Bibliographic Cite	PMID Link	Literature Type	Level of Evidence	Purpose	Population	Intervention and Outcome Measures	Results/ Recommendations	Study Limitiations
Aggarwal R, Lam AC, McGregor M, et al. Outcomes of long-term interval rescreening for lung cancer in different risk cohorts. J Thorac Oncol. 2019; 14(6):1003-1011.	30771523	Prospective, single-center, single-reader	Low	To determine how to best prioritize participants practically for rescreening, after a long interval between LDCT scans that were originally negative.	Inclusion criteria were those who, at study entry, had a smoking history of ≥ 10 pack-years, were ≥ 50 years old, had no history of any cancer, and had no positive findings on their pre-hiatus LDCT scan (defined as no solid nodules ≥ 5 mm and no nonsolid nodules ≥ 8 mm). Exclusion criteria were any participants diagnosed with LC during the study hiatus, those who had a CT scan of the thorax performed within the past 5 years, or those with significant comorbidity that made screening inappropriate.	Individuals with negative baseline screening results before 2009 underwent low-dose CT rescreening from 2015-2018. Individuals were contacted in order of descending risk, and then categorized into three risk cohorts according to their baseline risks. The incidence of LC in each risk cohort was determined and compared. Chi-square testing was used for categorical variables and one-way analysis of variance on ranks was used for continuous variables.	Of the 1261 participants the authors attempted to recontact, 359 participants returned for a rescreening scan (mean of 7.6 years between scans). Participants were divided into low (<2%), moderate (2% to <3.5%), and high baseline risk (≥ 3.5%) cohorts. On average, those in the high-risk cohort compared to the moderate- and low-risk cohorts were older (66 years versus 62 and 59 years) and had a greater smoking history (54 pack-years versus 47 and 29 pack-years). The incidence of cancer in the high-risk cohort was significantly higher than in the moderate-risk cohort (11% versus 1.7%, p ¼ 0.002). The authors conclude that there was a significantly higher incidence of LC in the high-risk cohort than in the moderate-risk cohort. The cut-point between the high- and moderate-risk was determined to be greater than or equal to 3.5% of the 6- year baseline risk.	The authors note two major limitations. First, only 64 participants were in the low-risk cohort. As a result, authors did not compare this cohort with other cohorts for the primary outcome. Second, risk scores were calculated using variables collected when participants first were entered into the pre-2009 trial, and not at the time of the pre-hiatus scan.
Bradley SH, Fielding Hatton NL, Aslam R, et al. Estimating lung cancer risk from chest x-ray and symptoms: A prospective cohort study. Br J Gen Pract. 2021; 71(705):e280-e286.	33318087	Prospective, single-center, multi-reader	Low	To establish the sensitivity and specificity of chest x-ray (CXR); determine the positive predictive values (PPVs) of each presenting symptom of lung cancer following a negative CXR; and determine whether lung cancer symptoms are different in those with positive CXR compared to those with negative CXR.	Patients aged > 50 years who had lung cancer symptoms (cough, hemoptysis, dyspnea, chest pain, weight loss, and change in voice) warranting investigation with CXR were included. Patients who had received chest radiography in the previous three months were not eligible. Patients who had a history of prior lung cancer prior were excluded, as were those who were diagnosed with an intrathoracic malignancy other than lung cancer in the 2 years following screening.	A prospective cohort study was conducted, based on routinely collected data from a service that allowed patients with symptoms of lung cancer to request CXR. Symptom data were combined with a diagnostic category (positive or negative) for each CXR, and the sensitivity and specificity of CXR for lung cancer were calculated. The PPV of lung cancer associated with each symptom or combination of symptoms was estimated for those patients with a negative CXR.	In total, 114 (1.3%) of 8996 patients (mean age 69) who requested a CXR were diagnosed with lung cancer within 1 year. Sensitivity was 75.4% and specificity was 90.2%. The PPV of all symptoms for a diagnosis of lung cancer within 1 year of CXR was <1% for all individual symptoms except for hemoptysis, which had a PPV of 2.9%. PPVs for a diagnosis of lung cancer within 2 years of CXR was <1.5% for all single symptoms except for haemoptysis, which had a PPV of 3.9%. The authors note that, even in patients who appear to be at low risk, a negative CXR does not eliminate the possibility of lung cancer and, in some cases, further investigation should be considered if symptoms persist or evolve. Additionally, findings support guidance that unexplained hemoptysis warrants urgent referral, regardless of CXR result. Findings also support guidance that unexplained hemoptysis warrants urgent referral, regardless of CXR result.	The study population had a low prevalence of lung cancer with only 154 (1.7%) diagnosed with the disease within 2 years, of whom 57 (37.0%) had had a negative SR-CXR result. This meant that insufficient cases were present to calculate PPVs for several symptom combinations. In addition, the lack of a control group meant the calculation of adjusted PPVs was calculated using a within-study comparator based on the patients at lowest risk of developing lung cancer.
