| **Author, year, title** | **Population** | **Risk group** | **Screening comparison(In vs. Co)** | **Imaging evaluation strategy** | **Suspicious abnormality finding evaluation strategy** |
| --- | --- | --- | --- | --- | --- |
| **National Lung Screening Trial (NLST)** |
| National Lung Screening Trial Research Team et al, 201154*Reduced lung-cancer mortality with low-dose computed tomographic screening* | Ages 55 to 74 years | Current or former (quit ≤15 years ago) smoker with ≥30 pack-year smoking history | CT vs. CXR:CT: Low-dose (1.5 mSv), multidetector, ≥4 channelsCXR: 1 view, PA with deep inspiration | Certified radiologists and technicians by appropriate boardsRadiologists trained in image quality and standardized image acquisitionNCN ≥4 mm were classified positive, suspicious for lung cancerAdenopathy, effusion could be positive, suspiciousOther abnormal findings suggesting clinically important, nonlung cancer diagnosis reportedStability on year 2 scan could be classified as minor rather than positive | Results and recommendations from radiologist to subject's community provider |
| **Lung Screening Study (LSS)** |
| Gohagan et al, 200455*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*  | Ages 55 to 74 years | Former or current smokers ≥30 pack-years who quit <10 years prior | LDCT vs. single PA CXR examination | Encouraged via study to be evaluated Diagnostic evaluation assessed by record review | Positive = any nodule ≥4 mm (although varied with time) |
| Gohagan et al, 200574*Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest x-ray screening for lung cancer* | Ages 55 to 74 years | Former or current smokers ≥30 pack-years who quit <10 years prior | LDCT vs. single PA CXR examination | Encouraged via study to be evaluated Diagnostic evaluation assessed by record review | Positive = any nodule ≥4 mm (although varied with time) |
| Pinsky et al, 200575*Diagnostic procedures after a positive spiral computed tomography lung carcinoma screen* | Ages 55 to 74 years | Former or current smokers ≥30 pack-years who quit <10 years prior | LDCT vs. single PA CXR examination | Encouraged via study to be evaluated Diagnostic evaluation assessed by record review | Positive = any nodule ≥4 mm (although varied with time) |
| Croswell et al, 201073*Cumulative incidence of false-positive test results in lung cancer screening*  | Ages 55 to 74 years | Former or current smokers ≥30 pack-years who quit <10 years prior | LDCT vs. single PA CXR examination | Encouraged via study to be evaluated Diagnostic evaluation assessed by record review | Positive = any nodule ≥4 mm (although varied with time) |
| **Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays (DANTE)** |
| Infante et al, 200951*A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial* | Screening vs. noneMean age: 64.3 vs. 64.6 yearsCurrent smoker: 56% vs. 57%Mean pack-years: 47.3 vs. 47.2Prior cancer (considered cured): 1.0% vs. 0.6%Respiratory comorbidity: 35% vs. 31% (p=0.04) | Asymptomatic male current or former smokers with ≥20 pack-years Ages 60 to 74 years | CT vs. annual clinical review | Per study protocol:Case-by-case basis for nonsmooth ≥6 but ≤10 mm lesion that has not regressed after antibiotics on repeat imaging.PET positive nonsmooth ≥10 but ≤20 mm lesion that has not regressed with antibioticsPET positive nonsmooth lesion ≥20 mmCase-by-case for focal ground glass opacities that have not responded to antibiotics or regressed on repeat imaging  | Pursued within the study via established diagnostic protocol |
| **Danish Lung Cancer Screening Study (DLCST)** |
| Pedersen et al, 200976*The Danish Randomized Lung Cancer CT Screening Trial—overall design and results of the prevalence round* | CT vs. controlMean age: 57.9 vs. 57.8Mean pack-years: 36.4 vs. 35.9Current/former smokers: 1545/507 vs. 1579/473 | Healthy volunteer men and women ages 50 to 70 years Current and former smokers (<10 years and >4 weeks since smoking cessation) with ≥20 pack-years smoking history | LDCT vs. usual care | Imaging assessed and followup imaging within study | Screen-detected findings, single center affiliated with study Control group outside study, but mostly with same specialists |
| Saghir et al, 201252*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* | CT vs. controlMean age: 57.9 vs. 57.8Mean pack-years: 36.4 vs. 35.9Current/former smokers: 1545/507 vs. 1579/473 | Healthy volunteer men and women ages 50 to 70 years Current and former smokers (<10 years and >4 weeks since smoking cessation) with ≥20 pack-years smoking history | LDCT vs. usual care | All CT scans reviewed by 2 study radiologists, within study protocol | Referred to chest physicians for diagnostic evaluation at 2 lung cancer centers when HRCT, PET-CT, bronchoscopy, and/or biopsy performed In control group, lung cancer diagnosed and treated by the usual clinical practice, which mostly involved the same centers/strategies |
