to 381 mins)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Shapiro, 2012[247] N=4,975 (4,975 for most outcomes; 4,645 for hospital stay outcomes) KQ 7 Fair	NR	NR	30-day mortality Total: *178* (3.6) (95% CI, 3.1 to 4.1) ≤10 LNs: 135 (3.6) >10 LNs: 43 (3.6)	Extrapulmonary infections (shock, septicemia, bacterial infection, postoperative infection, bacteremia, kidney infection, and infection-related procedure) Total: *295 (5.9)* ≤10 LNs: 220 (5.8) >10 LNs: 75 (6.3) Transfusion Total: *180 (3.6)* ≤10 LNs: 143 (3.8) >10 LNs: 37 (3.1) 30-day readmission Total: *380 (7.6)* ≤10 LNs: 301 (8.0) >10 LNs: 79 (6.6) Prolonged LOS Total: *808 (16.2)* ≤10 LNs: 633 (18.0) >10 LNs: 175 (5.5) Postoperative ICU stay Total: *3,390 (68.1)* ≤10 LNs: 2,547 (72.4) >10 LNs: 843 (74.9) Cardiovascular complications (acute MI and acute coronary occlusion without MI) Total: *82 (1.6)* ≤10 LNs: 64 (1.7) >10 LNs: 18 (1.5)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Shapiro, 2012[247] (continued)				Thromboembolic complications (DVT and pulmonary embolism) Total: *98 (2)* ≤10 LNs: 64 (1.7) >10 LNs: 34 (2.8) Respiratory complications (adult respiratory distress syndrome, respiratory failure, bronchitis, pneumonia, empyema, abscess of lung, abscess of mediastinum and respiratory infection) Total: *1,414 (28.4)* ≤10 LNs: 1,095 (29.0) >10 LNs: 319 (26.7) Reoperation (thoracotomy for postoperative complications, reoperation for emphysema, bronchial fistula repair, and hemorrhage control) Total: *73 (1.5)* ≤10 LNs: 48 (1.3) >10 LNs: 25 (2.1)
Shirvani, 2012[237] N=7,808 for surg (total=7,808; SLR=1,277; L=6,531) KQ 7 Fair	NR	NR	30-day mortality SLR: 15.32 (1.2) L: 84.90 (1.3) 90-day mortality SLR: 52.36 (4.1) L: 267.77 (4.1)	NR
Shirvani, 2014[241] N=8,711 for surg (total=8,711; L=7,215; SLR=1,496) KQ 7 Fair	NR	NR	90-day mortality L: 289 (4.0) SLR: 55 (3.7)	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Speicher, 2016[187] N=39,403 (total=11,990; NR for L or SLR) KQ 6 Fair	5-yr OS Total: NR L: 66.2 (NR) SLR: 51.2 (NR)	NR	NR	NR
Stephens, 2014[182] N=963 (963) KQs 6, 7 Fair	5-yr OS Total: NR VATS L: 78 (NR) Open L: 68 (NR)	NR	30-day mortality Total: *10 (1.0)* VATS L: 1 *(0.3)* Open L: 9 (1) 90-day mortality Total: *19 (2.0)* VATS L: 3 (1) Open L: 16 (2)	Pneumonia Total: *72 (7.5)* VATS L: 17 (6) Open L: 55 (8) Sepsis Total: *13 (1.3)* VATS L: 3 (1) Open L: 10 (2) Bleeding Total: *10 (1.0)* VATS L: 3 (1) Open L: 7 (1) Bronchopleural fistulas Total: *2 (0.2)* VATS L: 0 (0) Open L: 2 *(0.3)* Respiratory arrest Total: *11 (1.1)* VATS L: 2 (1) Open L: 9 (1)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Stephens, 2014[182] (continued)				Pulmonary morbidity Total: *139 (14.4)* VATS L: 29 (9) Open L: 110 (17) Overall morbidity Total: *279 (29.0)* VATS L: 59 (19) Open L: 220 *(33.5)* Atelectasis Total: *26 (2.7)* VATS L: 5 (2) Open L: 21 (3) Air leak >5 days Total: *64 (6.6)* VATS L: 13 (4) Open L: 51 (8) Tracheostomy Total: *15 (1.6)* VATS L: 3 (1) Open L: 12 (2) Reintubation Total: *25 (2.6)* VATS L: 7 (2) Open L: 18 (3) Acute respiratory distress syndrome Total: *12 (1.2)* VATS L: 3 (1) Open L: 9 (1) Myocardial infarction Total: *10 (1.0)* VATS L: 2 (1) Open L: 8 (1)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Stephens, 2014[182] (continued)				Atrial arrhythmia Total: *168 (17.4)* VATS L: 36 (12) Open L: 132 (20) Ventricular arrhythmia Total: *4 (0.4)* VATS L: 0 (0) Open L: 4 (1) Cerebrovascular accident Total: *4 (0.4)* VATS L: 1 *(0.3)* Open L: 3 (1) Pulmonary embolism Total: *2 (0.2)* VATS L: 1 *(0.3)* Open L: 1 *(0.2)* DVT Total: 0 (0) VATS L: 0 (0) Open L: 0 (0) Emphysema Total: 3 *(0.3)* VATS L: 0 (0) Open L: 3 (1) Renal failure Total: *13 (1.3)* VATS L: 1 *(0.3)* Open L: 12 (2) Reoperation Total: *15 (1.6)* VATS L: 9 (3) Open L: 6 (1)

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Stephens, 2014[182] (continued)				Chest tube duration, median days (IQR) Total: NR VATS L: 2 (4) Open L: 3 (20) Operative time, median mins (IQR) Total: NR VATS L: 173 (57) Open L: 160 (57) LOS, median days (IQR) Total: NR VATS L: 4 (8) Open L: 6 (7)
Stokes, 2018[251] N=76,623 for surg (all surg=76,623; L=59,536; p=1,532; SLR=15,555) KQ 7 Fair	NR	NR	30-day mortality All surg: *1,586* (2.07) L: *1,191* (2.0) P: *120* (7.82) SLR: *275* (1.77) 30-day mortality stratified by age <u>≤55 yrs</u> All surg: 95 (0.97) L: 64 (0.8) P: 18 (5.2) SLR: 13 (0.96) <u>56 to 60 yrs</u> All surg: 83 (0.98) L: 64 (0.9) P: 12 (5.1) SLR: 7 (0.5)	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Stokes, 2018[251] (continued)			61 to 65 yrs All surg: 160 (1.33) L: 119 (1.25) P: 19 (7.12) SLR: 22 (0.96) 66 to 70 yrs All surg: 272 (1.77) L: 207 (1.73) P: 23 (7.69) SLR: 42 (1.38) 71 to 75 yrs All surg: 352 (2.51) L: 271 (2.51) P: 24 (11.88) SLR: 57 (1.88) 76 to 80 yrs All surg: 383 (3.56) L: 283 (3.54) P: 20 (15.27) SLR: 80 (3.02) ≥81 yrs All surg: 242 (3.94) L: 185 (4.44) P: 2 (6.9) SLR: 55 (2.83) 90-day mortality All surg: *2,751* (3.59) L: *2,060* (3.46) P: *182* (11.86) SLR: *509* (3.27)	

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Stokes, 2018[251] (continued)			90-day mortality stratified by age <u>≤55 yrs</u> All surg: 152 (1.55) L: 108 (1.33) P: 28 (8.12) SLR: 16 (1.19) <u>56 to 60 yrs</u> All surg: 145 (1.71) L: 106 (1.53) P: 20 (8.47) SLR: 19 (1.47) <u>61 to 65 yrs</u> All surg: 278 (2.3) L: 211 (2.22) P: 29 (10.86) SLR: 38 (1.67) <u>66 to 70 yrs</u> All surg: 471 (3.07) L: 354 (2.95) P: 33 (11.04) SLR: 84 (2.76) <u>71 to 75 yrs</u> All surg: 626 (4.46) L: 486 (4.5) P: 35 (17.33) SLR: 105 (3.46) <u>76 to 80 yrs</u> All surg: 629 (5.85) L: 462 (5.79) P: 32 (24.43) SLR: 135 (5.1) <u>≥81 yrs</u> All surg: 448 (7.3) L: 333 (8.0) P: 2 (6.9) SLR: 113 (5.81)	

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Strand, 2006[194] N=1,375 eligible (total=1,375; Stage 1A=559; stage 1B=816) KQ 6 Good	5-yr OS Total: 50.8 (NR) Stage 1A: 63.5 (NR) Stage 1B: 42.1 (NR)	NR	NR	NR
Su, 2014[174] N=578 (578 for OS, 542 for DFS) – T1 patients only KQ 6 Fair	5-yr OS 72 (68 to 76)	5-yr DFS 77 (73 to 81)	NR	NR
Tsutani, 2014[179] N=618 (325 with N0 status only) KQs 6, 7 Good	N0 patients only 5-yr OS 95.9 (NR)	NR	No 30-day mortality	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Valle, 2016[246] Surg N=1,183 *(1,067* for perioperative death, 1,033 for acute toxicity) KQ 7 Fair	NR	NR	30-day mortality 16 (1.5)	Any acute toxicity (within 60 days of surg) 241 (23) reporting 381 toxicity events Pneumonia (infectious) *41* (4) Hemoptysis 0 (0) Respiratory failure *31* (3) Home oxygen *93* (9) Pleural effusion (nonmalignant) *62* (6) Pneumothorax *41* (4) ICU admission *31* (3) Dyspnea requiring hospitalization *10* (1) Hospitalization (other) *31* (3)
Yang, 2016[250] N=20,191 (for open L vs. MIS L analysis: total=18,780; open L=9,390; MIS L=9,390; for VATS L vs. robotic L analysis: total=3,876; VATS L=1,938; robotic L=1,938) KQ 7 Fair	NR	NR	30-day mortality <u>Open vs. MIS analysis</u> Open L: 117 (1.8) MIS L: 79 (1.5) <u>VATS vs. robotic analysis</u> VATS L: 17 (1.5) Robotic L: 12 (1.3) 30-day readmission <u>Open vs. MIS analysis</u> Open L: 375 (4) MIS L: 467 (5) <u>VATS vs. robotic analysis</u> VATS L: 103 (5.3) Robotic L: 89 (4.6) Conversion from MIS to open procedure <u>VATS vs. robotic analysis</u> VATS L: 340 (17.5) Robotic L: 200 (10.3)	NR

Appendix E Table 5. KQs 6 and 7: Surgery Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes, % (95% CI)*	Long-Term Progression-Related Outcomes, % (95% CI)*	Short-Term Mortality, N (%)*	Adverse Events, N (%)*
Zhai, 2014[172] N=724 (subset of sample with Stage 1 NSCLC) KQ 6 Fair	5-yr OS Total: 73.7 (NR) COPD: 72.8 (NR) No COPD: 74.0 (NR)	NR	NR	NR
Zhao, 2017[183] N=7,989 (total=7,989; S=564; L=7,425) KQ 6 Fair	5-yr OS Total: NR S: 69.0 (NR) L: 70.7 (NR)	5-yr LCSS Total: NR S: 81.3 (NR) L: 83.6 (NR)	NR	NR

* Unless otherwise specified.

Abbreviations: CI=confidence interval; COPD=chronic obstructive pulmonary disease; DSS=disease-specific survival; DVT=deep vein thrombosis; ICU=intensive care unit; KQs=key questions; L/Bi-L=bilobectomy; LC=lung cancer; LNs=lymph node; MI=myocardial infarction; N=number; NR=not reported; NSCLC=non-small cell lung cancer; OS=overall survival; PSM=propensity score-matched; R0 resection=resection for cure or complete remission; R1= microscopic residual disease; SD=standard deviation; SLR=sublobar resection; surg=surgery; ThRCRI=Thoracic Revised Cardiac Risk Index; VATS=video-assisted thoracoscopic surgery; VPI= visceral pleural invasion; vs=versus; yr=year.

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Allibhai, 2013[259] N=185 (185) KQ 7 Fair	NR	NR	NR	Radiation pneumonitis of any grade *18 (8.2)* Grade ≥2 radiation pneumonitis *15 (8.2)* Grade 3 radiation pneumonitis *3* (1.8) No Grade 4 or 5 radiation toxicities	NR
Arnold, 2017[199] N=127 (127) KQ 6 Fair	5-yr OS, % (95% CI) 20.4 (NR)	NR	NR	NR	NR
Badellino, 2017[270] N=148 (148) KQ 7 Fair	NR	NR	NR	RTOG grade ≥3 radiation pneumonitis SBRT 3D-CRT: *4* (3.8) SBRT VMAT: *1* (2.1)	NR
Bibault, 2015[254] N=205 (total=205; Monte Carlo dose calculation protocol=88; Type A dose calculation algorithm=117) KQ 7 Fair	NR	NR	NR	Radiation pneumonitis 14 (6.8) Death during followup 24 (12)	Lung fibrosis 56 *(27.0)* Rib fracture 2 *(1.0)*

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Brooks, 2017[204] N=772 (772) KQs 6, 7 Fair	5-yr OS, % (95% CI) <75 yrs: 51.5 (NR) ≥75 yrs: 39.5 (NR)	5-yr TTP, % (95% CI) <75 yrs: 69.7 (NR) ≥75 yrs: 66.9 (NR)	NR	Radiation Toxicities Fatigue: *48 (6.2)* Dermatitis: *16 (2.1)* Esophagitis: *7 (0.9)* Pneumonitis: *36 (4.7)* Chest wall pain: *31 (4.0)* Hemoptysis: *1 (0.1)* Brachial plexopathy: *1 (0.1)* Rib fracture: *17 (2.2)* Severity of toxicity measured with CTCAE v4.0 Grade 5 toxicity Overall: *1 (0.1)* Hemoptysis: *1 (0.1)* Grade 4 toxicity: None Grade 3 toxicity Overall: NR Fatigue: 4 *(0.5)* Dermatitis: 3 *(0.4)* Pneumonitis: 7 *(0.9)* Chest wall pain: 4 *(0.5)* Grade 2 toxicity Overall: NR Fatigue: *44 (5.7)* Dermatitis: *13 (1.7)* Esophagitis: *7 (0.9)* Pneumonitis: *29 (3.7)* Chest wall pain: *27 (3.5)* Hemoptysis: *1 (0.1)* Brachial plexopathy: *1 (0.1)* Rib fracture: *17 (2.2)*	Cardiac events after SBRT *24 (3.1)*