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. 382(6):503-513.	31995683	Prospective, multi-center, single-reader	High	To report lung-cancer incidence, mortality, and the performance of four screening rounds in the NELSON trial among male participants (main analysis) and female participants (subgroup analysis).	A total of 13,195 men and 2594 women between the ages of 50 and 74 (median age 58) were included. Eligible participants were current or former smokers [those who had quit ≤ 10 years ago] who had smoked > 15 cigarettes a day for > 25 years or > 10 cigarettes a day for > 30 years. Exclusion criteria were patient report of moderate or severe health problems and an inability to climb two flights of stairs; a body weight of more than 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.	Participants were randomly assigned to undergo CT screening at T0 (baseline), year 1, year 3, and year 5.5 or no screening. Data was obtained on cancer diagnosis and date and cause of death through linkages with national registries, and a review committee confirmed lung cancer as the cause of death when possible. A minimum follow up of 10 years was completed for all participants.	Among men, average adherence to CT screening was 90.0%. On average, 9.2% of the screened participants underwent at least one additional CT scan. The overall referral rate for suspicious nodules was 2.1%. At 10 yrs of follow-up, the incidence of lung cancer was 5.58 cases per 1000 person-years in the screening group and 4.91 cases per 1000 person-years in the control group; lung-cancer mortality was 2.50 deaths per 1000 person-years and 3.30 deaths per 1000 person-years, respectively. The cumulative rate ratio for death from lung cancer at 10 years was 0.76 (95% CI, 0.61 to 0.94; P = 0.01) in the screening group as compared with the control group, similar to the values at years 8 and 9. Among women, the rate ratio was 0.67 (95% CI, 0.38 to 1.14) at 10 years of follow-up, with values of 0.41 to 0.52 in years 7 through 9. The authors conclude that, among high-risk persons, lung-cancer mortality was significantly lower among those who underwent volume CT screening than among those who underwent no screening. There were low rates of follow-up procedures for results suggestive of lung cancer.	At the time of initiation (2000 through 2004), only a small number of women were eligible, because smoking was much less prevalent and much less intensive among women than among men. The NELSON trial was not powered to show a possible favorable difference in all-cause mortality (expected within the range of 2.5%), because it would have required unrealistic sample sizes.
Field JK, Vulkan D, Davies MP, et al. Lung cancer mortality reduction by LDCT screening: UKLS randomized trial results and international meta-analysis. Lancet Reg Health Eur. 2021; 10:100179.	34806061	Prospective, multi-center, multi-reader	High	To report on incidence and morality outcome for participants with cancer registry and mortality data available from the UKLS trial, and to undertake a meta-analysis of the randomized, controlled LDCT screening trials which have reported lung cancer mortality with at least a median of three years' follow-up.	Included were individuals at high risk of developing lung cancer over the next five years defined as a risk score of at least 4.5% as per version 2 of the validated Liverpool Lung Project risk model (LLPv2). Exclusion criteria were: inability to give consent, or any condition precluding written informed consent; any comorbidity which would contraindicate either screening or treatment if lung cancer were to be detected; a chest CT performed within the preceding year; inability to lie flat.	From October 2011 to February 2013, authors randomly allocated a total of 4,055 participants to either a single invitation to screening with LDCT or to no screening (usual care). Data were collected on lung cancer cases through linkage to national registries. The primary outcome was mortality due to lung cancer. The authors included results in a random effects meta-analysis to provide a synthesis of the latest randomized trial evidence.	1,987 participants in the intervention and 1,981 in the usual care arms were followed for a median of 7.3 years (IQR 7.1 7.6), 86 cancers were diagnosed in the LDCT arm and 75 in the control arm. 30 lung cancer deaths were reported in the screening arm, 46 in the control arm, (relative rate 0.65 [95% CI 0.41 1.02]; p=0.062). The meta-analysis indicated a significant reduction in lung cancer mortality with a pooled overall relative rate of 0.84 (95% CI 0.76 0.92) from nine eligible trials. The authors conclude that the UKLS trial of single LDCT indicates a reduction of lung cancer death of similar magnitude to the NELSON and NLST trials and was included in a meta-analysis of nine randomized trials which provides unequivocal support for lung cancer screening in identified risk groups.	The number of individuals recruited into the UKLS pilot trial is its major limitation when considering the effect on lung cancer mortality. Pragmatically, authors relied on nationally curated data (ONS) rather than having a cause of death committee. This, however, does mean that the cause of death was determined in the absence of knowledge of which trial group the subjects belonged to. UKLS predates introduction of British Thoracic Society pulmonary nodule guidelines, but utilized similar nodule categorization to NELSON.

