| **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 channels CXR: 1 view, PA with deep inspiration | Certified radiologists and technicians by appropriate boards Radiologists trained in image quality and standardized image acquisition NCN ≥4 mm were classified positive, suspicious for lung cancer Adenopathy, effusion could be positive, suspicious Other abnormal findings suggesting clinically important, nonlung cancer diagnosis reported Stability 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. none Mean age: 64.3 vs. 64.6 years Current smoker: 56% vs. 57% Mean pack-years: 47.3 vs. 47.2 Prior 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 antibiotics PET positive nonsmooth lesion ≥20 mm Case-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. control Mean age: 57.9 vs. 57.8 Mean pack-years: 36.4 vs. 35.9 Current/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. control Mean age: 57.9 vs. 57.8 Mean pack-years: 36.4 vs. 35.9 Current/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. control  Mean age: 57.9 vs. 57.8  Mean pack-years: 36.4 vs. 35.9  Current/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 |
| **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 study 3 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 study  3 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 years 63% to 68% male 10% former smokers Mean 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 schedule 60–250 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 nodules PET scan for nodules >250 mm3 No 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 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, 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: NR Number eligible: NR Number enrolled: 53,454 (26,722 vs. 26,732) | United States Multicenter (10 LSS centers and 23 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: 653,417 Number eligible: 4828 Number 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: 653,417 Number eligible: 4828 Number 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: 653,417  Number eligible: 4828  Number 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: 653,417 Number eligible: 4828 Number 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: 5861 Number eligible: NR Number enrolled: 4104 (2052 vs. 2052) | Denmark, single site University 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: 5861 Number eligible: NR Number enrolled: 4104 (2052 vs. 2052) | Denmark, single site University 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: 5861  Number eligible: NR  Number enrolled: 4104 (2052 vs. 2052) | Denmark, single site  University 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: 71,232 Number eligible: NR Number 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: 71,232  Number eligible: NR  Number 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: NR Number 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: NR Number eligible: NR Number 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: 548,489 Number eligible: NR Number 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 survey  Number eligible: NR  Number 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 survey  Number eligible: NR  Number 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: NR Number eligible: NR Number 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: NR Number eligible: NR Number 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: 1998 Adherence 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: 325/1586 Any procedure: 309 Clinical evaluation: 244 Comparison with prior: 155 Chest CT: 232 CXR: 92 PFT: 73 Any invasive procedure: 53 Lung cancer: 30 Lung cancer incidence: 1.9% Stage I: 16 (53%) Stage IV: 3 (10%) Adenocarcinoma: 19 (63%) | Positive: 152/1550 Any procedure: 140 Clinical evaluation: 71 Comparison with prior: 71 Chest CT: 76 CXR: 68 PFT: 20 Any invasive procedure: 15 Lung cancer: 7 Lung cancer incidence: 0.5% Stage I: 6 (86%) Stage IV: 0 Adenocarcinoma: 3 (43%) | Baseline:  PPV CXR or CT: 9.2% CT: 30 lung cancers and 325 positive exams  CXR: 7 lung cancers and 152 positive exams Sensitivity: 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: 360 Followup status known: 351 Any procedure: 332 Comparison with prior imaging: 231 CXR: 64 Chest CT: 140 PFT: 70 Bronchoscopy: 14 Biopsy/resection: 18 Lung cancer: 8 (0.6%) Cumulative results: Positive: 35% Screen-detected lung cancer: 38/40 (2 interval cancer) Stage I: 48% | Year 1 results: Positive: 115 Followup status known: 111 Any procedure: 101 Comparison with prior imaging: 57 CXR: 45 Chest CT: 55 PFT: 14 Bronchoscopy: 8 Biopsy/resection: 10 Lung 