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Bryant, 2018[196] N=3,620 for SBRT/SABR (total=3,620; L=2,986; SLR=634) KQs 6, 7 Fair	5-yr OS, % (95% CI) 44 (NR) 5-yr cancer-specific mortality, N (%) *202* (45)	NR	30-day mortality, N (%) *2* (0.5) 90-day mortality, N (%) *6* (1.4) 90-day mortality stratified by age, N (%) ≤55 yrs 7 (2.9) 56 to 60 yrs, N (%) 8 (1.92) 61 to 65 yrs, N (%) 19 (2.38) 66 to 70 yrs, N (%) 33 (2.58) 71 to 75 yrs, N (%) 38 (2.44) 76 to 80 yrs, N (%) 56 (3.26) ≥81 yrs, N (%) 80 (3.63)	NR	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Crabtree, 2013[265] Timmerman, 2010[272] N=55 (55) KQ 7 Fair	NR	NR	None	Protocol-specified AEs related to treatment (grade 3 measures of lung injury, esophageal injury, heart injury, and nerve damage, and any grade 4-5 toxicity related to treatment) FEV1: *2 (3.6)* Hypocalcemia: *1 (1.8)* Hypoxia: *2 (3.6)* Pneumonitis NOS: *2 (3.6)* Pulmonary function test decreased NOS: *4 (7.3)* Maximum for protocol: *4 (7.3)* Grade 3 AEs: 7 (12.7) (95% CI, 9.6 to 15.8) Grade 3+ AEs at 30 days: 5 (9.1) Grade 3+ AEs at 90 days: 12 (21.8) Grade 4 AEs: 2 (3.6) (95% CI, 2.7 to 4.5) No grade 5 treatment-related AEs reported Additional patients with AEs attributable to SBRT but not classified prospectively as protocol-specified: 6 (10.9) (95% CI, 8.2 to 13.6)	AEs related (or not) to treatment Overall: *45 (81.8)* Blood or bone marrow: *6 (10.9)* Cardiovascular: *2 (3.6)* Constitutional symptoms: *20 (36.4)* Dermatology or skin: *7 (12.7)* GI tract: *6 (10.9)* Lymphatics: *2 (3.6)* Metabolic or laboratory: *5 (9.1)* Musculoskeletal or soft tissue: *11 (20)* Neurology: *6 (10.9)* Pain: *14 (25.5)* Pulmonary or upper respiratory tract: *33 (60)* Renal or genitourinary: *1 (1.8)* Infection: *3 (5.5)* Coagulation: *2 (3.6)* Hemorrhage or bleeding: *2 (3.6)*
Eba, 2016[201] N=40 (40) KQ 6 Fair	5-yr OS, % (95% CI) 67.0 (50.0 To 79.3)	NR	NR	NR	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Ferrero, 2015[262] N=30 (30) KQ 7 Fair	NR	NR	NR	Any toxicity: 16 *(53.3)* Asthenia: 15 *(50)* Cough: 3 *(10)* Thoracic pain: 1 *(3.3)* Severity measured using RTOG scoring system Grade 1: 5 (15) Grade 2: 6 (20) Grade 3: 4 (13.3) Grade 4: 1 (3.3)	NR
Grills, 2012[256] N=483 (483) KQs 6, 7 Fair	NR	NR	NR	Grade 2 or higher pneumonitis *34* (7) Rib fracture *39* (8)	Respiratory failure 1 *(0.2)* Chronic myositis *24* (5) Grade 2 or higher dermatitis *10* (2)

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Haidar, 2014[257] N=55 (total=55; NPC=23; PC=32) KQ 7 Fair	NR	NR	NR	NPC Acute toxicity: 2 (8.7) Chronic toxicity: 3 (13) PC Acute toxicity: 4 (13) Chronic toxicity: 6 (19) NPC Acute toxicity 2 (8.7): Grade 1 hemoptysis and Grade 2 pleural effusion Chronic toxicity 3 (13): Grade 2 dyspnea, Grade 2 cough and Grade 1 pulmonary fibrosis PC Acute toxicity 4 (13): Grade 3 esophagitis, Grade 2 pneumonitis, Grade 1 cough, and Grade 1 pruritis Chronic toxicity 6 (19): Grade 2 pneumonitis, Grade 1 cough, Grade 1 pneumonitis, Grade 2 dyspnea, and Grade 2 atelectasis	NR
Jeon, 2018[268] N=53 (53) KQ 7 Fair	NR	NR	NR	Chest pain, including rib fracture: 5 (9.4) Rib fracture: *2 (3.8)* Dyspnea: *6 (11.3)* Grade 1 Overall: 5 (9.4) Chest pain, including rib fracture: 5 (9.4) Rib fracture: *2 (3.8)* Grade 3 Overall: 4 *(7.5)* Dyspnea: 4 *(7.5)* Grade 4 Overall: 2 *(3.8)* Dyspnea: 2 *(3.8)*	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Jeppesen, 2018[203] N=136 (136) KQs 6, 7 Fair	5-yr OS, % (95% CI) 35 (NR)	NR	None	"Most common side effects were skin rash, rib fracture, cough and radiological pneumonitis/fibrosis without clinical symptoms" No acute grade 3+ toxicity	NR
Katoh, 2017[255] N=283 (283) KQs 6, 7 Fair	NR	NR	NR	Grade 2 or higher radiation pneumonitis 38 *(13.4)*	NR
Koshy, 2015[200] N=498 (498) KQ 6 Fair	5-yr OS, %, 95% CI 30 (NR)	NR	NR	NR	NR
Lam, 2018[202] N=4,454 (4,454) KQs 6, 7 Fair	Unmatched 5-yr OS, % (95% CI) 33.4 (NR)	NR	NR	NR	Unplanned readmissions within 30 days 17 (0.4)

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Lindberg, 2015[207] N=57 (57 for survival and early toxicity; 34 for late toxicity) KQs 6, 7 Fair	5-yr OS, % (95% CI) 30 (18 To 42)	5-yr LCSS, % (95% CI) 74 (59 to 89) 5-yr PFS, % (95% CI) 52 (33 to 70)	None	Early toxicity (≤36 mos) Overall: NR Atelectasis: 2 *(3.5)* Cough: *6 (10.5)* Dyspnea: *12 (21.1)* Exudate: *4 (7.0)* Fatigue: *9 (15.8)* Fibrosis: *12 (21.1)* Heart: *2 (3.5)* Lung infection: *2 (3.5)* Pain: *4 (7.0)* Pericardial effusion: 1 *(1.8)* Pneumonitis: 6 *(10.5)* Rib fracture: 2 *(3.5)* Skin and subcutaneous tissue: 5 *(8.8)* Upper airway infection: 1 *(1.8)* Late toxicity (>36 mos), N(%) Overall: NR COPD exacerbation: 2 (6) Cough: 1 (3) Dyspnea: *3 (8.8)* Exudate: 1 (3) Lung infection: 1 (3) Rib fracture: *6 (17.6)* Upper airway infection: 1 (3) Ventricle tachycardia: 1 (3) Severity of toxicity measured with CTCAE v4.0 or, for fibrosis, RTOG late toxicity scale (early=occurring within 36 mos of treatment; late=occurring after 36 mos of treatment) Grade 5 toxicity: None Grade 3-4 early toxicity (≤36 mos) Overall: NR Cough: 1 *(1.8)* Dyspnea: 3 *(5.3)* Exudate: 1 *(1.8)*	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Lindberg, 2015[207] (continued)				Fatigue: 1 *(1.8)* Fibrosis: 3 *(5.3)* Heart: 1 *(1.8)* Lung infection: 1 *(1.8)* Pain: 2 *(3.5)* Pericardial effusion: 1 *(1.8)* <u>Grade 3-4 late toxicity (>36 mos) (N analyzed=34)</u> Overall: NR Dyspnea: 1 (3) Rib fracture: 1 (3) Ventricle tachycardia: 1 (3) <u>Grade 2 early toxicity (≤36 mos)</u> Overall: NR Atelectasis: 2 *(3.5)* Cough: 5 *(8.8)* Dyspnea: 9 *(15.8)* Exudate: 3 *(5.3)* Fatigue: 8 *(14.0)* Fibrosis: 9 *(15.8)* Heart: 1 *(1.8)* Lung infection: 1 *(1.8)* Pain: 2 *(3.5)* Pneumonitis: 6 *(10.5)* Rib fracture: 2 *(3.5)* Skin and subcutaneous tissue: 5 *(8.8)* Upper airway infection: 1 *(1.8)* <u>Grade 2 late toxicity (>36 mos) (N analyzed=34)</u> Overall: NR COPD exacerbation: 2 (6) Cough: 1 (3) Dyspnea: 2 (6) Exudate: 1 (3) Lung infection: 1 (3) Rib fracture: 5 *(14.7)* Upper airway infection: 1 (3)	

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Ma, 2017[269] N=155 (155) patients with 159 (159) tumors KQ 7 Fair	NR	NR	NR	Pulmonary embolism Total: 1 *(0.6)* Single-fx SBRT: 0 (0) Triple-fx SBRT: 1 *(1.1)* Severity of toxicity measured with CTCAE v4.0 Grade ≥3 pulmonary toxicity Total: 1 *(0.6)* Single-fx SBRT: 0 (0) Triple-fx SBRT: 1 *(1.1)*, a case of pulmonary embolism No Grade ≥3 pulmonary toxicity occurred within 6 months of SBRT	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Mathieu, 2015[260] N=45 (45) KQ 7 Fair	NR	NR	NR	Radiation pneumonitis of any grade *2 (4.4)* Mortality due to radiation pneumonitis 1 *(2.2)* Dyspnea *4 (8.9)* Cough 1 *(2.2)* Radiation-induced rib fractures 3 (7) Pneumothorax requiring chest tube placement 2 *(4.4)* <u>Severity of toxicity measured with CTCAE v3.0</u> (acute=occurring within 4 mos of treatment; late=occurring after 4 mos of treatment) Grade 5 toxicity: Radiation pneumonitis: 1 *(2.2)* Grade 3 toxicity Overall: *4 (8.9)* Acute dyspnea: 1 *(2.2)* Late: 3 (7), of which 2 were cases of dyspnea and 1 was case of dyspnea, cough, and radiation pneumonitis Grade ≤2 toxicity (measured with CTCAE v3.0) Overall: 3 (7) Acute: 0 (0) Late radiation-induced rib fractures: 3 (7)	NR
Matsuo, 2014[198] N=115 (115) KQs 6, 7 Fair	5-yr OS, % (95% CI) 40.3 (31.1 To 49.3)	5-yr cause-specific death, % (95% CI) 33.8 (25.1 to 42.6)	NR	NR	No treatment-related deaths

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Nagata, 2015[205] N=164 (total=164; operable=64; inoperable=100) KQs 6, 7 Fair	5-yr OS, % (95% CI) Operable 54.0 (41.0 To 65.4) Inoperable 42.8 (33.0 To 52.3)	NR	NR	Grade 2 toxicities using CTCAE v3.0 Total: NR, but 17 events reported Mild symptomatic fractures: 7 *(4.1)* Chest wall pain: 3 *(1.8)* Cough: 3 *(1.8)* Chest pain: 2 *(1.2)* Brachial plexopathy: 1 *(0.6)* Dermatitis: 1 *(0.6)* Grade 3 toxicities using CTCAE v3.0 Total: *15 (8.9)* Dyspnea: *13 (7.7)* Hypoxia: *9 (5.3)* Pneumonitis: *10 (5.9)* Chest pain: *3 (1.8)* Cough: 1 *(0.6)* Grade 4 toxicities using CTCAE v3.0 Total: 2 *(1.2)* Dyspnea: 2 *(1.2)* Hypoxia: 1 *(0.6)* Pneumonitis: 1 *(0.6)*	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Nyman, 2016[267] N=49 (49) KQ 7 Fair	NR	NR	NR	Esophagitis: 4 (8) Pneumonitis: *9 (18.4)* Dyspnea: *32 (65.3)* Fibrosis: *24 (49.0)* Cough: *25 (51.0)* Skin reactions: *16 (32.7)* Rib fractures: *8 (16.3)* Severity measured using CTCAE v3.0 grading system <u>Grade 1</u> Esophagitis: 4 (8) Pneumonitis: 7 (15) Dyspnea: 19 (40) Fibrosis: 20 (42) Cough: 19 (40) Skin reactions: 13 (27) Rib fractures: 6 (13) <u>Grade 2</u> Esophagitis: 0 (0) Pneumonitis: 2 (4) Dyspnea: 8 (17) Fibrosis: 4 (8) Cough: 5 (10) Skin reactions: 2 (4) Rib fractures: 2 (4) <u>Grade 3</u> Esophagitis: 0 (0) Pneumonitis: 0 (0) Dyspnea: 5 (10) Fibrosis: 0 (0) Cough: 1 (2) Skin reactions: 1 (2) Rib fractures: 0 (0) No Grade 4 or 5 toxicities	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Robinson, 2013[266] N=78 (78) KQ 7 Fair	NR	NR	NR	Esophagitis: 2 *(2.6)* Pneumonitis: 6 (7.7) Brachial plexopathy: 1 *(1.3)* Pleural effusion: 1 *(1.3)* Soft-tissue necrosis: 1 *(1.3)* Chest-wall pain: 15 (19.2) Severity measured using CTCAE v4.0 grading system <u>Grade 1</u> Total: *12 (15.4)* Acute: 18 *(1.3)* Late: *11 (14.1)* <u>Grade 2</u> Total: *11 (14.1)* Acute: 1 *(1.3)* Late: *10 (12.8)* <u>Grade 3</u> Total: *4 (5.1)* Acute: 0 (0) Late: *4 (5.1)*	NR
Rosen, 2014[258] N=79 (79) KQ 7 Fair	NR	NR	None	Chest wall pain 6 (7.6) (95% CI, 3.5 to 15.9) Rib fracture, N (%) 2 (2.5) (95% CI, 0.7 to 8.7) Significant skin reactions 3 (3.8) (95% CI, 1.3 to 10.5) No cases of life-threatening radiation pneumonitis, clinically significant pulmonary complications, necrosis, or fatal hemoptysis "All cases of rib fracture were late findings and resolved without intervention beyond topical creams and oral pain medications"	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Rosen, 2016[185] Primary analyses (i.e., patients selected for Charlson-Deyo score=0) N=1,781 for SBRT/SABR (1,781 for both unmatched and PSM sets) Secondary analyses (i.e., patients unselected based on Charlson-Deyo score) N=235 for SBRT/SABR (235 for both unmatched and PSM sets) KQs 6, 7 Good	5-yr OS, % (95% CI) Primary Analysis Propensity-Matched Healthy Subset 29 (NR) Secondary Analysis Propensity-Matched Healthy Subset With SBRT Patients Refusing Surgery 40 (NR)	NR	NR	NR	NR
Shirvani, 2012[237] N=124 for SABR/SBRT (124) KQ 7 Fair	NR	NR	30-day mortality, N (%) 0 (0) 90-day mortality, N (%) *1* (0.8)	NR	NR
Shirvani, 2014[241] N=382 (382) KQ 7 Fair	NR	NR	90-day mortality, N (%) *5* (1.3)	NR	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Stokes, 2018[251] N=8,216 for SBRT (8,216) KQ 7 Fair	NR	NR	30-day mortality, N (%) *60* (0.7) 30-day mortality stratified by age, N (%) <u>≤55 yrs</u> 3 (1.2) <u>56 to 60 yrs</u> 2 (0.5) <u>61 to 65 yrs</u> 3 (0.38) <u>66 to 70 yrs</u> 9 (0.7) <u>71 to 75 yrs</u> 10 (0.64) <u>76 to 80 yrs</u> 13 (0.76) <u>≥81 yrs</u> 20 (0.91) 90-day mortality, N (%) *241* (2.9) 90-day mortality stratified by age, N (%) <u>≤55 yrs</u> 7 (2.9) <u>56 to 60 yrs</u> 8 (1.92) <u>61 to 65 yrs</u> 19 (2.38)	NR	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Stokes, 2018[251] (continued)			66 to 70 yrs 33 (2.58) 71-75 yrs 38 (2.44) 76-80 yrs 56 (3.26) ≥81 yrs 80 (3.63)		
Sun, 2017[197] N=73 (65) KQs 6, 7 Fair	5-yr OS, % (95% CI) 55.7 (49.4 To 62.0) 5-yr mortality, % (95% CI) NR 10-yr mortality, % (95% CI) NR		NR	NCI CTCAE (v. 3) Grade 1: 49 (75.4) Grade 2: 7 (10.8) Grade 3: 1 (1.5) Radiation pneumonitis, N (%) 57 *(87.7)*	Dermatitis Total: 21 *(32.3)* Grade 1: 16 (24.6) Grade 2: 3 (4.6) Grade 3: 2 (3.1) Hemoptysis Total: 1 (1.5) Grade 1: 1 (1.5) Grade 2: 0 (0) Grade 3: 0 (0) Dyspnea/shortness of breath Total: 19 *(29.2)* Grade 1: 11 (16.9) Grade 2: 8 (12.3) Grade 3: 0 (0) Fatigue Total: 9 *(13.9)* Grade 1: 7 (10.8) Grade 2: 2 (3.1) Grade 3: 0 (0) Chest wall pain Total: 23 *(35.4)* Grade 1: 15 (23.1) Grade 2: 7 (10.8) Grade 3: 1 (1.5) Rib fracture Total: 16 *(24.6)* Grade 1: 13 (20.0) Grade 2: 3 (4.6) Grade 3: 0 (0)