Hammer MM, Palazzo LL, Kong CY, Hunsaker AR. Cancer risk in subsolid nodules in the National Lung Screening Trial. Radiology. 2019; 293(2):441-448.	31526256	Retrospective, multi-center, single-reader	Low	To evaluate Lung-RADS estimates of the malignancy rates of subsolid nodules, using nodules from the National Lung Screening Trial (NLST), and to compare Lung-RADS to the NELSON trial classification as well as the Brock University calculator.	This retrospective study used nonidentifiable patient data for secondary data analysis. Subsets of patients (nodules) were selected by using the following queries: (a) GGNs smaller than 10mm; (b) GGNs measuring 10 mm or larger; and (c) "mixed" nodules (PSNs) measuring 6 mm or larger. Only patients in the NLST with at least two CT scans were included to identify nodule growth over time.	A thoracic radiologist reviewed the baseline and follow-up CT images, confirmed that they were true subsolid nodules, and measured the nodules. The primary outcome for each nodule was the development of malignancy within the follow-up period (median, 6.5 years). Nodules were stratified according to Lung-RADS, NELSON trial criteria, and the Brock model. For analyses, nodule subsets were weighted on the basis of frequency in the NLST data set. Nodule stratification models were tested by using receiver operating characteristic curves.	434 patients were included in the analysis. 220 were women (51%) and 245 (56%, 54% weighted) were former rather than current smokers. The median age was 62 years (range, 55–74 years), and the median smoking history was 48 pack-years. At baseline, 304 nodules were classified as Lung-RADS category 2, with a malignancy rate of 3%, which is greater than the 1% in Lung-RADS (P = .004). The malignancy rate for GGNs smaller than 10 mm (two of 129, 1.3%) was smaller than that for GGNs measuring 10–19 mm (11 of 153, 6%) (P = .01). The malignancy rate for Lung-RADS category 3 was 14% (13 of 67), which is greater than the reported 2% in Lung-RADS (P , .001). The Brock model predicted malignancy better than Lung-RADS and the NELSON trial scheme (area under the receiver operating characteristic curve = 0.78, 0.70, and 0.67, respectively; P = .02 for Brock model vs NELSON trial scheme). The authors conclude that subsolid nodules classified as Lung-RADS category 2 or 3 have a higher risk of malignancy than reported. The Brock risk calculator performed better than measurement-based classififcation schemes such as Lung-RADS.	This study has several noted limitations. First, the NLST data cancers were assigned to a lobe rather than a nodule. Thus, authors cannot know for certain if a malignancy identified within the lobe was the result of the most suspicious nodule seen at that time or of a new (incident) nodule. Authors also note that unresected subsolid nodules in NLST may still represent indolent malignancies that have simply not been detected during the follow-up period. Being derived from NLST, the authors note that the applicability to Asian screening populations, which tend to include many nonsmokers, is uncertain. Finally, authors note that they did not apply radiomic analysis to these subsolid nodules, which may have improved the malignancy risk assessment
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; 113:45-50.	29110848	Retrospective, multi-center, multi-reader	Moderate	To explore the relationship between nodule count and lung cancer probability in baseline low-dose CT lung lung cancer screening.	Included were participants from the NELSON trial with at least one baseline nodule (3,392 participants [45% of screen-group], 7,258 nodules). The NELSON trial consisted of current and former smokers, aged 50-75 years, who smoked > 15 cigarettes daily for over 25 years or > 10 cigarettes daily for over 30 years. Median participant age was 58 years (IQR 55–63 years); 84.4% (2863/3392) were male.	Authors determined nodule count per participant. Malignancy was confirmed by histology. Nodules not diagnosed as screen-detected or interval cancer until the end of the fourth screening round were regarded as benign. Authors compared lung cancer probability per nodule count category.	1746 (51.5%) participants had one nodule, 800 (23.6%) had two nodules, 354 (10.4%) had three nodules, 191 (5.6%) had four nodules, and 301 (8.9%) had > 4 nodules. Lung cancer in a baseline nodule was diagnosed in 134 participants (139 cancers; 4.0%). At baseline, malignancy was detected mostly in the largest nodule (64/66 cancers). Lung cancer probability was 62/1746 (3.6%) in participants thst had one nodule, 33/800 (4.1%) for two nodules, 17/354 (4.8%) for three nodules, 12/191 (6.3%) for four nodules and 10/301 (3.3%) for > 4 nodules (p =NS). The authors conclude that in baseline lung cancer CT screening, half of participants with lung nodules have more than one nodule, and lung cancer probability does not significantly change with number of nodules. Each nodule found in screening should be assessed separately independent of the presence of other nodules.	Authors note that they included all non-calcified nodules, and did not differentiate between solid, part- solid and pure nonsolid nodules. Therefore, more detailed research on the influence of multiple nodules from different subtypes (solid, sub-solid) on lung cancer probability is recommended. Furthermore, authors note that external validation of the nodule count and lung cancer probability in high-risk screening participants needs to be performed to confirm these findings.