| Ashraf et al, 200862*Smoking habits are unaffected by CT screening at 1-year follow-up in the Danish Lung Cancer Screening Trial*  | CT vs. controlMean age: 57.9 vs. 57.8Mean pack-years: 36.4 vs. 35.9Current/former smokers: 1545/507 vs. 1579/473 | Healthy volunteer men and women ages 50 to 70 years Current and former smokers (<10 years and >4 weeks since smoking cessation) with ≥20 pack-years smoking history | LDCT vs. usual care | Imaging assessed and followup imaging within study | Screen-detected findings, single center affiliated with studyControl group outside study, but mostly with same specialists |
| **ITALUNG** |
| Lopes Pegna et al, 200957*Design, recruitment and baseline results of the ITALUNG trial for lung cancer screening with low-dose CT* | Mean age: 64 years (range: 55 to 69) | ≥20 pack-years since the last 10 years (former smokers who quit >10 years ago excluded) | CT vs. usual care | 5 SCT scanners (1 single row, 4 multirow detectors)Subsequent management per ELCAP study3 radiologists read first reading, 15 read second | Negative study = no focal findings, <5 mm solid NCN, or <10 mm nonsolid nodule |
| Mascalchi et al, 201182*Dose exposure in the ITALUNG trial of lung cancer screening with low-dose CT* | Mean age: 64 years (range: 55 to 69) | ≥20 pack-years since the last 10 years (former smokers who quit >10 years ago excluded) | CT vs. usual care | 8 SCT scanners Subsequent management per ELCAP study3 radiologists read first reading, 15 read second | Negative study = no focal findings, <5 mm solid NCN, or <10 mm nonsolid nodule |
| Mascalchi et al, 200681*Risk–benefit analysis of x-ray exposure associated with lung cancer screening in the ITALUNG-CT trial* | Mean age: 64 years (range: 55 to 69) | ≥20 pack-years since the last 10 years (former smokers who quit >10 years ago excluded) | CT vs. usual care | Followed in study per ELCAP criteria | Negative study = no focal findings, <5 mm solid NCN, or <10 mm non-solid nodule |
| **Multi-centric Italian Lung Detection (MILD)** |
| Pastorino et al, 201253*Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial* | Age ≥49 years63% to 68% male10% former smokersMean pack-years: 38 to 39 | Smokers with a smoking history >20 pack-years or quit <10 years ago | LDCT (annual vs. biennial) vs. usual care | Volumetrics used:<60 mm3 (4.8 mm) continue 1–2 year schedule60–250 mm3 (5 to 8 mm) repeat in 3 months, if <25% increase in volume, resume 1 or 2 year schedule>250 mm3 (>8 mm) referred for evaluation, generally with PET | Volumetric followup of intermediate nodulesPET scan for nodules >250 mm3No further description |
| **Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON)** |
| van Iersel et al, 200679*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)*Xu et al, 200664*Nodule management protocol of the NELSON randomised lung cancer screening trial*van den Bergh et al, 200978*Informed participation in a randomised controlled trial* *of computed tomography screening for lung cancer*van Klaveren et al, 200956*Management of lung nodules detected by volume CT scanning* | Median age: 59 years (SD 6)16% female | Asymptomatic current or former smokers with 15 cigarettes/day for >25 years or >10 cigarettes/day for >30 years smoking history, and if former smoker, quit ≤10 years ago Could have prior lung cancer if >5 years prior and not being treated | CT vs. no screening  | Imaging assessment and followup dictated by the study using volumetric indices | Positive test: solid nodule, >500 mm3 were referred to pulmonologistPositive test: solid, between 50 to 500 mm3; solid, pleural-based between 5 to 10 mm in diameter, partially solid with nonsolid component >7 mm; partially solid with solid component between 50 to 500 mm3; or nonsolid, >7 mm diameter: referred for repeat CT scan in 3 to 4 months |
| van den Bergh et al, 201077 *Short-term health-related quality of life consequences in a lung cancer CT screening trial (NELSON)* | Median age: 59 years (SD 6)16% female | Asymptomatic current or former smokers with 15 cigarettes/day for >25 years or >10 cigarettes/day for >30 years smoking history, and if former smoker, quit ≤10 years ago Could have prior lung cancer if >5 years prior and not being treated | CT vs. no screening  | Imaging assessment and followup dictated by the study using volumetric indices | Positive test: solid nodule, >500 mm3 were referred to pulmonologist Positive test: solid, between 50 to 500 mm3; solid, pleural-based between 5 to 10 mm in diameter, partially solid with nonsolid component >7 mm; partially solid with solid component between 50 to 500 mm3; or nonsolid, >7 mm diameter: referred for repeat CT scan in 3 to 4 months |