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Sun, 2017[197] (continued)					Brachial plexopathy Total: 5 *(7.7)* Grade 1: 3 (4.6) Grade 2: 2 (3.1) Grade 3: 0 (0)
Taremi, 2012[261] N=46 (total=46; female=24; male=22; COPD=29; diabetes=8) KQ 7 Fair	NR	NR	NR	RIBI Total: 17 (37) Female: 11 *(45.8)* with 30 fractures Male: 6 *(27.3)* with 13 fractures COPD: 11 *(37.9)* Diabetes: 2 *(25.0)* Total N of rib fractures: 41 ribs with 43 fracture sites Median time to developing a rib fracture (range) 21 mos (7 to 40 mos) <u>Chest wall pain toxicity</u> Patients without rib fractures 7 *(24)* Patients with rib fractures 14 *(82)* Patients with chest wall pain received higher dose of radiation to the ribs compared to patients without chest wall pain (62.76 Gy, range: 28.4 to 88.05 Gy vs. 47.21 Gy, range: 15.9 to 73.19 Gy; p value: 0.008).	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Taremi, 2012[261] (continued)				In all patients except one (with 6 fractured ribs), pain became more stable after 6–8 months. Multivariate analysis found that D to 0.5 cc of the ribs (D0.5) and volume of rib receiving ≥25 Gy (V25) were significantly associated with RIBI Grading of chest wall pain and rib fractures using CTCAE v3.0 <u>Grade 1</u> With rib fractures 5 *(29.4)* Without rib fractures 4 *(13.8)* Radiologic fractures (denominator is total N of fracture sites) 10 *(23.3)* <u>Grade 2</u> With rib fractures 6 *(35.3)* Without rib fractures 3 *(10.3)* Radiologic fractures (based on total N of fracture sites) 19 *(44.2)* <u>Grade 3</u> With rib fractures 3 *(17.6)* Without rib fractures 0 (0) Radiologic fractures (based on total N of fracture sites) 14 *(32.5)*	

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Taremi, 2012[264] N=108 KQ 7 Fair	NR	NR	None	<u>Any acute/early toxicity (i.e., ≤3 mos after SBRT)</u> Overall N of patients with acute/early toxicity: 77 *(71.3)* Fatigue: 54 (50) Cough/dyspnea: 39 *(36.1)* Pneumonitis: 4 *(3.7)* Anorexia: 3 *(2.8)* Chest wall pain: 12 *(11.1)* Dyspepsia/dysphagia: 13 *(12)* Skin toxicity: 12 *(11.1)* <u>Any late toxicity (i.e., >3 mos after SBRT)</u> Overall N of patients with late toxicity: 74 *(68.5)* Fatigue: 38 *(35.2)* Cough/dyspnea: 43 *(39.8)* Pneumonitis: 24 *(22.2)* Chest wall pain: 16 *(14.8)* Rib fracture: 27 *(25)* Pleural effusion: 2 *(1.9)* Hemoptysis: 5 *(4.6)* Skin toxicity: 1 *(0.9)* <u>Grading of acute/early toxicities using CTCAE v3.0</u> Grade 1: Patients NR, but 102 *(74.4%)* total events Grade 2: Patients NR, but 31 *(22.6%)* total events Grade 3: 4 *(3.7)* <u>Grading of late toxicities using CTCAE v3.0</u> Grade 1: Patients NR, but 96 *(59.3%)* total events Grade 2: Patients NR, but 54 *(33.3%)* total events Grade 3: 6 *(5.6)*	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Ubels, 2015[206] N=39 (39) KQs 6, 7 Fair	5-yr OS, % (95% CI) 31 (NR)	5-yr DFS, % (95% CI) 52 (NR)	Mortality during surgery, N (%) 1 *(2.6)*	Patients with grade 2-3 events (grade 1 events NR) Any acute toxicity: *27 (69.2)* Dyspnea: *15 (38.5)* Esophageal pain: 1 *(2.6)* Thoracic pain: *10 (25.6)* Coughing: *6 (15.4)* Severity of toxicity measured with CTCAE v3.0 (acute=occurring within 4 mos of treatment; late=occurring after 4 mos of treatment) Grade 5 toxicity: None Grade 4 toxicity: None Grade 3 acute toxicity Overall: 2 *(5.1)* Dyspnea: 1 *(2.6)* Thoracic pain: 1 *(2.6)* Grade 3 late toxicity Overall: 4 *(10.3)* Dyspnea: 2 *(5.1)* Thoracic pain: 2 *(5.1)* Grade 2 acute toxicity Overall: 12 *(30.8)* Dyspnea: 6 *(15.4)* Esophageal pain: 1 *(2.6)* Thoracic pain: 1 *(2.6)* Coughing: 4 *(10.3)* Grade 2 late toxicity Overall: 14 *(35.9)* Dyspnea: 6 *(15.4)* Thoracic pain: 6 *(15.4)* Chronic cough: 2 *(5.1)*	NR

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Valle, 2016[246] N=*184* (*176* for perioperative death, *148* for acute toxicity) KQ 7 Fair	30-day mortality 3 (1.7)	NR	NR	Any acute toxicity (i.e., within 180 days of treatment completion): 34 (23) reporting 60 toxicity events Radiation pneumonitis: *13* (9) Home oxygen: *4* (3) Pleural effusion (nonmalignant): *4* (3) Pneumonia (infectious): *15* (10) Pneumothorax: 0 (0) ICU admission: 0 (0) Respiratory failure: *2* (1) Dyspnea requiring hospitalization: *4* (3) Hemoptysis: *3* (2) Hospitalization (other): *6* (4)	NR
Videtic, 2014[271] N=80 (80) KQ 7 Fair	NR	NR	NR	<u>Patients experiencing any toxicity</u> Single-fx SBRT at 30 Gy: *4 (7.3)* Single-fx SBRT at 34 Gy: *4 (16)* <u>Chest wall pain/neuropathy</u> Single-fx SBRT at 30 Gy: *2 (3.6)* Single-fx SBRT at 34 Gy: *4 (16)* <u>Pneumonitis</u> Single-fx SBRT at 30 Gy: *2 (3.6)* Single-fx SBRT at 34 Gy: 0 (0) <u>Grade 1 toxicity</u> Single-fx SBRT at 30 Gy: 0 (0) Single-fx SBRT at 34 Gy: *1 (4)* <u>Grade 2 toxicity</u> Single-fx SBRT at 30 Gy: *4 (7.3)* Single-fx SBRT at 34 Gy: *3 (12)*	NR
Videtic, 2015[263] N=84 (84) KQ 7 Fair	NR	NR	30-day mortality, N (%) SBRT at any dose: 1 *(1.2)* SBRT 34 Gy x 1 fx: 1 *(2.6)* SBRT 48 Gy x 4 fx: 0 (0)	<u>Rates of prespecified grade 3 or higher toxicities at 1 year</u> SBRT at any dose: *10 (11.9)* SBRT 34 Gy x 1 fx: 4 (10.3) (95% CI, 2.9 to 24.2) SBRT 48 Gy x 4 fx: 6 (13.3) (95% CI, 5.1 to 26.8)	<u>Respiratory failure leading to death, possibly related to SBRT</u> SBRT at any dose: 1 *(1.2)* SBRT 34 Gy x 1 fx: 0 (0) SBRT 48 Gy x 4 fx: 1 *(2.2)*

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Videtic, 2015[263] (continued)				Fatigue/malaise SBRT at any dose: *11 (13.1)* SBRT 34 Gy x 1 fx: 6 (15) SBRT 48 Gy x 4 fx: 5 (11) Musculoskeletal disorders (including pain) SBRT at any dose: *11 (13.1)* SBRT 34 Gy x 1 fx: 8 (21) SBRT 48 Gy x 4 fx: 3 (7) Injury (including fracture) SBRT at any dose: *8 (9.5)* SBRT 34 Gy x 1 fx: 7 (18) SBRT 48 Gy x 4 fx: 1 (2) Respiratory disorders SBRT at any dose: *33 (39.3)* SBRT 34 Gy x 1 fx: 18 (46) SBRT 48 Gy x 4 fx: 15 (33) Adverse changes in DLCO SBRT at any dose: *6 (7.1)* SBRT 34 Gy x 1 fx: 4 *(10.3)* SBRT 48 Gy x 4 fx: 2 *(4.4)* Adverse changes in FVC SBRT at any dose: 1 *(1.2)* SBRT 34 Gy x 1 fx: 0 (0) SBRT 48 Gy x 4 fx: 1 *(2.2)* Pneumonitis SBRT at any dose: 2 *(2.4)* SBRT 34 Gy x 1 fx: 0 (0) SBRT 48 Gy x 4 fx: 2 *(4.4)* General disorder leading to death, but possibly unrelated to SBRT SBRT at any dose: 1 *(1.2)* SBRT 34 Gy x 1 fx: 1 *(2.6)* SBRT 48 Gy x 4 fx: 0 (0)	

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Videtic, 2015[263] (continued)				Respiratory failure leading to death, possibly related to SBRT SBRT at any dose: 1 *(1.2)* SBRT 34 Gy x 1 fx: 0 (0) SBRT 48 Gy x 4 fx: 1 *(2.2)* Severity measured using CTCAE v4.0 grading system Grade 1 fatigue/malaise SBRT at any dose: *7 (8.3)* SBRT 34 Gy x 1 fx: 2 (5) SBRT 48 Gy x 4 fx: 5 (11) Grade 1 musculoskeletal disorders (including pain) SBRT at any dose: *8 (9.5)* SBRT 34 Gy x 1 fx: 5 (13) SBRT 48 Gy x 4 fx: 3 (7) Grade 1 injury (including fracture) SBRT at any dose: 4 *(4.8)* SBRT 34 Gy x 1 fx: 4 (10) SBRT 48 Gy x 4 fx: 0 (0) Grade 1 respiratory disorders SBRT at any dose: *21 (25)* SBRT 34 Gy x 1 fx: 13 (33) SBRT 48 Gy x 4 fx: 8 (18) Grade 2 fatigue/malaise SBRT at any dose: *4 (4.8)* SBRT 34 Gy x 1 fx: 4 (10) SBRT 48 Gy x 4 fx: 0 (0) Grade 2 musculoskeletal disorders (including pain) SBRT at any dose: 3 *(3.6)* SBRT 34 Gy x 1 fx: 3 (8) SBRT 48 Gy x 4 fx: 0 (0)	

Appendix E Table 6. KQs 6 and 7: SBRT Results

Study Identifiers Author, Year N Enrolled (Analyzed) KQs Addressed Quality	Long-Term Survival and Mortality Outcomes	Long-Term Progression-Related Outcomes	Short-Term Mortality	Radiation Toxicities Rib Fractures Radiation Pneumonitis, N (%) Patients* Rib Fracture, N (%) Patients*	Other Adverse Events Specific Outcome, N (%) Patients*
Videtic, 2015[263] (continued)				Grade 2 injury (including fracture) SBRT at any dose: *4 (4.8)* SBRT 34 Gy x 1 fx: 3 (8) SBRT 48 Gy x 4 fx: 1 (2) Grade 2 respiratory disorders SBRT at any dose: *7 (8.3)* SBRT 34 Gy x 1 fx: 5 (13) SBRT 48 Gy x 4 fx: 2 (4) Grade 3 SBRT at any dose: *9 (10.7)* SBRT 34 Gy x 1 fx: 4 *(10.3)* SBRT 48 Gy x 4 fx: *5 (11.1)* Grade 5 SBRT at any dose: *2 (2.4)* SBRT 34 Gy x 1 fx: 1 *(2.6)* SBRT 48 Gy x 4 fx: 1 *(2.2)*	

* Unless otherwise specified.

Abbreviations: 3D-CRT=three-dimensional conformal radiation therapy; 95% CI=95% confidence interval; AE(s)=adverse event(s); cc=cubic centimeters; COPD=chronic obstructive pulmonary disease; CTCAE=Common Terminology Criteria for Adverse Events; FVC=forced vital capacity; fx=fraction(s); D0.5=dose to 0.5 cc of the ribs; DVT=deep vein thrombosis; Gy=Gray; ICU=intensive care unit; IQR=interquartile range; LC=lung cancer; LN(s)=lymph node(s); LOS=length of stay; MI=myocardial infarction; N=number; NCI=National Cancer Institute; NR=not reported; OS=overall survival; PSM=propensity score matching (or matched); RIBI=radiation-induced bone injury; RTOG=Radiation Therapy Oncology Group; SBRT/SABR=stereotactic body radiotherapy/stereotactic ablative radiotherapy; SD=standard deviation; SLR=sublobar resection; surg=surgery; ThRCRI=Thoracic Revised Cardiac Risk Index; TTP=time-to-progression; V25=volume of rib receiving ≥25 Gy; VATS=video-assisted thoracoscopic lobectomy; VMAT=volumetric modulated arc therapy; VPI=visceral pleural invasion; vs.=versus.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Ackerson, 2018[295] SBRT N=70 KQ 7 Fair	NA United States 2007-2014 Followup: 65 mos.	Age: 74 (IQR 69 to 79) Female: 35 (50) Race/Ethnicity: NR Smoking Status: Never: 2 (2.9) Current: 14 (20) Past: 54 (77) Comorbidities: 89% of SBRT patients were deemed medically inoperable prior to treatment Charlson Comorbidity Index: Mean (SD): 3.7 (1.4) Median (IQR): 3 (3 to 5)	Clinical T-Stage T1a: 25 (36) T1b: 29 (41) T2a: 15 (21) T2b: 1 (1) Histology: NR SBRT Dosing and Frequency: SBRT was given every 48-72 hours using 3-5 fractions. Overall, 34 (49%) patients received 12–12.5 Gy x 4; 24 (34%) patients received 18–20 Gy × 3; and 8 (11%) patients received 10 Gy × 5. Less common fractionation schemes were used to treat 4 (6%) patients.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Baine, 2019[232] SBRT N=26,725 KQs 6 & 7 Fair	NCDB United States 2004-2014 Followup: 26.7 mos.	Age: 75 (IQR 69 to 81) Female: 14,265 (53.4) Race/Ethnicity White: 23,861 (89.3) Black: 2,230 (8.3) Indian: 76 (0.3) Pacific Islander: 258 (1.0) Other: 72 (0.3) Missing: 228 (0.9) Smoking Status: NR Comorbidities Charlson-Deyo Comorbidity Score, N (%) 0-2: 25,485 (95.4) ≥3: 1,240 (4.6)	Stage IA: 19,856 (74.3) IB: 5,659 (21.2) I NOS: 1,210 (4.5) Histology Squamous: 9,160 (34.3) Adenocarcinoma: 11,672 (43.7) NSCLC NOS: 4,457 (16.7) Other: 1,436 (5.4) SBRT Dosing, N (%) 48 Gy: 5,727 (21.4) 50 Gy: 9,677 (36.2) 54 Gy: 4,368 (16.3) 60 Gy: 6,953 (26) SBRT Fractions, N (%) 3: 7,835 (29.3) 4: 7,212 (27) 5: 9,291 (34.8) Other: 2,387 (8.9)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Ball, 2019[293] SABR N=66 KQ 7 Fair	CHISEL Australia/New Zealand Dec. 2009-June 2015 Followup: 2.6 yrs (IQR 1.6 to 3.6 yrs)	Age, Mean (SD): 74 (8) Female: 30 (45) Race/Ethnicity: NR Smoking status Current or previous smoker: 63 (97) Current smoker: 20 (31) Smoker pack-years Mean (SD): 51 (30) Median (IQR): 42 (33 to 60) Comorbidities Medically inoperable: 58 (88) Previous cancer: 28 (43) Colinet Simplified Comorbidity Score[†] Mean (SD): 10 (3) Median (IQR): 9 (8 to 11)	T Stage 1: 47 (71) 2a: 19 (29) Histology Adenocarcinoma: 32 (48) LCC: 1 (2) Mixed: 2 (3) Non-small-cell carcinoma NOS: 9 (14) SCC: 22 (33) SABR Dosing and Frequency: Overall, 8 (13%) of the 63 patients not withdrawing before treatment received 54 Gy total in 3 fractions x 18 Gy. Because their tumors were <2 cm from the chest wall, the other 55 (87%) of 63 patients received 48 Gy total in 4 fractions x 12 Gy. Treatment was initiated ideally within 4 weeks, but later than 6 weeks after, randomization.
Barriger, 2012[290] SBRT N=251 KQ 7 Fair	NA United States Feb. 2000-Oct. 2008 Followup: 17 mos. (0.3-89 mos.)	Age: 74 (45 to 100) Female: 109 (43) Race/Ethnicity: NR Smoking Status Never smoker: 6 (2) Quit >30 years: 15 (6) Quit 3 mos. to 30 years: 145 (58) Current or quit <3 months: 82 (33) Unknown: 3 (1) Comorbidities All patients were medically inoperable COPD: 192 (76) Oxygen dependent: 56 (22)	Stage IA: 138 (55) IB: 108 (43) IIB: 5 (2) Histology SCC: 76 (30) Adenocarcinoma: 70 (28) NSCLC unspecified: 105 (42) SBRT Dosing and Frequency: Median prescribed dose was 60 Gy (range: 24 to 72 Gy) delivered in 3 fractions, with a dose/fraction of 8 to 24 Gy, each separated by 2-3 days, to the 80% isodose line. Treatment time was a median of 8 days (range: 4 to 84 days).