Kato K, Gemba K, Ashizawa K, et al. Low-dose chest computed tomography screening of subjects exposed to asbestos. Eur J Radiol. 2018; 101:124-128.	29571785	Prospective, multi-center, multi-reader	Moderate	To reveal the prevalence of lung cancer (LC) and malignant pleural mesothelioma (MPM) in subjects with past asbestos exposure (AE). Additionally, to examine pulmonary or pleural changes correlated with the development of LC.	Included were 1) those who had engaged in asbestos-product manufacturing > 1 year, 2) those who had engaged in other industries related to AE for > 10 years, or 3) those who had engaged in industries related to AE and demonstrated pleural plaques on chest X-ray or CTA. A total of 2,132 subjects were enrolled. 96.2% were men, with a mean age of 76.1 years; 78.8% former or current smokers; and 21.2% never smokers.	Authors screened subjects using low-dose computed tomography (CT). The CT images were taken with a CT dose Index of 2.7 mGy. The evaluated CT findings included subpleural curvilinear shadow/subpleural dots, ground glass opacity or interlobular reticular opacity, traction bronchiectasia, honeycombing change, parenchymal band, emphysema changes, pleural effusion, diffuse pleural thickening, rounded atelectasis, pleural plaques (PQs), and tumor formation.	The PQs were detected in most of subjects (89.4%) and emphysema changes were seen in 46.0%. Fibrotic changes were detected in 565 cases (26.5%). A pathological diagnosis of LC was confirmed in 45 cases (2.1%) and MPM was confirmed in 7 cases (0.3%). The prevalence of LC was 2.5% in patients with a smoking history, which was significantly higher than that in never smokers (0.7%, p=0.027). The prevalence of LC was 2.8% in subjects with emphysema changes, which+ was higher than that of subjects without those findings (1.6%); although, the difference was not statistically significant (p=0.056). The prevalence of LC in subjects with both fibrotic plus emphysema changes was 4.0%, which was significantly higher than that of subjects with neither of those findings (1.8%, p=0.011). Logistic regression analysis revealed smoking history, fibrotic plus emphysema changes, and pleural effusion as significant explanatory variables. The authors conclude that smoking history, fibrotic plus emphysema changes, and pleural effusion were correlated with the prevalence of LC.	The authors note that there are limitations to the current study. It is a cross-sectional study. The causal connection between LC and some CT pulmonary findings were suggested; however, these should be clarified in a future prospective study.
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; 289(1):218-224.	29989522	Prospective, multi-center, single-reader	Low	To assess the incidence of lung cancer in a cohort of patients with negative fidings at previous lung cancer screening.	Study consisted of subset of the 4,782 individuals who had negative screening results as part of the International Early Lung Cancer Action Program (1993–2005). If there was a history of lung cancer or if chest CT had been performed during the previous 3 years, authors collected this information, but these individuals were not invited to undergo low-dose CT.	Subjects were assigned a lung cancer risk score by using a validated risk model. Starting with those at highest risk, subjects were interviewed by phone and invited to undergo low-dose CT between March 2013 and October 2016. Subjects with a diagnosis of lung cancer and those who had died of lung cancer were determined. Descriptive statistics were used to summarize data. The independent samples t test and Fisher exact test were used to compare age, sex, and risk scores.	A total of 327 study participants were contacted, and 200 subjects participated in this study. The average age was 74 years (range, 57–88 years), and the median time since previous CT was 7 years. The incidence rate of developing lung cancer during the next 6 years was estimated at 5.6%. The period prevalence of lung cancer was 20.8% (new and preexisting lung cancer, 68 of total cohort of 327). The detection rate of low-dose CT was 7% (14 of 200 subjects). Of the 14 screening detected cancers, 12 were stage I or II. The authors conclude that high-risk individuals have a high incidence of lung cancer after previous negative lung cancer screening. Early-stage lung cancer can be successfully detected in older high-risk individuals.	Because authors contacted individuals with the highest risk first, the lung cancer incidence is likely to decrease as patients with lower calculated risk scores continue to be enrolled. Given that most of the diagnosed malignancies were stages I and II, overdiagnosis is a possibility, especially in this older cohort. With regard to the group comparisons, the lack of significant associations may be attributed to underpowering resulting from small sample sizes for the outcome and/or key comparison subgroups.

Kim M, Suh CH, Lee SM, et al. Development of brain metastases in patients with non-small cell lung cancer and no brain metastases at initial staging evaluation: Cumulative incidence and risk factor analysis. AJR Am J Roentgenol. 2021; 217(5):1184-1193.	34037408	Retrospective, single-center, multi-reader	Low	To estimate the cumulative incidence of an risk factors for brain metastasis development in patients with NSCLC without brain metastases at initial presentation.	Study included 1,495 patients with NSCLC (mean [± SD] age, 65 ± 10 years; 920 men and 575 women) without brain metastases at initial evaluation that included brain MRI. Excluded were those with no initial staging contrast-enhanced brain RI, brain metastasis at initial evaluation, incomplete staging of NSCLC because of absence of contrast-enhanced chest CT at initial evaluation, and malignancy other than lung cancer.	Follow-up brain MRI was ordered at the discretion of the referring physicians. MRI examinations were reviewed in combination with clinical records for brain metastasis development; patients not undergoing MRI were deemed to have not had metastases develop through last clinical follow-up. The cumulative incidence of brain metastases was determined, with death considered a competing risk, and was stratified by clinical stage group, cell type, and epidermal growth factor receptor (EGFR) gene mutation status. Univariable and multivariable Cox proportional hazards regression analyses were performed.	A total of 258 of 1495 patients (17.3%) underwent follow-up brain MRI, and 72 (4.8%) had brain metastases develop at a median of 12.3 months after initial diagnosis of NSCLC. Of the patients who had metastases develop, 44.4% had no neurologic symptoms, and 58.3% had stable primary thoracic disease. The cumulative incidence of brain metastases at 6, 12, 18, and 24 months after initial evaluation was 0.6%, 2.1%, 4.2%, and 6.8%, respectively. Cumulative incidence at 6, 12, 18, and 24 months was higher (p < .001) in patients with clinical stage III–IV disease (1.3%, 3.9%, 7.7%, and 10.9%, respectively) than in those with clinical stage I–II disease (0.0%, 0.8%, 1.2%, and 2.6%, respectively), and it was higher (p < .001) in patients with EGFR mutation–positive adenocarcinoma (0.7%, 2.5%, 6.3%, and 12.3%, respectively) than in those with EGFR mutation– negative adenocarcinoma (0.4%, 1.8%, 2.9%, and 4.4%, respectively). The incidence of brain metastasis over the study interval was 8.7% among patients with clinical stage III–IV disease and 17.4% among those with EGFR mutation–positive adenocarcinoma.	The authors note that a primary limitation of the study is its single-center, retrospective design. However, they included 1495 consecutive patients with NSCLC who had no brain metastases at initial evaluation, which to their knowledge is the largest such cohort reported to date. In addition, 74.2% of patients in the cohort had adenocarcinoma, which is higher than the reported prevalence of approximately 50% for adenocarcinoma in NSCLC. The EGFR or ALK mutation status was unknown for some patients. This reflects real-world data, because molecular markers may not be tested in early-stage NSCLC that is treated surgically. Finally, only 17.3% of patients underwent surveillance brain MRI at authors' institution; the remaining patients were deemed to be free of brain metastases on the basis of clinical follow-up without having undergone brain MRI. This approach may have underestimated the true incidence of brain metastases developing.