| van den Bergh et al, 201169*Long-term effects of lung cancer computed tomography screening on health-related quality of life: the NELSON trial* | Median age: 59 years (SD 6)16% female | Asymptomatic current or former smokers with 15 cigarettes/day for >25 years or >10 cigarettes/day for >30 years smoking history, and if former smoker, quit ≤10 years ago Could have prior lung cancer if >5 years prior and not being treated | CT vs. no screening  | Imaging assessment and followup dictated by the study using volumetric indices | Positive test: solid nodule, >500 mm3 were referred to pulmonologist Positive test: solid, between 50 to 500 mm3; solid, pleural-based between 5 to 10 mm in diameter, partially solid with nonsolid component >7 mm; partially solid with solid component between 50 to 500 mm3; or nonsolid, >7 mm diameter: referred for repeat CT scan in 3 to 4 months |
| **Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial**  |
| Croswell et al, 200973*Cumulative incidence of false-positive results in repeated, multimodal cancer screening* | CXR vs. usual care Men: 50% vs. 50%White: 86% vs. 85%Current smokers: 10% vs. 10%Former smokers: 42% vs. 42%Never smokers: 45% vs. 44%NLST eligible: 20% vs. 21%Family history: 11% vs. 11% | Those with ≥30 pack-year smoking history; current smokers or quit <15 years ago | CXR vs. usual care | Advised to seek diagnostic evaluation which was decided outside of study; study obtained their records Participants/ health care providers notified of results and evaluation determined by patient with provider | Positive result = nodule, mass, infiltrate, or other abnormality suspicious for lung cancer |
| Hocking et al, 201084*Lung cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial* | CXR vs. usual care Men: 50% vs. 50%White: 86% vs. 85%Current smokers: 10% vs. 10%Former smokers: 42% vs. 42%Never smokers: 45% vs. 44%NLST eligible: 20% vs. 21%Family history: 11% vs. 11% | Those with ≥30 pack-year smoking history; current smokers or quit <15 years ago | CXR vs. usual care | Advised to seek diagnostic evaluation which was decided outside of study; study obtained their records Participants/ health care providers notified of results and evaluation determined by patient with provider | Positive result = nodule, mass, infiltrate, or other abnormality suspicious for lung cancer |

| **Author, year, title** | **Inclusion criteria** | **Exclusion criteria** | **Number of subjects** | **Country and setting** | **Sponsor** |
| --- | --- | --- | --- | --- | --- |
| **National Lung Screening Trial (NLST)** |
| National Lung Screening Trial Research Team et al, 201154*Reduced lung-cancer mortality with low-dose computed tomographic screening* | Asymptomatic men and women ages 55 to 74 years with ≥30 pack-year smoking history and if former smoker quit ≤15 years ago  | Hemoptysis or unexplained >15 lb weight loss in preceding year, chest CT within 18 months | Number approached: NRNumber eligible: NRNumber enrolled: 53,454 (26,722 vs. 26,732) | United StatesMulticenter(10 LSS centers and23 ACRIN centers) | NCI |
| **Lung Screening Study (LSS)** |
| Gohagan et al, 200455*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*  | Men and women ages 55 to 74 years with ≥30 pack-year smoking history and quit during <10 years | Prior lung cancer, prior lung surgery, prior chest CT ≤2 years, current treatment for any cancer (other than nonmelanoma skin cancer), participation in another lung cancer screening trial | Number approached: 653,417Number eligible: 4828Number enrolled: 3318 (1660 vs. 1658) | 6 centers in United States | NCI |
| Gohagan et al, 200574*Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest x-ray screening for lung cancer* | Men and women ages 55 to 74 years with ≥30 pack-year smoking history and quit during <10 years | Prior lung cancer, prior lung surgery, prior chest CT ≤2 years, current treatment for any cancer (other than nonmelanoma skin cancer), participation in another lung cancer screening trial | Number approached: 653,417Number eligible: 4828Number enrolled: 3318 (1660 vs. 1658)Number at 1 year: 2715 (1398 vs. 1317) | 6 centers in United States | NCI |
| Pinsky et al, 200575*Diagnostic procedures after a positive spiral computed tomography lung carcinoma screen* | Men and women ages 55 to 74 years with ≥30 pack-year smoking history and quit during <10 years | Prior lung cancer, prior lung surgery, prior chest CT ≤2 years, current treatment for any cancer (other than nonmelanoma skin cancer), participation in another lung cancer screening trial | Number approached: 653,417Number eligible: 4828Number enrolled: 3318 (1660 vs. 1658)Number at 1 year: 2715 (1398 vs. 1317) | 6 centers in United States | NCI |
| Croswell et al, 201073*Cumulative incidence of false-positive test results in lung cancer screening*  | Men and women ages 55 to 74 years with ≥30 pack-year smoking history and quit during <10 years | Prior lung cancer, prior lung surgery, prior chest CT ≤2 years, current treatment for any cancer (other than nonmelanoma skin cancer), participation in another lung cancer screening trial | Number approached: 653,417Number eligible: 4828Number enrolled: 3318 (1660 vs. 1658)Number analyzed: 3190 (1610 vs. 1580) | 6 centers in United States | NCI |