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Baumann, 2006[227] SBRT N=141 KQs 6 & 7 Fair	NA Sweden/Denmark 1996-2003 Followup: 33 mos. (1 to 107 mos.)	Age, mean (range): 74 (56 to 90) Female: 72 (51) Race/Ethnicity: NR Smoking Status: NR Comorbidities All patients were medically inoperable COPD: 78 (55) CVD: 25 (18) COPD+CVD: 21 (15) Other malignancies: 14 (10) Other compromising diseases: 3 (2)	T Stage 1: 56 (40) 2: 85 (60) Histology SCC: 39 (28) Adenocarcinoma: 44 (31) BAC: 3 (2) NSCLC NOS: 21 (15) No histology: 34 (24) SBRT Dosing and Frequency: A total dose of 30 to 48 Gy was given in 2 to 4 fractions, with a dose/fraction of 10 to 20 Gy, generally 2 to 3 days apart.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Berry, 2018[216] Surgery N=14,545 KQ 6 Fair	California Cancer Registry United States Jan. 2003-Dec. 2014 Followup: NR	Age at diagnosis, N (%) <60: 2401 (16.5) 60-69: 4746 (32.6) 70-79: 5450 (37.5) ≥80: 1948 (13.4) Female: 7948 (54.6) Transgender: <5 Race/Ethnicity Non-Hispanic white: 10,621 (73.0) Non-Hispanic black: 861 (5.9) Hispanic: 1,258 (8.6) Asian/Pacific Islander: 1,711 (11.8) Other/unknown: 94 (0.6) Smoking Status: NR Comorbidities: NR	c-stage 1: 14,545 (100) T Stage T1: 8305 (57.1) T2: 6202 (42.6) Unknown: 38 (0.3) Histology Adenocarcinoma: 9474 (65.1) SCC: 3227 (22.2) Large cell neuroendocrine carcinoma: 382 (2.6) Other: 964 (6.7) NSCLC NOS: 498 (3.4) Surgical Approach Lobar resection: 11,536 (79.3) SLR: 2783 (19.1) Wedge resection (SLR subtype): 2119/2783 (76.1) Segmentectomy (SLR subtype): 560/2783 (20.1) Not specified (SLR subtype): 104*/2783 (3.7*) Pneumonectomy: 226 (1.6)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Bongers, 2011[286] SABR N= 500 (530 tumors) KQ 7 Fair	NA Netherlands April 2003-April 2009 Followup: 33 mos. (13 to 86 mos.)	Age: 74 (42 to 92) Female: 209 (41.8) Race/Ethnicity: NR Smoking Status: NR Comorbidities 374 (74.8%) medically inoperable	T Stage (n=530) 1: 307 (57.9) 2: 223 (42.1) Histology (n=500) Adenocarcinoma: 61* (12.2*) SCC: 57* (11.4*) NSCLC NOS: 64* (12.8*) Not obtained: 318 (63.6) SABR Dosing and Frequency (n=530) 3 x 20 Gy: 215 (40.6) 5 x 12 Gy: 226 (42.6) 8 x 7.5 Gy: 89 (16.8)
Chang, 2012[282] SABR N=130 KQ 7 Fair	NA United States Feb. 2005-Dec. 2009 Followup: 26 mos. (6-78 mos.)	Age: 74 (48-91) Female: 63 (48.5) Race/Ethnicity: NR Smoking Status: NR Comorbidities: COPD Stage 0-II: 73 (56) COPD Stage III-IV: 57 (44) History of other type of cancer: 37 (28.5)	Stage IA: 112 (86) IB: 18 (14) Histology SCC: 36 (28) Adenocarcinoma: 58 (45) NSCLC NOS: 36 (28) SABR Dosing and Frequency: 50 Gy total, (to PTV between 75% & 90% isodose lines) administered in 4 fractions over 4 consecutive days.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Cummings, 2018[233] SBRT N=163 KQs 6 & 7 Fair	NA United States 2007-2015 Followup 1-Fraction (SF): 24 mos. (1.6 to 64 mos) 5-Fraction (FF): 40 mos. (3 to 97 mos.)	Age: 77 (52 to 97) Female: 89* (54.6*) Race/Ethnicity: NR Pack-years smoking, years (range) SF: 50 (0 to 140) FF: 47.5 (0 to 125) Comorbidities: NR	T Stage T1b: 92 (56.4*) T1c: 34 (20.9*) NR: 37* (22.7*) Histology Adenocarcinoma: 77 (47.2*) SCC: 46 (28.2*) LCC: 1 (0.6*) BAC: 9* (5.5*) Other: 7 (4.3*) No pathology: 23* (14.1*) SBRT Dosing and Frequency: Median doses were 30 Gy in the SF arm and 50 Gy in the FF arm. In the latter, most patients received 50 Gy total in 5 fractions; 18 patients received 60 Gy total in 5 fractions.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Detillon, 2019[231] SBRT N=378 (159 and 36 for primary and secondary PSM analyses, respectively) KQ 6 Fair	Netherlands Cancer Registry Netherlands 2010-2015 Followup Unmatched analysis: 32 mos. Primary PSM analysis: 32 mos. Secondary PSM analysis: 33 mos.	Age, Mean (SD) Unmatched analysis: 74.9 (5.9) Primary PSM analysis: 74.3 (5.4) Secondary PSM analysis: 73.5 (5.8) Female Unmatched analysis: 154 (40.7) Primary PSM analysis: 61 (38.4) Secondary PSM analysis: 14 (38.9) Race/Ethnicity: NR Smoking Status: NR Comorbidities Unmatched analysis Pulmonary: 221 (61.9) Cardiac: 158 (44.3) Hypertension: 139 (38.9) Previous malignancy: 126 (35.3) Vascular: 116 (32.5) Diabetes: 73 (20.4) Unknown: 21 (5.6) Primary PSM analysis Pulmonary: 82 (51.6) Cardiac: 67 (42.1) Hypertension: 66 (41.5) Previous malignancy: 68 (42.8) Vascular: 53 (33.3) Diabetes: 27 (17.0) Secondary PSM analysis Pulmonary: 20 (55.6) Cardiac: 14 (38.9) Hypertension: 15 (41.7) Previous malignancy: 12 (33.3) Vascular: 13 (36.1) Diabetes: 6 (16.7)	T Stage Unmatched analysis 1a: 139 (36.8) 1b: 117 (31.0) 2a: 91 (24.1) Unknown: 31 (8.2) Primary PSM analysis 1a: 49 (30.8) 1b: 53 (33.3) 2a: 57 (35.8) Secondary PSM analysis 1a: 14 (38.9) 1b: 12 (33.3) 2a: 10 (27.8) Histology Unmatched analysis Adenocarcinoma: 77 (20.4) SCC: 65 (17.2) Other: 50 (13.2) Unknown: 186 (49.2) Primary PSM analysis Adenocarcinoma: 63 (39.6) SCC: 54 (34.0) Other or unknown: 42 (26.4) Secondary PSM analysis Adenocarcinoma: 8 (22.2) SCC: 5 (13.9) Other or unknown: 23 (63.9) SBRT Dosing and Frequency: Total Gy NR, schedules varied between 3 to 8 fractions, delivered 2-3 times per week in the case of multiple fractions.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Detillon, 2019[231] SBRT N=378 (159 and 36 for primary and secondary PSM analyses, respectively) KQ 6 Fair (continued)		N (%) of Comorbidities <u>Unmatched analysis</u> None: 9 (2.5) 1: 73 (20.5) 2: 105 (29.4) 3: 75 (21.0) ≥4: 95 (26.6) <u>Primary PSM analysis</u> None: 6 (3.8) 1: 27 (17.0) 2: 54 (34.0) 3: 34 (21.4) ≥4: 38 (23.9) <u>Secondary PSM analysis</u> None: 2 (5.6) 1: 7 (19.4) 2: 12 (33.3) 3: 8 (22.2) ≥4: 7 (19.4) Charlson Comorbidity Score, N (%) <u>Unmatched analysis</u> 0: 9 (2.5) 1: 61 (17.1) 2: 79 (22.1) 3: 83 (23.2) ≥4: 125 (35.0) <u>Primary PSM analysis</u> 0: 6 (3.8) 1: 17 (10.7) 2: 42 (26.4) 3: 40 (25.2) ≥4: 54 (34.0)	

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Detillon, 2019[231] SBRT N=378 (159 and 36 for primary and secondary PSM analyses, respectively) KQ 6 Fair (continued)		Secondary PSM analysis None: 2 (5.6) 1: 6 (16.7) 2: 10 (27.8) 3: 6 (16.7) ≥4: 12 (33.3)	
Dziedzic, 2017[217] Surgery N=6,905 KQs 6 & 7 Fair	Polish National Lung Cancer Registry Poland Jan. 2007-Dec. 2013 Followup: 36.9 mos. (95% CI, 36.1 to 37.9 mos.)	Age: 63.3 (IQR, 57.6 to 70.1) Female: 2,865 (41.5*) Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	Stage IA: 5,147* (74.5*) IB: 1,758* (25.5*) Histology Adenocarcinoma: 3,181* (46.1*) SCC: 2,235* (32.4*) Other: 1,489* (21.6*) Surgical Approach Lobectomy: 5,911 (85.6*) Segmentectomy: 233 (3.4*) Wedge resection: 761 (11*)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Ezer, 2018[273] Surgery N=9,508 KQ 7 Fair	SEER United States 2000-2009 Followup: NR	Age Total: 74.5* Open Lobectomy: 74 (5) VATS Lobectomy: 75 (6) Female Total: 5,143* (54.1*) Open Lobectomy: 4,414 (53) VATS Lobectomy: 729 (61) Race/Ethnicity White Total: 8,489* (89.3*) Open Lobectomy: 7,429 (88) VATS Lobectomy: 1,060 (89) African American Total: NR Open Lobectomy: 426 (5) VATS Lobectomy: >11 (exact N was NR) Hispanic Total: 105* (1.1*) Open Lobectomy: 94 (1) VATS Lobectomy: ≤11 (exact N was NR) Other Total: 445* (4.7*) Open Lobectomy: 374 (5) VATS Lobectomy: 71 (6) Smoking Status: NR Comorbidity score, N (%) <1 Total: 2,930* (30.8*) Open Lobectomy: 2,504 (30) VATS Lobectomy: 426 (36)	Stage I Total: 8,281* (87.1*) Open Lobectomy: 7,204 (87) VATS Lobectomy: 1,077 (91) Stage II Total: 1,227* (12.9*) Open Lobectomy: 1,119 (13) VATS Lobectomy: 108 (9) Histology Adenocarcinoma Total: 5,681* (59.7*) Open Lobectomy: 4,943 (60) VATS Lobectomy: 738 (62) SCC Total: 2,902* (30.5*) Open Lobectomy: 2,616 (32) VATS Lobectomy: 286 (24) LCC Total: 295* (3.1*) Open Lobectomy: 271 (3) VATS Lobectomy: 24 (2) Other Total: 630* (6.6*) Open Lobectomy: 493 (6) VATS Lobectomy: 137 (12) Surgical Approach Open Lobectomy: 8,323 (87.5*) VATS Lobectomy: 1,185 (12.5*)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Ezer, 2018[273] Surgery N=9,508 KQ 7 Fair (continued)		1-1.5 Total: 3,081* (32.4*) Open Lobectomy: 2,679 (32) VATS Lobectomy: 402 (34) 1.5-2.5 Total: 1,125* (11.8*) Open Lobectomy: 1,029 (12) VATS Lobectomy: 96 (8) >2.5 Total: 2,372* (24.9*) Open Lobectomy: 2,111 (25) VATS Lobectomy: 261 (22)	
Factor, 2014[278] SBRT N=74 (78 tumors) KQ 7 Fair	NA United States Dec. 2006-Jul. 2012 Followup: Local control: 14.4 mos. Overall survival: 18.8 mos.	Age: 78.5 (56 to 93) Female: Patients NR, but 42 (54) tumors Race/Ethnicity: NR Smoking Status: NR Comorbidities: Patients were either medically inoperable or refused surgery	Stage IA: Patients NR, but 52 (67) tumors IB: Patients NR, but 26 (33) tumors Histology Adenocarcinoma: Patients NR, but 41 (53) tumors SCC: Patients NR, but 23 (29) tumors NSCLC NOS: Patients NR, but 10 (13) tumors Unknown: Patients NR, but 4 (5) tumors SBRT Dosing and Frequency: Median dose of 4800 cGy total, administered in 4 fractions over 4 consecutive days

