**openMetaAnalysis: Risk of bias**

**Studies of interventions**

**Under construction!**

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| **Table.** Risk of bias for included studies. Criteria for determinations are from the Cochrane Handbook, Table 8.5.d. Available at <http://handbook-5-1.cochrane.org/chapter_8/table_8_5_d_criteria_for_judging_risk_of_bias_in_the_risk_of.htm> . | | | | | | | | |
| **Study** | **Subjects and summary risk\*** | **Selection bias** | | **Performance bias** | **Detection bias** | **Attrition bias** | **Reporting bias** | **Other biases** |
| **Random sequence generation** | **Allocation concealment** | **Blinding of participants and personnel** | **Blinding of outcome assessment** | **Incomplete outcome data** | **Selective reporting** | **E.g. imbalanced compliance, co-interventions, or other.** |
| **Summary** | Total: 1125 Low risk 0% Unclear risk: 0% High risk: 100% |  |  |  |  |  |  |  |
| National Lung Screening Trial (NLST), 2011 PMID: [25372087](http://pubmed.gov/25372087)  [NCT00047385](http://clinicaltrials.gov/show/NCT00047385)  Roger | 53,452  Unclear risk | Unclear:  Not explicitly stated | Low risk:  The RA will register the participant by logging onto the ACRIN web site. Stratified randomization was accomplished by use of a block size of six or eight, with block size chosen at random. | Low risk:  No blinding or incomplete blinding. Reviewers judged it did not affect outcomes | Low Risk:  The members of the [end-point verification team] were not aware of the group assignments | Low Risk:  Vital status known for 97% in LDCT group, 96% in CXR group | Low Risk:  Primary outcomes are lung cancer and overall mortality. Specified in protocol. | Low risk |
| Multicentric Italian Lung Detection (MILD), 2013 (PMID [22465911](http://pubmed.gov/22465911)) and 2019 (PMID [30937431](http://pubmed.gov/30937431))  Roger | 3,466  High risk | High risk ‡  Method not described, But, reported as “central stratified randomization”. Large heterogeneity of baseline characteristics including current smokers versus former. | Unclear: Reported as “central stratified randomization” Baseline not reported among the randomized patients. | Low risk:  Unblinded, not deemed to have interfered with results. | Low risk:  Outcome info obtained by phone calls, emails, appointments and confirmed with national statistic and cancer registries. | Low risk:  Only one subject lost to follow up. | Low Risk: Primary outcomes of lung cancer and overall mortality reported | MILD was not properly registered. Originally stratified to annual and biennial then did not explain why they were pooled.  Did not include control group until after enrolling 653 subjects.  Did not report baseline comparisons—or deaths in intervention group--for contemporaneously randomized subjects |
| Dante, 2015 PMID: [25760561](http://pubmed.gov/25760561)  Roger | 2,811  Low Risk | Low risk:  Randomized 1:1 scheme from computer generated list. Possible inadequate randomization based on the fact 16 patients diagnosed at baseline by sputum and x-ray versus 9 in control group. LDCT had statistically significant higher rates of chronic bronchitis. Higher rate of enrollment decline in control group compared to LDCT (LDCT, 91; control, 166). Only males studied. | Low Risk:  Randomized in blocks of 4, stratified by center according to computer generated list. | Low: No blinding. Annual review for controls performed to monitor for cross contamination. Powered for 80% to detect 35% reduction in lung cancer mortality. Not deemed to have affected results | Unclear Risk: Patients aware they are included in lung cancer study and undergoing annual clinical reviews. Larger number of control group reported symptoms and larger number of cancers diagnosed in control group based on symptoms (LDCT 13, control 23). | Low Risk: Information regarding vital status, causes of death and malignancy diagnosis available for 96.6% of LDCT and 94.7% of controls | Low Risk: Primary outcomes are lung cancer and overall mortality. | Low Risk:  Single center study. |
| German Lung Cancer Screening Intervention Trial (LUSI), 2015 PMID: [25783198](http://pubmed.gov/25783198)  Roger | 4,052  Unclear risk | Low Risk:  Electronic randomization was in blocks and  stratified by age, gender,  and smoking status | Low Risk:  Electronic randomization reported but not explicitly defined. | Low risk:  No blinding or unclear blinding, but unlikely to have influence | Unclear:  Data on incident lung cancers were obtained for the screening group from the annual MSCT scans.  Control group data on lung cancer incidence was obtained from the annual questionnaires, followed by data collection from the treating physicians in case of self-reported lung cancer diagnosis. In addition, a linkage with the local cancer registry as well as the local population registries was carried out. | Low Risk: One in intervention group lost to follow up, 5 in control group non-adherent. | Low Risk: Primary outcome reported: Lung cancer mortality. | Low Risk |
| Danish Lung Cancer Screening Trial (DLCST), 2016 PMID: [26485620](http://pubmed.gov/26485620)  [NCT00496977](http://clinicaltrials.gov/show/NCT00496977)  RAMI | 4104  Unclear Risk | Low Risk  Participants were randomized in random permuted blocks of 10 participants | Unclear risk  Method of allocation concealment not described | Low Risk  No blinding or incomplete blinding, but the review authors judge that the outcome  is not likely to be influenced by lack of blinding | Low Risk  Final conclusions regarding cause of death were established by the local review board without awareness of group assignment | Low risk: The vital status of all participants is checked annually in the Danish Civil Registration System which registers all national deaths within 2 weeks. | Low Risk  The primary outcome was assessment of lung cancer mortality and all-cause mortality in the two groups.  Secondary outcomes were lung cancer diagnoses, survival, stages, and histology. Post hoc analyses of the effects of age, amount of smoking, and COPD at baseline on mortality of lung cancer were conducted. | Participants who emigrated from Denmark were lost to follow-up. |