| **Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays (DANTE)** |
| Infante et al, 200951*A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial* | Male current or former smokers with a history of ≥20 pack-years and ages 60 to 74 years  | Comorbid conditions carrying a life expectancy of <5 years, a history of previous malignancy treated within 10 years before accrual (exceptions allowed for early laryngeal cancer and nonmelanoma skin cancer if 5-year disease free interval met), or if unable to comply with the followup protocol for any reason | Number approached: 2811 (1403 vs. 1408)Number enrolled: 2472 patients (1276 vs. 196) | Italy, 3 hospitals from same hospital network | Italian Association for the Fight Against Cancer (donations from benefactors and charities directed at financing the study) |
| **Danish Lung Cancer Screening Study (DLCST)** |
| Pedersen et al, 200976*The Danish Randomized Lung Cancer CT Screening Trial—overall design and results of the prevalence round* | Current or former smokers with history of ≥20 pack-years, ages 50 to 70 years Former smokers who quit smoking after age 50 years and <10 years ago, able to climb 2 flights of stairs without pausing, PFT baseline forced expiratory volume-1 was ≥30% of predicted normal  | Body weight >130 kg; previous treatment for lung cancer, breast cancer, malignant melanoma, or hypernephroma; history of any other cancer within previous 5 years; tuberculosis within 2 years; any other serious illness that would shorten life expectancy to <10 years | Number approached: 5861Number eligible: NRNumber enrolled: 4104 (2052 vs. 2052) | Denmark, single siteUniversity Hospital, enrolled from October 2004 to March 2006 | Danish Ministry of Interior and Health |
| Saghir et al, 201252*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* | Current or former smokers with history of ≥20 pack-years, ages 50 to 70 years Former smokers who quit smoking after age 50 years and <10 years ago, able to climb 2 flights of stairs without pausing, PFT baseline forced expiratory volume-1 was ≥30% of predicted normal | Body weight >130 kg; previous treatment for lung cancer, breast cancer, malignant melanoma, or hypernephroma; history of any other cancer within previous 5 years; tuberculosis within 2 years; any other serious illness that would shorten life expectancy to <10 years | Number approached: 5861Number eligible: NRNumber enrolled: 4104 (2052 vs. 2052) | Denmark, single siteUniversity Hospital, enrolled from October 2004 to March 2006 | Danish Ministry of Interior and Health |
| Ashraf et al, 200862*Smoking habits are unaffected by CT screening at 1-year follow-up in the Danish Lung Cancer Screening Trial*  | Current or former smokers with history of ≥20 pack-years, ages 50 to 70 years Former smokers who quit smoking after age 50 years and <10 years ago, able to climb 2 flights of stairs without pausing, PFT baseline forced expiratory volume-1 was ≥30% of predicted normal | Body weight >130 kg; previous treatment for lung cancer, breast cancer, malignant melanoma, or hypernephroma; history of any other cancer within previous 5 years; tuberculosis within 2 years; any other serious illness that would shorten life expectancy to <10 years | Number approached: 5861Number eligible: NRNumber enrolled: 4104 (2052 vs. 2052) | Denmark, single siteUniversity Hospital, enrolled from October 2004 to March 2006 | Government grant |
| **ITALUNG** |
| Lopes Pegna et al, 200957*Design, recruitment and baseline results of the ITALUNG trial for lung cancer screening with low-dose CT* | ≥20 pack-years since the last 10 years | History of cancer and inability to tolerate lung cancer resection surgery, former smokers who quit >10 years ago | Number approached: 71,232Number eligible: NRNumber enrolled: 1613 (1406 vs. 1593) | Italy, general population | Regional Health Public Authority |
| Mascalchi et al, 201182*Dose exposure in the ITALUNG trial of lung cancer screening with low-dose CT* | ≥20 pack-years since the last 10 years | History of cancer and inability to tolerate lung cancer resection surgery, former smokers who quit >10 years ago | Number approached: 71,232Number eligible: NRNumber enrolled: 1613 (1406 vs. 1593) | Italy, general population | Regional Health Public Authority |
| Mascalchi et al, 200681*Risk–benefit analysis of x-ray exposure associated with lung cancer screening in the ITALUNG-CT trial* | ≥20 pack-years since the last 10 years | History of cancer and inability to tolerate lung cancer resection surgery, former smokers who quit >10 years ago | Number approached: NRNumber eligible: NR Number analyzed: 60 (210 CT scans) | Italy, general population | Health Department of the Region of Tuscany, Italian League Against Tumors, and the Ministry of Education, Universities, and Research |
