Diagnostic performance of dual-time 18F-FDG PET in the diagnosis of pulmonary nodules: a meta-analysis
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CRD summary
This review concluded that dual time-point 18F-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) had similar sensitivity and specificity to single time-point FDG-PET in the diagnosis of malignant pulmonary nodules, with no additional value. Weaknesses in the reporting and analytic methods and the absence of data on single time-point FDG-PET make these conclusions unreliable.

Authors' objectives
To assess the performance of two time-point 18F-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) in the diagnosis of malignancy in pulmonary nodules.

Searching
MEDLINE and EMBASE were searched for items from January 2000 to January 2011, without language restriction, and the search terms were reported. The bibliographies of textbooks and retrieved articles were screened for additional studies. Conference abstracts were excluded.

Study selection
Studies assessing the performance of dual time-point FDG-PET in the diagnosis of malignancy in pulmonary nodules were eligible for inclusion if they included 10 or more participants. Included studies were required to use pathology or clinical follow-up as the reference standard to confirm diagnosis, and to report the numbers of true-positive, false-negative, false-positive, and true-negative results.

Where reported, the mean age of study participants ranged from 54 to 69 years, and the mean nodule size ranged from 1.1 to 3.3cm. All studies defined a pulmonary nodule as a round, three-dimensional structure of less than 3cm. The initial and delayed maximum standard uptake values (SUVmax) used to define malignancy varied between studies (reported in the article). The manufacturers and, in some cases, models of the scanners were reported, but no further technical details were provided. All but one of the studies were published between 2007 and 2010. Three studies used pathology as the reference standard and the remaining seven used a combination of pathology and clinical follow-up; only two studies reported the suggested minimum (24 months) follow-up to confirm benign nodules.

The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality
The methodological quality of included studies was assessed using a modification of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool, but no further details were reported.

The authors did not state how many reviewers assessed study quality.

Data extraction
Data were extracted on the numbers of true-positive, false-negative, false-positive, and true-negative results, and used to calculate sensitivity and specificity, with 95% confidence intervals.

The authors did not state how many reviewers extracted these data.

Methods of synthesis
Pooled estimates of per patient sensitivity and specificity, with 95% confidence intervals, were calculated using a random-effects model. Between-study heterogeneity was assessed visually, using forest plots, and quantified using $I^2$.

Results of the review
Ten studies, with 816 participants (range 27 to 255), were included in the review. Seven studies were retrospective. The mean quality score was 8.3 (range 7 to 10).

The pooled estimate of sensitivity was 85% (95% CI 82 to 89; 10 studies) and the pooled estimate of specificity was 77% (95% CI 72 to 81; 10 studies). There was substantial heterogeneity in both measures ($I^2=77\%$ for sensitivity and 91% for specificity). The summary positive likelihood ratio was 2.7 (95% CI 1.4 to 5.2) and the summary negative likelihood ratio was 0.26 (95% CI 0.14 to 0.49).

**Authors’ conclusions**
Dual time-point FDG-PET had similar sensitivity and specificity to single time-point FDG-PET for the diagnosis of malignant pulmonary nodules. Its additional value was questionable due to the overlap between benign and malignant nodule characteristics and the lack of an agreed definition for a malignant nodule.

**CRD commentary**
The review reported a clear objective and inclusion criteria. Literature searches were conducted, without language restrictions, but were limited to two databases. No measures to minimise error and bias in the review process were reported and the results of the quality assessment were only given as a mean and range of scores, which is not recommended in the guidance for the QUADAS. It is therefore impossible to assess the impact on the findings of weaknesses in the included studies or in the review methods.

A simple random-effects model is not generally recommended for generating pooled estimates of sensitivity and specificity across studies with varying diagnostic thresholds and reference standards, and significant statistical heterogeneity. The authors discussed several possible sources of heterogeneity, but the reliability and value of the pooled estimates is questionable. The authors’ conclusions drew comparisons between the accuracy of dual time-point FDG-PET and that of single time-point FDG-PET, but their review included no comparative data and no studies of single time-point FDG-PET.

Weaknesses in the reporting of the review and the analytical methods mean that the pooled estimates of sensitivity and specificity and the authors’ conclusions are not likely to be reliable.

**Implications of the review for practice and research**
**Practice:** The authors did not specify any recommendations for clinical practice.

**Research:** The authors stated that further, larger, prospective studies, using different thresholds to define malignant pulmonary nodules, might be helpful.

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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.