Kim M, Suh CH, Lee SM, et al. Diagnostic yield of staging brain MRI in patients with newly diagnosed non-small cell lung cancer. Radiology. 2020; 297(2):419-427.	32840470	Retrospective, single-center, multi-reader	Low	To evaluate the diagnostic yield of staging brain MRI in the initial evaluation of lung cancer.	Study included patients with newly diagnosed NSCLC who underwent staging chest CT and staging brain MRI. A total of 1,712 patients (mean age, 64 years; 1,035 men) were included. Patients with malignancy other than lung cancer, with no staging brain MRI, with no chest CT report, and with clinical staging as Tis were excluded.	Diagnostic yield was defined as the proportion of patients with brain metastases among all patients. Yield was stratified into clinical stage groups per the eighth edition of the American Joint Committee on Cancer staging guidelines, based on staging chest CT and in adenocarcinoma with epidermal growth factor receptor (EGFR) gene mutation and anaplastic lymphoma kinase (ALK) gene rearrangement. Subgroup analyses were performed on the basis of cell types and molecular markers.	The diagnostic yield of staging brain MRI in newly diagnosed NSCLC was 11.9% (203 of 1712; 95% CI: 10.4%, 13.5%). In clinical stage IA, IB, and II disease, the diagnostic yields were 0.3% (two of 615; 95% CI: 0.0%, 1.2%), 3.8% (seven of 186; 95% CI: 1.5%, 7.6%), and 4.7% (eight of 171; 95% CI: 2.0%, 9.0%), respectively. The diagnostic yield was higher in patients with adenocarcinoma (13.6%; 176 of 1297; 95% CI: 11.8%, 15.6%) than squamous cell carcinoma (5.9%; 21 of 354; 95% CI: 3.7%, 8.9%) and in patients with EGFR mutation–positive adenocarcinoma (17.5%; 85 of 487; 95% CI: 14.2%, 21.1%) than with EGFR mutation– negative adenocarcinoma (10.6%; 68 of 639; 95% CI: 8.4%, 13.3%) (P , .001 for both).	Authors note the major limitation was its single- center retrospective nature. There was a higher proportion of adenocarcinoma (75.8%) in this study sample in comparison with the reported prevalence of about 50% of adenocarcinoma in NSCLC, which could potentially result in overestimation of overall diagnostic yield. Authors were also unable to evaluate overall survival of patients with brain metastases or examine the prognostic value of staging brain MRI, primarily owing to the relatively short follow-up period available following the recent introduction of the AJCC eighth edition.
Quartuccio N, Evangelista L, Alongi P, et al. Prognostic and diagnostic value of [18F]FDG-PET/CT in restaging patients with small cell lung carcinoma: An Italian multicenter study. Nucl Med Commun. 2019; 40(8):808-814.	31136534	Retrospective, multi-center, multi-reader	Low	To evaluate the prognostic value yielded by [18F] FDG-PET/CT and to assess the diagnostic agreement between [18F] FDG-PET/CT and contrast-enhanced computed tomography (ceCT).	Included were 164 patients with SCLC from a multicenter database who underwent [18F] FDG-PET/CT for restaging purposes. Eighty-three (50.6%) patients were smokers and 110 had a central SCLC (67.1%). Thirteen (7.9%) patients received chemotherapy before [18F]FDG PET/CT and 75 (45.7%) had been treated with radiotherapy.	PET scans were evaluated visually to identify the presence of recurrence. The maximum and mean standardized update value, metabolic tumor volume, and total lesion glycolysis were calculated. Kaplan-Meier curves were computed to assess the effects of [18F] FDG-PET/CT findings on overall survival and progression-free survival. The agreement between PET/CT and ceCT in detecting metastases was evaluated in 199 patients on a patient-based analysis (Cohen's K; P < 0.05).	The median follow-up from restaging [18F]FDG-PET/CT was 441 days. The presence of metastatic lesions at [18F] FDG-PET/CT was associated with a significantly shorter overall survival (P = 0.039) and progression-free survival (P < 0.001). Higher maximum standardized uptake value showed a trend toward a shorter overall survival (P = 0.065). The K-agreement between ceCT and PET/CT in recurrent SCLC was 0.37 (P < 0.001). PET/CT and ceCT showed the same number of lesions in 52 (43.7%) patients, whereas PET/CT detected additional lesions in 35 (29.4%) patients. The authors conclude that detection of metastatic lesions at restaging by [18F] FDG-PET/CT can predict a higher rate of progression and negatively influence overall survival in patients with SCLC. [18F] FDG-PET/CT and ceCT seem to be complementary imaging modalities in patients with metastatic SCLC.	Authors note that the lack of stratification for treatment may constitute a bias for evaluating the real prognostic power of semiquantitative [18F] FDG-PET/CT-derived parameters. Other limitations of this work, on the basis of the study design, included the mixture of patients with limited and extended disease at initial presentation and a significant portion of missing data, which may have hampered the accurate assessment of the prognostic power of clinical or [18F] FDG-PET/CT-derived semiquantitative variables.