| **Multi-centric Italian Lung Detection (MILD)** |
| Pastorino et al, 201253*Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial* | Smokers ages ≥49 years with ≥20 pack-year smoking history or if former smoker quit <10 years ago  | History of cancer in past 5 years | Number approached: NRNumber eligible: NRNumber enrolled: 4099 (1190 vs. 1186 vs. 1723) | Single institution, Milan | Foundations and Ministry of Health |
| **Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON)** |
| van Iersel et al, 200679*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)*Xu et al, 200664*Nodule management protocol of the NELSON randomised lung cancer screening trial*van den Bergh et al, 200978*Informed participation in a randomised controlled trial of computed tomography screening for lung cancer*van Klaveren et al, 200956*Management of lung nodules detected by volume CT scanning* | Men born between 1928 and 1956 who smoked >15 cigarettes/day during >25 years or smoked >10 cigarettes/day during >30 years, current or former smokers who quit smoking ≤10 years ago | Moderate or bad self-reported health who were unable to climb 2 flights of stairs; body weight ≥140 kg; current or past renal cancer, melanoma, or breast cancer; lung cancer diagnosed <5 years ago or ≥5 years ago but still under treatment; chest CT examination <1 year before starting study | Number approached: 548,489Number eligible: NRNumber enrolled: 15,822 (7907 vs. 7915) | Belgium, the Netherlands, Denmark | Netherlands Organisation of Health Research and Development, Dutch Cancer Society, Health Insurance Innovation Foundation, Siemens Germany, Roche Diagnostics, G. Ph. Verhagen Stichting, Rotterdam Oncologic Thoracic Study Group, Erasmus Trust Fund, Stichting tegen Kanker, Vlaamse Liga tegen Kanker, and LOGO Leuven |
| van den Bergh et al, 201077 *Short-term health-related quality of life consequences in a lung cancer CT screening trial (NELSON)* | Men born between 1928 and 1956 who smoked >15 cigarettes/day during >25 years or smoked >10 cigarettes/day during >30 years, current or former smokers who quit smoking ≤10 years ago Consecutive sample of 733 patients in CT group sent surveys on health related quality of life | Moderate or bad self-reported health who were unable to climb 2 flights of stairs; body weight ≥140 kg; current or past renal cancer, melanoma, or breast cancer; lung cancer diagnosed <5 years ago or ≥5 years ago but still under treatment; chest CT examination <1 year before starting study | Number approached:692 sent 1st survey, 685 sent 2nd survey, 667 sent 3rd survey, 684 sent 4th surveyNumber eligible: NRNumber analyzed: 630 returned 1st survey, 641 returned 2nd survey, 620 returned 3rd survey, 600 returned 4th survey | The Netherlands/ Belgium | Netherlands Organisation of Health Research and Development, Dutch Cancer Society, Health Insurance Innovation Foundation, Siemens Germany, Roche Diagnostics, G. Ph. Verhagen Stichting, Rotterdam Oncologic Thoracic Study Group, Erasmus Trust Fund, Stichting tegen Kanker, Vlaamse Liga tegen Kanker, and LOGO Leuven |
| van den Bergh et al, 201169*Long-term effects of lung cancer computed tomography screening on health-related quality of life: the NELSON trial* | Men born between 1928 and 1956 who smoked >15 cigarettes/day during >25 years or smoked >10 cigarettes/day during >30 years, current or former smokers who quit smoking ≤10 years ago Consecutive sample of 733 patients in CT group sent surveys on health related quality of life | Moderate or bad self-reported health who were unable to climb 2 flights of stairs; body weight ≥140 kg; current or past renal cancer, melanoma, or breast cancer; lung cancer diagnosed <5 years ago or ≥5 years ago but still under treatment; chest CT examination <1 year before starting study | Number approached: 1466 sent 1st survey, 684 sent 2nd survey, 1180 sent 3rd survey, 684 sent 4th surveyNumber eligible: NRNumber analyzed:1288 returned 1st survey (90% vs. 86%), 600 returned 2nd survey, 931 returned 3rd survey (89% vs. 65%),600 returned 4th survey | The Netherlands/ Belgium | Netherlands Organisation of Health Research and Development, Dutch Cancer Society, Health Insurance Innovation Foundation, Siemens Germany, Roche Diagnostics, G. Ph. Verhagen Stichting, Rotterdam Oncologic Thoracic Study Group, Erasmus Trust Fund, Stichting tegen Kanker, Vlaamse Liga tegen Kanker, and LOGO Leuven |
| **Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial**  |
| Croswell et al, 200973*Cumulative incidence of false-positive results in repeated, multimodal cancer screening* | Men and women ages 55 to 74 years, eligible for NLST | History of a PLCO cancer, prior pneumonectomy, current cancer treatment | Number approached: NRNumber eligible: NRNumber enrolled: 154,901 (77,445 vs. 77,456)Number with false-positives in intervention: 11,851 (6320 men and 5531 women) | 10 centers | NCI |