| ITALUNG, 2017 PMID: [28377492](http://pubmed.gov/28377492) [NCT02777996](http://clinicaltrials.gov/show/NCT02777996)  RAMI | 3206  Summary: Low risk | **Low Risk**  Eligible sub- jects were centrally randomised by a software procedure into an active group receiving an annual invitation to LDCT screening for 4 years and a control group receiving usual care. | **Low Risk**  Eligible sub- jects were centrally randomised by a software procedure into an active group receiving an annual invitation to LDCT screening for 4 years and a control group receiving usual care. | **Low risk**  No blinding or incomplete blinding, but the review authors judge that the outcome  is not likely to be influenced by lack of blinding | **Low Risk**  An independent committee reviewed and revised the causes of death in a blinded fashion using a spe- cific algorithm presented in the online supplementary appendix (section 2). | **Low Risk**  207 dropouts between ran- domisation and the baseline screening test were mainly due to refusal to undergo baseline LDCT after randomisation (79.2%) | **Low risk**  primary endpoint was the comparison of LC mor- tality between the active and control groups using the rate ratio (RR) with 95% CI. |  |
| NELSON, 2014 PMID: [25282284](https://www.ncbi.nlm.nih.gov/pubmed?term=25282284) [NL580](https://www.trialregister.nl/trial/580)  RAMI | 15,822  Unclear risk | **Unclear Risk**  **NMS SYSTEM**  To conduct this logistically complex multi-center study, the NELSON management system (NMS) has been developed. It is a web-based interactive database application used for data collection and management of all study related processes such as the selection and randomisation of participants, electronic storage of questionnaires and informed consent forms, completely trackable data collection, study monitoring, reporting of scan results and scheduling of appointments for follow-up scan | **Unclear?**  **NMS SYSTEM**  To conduct this logistically complex multi-center study, the NELSON management system (NMS) has been developed. It is a web-based interactive database application used for data collection and management of all study related processes such as the selection and randomisation of participants, electronic storage of questionnaires and informed consent forms, completely trackable data collection, study monitoring, reporting of scan results and scheduling of appointments for follow-up scan | **Low risk**  No blinding or incomplete blinding, but the review authors judge that the outcome  is not likely to be influenced by lack of blinding | **Unclear risk**  **(no description)** | **Low risk**  **National registries were used to determine cancer diagnosis, date of death, and cause of death** | **Low risk**  **Lung cancer mortality (reduction)**  <http://www.isrctn.com/ISRCTN63545820> | Individuals who are younger, have a high socioeconomic background and/or more physically active are more inclined to participate in this screening trial.  Belgian participants not included (no data available from Belgian registry) |
| LSS, 2005 PMID: [15603850](https://www-ncbi-nlm-nih-gov.proxy.kumc.edu/pubmed/?term=Final+results+of+the+Lung+Screening+Study%2C+a+randomized+feasibility+study+of+spiral+CT+versus+chest+X-ray+screening+for+lung+cancer) [NCT00006382](https://clinicaltrials.gov/ct2/show/NCT00006382?term=lung+screening+study&rank=1)  RAMI | 3,318  Unclear | Unclear Risk  Not explicitly stated | Low Risk  Randomized using a secure web-based system that maintained by the coordinating center, to one of the two study arms, LDCT scan or CXR. | Low Risk  No blinding or incomplete blinding, but the review authors judge that the outcome  is not likely to be influenced by lack of blinding | Unclear Risk  No endpoint verification was performed. | Low Risk: Linkage with National Death Index. All deaths through 2005. | Low: Primary outcomes were lung cancer incidence and feasibility. However, LSS was pilot for NLST which was looking at lung cancer and over mortality. | Definition of a positive screen, changed somewhat between the baseline and year one screening visit.  According to the original study protocol, which was in effect at the time of the baseline screen, several specific findings other than a non-calcified nodule ≥ 4 mm (e.g., a spiculated nodule ≤ 3 mm in the LDCT arm) necessitated a finding of a positive screen |
|  |  | **Random sequence generation** | **Allocation concealment** | **Blinding of participants and personnel** | **Blinding of outcome assessment** | **Incomplete outcome data** | **Selective reporting** | **E.g. imbalanced compliance, co-interventions, or other.** |
| **Selection bias** | | **Performance bias** | **Detection bias** | **Attrition bias** | **Reporting bias** | **Other biases** |
| **Notes:**  \* Summary determination based on Cochrane Handbook, Table 8.7. Available at <http://handbook-5-1.cochrane.org/chapter_8/table_8_5_d_criteria_for_judging_risk_of_bias_in_the_risk_of.htm>  † Trial was not prospectively registered.  ‡ Descriptions of randomization suggest low risk of bias; however, uneven distribution of smoking and airway obstruction.  §  ||  ¶ | | | | | | | | |