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Fischer-Valuck, 2012[281] SBRT N=62 KQ 7 Fair	NA United States March 2005-Aug. 2010 Followup: 28 mos. (4 to 78 mos.)	Age, Mean (Range): 72.6 (27 to 92) Female: 35 (56.5) Race/Ethnicity: NR Smoking history: Yes: 52 (83.8) No: 10 (16.2) Comorbidities: NR	Stage IA: 44 (70.9) IB: 18 (29.1) Histology Adenocarcinoma: 22 (35.4) SCC: 22 (35.4) BAC: 3 (4.8) NSCLC NOS: 15 (24.1) SBRT Dosing and Frequency Dosing, N (%) 48 Gy (4 x 12 Gy): 13 (20.9) 60 Gy (5 x 12 Gy): 49 (79.1)
Guckenberger, 2013[280] SBRT N=582 KQ 7 Fair	NA Germany/Austria Study Years: 1998-2011 Followup, Mean: 21.4 mos	Age: 72.2 (30.9 to 92.4) Female: 177 (30.4) Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	Stage IA: 327 (56.2) IB: 236 (40.5) I (unclear): 19 (3.3) Histology Adenocarcinoma: 231 (39.7) SCC: 195 (33.5) Other: 55 (9.5) Unknown or no biopsy: 101 (1.9) SBRT Dosing and Frequency, Median (Range): N of SBRT Fractions: 3 (1 to 20) Single-fraction dose PTV-encompassing (Gy): 12.5 (2.9 to 33) Total dose PTV-encompassing (Gy): 37.5 (12 to 64)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Haasbeek, 2010[291] SBRT N=193 (203 tumors) KQ 7 Fair	NA Netherlands 2003-2008 Followup: 12.6 mos. (3 to 52 mos.)	Age: 79 (57 to 91) Female: 62 (32) Race/Ethnicity: NR Smoking Status: NR Comorbidities Medically inoperable: 155 (80) COPD: 140* (72.5*)	T Stage (n=203) T1: 118 (58) T2: 85 (42) Histology (n=75) Adenocarcinoma: 23 (30.7*) SCC: 18 (24*) Undifferentiated NSCLC: 34 (45.3*) SBRT Dosing and Frequency: All patients received 60 Gy total. Half of the patients (101) received 12 Gy in 5 fractions; 69 (34%) received 20 Gy in 3 fractions; 33 (16%) received 7.5 Gy in 8 fractions.
Handa, 2018[218] Surgery N=711 KQ 6 Fair	NA Japan April 2000-Dec. 2015 Followup: 52.3 mos.	Age: NR Female: NR Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	Stage: NR Histology: NR Surgical Approach: Lobectomy or bilobectomy

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Inoue, 2013[224] SBRT N=109 KQs 6 & 7 Fair	NA Japan June 2005-Nov. 2010 Followup: 25 mos (4 to 72 mos.)	Age: 78 (47 to 90) Female: 35 (32.1*) Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	Stage (all N0M0) T1a: 47 (43.1*) T1b: 32 (29.4*) T2: 30 (27.5*) Histology Adenocarcinoma: 65 (59.6*) SCC 29 (26.6*) LCC: 1 (0.9*) NSCLC NOS: 8 (7.3*) Unproven: 6 (5.5*) SBRT Dosing and Frequency: Treatment period of 4 to 7 days 2005-2006: 48 Gy total, administered in 4 fractions 2007-2010: 40 Gy total, administered in 4 fractions to 95% volume of PTV (~45 to 50 Gy)
Jeppesen, 2013[223] SBRT N=100 KQ 6 Fair	NA Denmark Aug. 2005-June 2012 Followup: 35.4 mos. (8.8 to 90.5 mos.)	Age, Mean (Range): 73.3 (52 to 88) Female: 55 (55) Race/Ethnicity: NR Smoking Status: Smoker or ex-smoker: 81 (81) Never smoker: 19 (19) Comorbidities: All patients were medically inoperable	T-Stage T1: 72 (72) T2: 28 (28) Histology: Adenocarcinoma: 59 (59) SCC: 28 (28) Other: 13 (13) SBRT Dosing and Frequency: 15 to 22 Gy x 3, delivered in 9 days

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Karasawa, 2018[229] SABR N=56 KQs 6 & 7 Fair	NA Japan Oct. 2003-Dec. 2010 Followup: 10.6 yrs	Age: 79 (49 to 91) Female: 17 (30.4*) Race/Ethnicity: NR Smoking Status: NR Comorbidities High risk operable: 27 (48.2*) Medically inoperable: 21 (37.5*) Pulmonary risk factor: 31 (55.4*) Cardiac risk factor: 8 (14.3*) Central nervous system factor: 4 (7.1*) Hepatic risk factor: 1 (1.8*)	T Stage T1: 41 (73.2*) T2: 15 (26.8*) Histology: Adenocarcinoma: 34 (60.7*) SCC: 18 (32.1*) Large cell neuroendocrine cancer: 1 (1.8*) NSCLC NOS: 2 (3.6*) Unproven: 1 (1.8*) SBRT Dosing and Frequency: Patients primarily received 48 Gy total, delivered in 4 fractions over 1 week.
Lagerwaard, 2012[283] SABR N=382 KQ 7 Fair	NA Netherlands April 2003-Nov. 2008 Followup: 23 mos.	Age: 74 (47 to 91) Female: 152 (39.8) Race/Ethnicity: NR Smoking Status: NR Comorbidities: History of prior lung cancer: 65 (17) COPD (mild, moderate, severe, or very severe) (n=361): 304* (84*) Medically inoperable: 323 (84.6)	Stage IA: 230 (60.2) IB: 152 (39.8) Histology: NR SABR Dosing and Frequency: 60 Gy total, administered in 3, 5, or 8 fractions (depending on tumor diameter and location)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Lagerwaard, 2012[225] SABR N=177 KQs 6 & 7 Fair	NA Netherlands April 2003-Dec. 2010 Followup: 31.5 mos.	Age: 76 (50 to 91) Female: 76 (43) Race/Ethnicity: NR Smoking Status: Current or former: 168 (95) Never smoked: 9 (5) Comorbidities: COPD: 112* (63*) Charlson Comorbidity Score: Median (range): 2 (0 to 5) 0: 18 (10) 1: 59 (33) 2: 38 (22) 3: 39 (22) 4: 16 (9) 5: 7 (4)	Stage IA: 106* (60) 1B: 71* (40) Histology (n=60) Adenocarcinoma: 20 (33) SCC: 16 (27) Undifferentiated NSCLC: 24 (38) SBRT Dosing and Frequency: 60 Gy total, delivered as 20 Gy in 3 fractions for 34% of patients; 12 Gy in 5 fractions for 46%; and 7.5 Gy in 8 fractions for 19%.
Lagerwaard, 2008[292] SBRT N=206 (219 tumors) KQ 7 Fair	NA Netherlands Study Years NR Followup: 12 mos. (3 to 44 mos.)	Age: 73 (NR) Female: 91 (44) Race/Ethnicity: NR Smoking Status: NR Comorbidities Medically inoperable: 167 (81) COPD: 151* (73.3*) Previous malignancy: 80* (39) Previous lung cancer: 37 (18)	T Stage (n=219) T1: 129 (59) T2: 90 (41) Histology (n=64) Adenocarcinoma: 23 (36) SCC: 19 (30) Undifferentiated NSCLC: 22 (34 SBRT Dosing and Frequency: Total Gy NR, delivered as 20 Gy in 3 fractions for 93/219 (43%) tumors; 12 Gy in 5 fractions for 99/219 (45%); and 7.5 Gy in 8 fractions for 27 (12%).

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Lee, 2017[234] SBRT/SABR N=169 (178 tumors) KQs 6 & 7 Fair	NA South Korea June 2000-May 2015 Followup: 32 mos. (2 to 195 mos.)	Age: 73 (40 to 91) Female: 38 (22) Race/Ethnicity: NR Smoking Status: NR Comorbidities Charlson Comorbidity Index Score, median (range): 5 (0 to 8) Poor lung function: 86 (51) Other comorbidity: 27 (16)	Stage T1a: 39 (22) T1b: 70 (39) T2a: 69 (39) Histology (n=178) Adenocarcinoma: 87 (49) SCC: 78 (44) NSCLC unspecified: 5 (3) Others: 3 (2) No biopsy: 5 (3) SABR Dosing and Frequency 82 (46%) patients received 60 Gy total in 4 fractions, 51 (29%) patients received 48 Gy total in 4 fractions, 18 (10%) patients received 54 Gy total in 3 fractions, 10 (6%) patients received 60 Gy total in 3 fractions, and 17 (10%) patients received other doses/fractionations.
Liu, 2018[219] Surgical resection N=3,219 KQ 6 Fair	SEER United States 2004-2013 Followup: 37 mos. (1 to 120 mos.)	Age: 69 (20 to 92) Female: 1,918 (59.6) Race/Ethnicity: White: 2,805 (87.1) Black: 271 (8.4) Other: 143 (4.5) Smoking Status: NR Comorbidities: NR	Stage IA: 3,219 (100) Histology Adenocarcinoma: 1,892 (58.8) SCC: 738 (22.9) LCC: 142 (4.4) Other: 447 (13.9) Surgical Approach Wedge: 2,327 (72.3) Segmental: 892 (27.7)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Lutz, 2018[220] Surgical resection N=632 KQs 6 & 7 Fair	NA France Jan. 2007-Aug. 2016 Followup, mean: 34.5	Age: 65 (IQR, 59 to 71) Female: 321 (50.8) Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	p-Stage IA: 281 (44.5) IB: 201 (31.8) IIA: 54 (8.5) IIB: 39 (6.2) IIIA: 57 (9) Histology Adenocarcinoma: 498 (78.8) SCC: 102 (16.1) LCC: 32 (5.1) Surgical Approach: All patients underwent surgical resection. The most common types of resection were right upper lobe (29.1%), segmentectomy (25.3%), and left upper lobe (15.5%).
Lv, 2018[221] Surgical resection N=861 KQ 6 Fair	SEER United States Jan. 2004-Dec. 2014 Followup: 39 mos. (0 to 131 mos.)	Age, mean (SD) Lobectomy (n=662): 65.9 (10.9) Sublobar resection (n=199): 66.6 (11.3) Female: 570* (66.2*) Race/Ethnicity White: 711* (82.6*) Black/other: 150* (17.4*) Smoking Status: NR Comorbidities: NR	Stage IA: 861 (100) Histology Adenocarcinoma: 656* (76.2*) SCC: 113* (13.1*) Other: 92* (10.7*) Surgical Approach: 662 (76.9) patients underwent lobectomy, and 199 (23.1) patients underwent sub-lobar resection.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Manyam, 2019[230] SBRT/SABR N=139 (146 tumors) KQs 6 & 7 Fair	NA United States 2009-2016 Followup: 23.8 mos. (3.1 to 87.9 mos.)	Age: 76 (47 to 92) Female: 74 (53.2*) Race/Ethnicity: NR Smoking Status Pack-years, median (range): 50 (0 to 160) Smoking during treatment: 38 (27.5) Comorbidities Pulmonary: 80 (58) Cardiac: 12 (9) Refusal: 5 (4) Other/multifactorial: 42 (29)	Stage IA: 135 (93) IB: 10 (6) IIA: 1 (1) Histology Adenocarcinoma: 39 (27) SCC: 38 (26) Others: 8 (6) Nondiagnostic: 14 (10) No biopsy: 47 (32) SBRT Dosing and Frequency: Of 146 lesions, 80 (55%) were treated with 30 Gy and 66 (45%) were treated with 34 Gy.
Matsuo, 2012[285] SBRT N=74 KQ 7 Fair	NA Japan Sept. 2003-March 2008 Followup: 31.4 mos. (4.2 to 65.0 mos.)	Age: 77 (63 to 88) Female: 19 (25.7*) Race/Ethnicity: NR Smoking Status: NR Comorbidities: Inoperable: 50 (67.6*)	Stage T1a: 26 (35.1*) T1b: 27 (36.5*) T2a: 21 (28.4*) Histology Adenocarcinoma: 36 (48.6*) SCC: 30 (40.5*) Other (LCC or NSCLC NOS): 8 (10.8*) SBRT Dosing and Frequency: 48 Gy total, administered in 4 fractions at the isocenter; median (range) overall treatment time was 5 days (4 to 12 days)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Moon, 2018[214] Surgical resection N=15,358 KQ 6 Fair	SEER United States 2000-2014 Followup: 56 mos. (IQR, 25 to 95 mos.)	Age, mean (SD) Lobectomy: 65.5 (10.2) Segmentectomy: 67.8 (10) Female: 9,037* (58.8*) Race/Ethnicity American Indian or Alaska Native: 47* (0.3*) Asian or Pacific Islander: 859* (5.6*) Black: 1,084* (7.1*) White: 13,318* (86.7*) Unknown: 50* (0.3*) Smoking Status: NR Comorbidities: NR	Stage IA: 15,358 (100) Histology Adenocarcinoma: 10,645* (69.3*) SCC: 2,881* (18.8*) Others: 1,832* (11.2*) Surgical Approach: Lobectomy: 14,549 (94.7*) Segmentectomy: 809 (5.3*)
Mutter, 2012[287] SBRT/SABR N=126 KQ 7 Fair	NA United States May 2006-July 2009 Followup: 16 mos. (3 to 43 mos.)	Age: 77 (55 to 95) Female: NR Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	Stage T1a: 63 (50*) T1b: 32 (25.4*) T2a: 27 (21.4*) Histology Adenocarcinoma: 93 (74) NSCLC unspecified: 2 (2) Not determined: 1 (1) Squamous: 30 (24) SBRT Dosing and Frequency Dose, Median (range): 54 Gy (40 to 60 Gy) Treatment time, Median (range): 7 days (4 to 19 days) Number of total fractions: 3 fractions: 73 (57.9*) 4 fractions: 38 (30.2*) 5 fractions: 15 (11.9*)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Olsen, 2011[288] SBRT/SABR N=130 KQ 7 Fair	NA United States June 2004-June 2009 11 mos. (2 to 33 mos.)	Age: 75 (31 to 92) Female: 65* (50*) Race/Ethnicity: NR Smoking Status: NR Comorbidities: 117 of 130 patients were considered medically inoperable	Stage T1a: 56 (43.1*) T1b: 44 (33.8*) T2a: 24 (18.5*) Histology Biopsy-proven: 110* (84.6*) SBRT Dosing and Frequency 9 Gy in 5 fractions: 8 (6.2*) 10 Gy in 5 fractions: 11 (8.5*) 18 Gy in 3 fractions: 111 (85.4*)
Onishi, 2007[226] SBRT/SABR N=257 KQs 6 & 7 Fair	NA Japan April 1995-March 2004 Followup: 38 mos. (2 to 128 mos.)	Age: 74 (39 to 92) Female: NR Race/Ethnicity: NR Smoking Status: NR Comorbidities Pulmonary chronic disease: 168 (65.4*) Medically inoperable: 158 (61.5*)	Stage IA: 164 (63.8*) IB: 93 (36.2*) Histology Adenocarcinoma: 120 (46.7*) SCC: 111 (43.2*) Other: 26 (10.1*) SBRT Dosing and Frequency: 10 to 75 Gy total (at isocenter) was administered in 1 to 22 fractions.
Palma, 2010[289] SBRT/SABR N=99* KQ 7 Fair	Amsterdam Cancer Registry Netherlands 1999-2007 Followup: 54 mos.	Age: NR Female: NR Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	T Stage IA or IB: 99* (100) Histology: NR SBRT Dosing and Frequency: NR