Su CC, Wu JT, Neal JW, et al. Impact of low-dose computed tomography screening for primary lung cancer on subsequent risk of brain metastasis. J Thorac Oncol. 2021; 16(9):1479-1489.	34091050	Retrospective, multi-center, single-reader	Low	To investigate the impact of LDCT screening for primary lung cancer (PLC) on the risk of developing brain metastasis (BM) after PLC diagnosis.	Study included 1,502 participants who were diagnosed with PLC and have follow-up data for BM. The mean age at PLC diagnosis was 65.9, 76.8% had early stage PLC, 41.8% had adenocarcinoma, and 55% had undergone surgery as primary treatment of their PLC	Study used the National Lung Screening Trial data to identify patients. Cause-specific competing risk regression was applied to evaluate an association between BM risk and the mode of PLC detection—that is, LDCT screen-detected versus non LDCT screen-detected. Subgroup analyses were conducted in patients with early stage PLC and those who underwent surgery for PLC.	Of 1,502 participants, 41.4% had PLC detected through LDCT screening versus 58.6% detected through other methods, for example, chest radiograph or incidental detection. Patients whose PLC was detected with LDCT screening had a significantly lower 3-year incidence of BM (6.5%) versus those without (11.9%), with a cause specific hazard ratio (HR) of 0.53 (p = 0.001), adjusting for age at PLC diagnosis, PLC stage, PLC histology, and smoking status. The authors conclude that early detection of PLC using LDCT screening is associated with lower risk of BM after PLC diagnosis.	The age of eligible participants in NLST was restricted to 55 to 74 years old, and the participants were predominantly white (90%) with a heavy smoking history. Authors also note that current data do not provide a full understanding of the mechanism behind the observed association between LDCT screen detected LCs and BM risk, especially among early stage patients or those who underwent surgery for PLCs. NLST lacked tumor mutation, detailed tumor radiomics, and patient genetic profiling data to evaluate the underlying biology between LDCT-screen and non–screen-detected LCs. Authors were also unable to compare the tumor doubling time between these two groups.

Subramanian M, Liu J, Greenberg C, et al. Imaging surveillance for surgically resected stage I non-small cell lung cancer: Is more always better? J Thorac Cardiovasc Surg. 2019; 157(3):1205-1217.	31130741	Retrospective, multi-center, single-reader	Low	To compare imaging surveillance in patients with pathologic stage I NSCLC. The primary aim was to determine if the intensity of surveillance with CT was associated with 5-year overall survival (OS).	2,442 patients were identified. These were pathologic stage I patients who underwent surgical resection and had their first surveillance imaging CT scan between 60–450 days after surgical resection. Additionally, patients must have been asymptomatic at the time of the first postoperative CT. Patients who underwent chemoradiation therapy or had positive surgical margins were excluded.	Cancer registrars at Commission on Cancer accredited institutions re-abstracted records to augment National Cancer Database patient data with information on comorbidities, imaging surveillance including intent and result of imaging, and recurrence. Pathologic stage I non-small cell lung cancer patients undergoing CT surveillance were placed into three imaging surveillance groups based on clinical practice guidelines: high intensity (3 month), moderate intensity (6 month), and low intensity (annual). Kaplan Meier analysis and Cox regression were used to compare overall survival among the three surveillance groups.	There were 805 (33%), 1216 (50%), and 421 (17%) patients in the high, moderate, and low surveillance intensity groups, respectively. Five-year overall survival was similar between intensity group (p = 0.547). Surveillance on asymptomatic patients detected 210 (63%) cases of locoregional recurrences and 128 (72%) cases of new primary lung cancer. The authors conclude that, in a unique national dataset of long term outcomes for stage I non-small cell lung cancer, surveillance intensity was not associated with 5-year overall survival.	The study consisted of patients that were diagnosed more than ten years ago. These patients were used so additional data abstraction on 5-year follow-up data could be performed. Thus, there was a trade-off required to capture complete 5-year follow-up information including recurrence and surveillance, which are not routinely captured in the NCDB.
