Systematic review of baseline low-dose CT lung cancer screening

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CRD summary
This review found that low-density computed tomography has the potential to lead to an effective screening programme for lung cancer. These findings are unlikely to be reliable as study quality was not appropriately assessed or considered in the results and a formal statistical analysis, including an investigation of variability between the studies, was not conducted.

Authors' objectives
To determine the accuracy of baseline low-dose computed tomography (LDCT) screening for lung cancer.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane Library were searched from inception to May 2006; the search terms were reported. In addition, relevant conference abstracts, ongoing trials, and reference lists from retrieved studies and major radiology and lung cancer textbooks were screened to identify additional relevant studies.

Study selection
Study designs of evaluations included in the review
Prospective and retrospective clinical studies were eligible for inclusion. Relevant studies reported as abstracts were noted but not included in the review. The included studies were randomised controlled trials (RCTs), non-randomised trials and prospective diagnostic cohort studies.

Specific interventions included in the review
Studies of LDCT screening were eligible for inclusion. Studies had to include at least a baseline LDCT screen with the aim of diagnosing lung cancer. Most studies described a positive screen as the detection of 1 to 6 non-calcified pulmonary nodules.

Reference standard test against which the new test was compared
Inclusion criteria were not specified in terms of the reference standard. The reference standards used were not reported clearly, but they appear to have been surgery or biopsy for positive screens and incidence scans (follow-up CT) for negative screens. The time between baseline and subsequent screens ranged from 3 to 24 months, with some studies reporting multiple subsequent screens.

Participants included in the review
Studies of primarily current and former smokers were eligible for inclusion. Studies of specific high-risk populations exposed to hazardous compounds (i.e. asbestos, nuclear fuel) were excluded. Where reported, the proportion of men in the included studies ranged from 50 to 88% and age ranged from 40 to 88 years.

Outcomes assessed in the review
Studies had to provide details on the number of lung cancers found. The outcomes reported in the review were the sensitivity, specificity and predictive values. The review also assessed the percentage of stage 1 lung cancers detected.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed studies for relevance. Any disagreements were resolved by referral to a third reviewer.

Assessment of study quality
The studies were assessed by independent reviewers on a 6-point scale which evaluated generalisability, sample size, adequacy of follow-up time/procedure, reproducibility and statistical methodology. Each category was given a score of 0, 0.5 or 1.0. A total score of at least 5.5 was considered excellent, 4.5 to 5.0 was good, 3.5 to 4.0 was fair, and 0 to 3 was poor.
Data extraction
The data were extracted as 2x2 tables of test performance for the baseline screen. The authors did not state how many reviewers performed the data extraction. Sensitivity, specificity, and positive and negative predictive values were calculated for each study.

Methods of synthesis
How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
Heterogeneity was not formally investigated.

Results of the review
Fifteen trials were included (29,607 patients screened with LDCT). There were 2 RCTs (one compared LDCT with no screening; the other compared LDCT with chest X-ray), 3 non-randomised trials that compared LDCT with other screening in the same patients (chest X-ray and/or sputum cytology), and 10 prospective diagnostic cohort studies.

Six studies were considered to be of excellent quality, five of good quality, and four of fair quality; none were considered poor quality.

Nine studies assessed accuracy. The sensitivity ranged from 50 to 100% (median 81%) and the specificity from 49 to 95% (median 81%).

Eleven studies assessed stage of cancer detected. The majority (80%) of the baseline cancers detected by LDCT were stage 1 non-small-cell lung cancer.

All 3 studies that compared LDCT with chest X-ray and/or sputum cytology in the same population reported that CT detected a greater proportion of cancers than the other tests.

Authors’ conclusions
The accuracy of baseline LDCT screening and the relatively high proportion of stage 1 cancers detected suggest that LDCT has the potential to lead to an effective screening programme for lung cancer.

CRD commentary
The review addressed a focused question and was supported by inclusion criteria clearly specified in terms of the intervention, participants, outcomes and study design. However, it is unclear why certain types of study were included when they did not report appropriate data to address the review objective and were not included in any synthesis of the results. The literature search was adequate and included some attempts to locate unpublished studies, but it was unclear whether any language restrictions were applied. Appropriate methods were used to avoid bias and error in the selection of studies and assessment of quality, but it is unclear whether such steps were also taken for the extraction of data. Although a formal quality assessment was conducted, this was not based on appropriate criteria for test accuracy studies and the results were presented as gradings of quality rather than showing which of the individual items assessed were fulfilled by each of the included studies.

A narrative synthesis of the results was presented. However, a more statistical analysis that included some investigation of heterogeneity would have been more informative. The authors’ conclusions appear to be based on summary measures of accuracy. These conclusions are unlikely to be reliable as follow-up was short-term, study quality was not appropriately assessed or considered in the results, and a formal statistical analysis including investigation of heterogeneity was not conducted.

Implications of the review for practice and research
Practice: The authors stated that LDCT has potential as a screening tool for lung cancer.
Research: The authors stated that the effect of LDCT on mortality and morbidity needs to be confirmed by well-designed RCTs prior to the implementation of any screening programme.

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