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Sekihara, 2017[222] Surgical resection N=1,356* KQ 6 Fair	NA Japan Jan. 2002-March 2013 Followup: 40 mos.	Age: NR Female: NR Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	Pathological Stage I: 1,356* Clinical Stage I: 1,612* (78.5*) Histology: NR Surgical Approach: NR
Shibamoto, 2012[236] SBRT N=180 KQs 6 & 7 Good	NA Japan May 2004-Nov. 2008 Followup: 36 mos.	Age: 77 (29 to 92) Female: 57 (31.7*) Race/Ethnicity: NR Smoking Status: NR Comorbidities Medically inoperable: 120 (66.7*)	Stage IA: 128 (71.1*) IB: 52 (28.9*) Histology Adenocarcinoma: 104 (57.8*) SCC: 60 (33.3*) NSCLC NOS: 16 (8.9*) SBRT Dosing and Frequency 44 Gy in 4 fractions: 4 (2.2*) 48 Gy in 4 fractions: 124 (68.9*) 52 Gy in 4 fractions: 52 (28.9*) Prescribed dose was 44 Gy in 4 fractions with ≥3 day interfraction intervals (tumors with a max dimension <1.5 cm); 48 Gy in 4 fractions (tumors with a max dimension of 1.5 cm to 3.0 cm); and 52 Gy in 4 fractions (tumors with a max tumor dimension >3 cm)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Stanic, 2014[279] SBRT N=55 KQ 7 Fair	RTOG 0236 United States Study Years: NR Followup: 2 yrs	Age: 72 (48 to 89) Female: 34 (61.8) Race/Ethnicity White: 51 (92.7) Asian: 2 (3.6) African American: 2 (3.6) Smoking Status: NR Comorbidities All patients were medically inoperable Total with >1 reason for being medically inoperable: 38 (69.1) Hypoxemia and/or hypercapnia: 10 (18.5) Severe pulmonary hypertension: 6 (10.9) Diabetes mellitus with severe end-organ damage: 3 (5.5) Severe cerebral, cardiac, or peripheral vascular disease: 24 (43.6) Severe chronic cardiac disease: 22 (40.0)	Stage IA: 44 (80) IB: 11 (20) Histology: All patients were confirmed to have NSCLC (histological details NR) SBRT Dosing and Frequency: 60 Gy total, administered in 3 fractions, separated by ≥40 hours, and the full regimen was completed within 14 days
Ueda, 2018[274] Surgical resection N=607 KQ 7 Fair	NA Japan Feb. 2008-March 2013 Followup: NR	Age Lobectomy: 67 (35 to 86) Segmentectomy: 67 (27 to 84) Female: 313* (51.6*) Race/Ethnicity: NR Smoking Status ≥40 pack years: 316* (52.1*) Comorbidities History of ischemic heart disease: 53* (8.7*) History of lung cancer resection: 36* (5.9*)	Stage IA: 607 (100) Histology: NR Surgical Approach Lobectomy: 443 (73*) Segmentectomy: 164 (27*)

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Uhlig, 2018[228] SBRT N=27,732 (1,070 in PSM analysis) KQs 6 & 7 Fair	NCDB United States 2004-2013 Followup, mean: 52.4 mos. (IQR, 32.1 to 75.2 mos.)	Age: 59 (IQR 53 to 65) Female: 601 (56.2) Race/Ethnicity African American: 55 (5.1) White: 984 (92) Other: 31 (2.9) Smoking Status: NR Comorbidities: Charlson comorbidity index score 0: 510 (47.7) 1: 335 (31.3) ≥2: 225 (21.0)	Stage I: 1,070 (100) Histology: NR SBRT Dosing and Frequency: NR for patients in PSM set, but in larger unmatched sample, the median biologic equivalent dose delivered was 100 Gy (IQR, 88 to 221 Gy). The median number of treatment sessions was 5 (IQR, 4 to 16 sessions) over a median duration of 10 days (IQR, 7 to 27 days).
Westover, 2012[284] SBRT N=15 (20 tumors) KQ 7 Fair	NA United States July 2008-Sept. 2010 Followup: 24.1 mos.	Age: 78 (62-89) Female: 12* (80*) Race/Ethnicity: NR Smoking Status: 14* (93.3*) Comorbidities COPD: 8 (53.3*) Interstitial lung disease: 1* (6.7*) History of prior lung cancer: 8* (53.3*) Systematic lupus erythematosus: 1* (6.7*)	Stage T1a: 16/20 (80) tumors T1b: 2/20 (10) tumors T2a: 2/20 (10) tumors Histology Adenocarcinoma: 9/20 (45*) tumors NSCLC NOS: 4/20 (20*) tumors SCC: 3/20 (15*) tumors No biopsy: 4/20 (20*) tumors SBRT Dosing and Frequency Median (range) total dose: 45 Gy (42-50 Gy) Median (range) fraction size: 14 Gy (10-16 Gy) 17/20 tumors (85%*) received 3 fractions

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Wink, 2019[235] SABR N=554 KQ 6 Fair	NA Netherlands/Germany 2007-2015 Followup: 36.1 mos. (1.1 to 118.3 mos.)	Age: 74 (42 to 91) Female: 234 (42.2) Race/Ethnicity: NR Smoking Status: NR Comorbidities: NR	Stage T1: 428 (77.2) T2: 124 (22.4) Histology Adenocarcinoma: 66 (11.9) SCC: 66 (11.9) LCC: 28 (5.1) AIS: 3 (0.5) NSCLC NOS: 14 (2.5) Suspicion of malignancy, but no histology: 377 (68.1) SABR Dosing and Frequency: The median prescribed dose was 54 Gy (range, 45 to 75 Gy in 3 to 8 fractions).
Ye, 2018[294] SBRT N=100 KQ 7 Fair	NA China Jan. 2010-June 2016 Followup: 26.5 mos.	Age: 73 Female: 27 (27*) Race/Ethnicity: NR Smoking Status Never: 38 (38*) Previous: 43 (43*) Current: 19 (19*) Comorbidities COPD: 55 (55*)	Stage T1: 69 (69*) T2a: 31 (31*) Histology Adenocarcinoma: 59 (59*) SCC: 22 (22*) Unknown: 19 (19*) SBRT Dosing and Frequency: Most patients received 60 Gy in 10 fractions, and the rest received 50 Gy in 5 fractions. The study's reported counts are NR here because they are incorrect.

Appendix E Table 7. KQs 6 and 7 Update Search Results: Study and Patient Characteristics

Study Identifiers Author, Year Treatment Type(s) N Enrolled KQs Addressed Quality	Study Characteristics Study or Database Name Country Study Years Followup, Median (Range)	Baseline Patient Characteristics Age, Median (Range) Gender, N (%) Race/Ethnicity, N (%) Smoking Status, N (%) Comorbidities, N (%)	NSCLC and Treatment Characteristics Stage, N (%) Histology, N (%) Surgical Approach or SBRT/SABR Dosing and Frequency
Zhou, 2017[215] Surgical resection N=20,850 KQ 6 Fair	SEER United States 2004-2013 Followup: 38 mos. (IQR, 17 to 66 mos.)	Age <60: 4,079 (19.6) 60-74: 11,112 (53.3) ≥75: 5,659 (27.1) Female: 11,339 (54.4) Race/Ethnicity White: 17,732 (85) Black: 1,665 (8) Other/unknown: 1,453 (7) Smoking Status: NR Comorbidities: NR	Stage IA1: 1,402 (6.7) IA2: 7,037 (33.8) IA3: 5,198 (24.9) IB: 7,213 (34.6) Histology Adenocarcinoma: 11,591 (55.6) SCC: 5,717 (27.4) BAC: 1,792 (8.6) Adenosquamous carcinoma: 578 (2.8) LCC: 411 (2.0) Other: 761 (3.6) Surgical Approach Lobectomy: 16,363 (78.5) Sublobar resection: 4,244 (20.4) Pneumonectomy: 243 (1.2)

*Indicates that data was calculated by abstractors

† Per the Colinet Simplified Comorbidity Score, a higher score indicates that a patient has a greater number of comorbidities.[396]

Abbreviations: AIS=adenocarcinoma in situ; BAC=bronchoalveolar carcinoma; cGy=centigray; COPD=chronic obstructive pulmonary disease; CVD=cardiovascular disease; ILD=interstitial lung disease; IQR=interquartile range; KQ=key question; LCC=large cell carcinoma; mos=months; NA=not applicable; NOS=not otherwise specified; NR=not reported; NSCLC=non-small cell lung cancer; PSM=propensity score matching; SABR=stereotactic ablative radiotherapy; SBRT=stereotactic body radiation therapy; SCC=squamous cell carcinoma**.**

Appendix E Table 8. KQs 6 and 7 Update Search Results: Surgery Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Perioperative Morbidity with ≥10% Incidence
Berry, 2018[216] Surgery N=14,545 KQ 6 Fair	Overall survival: 64.9 (95% CI, 64 to 65.8) Lung cancer-specific survival Total sample: 76.9 (95% CI, 76.1 to 77.7) SLR: 70.8 (95% CI, 68.6 to 72.9) Lobar resection: 78.5 (77.6 to 79.4) SLR vs. lobar resection: between-group p <0.0001 (both unadjusted and multivariable adjusted analyses)	NA
Dziedzic, 2017[217] Surgery N=6,905 KQs 6 & 7 Fair	Overall survival Unmatched population (n=6,905) Any resection: 76.6 (95% CI, 75.4 to 78) Wedge resection (n=761) Total: 58.1 (95% CI, 53.6 to 62.5) Stage IA: 61.3 (95% CI, 56.2 to 66.5) Stage IB: 44.8 (95% CI, 35.5 to 54.1) Lobectomy (n=5,911) Total: 79.1 (95% CI, 77.7 to 80.5) Stage IA: 80.5 (95% CI, 78.9 to 82.2) Stage IB: 75.3 (95% CI, 72.6 to 77.9) Segmentectomy (n=233) Total: 78.3 (95% CI, 70.6 to 86) Stage IA: 78 (95% CI, 68.8 to 87.1) Stage IB: 78.6 (95% CI, 64.3 to 92.9)95% CI,95% CI,95% CI,95% CI,	30-day mortality Any resection: 1.6 (95% CI, 1.3 to 1.9) Wedge resection: 1.4 (95% CI, 0.6 to 2.3) Lobectomy: 1.6 (95% CI, 1.2 to 1.9) Segmentectomy: 2.6 (95% CI, 0.5 to 4.6) 90-day mortality Any resection: 2.4 (95% CI, 2.1 to 2.8) Wedge resection: 3 (95% CI, 1.8 to 4.2) Lobectomy: 2.3 (95% CI, 1.9 to 2.7) Segmentectomy: 4.3 (95% CI, 1.7 to 6.9)
Ezer, 2018[273] Surgery N=9,508 KQ 7 Fair	NA	30-day mortality: 322* (3.4*) Respiratory complications: 3,000* (31.6*) Extended length of stay: 1,397* (14.7*)
Handa, 2018[218] Surgery N=711 KQ 6 Fair	Overall Survival: 81.3 (95% CI, NR)	NA

Appendix E Table 8. KQs 6 and 7 Update Search Results: Surgery Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Perioperative Morbidity with ≥10% Incidence
Liu, 2018[219] Surgical resection N=3,219 KQ 6 Fair	Lung cancer specific survival Total sample 1-6 examined LNs (n=2,410): 75 ≥7 examined LNs (n=809): 83 Wedge resection only 1-6 examined LNs (n=1,777): 74 ≥7 examined LNs (n=550): 81 Segmental only 1-6 examined LNs (n=633): 78 ≥7 examined LNs (n=259): 87	NA
Lutz, 2018[220] Surgical resection N=632 KQs 6 & 7 Fair	Overall survival Total: 75 (69.9 to 80.1) Stage IA: 79.5 (NR) Stage IB: 76.9 (NR) Lung cancer specific survival Total: 86.4 (82.3 to 90.5) Stage IA: 71.1 (NR) Stage IB: 63.6 (NR)	30-day or in-hospital mortality: 6 (0.95) Any complication: 185 (29.3)
Lv, 2018[221] Surgical resection N= 861 KQ 6 Fair	Overall survival: 75 (NR)	NA
Moon, 2018[214] Surgical resection N=15,358 KQ 6 Fair	Overall survival Lobectomy: 76.0 (75.2 to 76.8) Segmentectomy: 74.4 (95% CI, 67.7 to 75.4) Lung cancer specific survival Lobectomy: 86.0 (85.4 to 86.7) Segmentectomy: 84.7 (81.6 to 88)	NA

Appendix E Table 8. KQs 6 and 7 Update Search Results: Surgery Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Perioperative Morbidity with ≥10% Incidence
Sekihara, 2017[222] Surgical resection N=1,356* KQ 6 Fair	Overall survival, patients with Stage I: ILD (n=62): 44 (NR) Non-ILD (n=1,294): 84.6 (NR) Lung cancer specific survival: ILD (n=62): 56.6 (NR) Non-ILD (n=1,294): 89.8 (NR) Recurrence-free survival: ILD (n=62): 37.3 (NR) Non-ILD (n=1,294): 63.1 (NR)	NA
Ueda, 2018[274] Surgical resection N=607 KQ 7 Fair	NA	Post-operative atrial fibrillation Total: 37 (6.1*) Lobectomy (n=443): 34 (7.7*) Segmentectomy (n=164): 3 (1.8*)
Zhou, 2017[215] Surgical resection N=20,850 KQ 6 Fair	Overall death from any cause Pneumonectomy: 52.4 (44.5 to 59.2) Lobectomy: 33.0 (32.1 to 33.8) Sublobar: 47.8 (45.8 to 49.6) Cause-specific death Pneumonectomy: 34.9 (28.2 to 41.7) Lobectomy: 20.1 (19.4 to 20.9) Sublobar: 28.1 (26.5 to 29.7)	NA

*Indicates that data were calculated by abstractors.

Abbreviations: CI=confidence interval; ILD=interstitial lung disease; KQ=key question; NA=not applicable; NR=not reported; PSM=propensity score matching; SLR=sub-lobar resection.

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Ackerson, 2018[295] SBRT N=70 KQ 7 Fair	NA	30-day mortality 1 (1.4*) Adverse events Any: 12 (17) Dyspnea Total: 6 (8.6*) Grade 1: 4 (5.7*) Grade 2: 2 (2.9*) Chest Wall Toxicity: 6 (8.5)
Baine, 2019[232] SBRT N=26,725 KQs 6 & 7 Fair	Overall survival: 30.6 [95% CI, 29.9 to 31.4]	30-day mortality: 3 (0.01) 90-day mortality: 134 (0.5)
Ball, 2019[293] SABR N=66 KQ 7 Fair	NA	No treatment-related deaths occurred RP (Grades 1-2 only): 10 (18) Adverse events Grade 4: 1 (2*) Grade 3: 8* (12*) Grades 1-2 Total: 22 (39) Dyspnea: 22 (39) Cough: 33 (59) Fatigue: 32 (57) Chest wall pain: 21 (38) Pulmonary fibrosis: 22 (39) Dermatitis radiation: 6 (11) Nausea: 9 (16) Atelectasis: 9 (16) Pleural effusion: 7 (12) Fracture (type unspecified): 5 (9)

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Barriger, 2012[290] SBRT N=251 KQ 7 Fair	NA	RP Total: 42 (17) lesions Grade 4: 1 (0.4) Grade 3: 5 (2) Grade 2: 17 (7) Grade 1: 19 (8) Note: RP overall developed at a median time of 5.6 mos. (range: 0.5 to 32.2 mos.). Grade 1 RP developed at a median time of 8.4 mos. (range: 1.3 to 32.2 mos.), and symptomatic RP (Grades 2-4) developed at a median of 3.5 mos. (range: 0.5 to 12 months; p=0.002).
Baumann, 2006[227] SBRT N=141 (138 for results) KQs 6 & 7 Fair	Overall survival: 26 (95% CI, NR) Lung-cancer specific survival: 40 (95% CI, NR) Total failure-free survival: 36 (95% CI, NR)	Rib fractures: 8 (5.8*) Pneumonitis: 1 (0.7*) Any side effect: 55* (40*) Grade 3-4 toxicity: 14 (10*) Lung fibrosis: 21 (15.2*)
Bongers, 2011[286] SABR N= 500 (530 tumors) KQ 7 Fair	NA	Rib fractures (all late-onset [>3 mos. post-SABR]) (n=500): 8 (1.6) Note: Rib fractures developed at a median time of 24 mos. (range: 6 to 27 mos.) Chest wall pain (n=500 patients) Total: 57 (11.4), of which 32 (6.4) were early onset (i.e., ≤3 mos. post-SABR) and 25 (5) were late onset (i.e., >3 mos. post-SABR) Grade 3 (severe): 10 (2), of which 5 (1) were early onset and 5 (1) were late onset Grade 1-2: 47* (9.5*), of which 27 (5.4) were early onset and 20 (4.1) were late onset