Suh YJ, Park CM, Han K, et al. Utility of FDG PET/CT for preoperative staging of non-small cell lung cancers manifesting as subsolid nodules with a solid portion of 3 cm or smaller. AJR Am J Roentgenol. 2020; 214(3):514-523.	31846374	Retrospective, single-center, single-reader	Low	To investigate the utility of FDG PET/CT for the preoperative staging of subsolid non-small cell lung cancer (NSCLCs) with a solid portion size of 3 cm or smaller.	855 patients (335 men and 520 women; median age, 61.0 years) with pathologically proven NSCLCs manifesting as subsolid nodules with a solid portion of 3 cm or smaller on CT. Excluded were those with other dominant solid lung cancers (synchronously or metachronously) and patients with resected subsolid NSCLCs that were not the dominant lesions among multiple lung cancers.	Authors compared the diagnostic performances of FDG PET/CT and chest CT for detecting lymph node (LN), intrathoracic, or distant metastases in patients who underwent preoperative chest CT and FDG PET/CT. After propensity score matching, they next compared the diagnostic performance of FDG PET/CT in the group who underwent both chest CT and FDG PET/CT with that of chest CT in patients who did not undergo FDG PET/CT.	There were LN metastases in 25 of 765 patients (3.3%) who underwent surgical LN dissection or biopsy and intrathoracic or distant metastasis in two of 855 patients (0.2%). For LN staging, FDG PET/CT showed a sensitivity of 44.0%, specificity of 81.5%, positive predictive value of 9.6%, negative predictive value of 97.0%, and accuracy of 79.9%, which were lower than those of chest CT for accuracy (p < 0.0001). FDG PET/CT could not accurately detect any intrathoracic or distant metastasis. After propensity score matching, the diagnostic accuracy for LN staging of FDG PET/CT in the group who underwent both CT and FDG PET/CT was lower than that of chest CT in the group who did not undergo FDG PET/CT (p = 0.002), and the diagnostic accuracy for intrathoracic and distant metastases was not different (p > 0.999). The authors conclude that FDG PET/CT has limited utility in preoperatively detecting LN or distant metastasis in patients with subsolid NSCLCs with a solid portion size of 3 cm or smaller.	Authors note several limitations. First, because this study was a nonrandomized and retrospective study, significant differences were observed in clinical and lesion characteristics among the patients who underwent PET/CT and those who did not. Second, they could not use the latest lung cancer staging system from the 8th edition of the TNM classification for pathologic staging because of the retrospective study design and because the study population received treatment following the standard practices of that period. Third, they did not additionally review the individual images of PET/CT in this study, which may have affected the diagnostic performance of PET/CT.
Taralli S, Scolozzi V, Foti M, et al. ^{18}F-FDG PET/CT diagnostic performance in solitary and multiple pulmonary nodules detected in patients with previous cancer history: Reports of 182 nodules. Eur J Nucl Med Mol Imaging. 2019; 46(2):429-436.	30535767	Retrospective, single-center, multi-reader	Low	To evaluate the 18F-FDG PET/CT diagnostic performance in pulmonary nodules detected during follow-up in oncological patients and the relationship between malignancy and nodules' characteristics.	Study consisted of 182 pulmonary nodules (121 solitary, 61 multiple; mean size = 16.5 ± 8.1 mm, mean SUVmax = 5.2 ± 5.1) in 148 oncological patients (89 males; mean age = 69.5 ± 8.4 years). Included patients had (1) a history of previous cancer, considered to be disease-free at the time of PET/CT; (2) pulmonary nodules detected at CT during oncological follow-up and ranging from 5 mm to 40 mm in maximum axial diameter; and (3) availability of histopathological evidence or a radiological follow-up of at least 24 months as reference standard for nodules' final diagnosis. Oncological patients with history of prior pulmonary metastases or with pulmonary abnormalities described as "ground glass" (GGO) were excluded.	Final diagnosis was established by histology or radiological follow-up. Diagnostic performance of 18F-FDG visual analysis (malignancy-criterion: uptake ≥ mediastinal activity), ROC curve analysis for SUVmax and nodules' characteristics were assessed.	In 182 nodules, the prevalence of malignancy was 75.8%; PET/CT provided sensitivity = 79%, specificity = 81.8%, accuracy = 79.7%, PPV = 93.1%, NPV = 55.4%; ROC analysis (SUVmax cut-off = 1.7) provided sensitivity = 85.5%, specificity = 72.7%. In 121 solitary nodules, the prevalence of malignancy was 87.6%; PET/CT provided sensitivity = 82.1%, specificity = 73.3%, accuracy = 81%, PPV = 95.6%, NPV = 36.7%; ROC analysis (SUVmax cut-off = 2) provided sensitivity = 84%, specificity = 80%. In 61 multiple nodules, the prevalence of malignancy was 52.5%; PET/CT (nodule and patient-based analysis, respectively) provided sensitivity = 68.7%and 88.9%, specificity = 86.2%and 55.6%, accuracy = 77%and 77.8%, PPV = 84.4% and 80%, NPV = 71.8% and 71.5%; ROC analysis (nodule-based, SUVmax cut-off = 1.8) provided sensitivity = 71.9%, specificity = 82.8%. Malignant nodules were prevalent in males, in solitary pattern and in upper lobes, and had significantly greater size and metabolic activity (SUVmax and TLG) than benign ones. When comparing solitary and multiple patterns, malignant nodules had significantly greater size and metabolic activity than benign ones in both groups.	Limitations of our study are represented by the retrospective nature and the unavailability of information on the prevalence of smokers. Regarding this latter point, the authors note that smoking history is a well-recognized risk factor for malignancy in pulmonary nodules. Although they cannot evaluate this additional factor in their population, in previous similar reports focusing on oncological populations, no difference in smoking status between malignant and benign pulmonary nodules has been observed