| Hocking et al, 201084*Lung cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial* | Men and women ages 55 to 74 years, eligible for NLST | History of a PLCO cancer, prior pneumonectomy, current cancer treatment | Number approached: NRNumber eligible: NRNumber enrolled: 154,901 (77,445 vs. 77,456)Number with false-positives in intervention: 11,851 (6320 men and 5531 women) | 10 centers | NCI |

| **Author, year, title** | **Results** | **Sensitivity** |
| --- | --- | --- |
| **Intervention** | **Control** |
| **National Lung Screening Trial (NLST)** |
| National Lung Screening Trial Research Team et al, 201154*Reduced lung-cancer mortality with low-dose computed tomographic screening* | Lung cancer mortality: 356 (247/100,000 py); RR, 20% (95% CI, 6.8 to 27%)Overall mortality: 1877; RR, 6.7% (95% CI, 1.2 to 14%)Adherence to screening: 95% Positive screen (T0, T1, T2, total patients): 27%, 28%, 17%, 39%Incidence: 1060 (645/100,000 py) | Lung cancer mortality: 443 (309/100,000 py)Overall mortality: 1998Adherence to screening: 93% Positive screen (T0, T1, T2, total patients): 9.2%, 6.2%, 5.0%, 16%Incidence: 941 (572/100,000 py) | NR |
| **Lung Screening Study (LSS)** |
| Gohagan et al, 200455*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*  | Positive: 325/1586Any procedure: 309Clinical evaluation: 244Comparison with prior: 155Chest CT: 232CXR: 92PFT: 73Any invasive procedure: 53Lung cancer: 30Lung cancer incidence: 1.9%Stage I: 16 (53%)Stage IV: 3 (10%)Adenocarcinoma: 19 (63%) | Positive: 152/1550Any procedure: 140Clinical evaluation: 71Comparison with prior: 71Chest CT: 76CXR: 68PFT: 20Any invasive procedure: 15Lung cancer: 7Lung cancer incidence: 0.5%Stage I: 6 (86%)Stage IV: 0Adenocarcinoma: 3 (43%) | Baseline: PPV CXR or CT: 9.2%CT: 30 lung cancers and 325 positive exams CXR: 7 lung cancers and 152 positive examsSensitivity: NR at baseline |
| Gohagan et al, 200574*Final results of the Lung Screening Study, a randomized feasibility study of spiral CT versus chest x-ray screening for lung cancer* | Year 1 results:Positive: 360Followup status known: 351Any procedure: 332Comparison with prior imaging: 231CXR: 64Chest CT: 140PFT: 70Bronchoscopy: 14Biopsy/resection: 18Lung cancer: 8 (0.6%)Cumulative results:Positive: 35%Screen-detected lung cancer: 38/40 (2 interval cancer)Stage I: 48% | Year 1 results:Positive: 115Followup status known: 111Any procedure: 101Comparison with prior imaging: 57CXR: 45Chest CT: 55PFT: 14Bronchoscopy: 8Biopsy/resection: 10Lung cancer: 9 (0.7%)Cumulative results:Positive: 16%Screen-detected lung cancer: 16/20 (4 interval cancer)Stage I: 40% | NR |
| Pinsky et al, 200575*Diagnostic procedures after a positive spiral computed tomography lung carcinoma screen* | After 1st positive screen (n=522)Highest level procedure Biopsy/resection: 63 (12%)Invasive procedure without resection: 5 (1%)Chest CT: 287 (55%)Other (PET/MRI): 10 (2%)PFT/sputum cytology: 31 (6%)CXR: 26 (5%)Comparison with other imaging: 63 (12%)Clinical exam: 21 (4%)No evaluation: 16 (3%)FindingsLung cancer: 37 Other lung diseases: 114COPD/emphysema: 59Pulmonary fibrosis: 31Renal cancer: 1 | NR | NR |
| Croswell et al, 201073*Cumulative incidence of false-positive test results in lung cancer screening*  | Received ≥1 false-positive: 506 (31%)Baseline risk false-positive: 21%1st incident screen false-positive: 33% | Received ≥1 false-positive: 216 (14%)Baseline risk false-positive: 9%1st incident screen false-positive: 15%Baseline false-negative: 4 | NR |
| **Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays (DANTE)** |
| Infante et al, 200951*A randomized study of lung cancer screening with spiral computed tomography: three-year results from the DANTE trial* | All-cause mortality: 46 (3.6%)Lung cancer mortality: 20 (1.6%)Other mortality causes: 26 (2.0%)Patients with lung cancers: 60 (4.7%)Total number of lung cancers: 63 (4.9%)Stage IA: 20 (1.6%)All stage I: 33 (2.6%)Stage II: 4 (0.3%)Stage IIIA: 7 (0.6%)Stage IIIB: 6 (0.5%)Stage IV: 11 (0.9%)Any abnormality on CT or CXR: 351 (28%)Additional CT: 199 (16%)Diagnostic PET: 57 (4.5%)Any investigation: 226 (18%)Any invasive procedure: 96 (7.5%)Histology: 6 (0.5%)Small cell: 57 (4.4%) | All-cause mortality: 45 (3.8%) p=0.83Lung cancer mortality: 20 (1.7%) p=0.84Other mortality causes: 25 (2.1%) p=0.93Patients with lung cancers: 34 (2.8%) p=0.02Total number of lung cancers: 36 (3.0%)Stage IA: 4 (0.3%)All stage I: 12 (1.0%) p=0.004Stage II: 2 (0.2%)Stage IIIA: 4 (0.3%)Stage IIIB: 3 (0.3%)Stage IV: 14 (1.2%)Any abnormality on CT or CXR: 22 (1.8%)Additional CT: 4 (0.3%)Diagnostic PET: 153 (13%) p=0.001Any investigation: 36 (3.0%) p<0.0001Any invasive procedure: 2 (0.2%)Histology: 34 (2.8%)Small cell: NR | NR |
