Screening for lung cancer with low-dose computed tomography: a systematic review and meta-analysis of the baseline findings of randomized controlled trials

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CRD summary
This review of preliminary evidence concluded that there was no compelling baseline data for or against the use of low-dose computed tomography in screening for lung cancer; final results of the trials should improve understanding of the effectiveness of such screening. These cautious conclusions reflected the findings of the review and may be regarded as reliable.

Authors' objectives
To determine whether screening for lung cancer with low-dose computed tomography (CT) is effective in diagnosing lung cancers early in a high-risk population of smokers compared with no screening.

Searching
MEDLINE, EMBASE, CINAHL and The Cochrane Library were searched from 1966 to February 2010. Search terms were reported. The abstracts of the Radiologic Society of North America (2003 to 2009) and of the European College of Radiology (2001 to 2009) were screened, along with major radiology and lung cancer textbooks and reference lists. Completed but unpublished trials were also sought. No language restrictions were employed.

Study selection
Randomised controlled trials (RCTs) that compared low-dose CT with no screening or chest radiography for the diagnosis of lung cancer in a high-risk population of smokers were eligible for inclusion.

Outcomes included detection of stage 1 non-small cell lung cancer, all non-small cell lung cancer, all lung cancer, detection of false positive nodules, and rate of thoracotomy for benign lesions.

Participants in included trials had average ages between 50 and 60 years (range 49 to 80 years), with an average smoking history of 20 to 30 pack-years; all trials enrolled volunteers. Half of included trials used chest x-rays in the control group; the other trials used no screening. The collimation beam of low-dose CT scans varied from 0.6 to 5mm, as did the use of positron emission tomography and fine-needle aspiration work-ups of nodules detected.

Two reviewers independently selected the studies for inclusion in the review, with disagreements resolved by a third reviewer.

Assessment of study quality
Two reviewers independently assessed the validity of the included trials using the US Preventative Services Task Force guidelines and the Cochrane Collaboration's tool for the assessment of bias assessing generalisability, sample size, drop-outs, reproducibility and statistical methodology. Disagreements were resolved by a third reviewer.

Data extraction
Data were extracted to permit the calculation of event rates and odds ratios (OR) with 95% confidence intervals (CI).

Two independent reviewers carried out the data abstraction.

Methods of synthesis
Trials were combined in random-effects meta-analyses; pooled odds ratios and event rates, with 95% confidence intervals, were calculated.

A subgroup analysis of trials using chest x-ray in the control arm was conducted.
The potential for publication bias was assessed by calculating the fail safe N.

**Results of the review**

Six RCTs were included in the review (n=14,055 patients), including 7,078 patients in the low-dose CT groups and 6,977 in the control groups. Sample sizes ranged from 190 to 4,104 patients. Drop-out rates ranged from 0 to 21%.

The detection of stage 1 non-small cell lung cancer was statistically significantly higher in the low-dose CT groups than in the control groups (OR 3.91, 95% CI 2.05 to 7.43; six RCTs), as was the detection of any non-small cell lung cancer (OR 5.51, 95% CI 3.13 to 9.70; six RCTs).

The detection of false-positive nodules was statistically significantly higher in the low-dose CT (OR 3.12, 95% CI 2.62 to 3.72; six RCTs). The odds ratio for rate of thoracotomy for benign lesions was 3.71 (95% CI 3.55 to 3.87; seven comparisons) higher in the low-dose CT groups.

Analysis of the subgroup of three RCTs that used chest x-ray in the control groups did not differ substantially from the results of the main analysis.

The fail safe N was calculated as 14 for the outcome of stage 1 non-small cell lung cancer and 279 for the outcome of thoracotomies for benign lesions.

**Authors' conclusions**

There was no compelling baseline data from six RCTs in favour of or against the use of low-dose CT screening for lung cancer; the final results of these trials should improve understanding of the effectiveness of such screening.

**CRD commentary**

The review question and inclusion criteria were clear. The authors searched several relevant databases without language restrictions, and made attempts to locate unpublished studies. These factors reduced the chance that relevant studies were omitted or selection biases introduced. The authors reported using methods designed to reduce reviewer bias and error at all stages of the review process.

Appropriate criteria were used to assess trial quality, but there was only limited reporting of the results of this assessment. The synthesis appeared appropriate, although there was limited assessment or exploration of potential heterogeneity.

The authors' cautious conclusions reflected the findings of this review of preliminary evidence and may be regarded as reliable.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that the final results of these RCTs are awaited to improve the understanding of the effectiveness of low-dose CT in screening for lung cancer and its effect on mortality.

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