Toba H, Kawakita N, Takashima M, et al. Diagnosis of recurrence and follow-up using FDG-PET/CT for postoperative non-small-cell lung cancer patients. Gen Thorac Cardiovasc Surg. 2021; 69(2):311-317.	32909168	Retrospective, single-center, multi-reader	Low	To examine the diagnostic capability of FDG-PET/CT for detecting recurrence in postoperative NSCLC patients, and to evaluate the results of postoperative surveillance using FDG-PET/CT in asymptomatic patients.	187 NSCLC patients (110 males, median age 68 years) who had undergone potentially curative operations at a single institution. From these patients, there was a total of 496 FDG-PET/CT examinations.	FDG-PET/CT examinations were performed to detect recurrences. The median interval between the initial surgery and the first FDG-PET/CT examination was 13.0 months (range 2–43 months). Follow-up FDG-PET/CT was performed ≥ 1 × /year in principle in 172 asymptomatic patients without clinical or radiological evidence of recurrence, and the results were retrospectively reviewed.	In the asymptomatic PET-screening group, the median interval between the patients' initial surgery and their latest follow-up was 5.0 years (range 1.4–9.7 years). During the follow-up period, the median number of times that FDG-PET/CT was performed per patient was three times (range 1–6 times). FDG-PET/CT correctly diagnosed recurrence in 46 of 47 (97.9%) patients and 68 of 69 (98.6%) recurrent sites. The following were obtained: 97.9% sensitivity, 97.1% specificity, 92.0% positive predictive value, 99.3% negative predictive value, and 97.3% accuracy. In asymptomatic patients, the detection rate of recurrence in the stage III group was significantly higher than the detection rates in the stage I and II groups, and FDG-PET/CT performed ≤ 3 years post-resection detected significantly more FDG- positive lesions compared to that performed after 4 years. The authors conclude that FDG-PET/CT is very useful for detecting recurrence in NSCLC patients after a potentially curative operation.	The study design was retrospective, and as a result, patient selection bias was introduced. The study design was also single-arm, and thus the diagnostic capability was not compared to any other imaging modality.

Vella M, Meyer CS, Zhang N, et al. Association of receipt of positron emission tomography-computed tomography with non-small cell lung cancer mortality in the Veterans Affairs health care system. JAMA Netw Open. 2019; 2(11):e1915828.	31747036	Retrospective, multi-center, single-reader	Moderate	To examine the association of the use of PET/CT with non-small cell lung cancer (NSCLC) mortality in the US Department of Veterans Affairs (VA) health care system from 2000 to 2013.	64,103 veterans (98% male and 78.9% white) receiving care in the VA health care system who were diagnosed with incident NSCLC. Further inclusion criteria was that veterans had at least 1 health care visit at the VA in the 12 months before the date of lung cancer diagnosis	Main outcomes were all-cause and NSCLC-specific mortality. Secondary outcome was receipt of stage-appropriate treatment. Patient data, including stage at time of diagnosis as determined by contemporaneous American Joint Committee on Cancer staging manuals, were obtained from the VA Central Cancer Registry and merged with electronic medical records in the Corporate Data Warehouse. Dates of death were determined from the VA Vital Status File. Cause of deathwas obtained from the National Death Index. Patient characteristics, including sex, race, housing status, marital status, smoking status, and rural vs urban location of residence, were obtained from VA patient care files and Cancer Registry data.	51,844 (80.9%) patients had a PET-CT performed: 25,735 (40.1%) in the 12 months before diagnosis and 41,242 (64.3%) in the 5 years after diagnosis. Increased PET-CT use (597 of 978 veterans [59.2%] in 2000 vs 3649 of 3915 [93.2%] in 2013) and decreased NSCLC-specific 5-year mortality (879 of 978 veterans [89.9%] in 2000 vs 3226 of 3915 veterans [82.4%] in 2013)were found over time. Increased use of stage-appropriate therapy was also seen over time, from 346 of 978 veterans (35.4%) in 2000 to 2062 of 3915 (52.7%) in 2013 (P < .001). Use of PET-CT before diagnosis was associated with increased likelihood of stage-appropriate treatment for all stages of NSCLC and decreased mortality in a risk adjusted model among all participants and among veterans undergoing stage-appropriate treatment.	The observational design of the study carries with it the inherent limitation of not being able to determine causality. Additionally, the authors note that the nature of the veteran population (overwhelmingly white men) limits the generalizability of their data. Further studies are warranted in other populations to determine if these findings are more broadly applicable.