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Chang, 2012[282] SABR N=130 KQ 7 Fair	NA	RP Grade 2-3: 15* (11.5*) Grade 0-1: 115* (88.5*) Adverse events Chest pain: 12 (9.3*)
Cummings, 2018[233] SBRT N=163 KQs 6 & 7 Fair	Overall survival Total: 33 (95% CI, NR) SF: 17 (95% CI, NR) FF: 39 (95% CI, NR)	RP, Grade 3: 1 (0.6*) Hospitalization Total: 9* (5.5*) SF: 3 (1.8*) FF: 6 (3.7*)
Detillon, 2019[231] SBRT N=378 (159 and 36 for primary and secondary PSM analyses, respectively) KQ 6 Fair	Overall survival Unmatched analysis: 29 (95% CI, NR) Primary PSM analysis: 29 (95% CI, NR) Secondary PSM analysis (adjusted for cT1a, histology and pathological confirmation): 49 (95% CI, NR)	NA
Factor, 2014[278] SBRT N=74 (78 tumors) KQ 7 Fair	NA	Adverse events Grade 2 RP: 1 (1.4*) No other toxicities experienced
Fischer-Valuck, 2012[281] SBRT N=62 KQ 7 Fair	NA	Rib fractures: 2 (3.2) [95% CI, 0.3 to 11.6] RP: 1 (1.6) [95% CI, 0.3 to 8.6] Adverse events Chest wall pain: 6 (9.6) [95% CI, 3.5 to 21]
Guckenberger, 2013[280] SBRT N=582 KQ 7 Fair	NA	30-day mortality: 3 (0.5) 60-day mortality: 10 (1.7) RP ≥Grade 2: 38/512 (7.4) Grade 5: 2/512 (0.4)

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Haasbeek, 2010[291] SBRT N=193 (203 tumors) KQ 7 Fair	NA	Rib fractures: 3 (1.6) RP ≥Grade 3: 4 (2.1) Adverse events in the first 3 mos. Any: 116 (60) Fatigue: 63* (32.6) Respiratory symptoms: 21* (10.9*)
Inoue, 2013[224] SBRT N=109 KQs 6 & 7 Fair	5-year overall survival Overall sample: 64 (57-80) T1a patients: 75 (58-97)	RP Grade 3: 3 (2.8) Grade 2: 15 (13.8)
Jeppesen, 2013[223] SBRT N=100 KQ 6 Fair	5-year overall survival 34 (NR) 5-year lung cancer-specific survival: 61 (NR)	No acute toxicity

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Karasawa, 2018[229] SABR N=56 KQs 6 & 7 Fair	Overall survival: 44.6 (95% CI, 31.6 to 57.7) Women had better overall survival than men, although the difference was not statistically significant (p=0.078). Women: 64.7 (95% CI, 42 to 87.4) Men: 35.9 (95% CI, 20.8 to 51) No significant difference between patients with T1 vs. T2 tumors (p=0.288). T1: 48.8 (95% CI, 33.5 to 64.1) T2: 33.3 (95% CI, 9.5 to 57.2) No significant difference between operable cases and inoperable or high-risk operable cases (p=0.466). Operable: 62.5 (95% CI, 29 to 96) High-risk operable: 44.4 (95% CI, 25.7 to 63.2) Inoperable: 38.1 (95% CI, 17.3 to 58.9) No significant difference between patients aged ≤79 yrs vs. ≥80 yrs (p=0.337). Aged ≤79 yrs: 48.4 (95% CI, 36.7 to 63.3) Aged ≥80 yrs: 40 (95% CI, 20.8 to 59.2)	Grade 3 Pulmonary toxicity: 1 (2) Cholecystitis: 1 (2) Grade 4 Stomach perforation: 1 (2)
Lagerwaard, 2012[283] SABR N=382 KQ 7 Fair	NA	Rib fracture: 4 (1) RP: Early, ≥Grade 3: 7 (1.8*) Late, ≥Grade 3: 9 (2) Adverse effects: Clinician-reported early side effects: 145* (38) Fatigue: 103* (27)

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Lagerwaard, 2012[225] SABR N=177 KQs 6 & 7 Fair	Overall survival: 51.3 (95% CI, NR)	30-day mortality: 0 (0) Rib fractures Total: 5 (3) 3-fraction scheme: 2/61 (3.3*) 5-fraction scheme: 1/82 (1.2*) 8-fraction scheme: 2/34 (5.9*) RP (Grade ≥3): 4 (2) Early side effects (Grades 1-2) Any: 103* (58*) Fatigue: 44* (25) Cough 25* (14) Local chest wall pain: 20* (11) Dyspnea: 18* (10)
Lagerwaard, 2008[292] SBRT N=206 (219 tumors) KQ 7 Fair	NA	30-day mortality: 1 (0.5*) Rib fractures: 4 (2.3*) RP (late ≥Grade 3): 6 (3) Adverse effects Any adverse effects: 101* (49*) Early side effects Fatigue: 64* (31) Local chest wall pain: 25* (12)
Lee, 2017[234] SART/SABR N=169 (178 tumors) KQs 6 & 7 Fair	Overall survival: 46.7 (NR) Cancer-specific survival: 69.4 (NR) Progression-free survival: 49.3 (NR)	Rib fractures: 39/93 (42) Rib dislocation, Grade 2: 12/93 (13) Rib fracture accompanying myositis: 8/93 (9) RP Grade 2: 19/93 (11) ≥Grade 3: 2/93 (1.2*) Radiation toxicity induced lung fibrosis: 156/169* (92) Bronchial obstruction: 19/25 (76)

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Manyam, 2019[230] SBRT/SABR N=139 (146 tumors) KQs 6 & 7 Fair	Overall survival: 28.7 (19.6 to 37.9)	Rib fracture: 7/146 (4.8) Chest wall toxicity, overall: 18/146 (12.3) Grade 1: 3/146 (2.1*) Grade 2: 13/146 (8.9*) Grade 3: 2/146 (1.4)
Matsuo, 2012[285] SBRT N=74 KQ 7 Fair	NA	Symptomatic RP Total: 15 (20.3) Grade 2: 14 (18.9*) Grade 3: 1 (1.4*)
Mutter, 2012[287] SBRT/SABR N=126 KQ 7 Fair	NA	Rib fractures: 5 (4) Chest wall pain Grade 1: 19 (15) Grade 2: 16 (13) Grade 3: 19 (15) Grade ≥2 Estimated actuarial incidence over 2 yrs: 39%
Olsen, 2011[288] SBRT/SABR N=130 KQ 7 Fair	NA	RP, Grade 2: 4 (3.1*) Chest wall toxicity: 21 (16)
Onishi, 2007[226] SBRT/SABR N=257 KQs 6 & 7 Fair	Overall survival: 47.2 (38.7 to 53.5) For operable patients (n=99): 64.8 (53.6 to 75.9) For inoperable patients (n=158): 35 (25.9 to 44.1) Lung cancer specific survival: 73.2 (66.1 to 80.2)	Rib fracture: 4 (1.6) Symptomatic radiation-induced pulmonary complications Grade >1: 28 (10.9) Grade ≥2: 14 (5.4)
Palma, 2010[289] SBRT/SABR N=99* KQ 7 Fair	NA	30-day mortality: 1* (1.0)

Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Shibamoto, 2012[236] SBRT/SABR N=180 KQs 6 & 7 Good	Overall survival: 52 For operable patients (n=60): 70 For inoperable patients (n=120): 44	RP: ≥Grade 2: 24 (13.3) Grade 3: 2 (1.1)
Stanic, 2014[279] SBRT N=55 KQ 7 Fair	NA	RP Total: 9 (16.4*) Grade 1: 4 (7.3*) Grade 2: 3 (5.5*) Grade 3: 2 (3.6*) Adverse effects Pulmonary function toxicity at any time during 2-yr followup: 49 (89*) Grade 1 pulmonary/upper respiratory function toxicity: 11 (20*) Grade 2 pulmonary/upper respiratory function toxicity: 13 (23.6*) Grade 3 pulmonary/upper respiratory function toxicity: 8 (14.5*) Cough: 15* (27.3*) Dyspnea: 17* (30.9*) Pleural effusion: 5* (9.1*) Other pulmonary/upper respiratory toxicity: 7* (12.7*)
Uhlig, 2018[228] SBRT/SABR N=27,732 (1,070 in PSM analysis) KQs 6 & 7 Fair	Overall survival in PSM cohort: 26.1 (22.7 to 29.9)	30-day mortality: None 90-day mortality: None 30-day post-treatment unplanned hospital readmission rate in PSM cohort: 2 (0.2)

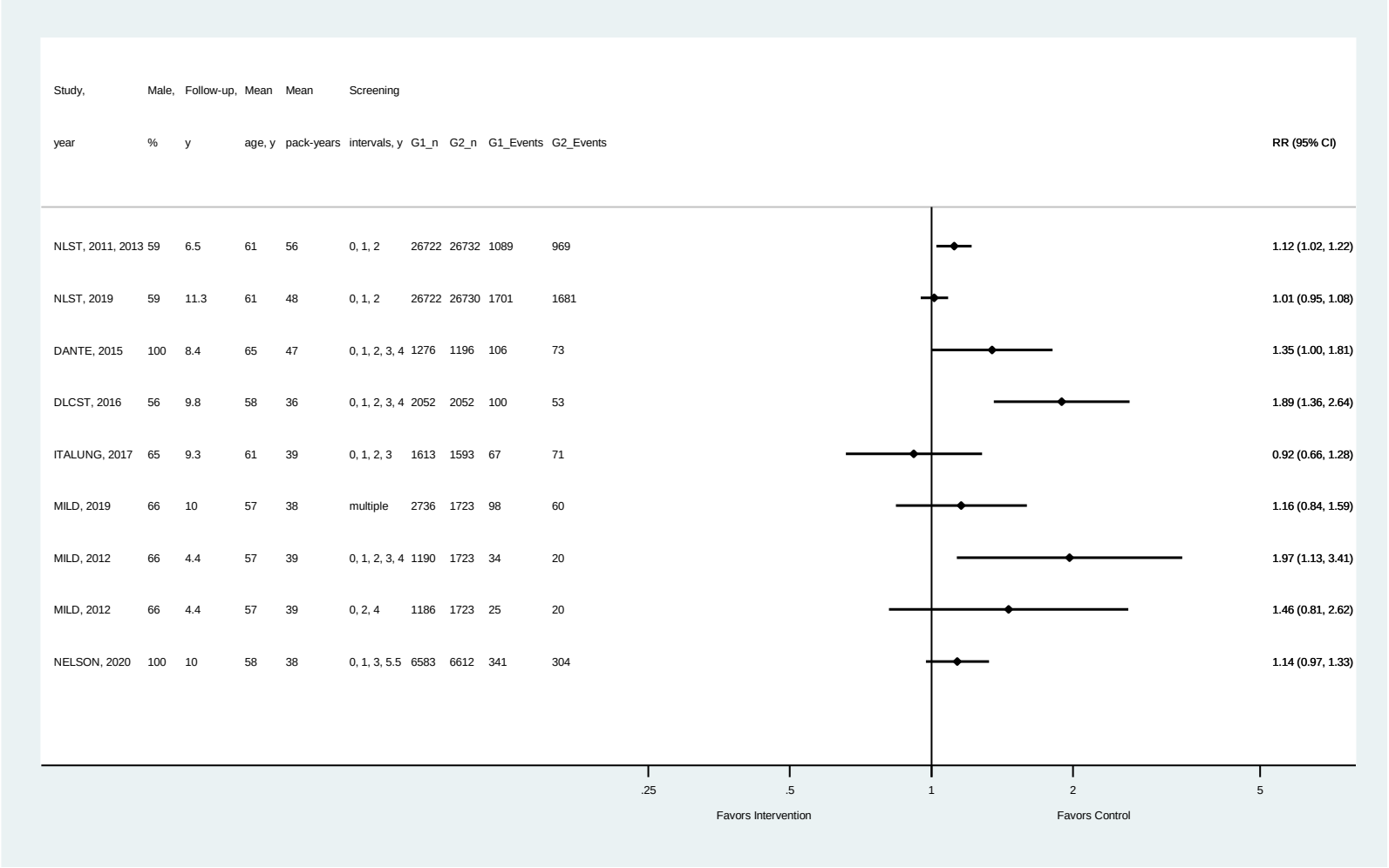
Appendix E Table 9. KQs 6 and 7 Update Search Results: SBRT Study Outcomes

Study Identifiers Author, Year Treatment Type N Enrolled (Analyzed) KQs Addressed Quality	5-Year Survival Outcomes Overall Survival, % (95 CI) Lung Cancer Specific Survival, % (95 CI) Progression- or Recurrence-Free Survival, % (95 CI)	Short-Term Outcomes 30-Day Mortality, N (%) 90-Day Mortality, N (%) Rib Fractures, N (%) Radiation Pneumonitis, N (%) Adverse Event with ≥10% Incidence, N (%)
Westover, 2012[284] SBRT N=15 (20 tumors) KQ 7 Fair	NA	Rib fracture: 3/20 (15*) tumors RP Total: 7/20 (35*) tumors Grade 3: 1/20 (5*) tumor Grade 1: 6/20 (30*) tumors Adverse events Dermatitis: 4/20 (20*) tumors Fatigue: 2/20 (10*) tumors
Wink, 2019[235] SBRT/SABR N=554 KQ 6 Fair	Overall survival: 47	NA
Ye, 2018[294] SBRT/SABR N=100 KQ 7 Fair	NA	30-day mortality: 0 Rib fracture: 0 Acute RP: 6 (6*) Late Grade 2 RP: 8 (8*)

*Indicates that data were calculated by abstractors.