| **Danish Lung Cancer Screening Study (DLCST)** |
| Pedersen et al, 200976*The Danish Randomized Lung Cancer CT Screening Trial—overall design and results of the prevalence round* | Prevalence round LDCT | NR | NR in study189/2052 (9.2%) with study requiring followup17 cases of lung cancer detected7.9% false-positive  |
| Saghir et al, 201252*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* | Overall69 lung cancers3 small cell66 NSCLC44 stage I or II21 stage III or IV53 pathologically identified within 1 year of CT first seen on1 interval cancerDeaths: 61 (3.0%)Lung cancer death: 15 (0.7%)All 5 rounds1029 nodules560 baseline469 incidence611 individuals with nodules/5 years198 (of 9800 scans) referred for diagnostic evaluation7 VATS benignBaseline false-positive rate: 7.9%Annual false-positive rate range: 1.6% to 2.0% | 24 lung cancers6 extensive SCLC17 NSCLC8 stage I or II16 stage III or IVDeaths: 42 (2.1%); p=0.059Lung cancer death: 11 (0.5%); p=0.42 | NR1 interval cancer diagnosed after 3rd incidence screen |
| Ashraf et al, 200862*Smoking habits are unaffected by CT screening at 1-year follow-up in the Danish Lung Cancer Screening Trial*  | Quit rate: 174/1545Relapse rate: 85/507 | Quit rate: 165/1579 Relapse rate: 98/473 | NR |
| **ITALUNG** |
| Lopes Pegna et al, 200957*Design, recruitment and baseline results of the ITALUNG trial for lung cancer screening with low-dose CT* | 639 nodules in 426 subjects366 followup CT, 4/5 with increased nodule size had PET59 had PET, bronchus in 1816 FNA biopsy in 15 subjects12 FNA biopsy positive for lung cancer, 2 indeterminate (later lung cancer), 1 benign20 with lung cancer, 1 with 2 primaryNSCLC: 86%; 10 stage I, 8 stage IA17 cancer in 16 subjects surgically resected; 1 resection for a benign lesion16 had cancer after baseline screen5 had cancer after 1 year followup | NR | NR |
| Mascalchi et al, 201182*Dose exposure in the ITALUNG trial of lung cancer screening with low-dose CT* | 1406 baseline CT3924 annual screen CT990 followup CT for 6320 total879 of 6320 scans on single-detector95 PETs for 90 patients 59 suspicious nodules at baseline, 36 during annual screen38 CT-guided biopsies in 34 patientsMean collective effective dose: 8.75 Sv to 9.36 SvMean effective dose per patient over 4 years: 6.2 mSv to 6.8 mSvMean number of radiation-induced cancers: 0.12 to 0.33 per 1000 patients (0.12 to 0.13 per 1000 men; 0.31 to 0.33 per 1000 women) | NR | NR |
| Mascalchi et al, 200681*Risk–benefit analysis of x-ray exposure associated with lung cancer screening in the ITALUNG-CT trial* | Actual radiation dose:Multidetector CT: 0.49 mSv/yearSingle-slice CT: 1.9 mSv/yearProjected radiation dose in full ITALUNG (assumed 10% of subjects would have indeterminate nodules):Multidetector CT: 0.83 mSv/yearSingle-slice CT: 1.78 mSv/yearLung cancer risk from radiation:Multidetector CT: 11.7/100,000Single-slice CT: 24.9/100,000 | NR | NA |
| **Multi-centric Italian Lung Detection (MILD)** |
| Pastorino et al, 201253*Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial* | Positive baseline CT: 177 vs. 158Recall rates: 14% vs. 15%Lung cancer incidence: 34 (662/100,000 py) vs. 25 (457/100,000 py)Stage IA lung cancer: 59% vs. 55%Stage IV lung cancer: 17% vs. 15% | Lung cancer incidence: 20 (216/100,000 py)Stage IA lung cancer: NRStage IV lung cancer: NR | NR |
| **Nederlands-Leuvens Longkanker Screenings Onderzoek (NELSON)** |
| van Iersel et al, 200679*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)*Xu et al, 200664*Nodule management protocol of the NELSON randomised lung cancer screening trial*van den Bergh et al, 200978*Informed participation in a randomised controlled trial of computed tomography screening for lung cancer*van Klaveren et al, 200956*Management of lung nodules detected by volume CT scanning* | Overall127 (1.6%) diagnosed with lung cancer3 with interval diagnosis between round 1 and 2 Round 1Negative scan: 5987 (79%)Indeterminate scan: 1451 (19%)Positive scan: 119 (1.6%)Total positive after followup imaging: 196 (2.6%)70 (35%) with diagnosis of lung cancer Round 2Negative scan: 6719 (92%)Indeterminate scan: 480 (6.6%)Positive scan: 90 (1.2%)Total positive after followup imaging: 128 (1.8%)54 (42%) with diagnosis of lung cancer Combining both roundsPositive scan: 209 (2.7 %) | NR | For diagnosis of lung cancer Round 1: 95% (95% CI, 87 to 98)Round 2: 96% (95% CI, 87 to 99) |
| van den Bergh et al, 201077 *Short-term health-related quality of life consequences in a lung cancer CT screening trial (NELSON)* | Mean scores (total, negative result, indeterminate)HRQOL: SF-12 T0 vs. T3SF-12 PCS: 49.5 vs. 50.0Neg: 49.7 vs. 50.3Ind: 48.5 vs. 48.9SF-12 MCS: 51.9 vs. 51.6Neg: 51.9 vs. 51.6Ind: 51.8 vs. 51.9 EuroQOL (EQ)-5D T0 vs. T1 vs. T2 vs. T3EQ-5D: 79.3 vs. 78.3 vs. 79.1 vs. 78.4Neg: 79.4 vs. 78.7 vs. 79.4 vs. 79.2Ind: 79.1 vs. 76.8 vs. 78.3 vs. 75.0STAI-6STAI-6: 33.2 vs. 34.6 vs. 32.7 vs. 33.0Neg: 33.1 vs. 34.4 vs. 32.5 vs. 32.6Ind: 33.6 vs. 35.2 vs. 33.5 vs. 34.8 IESIES-D: 4.2 vs. 5.9 vs. 4.5 vs. 3.6Neg: 4.1 vs. 5.8 vs. 4.5 vs. 2.4 Ind: 4.5 vs. 6.3 vs. 4.9 vs. 8.3 | NR | NR |
