

---

## Benefits and harms of CT screening for lung cancer: a systematic review

*Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, Byers T, Colditz GA, Gould MK, Jett JR, Sabichi AL, Smith-Bindman R, Wood DE, Qaseem A, Detterbeck FC*

---

### CRD summary

This review concluded that low-dose computed tomography screening might benefit those at an increased risk of lung cancer, but the potential harms of screening and the generalisability of the results were uncertain. There were some limitations to the review and the included studies, but the authors' conclusions are suitably cautious.

### Authors' objectives

To evaluate the benefits and harms of lung cancer screening, using low-dose computed tomography (CT).

### Searching

MEDLINE, EMBASE and The Cochrane Library were searched for studies published in English between 1996 and April 2012. Reference lists of related papers and reviews were scanned. The search strategy was available online.

### Study selection

Randomised controlled trials (RCTs) were eligible for inclusion if they compared low-dose CT to screen for lung cancer with no screening in patients who were at risk due to smoking. Uncontrolled cohort studies were eligible if they reported the nodule detection rate, frequency of additional imaging or invasive diagnostic procedures, complications associated with screening, or the rate of smoking cessation or re-initiation. RCTs evaluated these outcomes, as well as lung cancer-specific and all-cause mortality.

Across the included studies, patient age ranged from 40 to 85 years and there were more men than women. The minimum smoking history ranged from at least 10 to 30 pack-years; the maximum time since quitting ranged from less than six months to an unlimited number of years; most studies required less than 10 years. Most studies used a nodule size of at least 5mm to indicate the need for work-up. The underlying risk of lung cancer varied considerably across studies.

Two reviewers selected studies for the review; disagreements were resolved by a third reviewer. The third reviewer also checked any articles deemed to be ineligible.

### Assessment of study quality

The risk of bias was assessed by two reviewers for the clarity of the question; reproducibility of the methodology; randomisation; allocation concealment; sample size; comparability at baseline; blinding; validation and reliability of the outcome measures; attrition; the appropriateness of the analysis; the accuracy of the results; and conflicts of interests. Discrepancies were resolved by consensus.

### Data extraction

Mortality data were extracted from the RCTs; relative risks, with 95% confidence intervals, absolute differences and the number needed to treat were calculated. The other outcomes of interest data were extracted from all studies. Data extraction was conducted by two reviewers, with differences resolved by discussion.

### Methods of synthesis

Pooled odds ratios, with 95% confidence intervals, were calculated for mortality, using a Mantel-Haenszel model. A random-effects model was used for mortality associated with lung cancer and a fixed-effect model for all-cause mortality and smoking cessation. Heterogeneity was assessed using  $X^2$  and  $I^2$ . The other outcomes of interest were combined in a narrative synthesis, with average rates, ranges, or both reported. Differences were discussed in the text and study details and results were tabulated.

### Results of the review

Eight RCTs and 13 cohort studies (in 45 publications) met the inclusion criteria. Two of the RCTs were considered to be at low risk of bias; only preliminary reports of ongoing trials were available for the other six. The risk of bias in the

cohort studies was variable; several lacked justification for the sample size, a definition of the primary end point, or description of the funding sources, and were therefore considered to be at high risk.

**Mortality:** Three RCTs, with 60,030 participants (range 2,472 to 53,454) found that screening resulted in a statistically significant reduction in lung cancer-related deaths (OR 0.82, 95% CI 0.72 to 0.94), over a median of 6.5 years follow-up, but no such effect on deaths from other causes (OR 0.99, 95% CI 0.92 to 1.06).

**Nodule detection:** Eight RCTs and 11 cohort studies, with 60,325 participants (range 60 to 26,309) found that the average nodule detection rate per round of screening was 20% (range three to 30 in RCTs; five to 51 in cohort studies); more than 90% of nodules were benign in most studies.

**Further interventions:** The frequency of further CT among screened individuals ranged from 1% to 44.6%, positron emission tomography from 2.5% to 5.5%, and invasive evaluation (seven RCTs and eight cohort studies; 52,575 participants, range 336 to 26,309) from 0.9% to 5.6%.

There was no significant effect of screening on smoking cessation (OR 0.95, 95% CI 0.79 to 1.14; two RCTs, 4,208 participants). Only one study reported procedure-related complications and the results were reported in detail. The review discussed over-diagnosis, radiation exposure, quality of life, the characteristics of patients who were likely to benefit from screening, and the effect of screening setting.

### **Authors' conclusions**

Low-dose CT screening might benefit those at an increased risk of lung cancer, but the potential harms of screening and the generalisability of the results were uncertain.

### **CRD commentary**

The review addressed a clear question with reproducible inclusion criteria. Several relevant sources were searched, but only English-language publications were included; language and publication bias could be present. Diagnostic filters were used for the electronic search and some studies might have been missed. Study selection and the quality assessment were conducted by two people. It was unclear whether similar methods to reduce error and bias were used for data extraction.

The quality of the RCTs was assessed using appropriate criteria, and the results were reported in full in an online appendix. The cohort studies were assessed using the same criteria, but the results for each study were not reported. The quality of the studies was not considered during the synthesis. The choice of statistical model for the mortality data was not explained; all three analyses included only two or three studies and a random-effects model seems to have been inappropriate.

There were some limitations to the review and the included studies, but the authors' conclusions are suitably cautious.

### **Implications of the review for practice and research**

**Practice:** The authors stated that recommending a low-dose CT scan outside a structured process appeared to be beyond the evidence for low-dose CT lung cancer screening.

**Research:** The authors did not state any implications for research.

### **Funding**

No industry funding.

### **Bibliographic details**

Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, Byers T, Colditz GA, Gould MK, Jett JR, Sabichi AL, Smith-Bindman R, Wood DE, Qaseem A, Detterbeck FC. Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA* 2012; 307(22): 2418-2429

### **PubMedID**

22610500

**DOI**

10.1001/jama.2012.5521

**Original Paper URL**

<http://jama.jamanetwork.com/article.aspx?articleid=1163892>

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Cohort Studies; Humans; Lung Neoplasms /mortality /radiography; Radiation Dosage; Randomized Controlled Trials as Topic; Risk; Risk Reduction Behavior; Tomography, X-Ray Computed /adverse effects

**AccessionNumber**

12012044428

**Date bibliographic record published**

04/10/2012

**Date abstract record published**

10/10/2012

**Record Status**

This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.