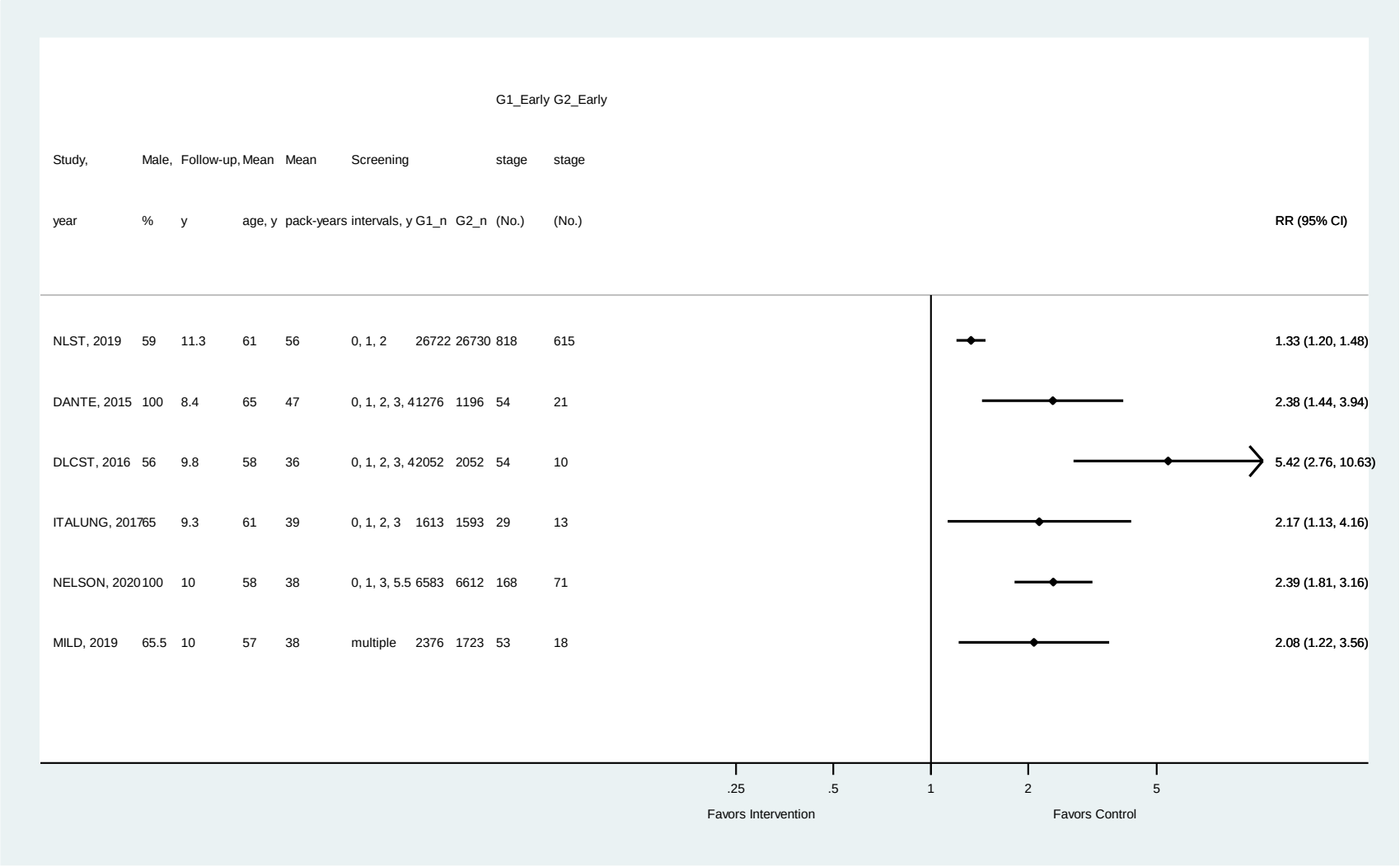
Abbreviations: CI=confidence interval; KQ=key question; Max=maximum; mos=months; NA=not applicable; PSM=propensity score matched; RP=radiation pneumonitis; RR=risk ratio; SABR=stereotactic ablative radiotherapy; SBRT=stereotactic body radiation therapy.

Appendix E Figure 1. Sensitivity Analysis for Trial Results for Lung Cancer Incidence (KQ 1), Including Studies Rated as Poor Quality



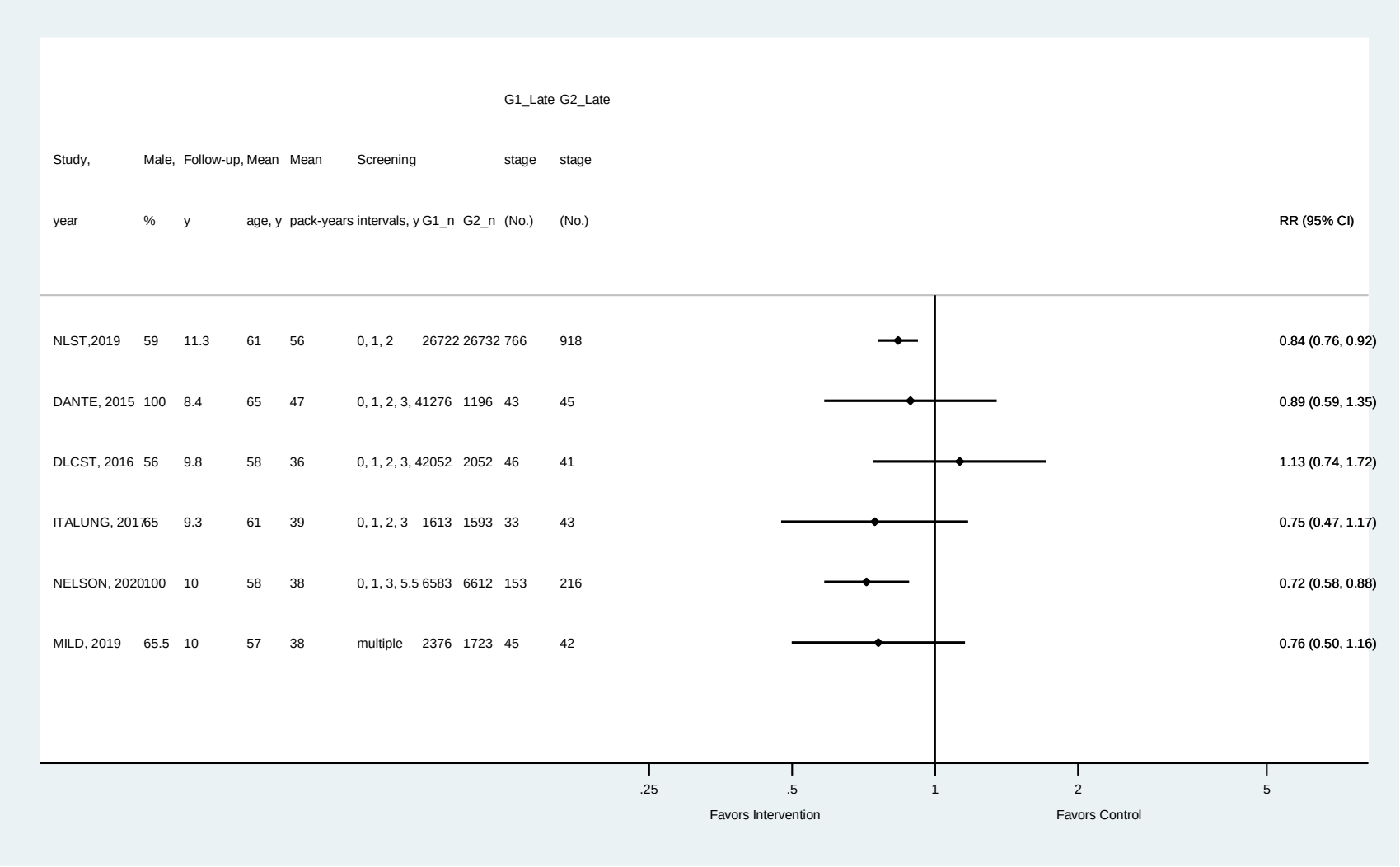
Note: G1=LDCT; G2=Control; The MILD trial randomized participants to annual screening, biennial screening, or a control group. For the 10-year followup, the annual and biennial screening groups were combined. At the 10-year followup, the median duration of screening for those in the screening groups was 6.2 years.
Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; MILD=Multicentric Italian Lung Detection; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

Appendix E Figure 2. Sensitivity Analysis for Early-Stage Lung Cancer Incidence (KQ 1), Including Studies Rated as Poor Quality



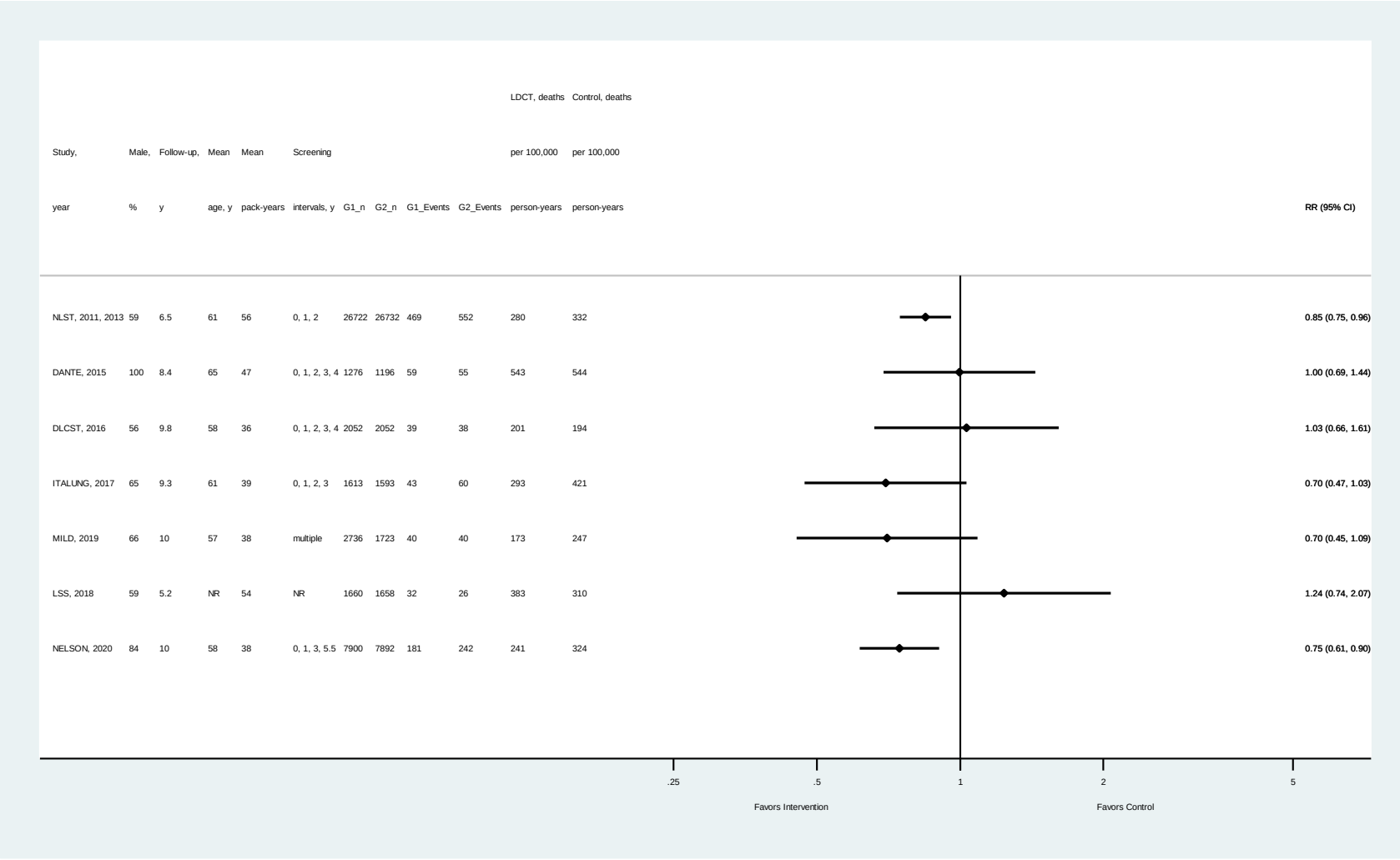
Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; MILD=Multicentric Italian Lung Detection; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

Appendix E Figure 3. Sensitivity Analysis for Late-Stage Lung Cancer Incidence (KQ 1), Including Studies Rated as Poor Quality



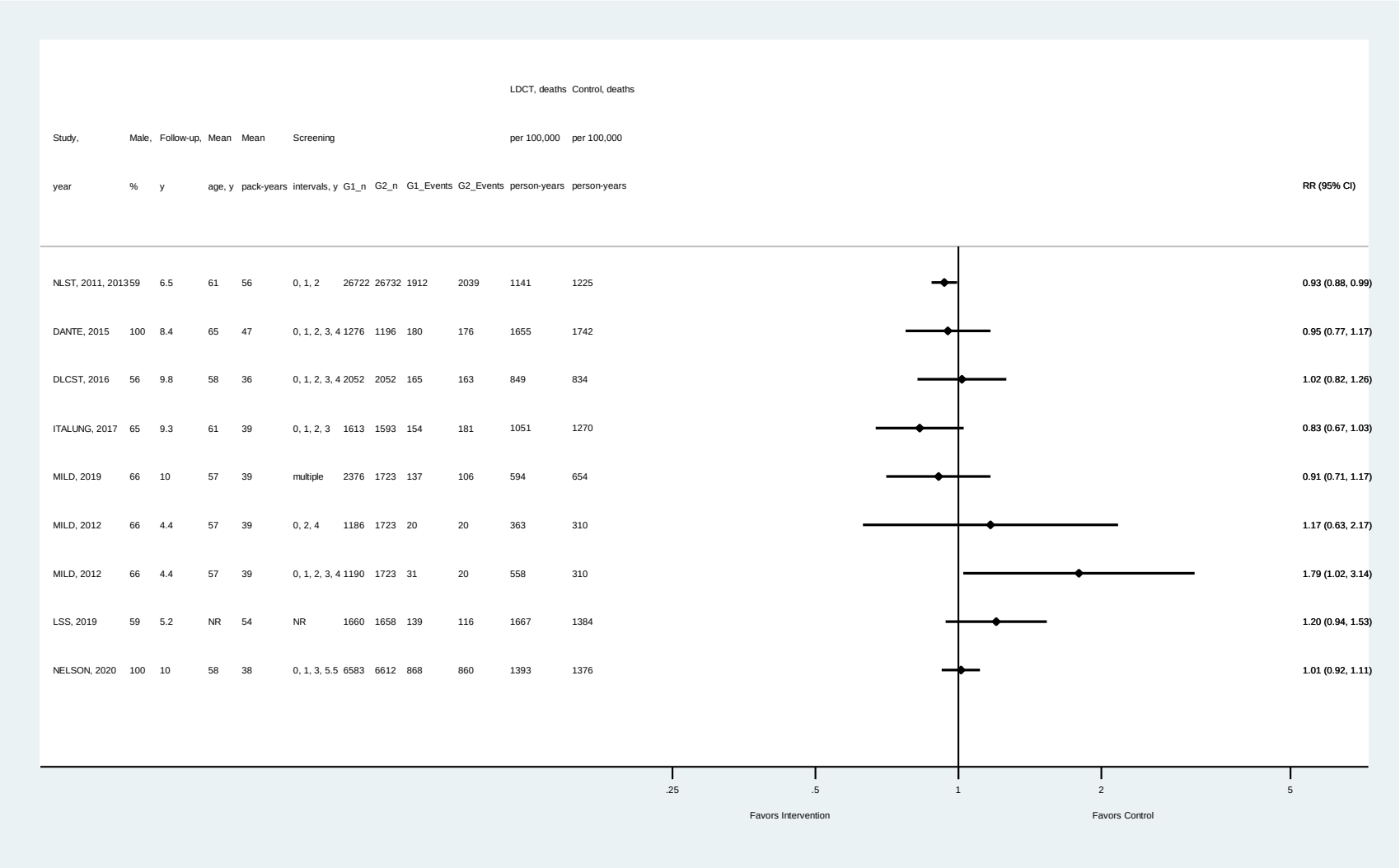
Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; MILD=Multicentric Italian Lung Detection; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

Appendix E Figure 4. Sensitivity Analysis for Trial Results for Lung Cancer Mortality (KQ 1), Including Studies Rated as Poor Quality



Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; LSS=Lung Screening Study; MILD=Multicentric Italian Lung Detection; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.

Appendix E Figure 5. Sensitivity Analysis for Trial Results for All-Cause Mortality (KQ 1), Including Studies Rated as Poor Quality



Abbreviations: DANTE=Detection and Screening of Early Lung Cancer with Novel Imaging Technology and Molecular Essays; DLCST=Danish Lung Cancer Screening Trial; ITALUNG=Italian Lung Cancer Screening Trial; LSS=Lung Screening Study; MILD=Multicentric Italian Lung Detection; NELSON=Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST=National Lung Screening Trial.