| van den Bergh et al, 201169*Long-term effects of lung cancer computed tomography screening on health-related quality of life: the NELSON trial* | At T0 and T2 no significant differences in HRQOL scores over time between groups or between the indeterminate or negative 2nd-round screening. There was a temporary increase in IES scores after an indeterminate baseline result:T0: mean 4.0 (95% CI, 2.8 to 5.3)T1: mean 7.8 (95% CI, 6.5 to 9.0)T2: mean 4.5 (95% CI, 3.3 to 5.8) At 2-year followup, the HRQOL of screened subjects was similar to that of control subjects, the unfavorable short-term effects of an indeterminate baseline screening result had resolved, and an indeterminate result at the 2nd screening round had no impact on HRQOL | NR | NR |
| **Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial**  |
| Croswell et al, 200973*Cumulative incidence of false-positive results in repeated, multimodal cancer screening* | Cumulative incidence-false positive (men vs. women)Underwent repeated screening: 3216 vs. 2907Underwent other imaging: 1466 vs. 1498Underwent minimally invasive procedure: 52 vs. 56Underwent moderately invasive procedure: 77 vs. 93Underwent major surgical procedure: 35 vs. 40Cumulative risk false-positive after 4 screens: 22% vs. 22% | NR | NR |
| Hocking et al, 201084*Lung cancer screening in the randomized Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial* | Positive scans: 7.5%Lung cancer diagnosis:306 (284 NSCLC)147 interval62 among nonscreenedPPV: 1.7% | NR | Calculated: 66% for NSCLC |
| National Lung Screening Trial Research Team et al, 201154*Reduced lung-cancer mortality with low-dose computed tomographic screening* | Positive CXRs: Baseline: 8.9%Round 1: 7.1%Round 2: 6.6%Round 3: 7.0%Cumulative lung cancer: 7.5%Lung cancer incidence: 20.1/10,000 pyScreening period # lung cancer: 505 (307 screen-detected) Interval: 198 (39%)Lung cancer never screened: 193 (during screening period)13 years followup: 1696 cancers (307 screen-detected)Lung cancers diagnosed after screening ended: 998 Stage I: 32%Stage III or IV: 373/1696 (22%)Cumulative death: 1213Cumulative incidence: 14/100,000 pyLung cancer mortality: RR, 0.99 (95% CI, 0.87 to 1.22)Lung cancer mortality women: RR, 0.92 (95% CI, 0.81 to 1.06)Lung cancer mortality men: RR, 1.02 (95% CI, 0.92 to 1.13)RR late-stage lung cancer after 6 years: 0.88 (95% CI, 0.78 to 0.99)RR late-stage lung cancer after 7 years: 0.94 (95% CI, 0.84 to 1.05)Other deaths: 12%Among the NLST eligible groupRR lung cancer: 1.0 (95% CI, 0.89 to 1.13)RR lung cancer death: 0.94 (95% CI, 0.81 to 1.10)Restricting analysis to lung cancer diagnosis within 6 years of screeningLung cancer mortality: RR, 0.89 (95% CI, 0.80 to 1.00)Lung cancer: 518Lung cancer deaths: 316Cumulative incidence lung cancer: 606/100,000 pyCumulative lung cancer mortality: 361/100,000 py | Lung cancer incidence: 19.2/10,000 pyStage I: 27%Stage III or IV: 895/1620 (55%)Cumulative death: 1230Cumulative lung cancer mortality: 14.2/100,000 pyOther deaths: 12%Lung cancer: 520Lung cancer deaths: 334Cumulative incidence lung cancer: 608/100,000 pyCumulative lung cancer mortality: 383/100,000 py | 307/505 during screening period |

Abbreviations: ACRIN = American College of Radiology Imaging Network; ARDS = acute respiratory distress syndrome; CI = confidence interval; Co = control group; COPD = chronic obstructive pulmonary disease; CT = computed tomography; 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; DVT = deep venous thrombosis; EBUS = endobronchial ultrasound; ELCAP = Early Lung Cancer Action Program; EUS = endoscopic ultrasound; FNA = fine needle aspiration; HRCT = high-resolution computed tomography; HRQOL = health-related quality of life; IES = Impact of Event Scale; In = intervention; LDCT = low-dose computed tomography; LSS = Lung Screening Study; MCS = Mental Health Composite Score; MILD = Multi-centric Italian Lung Detection; MRI = magnetic resonance imaging; NA = not applicable; NCI = National Cancer Institute; NCN = noncalcified nodule; NELSON = Nederlands-Leuvens Longkanker Screenings Onderzoek; NLST = National Lung Screening Trial; NSCLC = non-small cell lung cancer; NR = not reported; PA = posteranterior; PCS = Physical Health Composite Scores;

PET = positron emission tomography; PFT = pulmonary function testing; PLCO = Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; PPV = positive predictive value; py = person-years; RR = relative risk; SCLC = small-cell lung cancer; SCT = spiral computed tomography; SD = standard deviation; SF-12 = 12-item Health Survey; STAI = Spielberger State-Trait Anxiety Inventory; sV = short volume; VATS = video-assisted thoracic surgery