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%)  Findings  Lung cancer: 37  Other lung diseases: 114  COPD/emphysema: 59  Pulmonary fibrosis: 31  Renal 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=0.83 Lung cancer mortality: 20 (1.7%) p=0.84 Other mortality causes: 25 (2.1%) p=0.93 Patients with lung cancers: 34 (2.8%) p=0.02 Total number of lung cancers: 36 (3.0%) Stage IA: 4 (0.3%) All stage I: 12 (1.0%) p=0.004 Stage 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=0.001 Any investigation: 36 (3.0%) p<0.0001 Any 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 study 189/2052 (9.2%) with study requiring followup 17 cases of lung cancer detected 7.9% 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* | Overall 69 lung cancers 3 small cell 66 NSCLC 44 stage I or II 21 stage III or IV 53 pathologically identified within 1 year of CT first seen on 1 interval cancer Deaths: 61 (3.0%) Lung cancer death: 15 (0.7%) All 5 rounds 1029 nodules 560 baseline 469 incidence 611 individuals with nodules/5 years 198 (of 9800 scans) referred for diagnostic evaluation 7 VATS benign Baseline false-positive rate: 7.9% Annual false-positive rate range: 1.6% to 2.0% | 24 lung cancers 6 extensive SCLC 17 NSCLC 8 stage I or II 16 stage III or IV Deaths: 42 (2.1%); p=0.059 Lung cancer death: 11 (0.5%); p=0.42 | NR 1 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: 174/1545  Relapse 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 subjects 366 followup CT, 4/5 with increased nodule size had PET 59 had PET, bronchus in 18 16 FNA biopsy in 15 subjects 12 FNA biopsy positive for lung cancer, 2 indeterminate (later lung cancer), 1 benign 20 with lung cancer, 1 with 2 primary NSCLC: 86%; 10 stage I, 8 stage IA 17 cancer in 16 subjects surgically resected; 1 resection for a benign lesion 16 had cancer after baseline screen 5 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 CT  3924 annual screen CT  990 followup CT for 6320 total  879 of 6320 scans on single-detector  95 PETs for 90 patients  59 suspicious nodules at baseline, 36 during annual screen  38 CT-guided biopsies in 34 patients  Mean collective effective dose: 8.75 Sv to 9.36 Sv  Mean effective dose per patient over 4 years: 6.2 mSv to 6.8 mSv  Mean 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/year Single-slice CT: 1.9 mSv/year Projected radiation dose in full ITALUNG (assumed 10% of subjects would have indeterminate nodules): Multidetector CT: 0.83 mSv/year Single-slice CT: 1.78 mSv/year Lung cancer risk from radiation: Multidetector CT: 11.7/100,000 Single-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. 158 Recall 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: NR Stage 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* | Overall 127 (1.6%) diagnosed with lung cancer 3 with interval diagnosis between round 1 and 2  Round 1 Negative 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 2 Negative 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 rounds Positive 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. T3  SF-12 PCS: 49.5 vs. 50.0  Neg: 49.7 vs. 50.3  Ind: 48.5 vs. 48.9  SF-12 MCS: 51.9 vs. 51.6  Neg: 51.9 vs. 51.6  Ind: 51.8 vs. 51.9  EuroQOL (EQ)-5D T0 vs. T1 vs. T2 vs. T3  EQ-5D: 79.3 vs. 78.3 vs. 79.1 vs. 78.4  Neg: 79.4 vs. 78.7 vs. 79.4 vs. 79.2  Ind: 79.1 vs. 76.8 vs. 78.3 vs. 75.0  STAI-6  STAI-6: 33.2 vs. 34.6 vs. 32.7 vs. 33.0  Neg: 33.1 vs. 34.4 vs. 32.5 vs. 32.6  Ind: 33.6 vs. 35.2 vs. 33.5 vs. 34.8  IES  IES-D: 4.2 vs. 5.9 vs. 4.5 vs. 3.6  Neg: 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. 2907 Underwent other imaging: 1466 vs. 1498 Underwent minimally invasive procedure: 52 vs. 56 Underwent moderately invasive procedure: 77 vs. 93 Underwent major surgical procedure: 35 vs. 40 Cumulative 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 interval 62 among nonscreened PPV: 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 py  Screening 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: 1213  Cumulative incidence: 14/100,000 py  Lung 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 group  RR 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 screening  Lung cancer mortality: RR, 0.89 (95% CI, 0.80 to 1.00)  Lung cancer: 518  Lung cancer deaths: 316  Cumulative incidence lung cancer: 606/100,000 py  Cumulative lung cancer mortality: 361/100,000 py | Lung cancer incidence: 19.2/10,000 py  Stage I: 27%  Stage III or IV: 895/1620 (55%)  Cumulative death: 1230  Cumulative lung cancer mortality: 14.2/100,000 py  Other deaths: 12%  Lung cancer: 520  Lung cancer deaths: 334  Cumulative incidence lung cancer: 608/100,000 py  Cumulative 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