Pediatric thyroid fine-needle aspiration cytology: a meta-analysis
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CRD summary
This review concluded that fine needle aspiration biopsy of thyroid nodules may be a useful tool for excluding malignancy in young patients. Limitations in the review including the possibility of missing studies and failure to investigate heterogeneity together with the small number, size and variable quality of the included studies mean these conclusions are unlikely to be reliable.

Authors' objectives
To investigate the diagnostic performance of fine-needle aspiration (FNA) biopsy in the diagnosis of a thyroid nodule in the paediatric population.

Searching
MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, ACP Journal Club, DARE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from 1950 to December 2006. Diagnostic filters were used in the searches; other details of the search were lacking. Reference lists of articles were screened. The review was restricted to English-language studies.

Study selection
Studies that assessed the diagnostic accuracy of FNA biopsy of thyroid nodules against a reference standard (surgery or >12 months for all patients or mean >18 months follow-up) in children (age <18 to 21) who presented with undiagnosed thyroid nodules were eligible for inclusion. Case studies were excluded.

Studies were generally retrospective studies of children who had undergone FNA or thyroidectomies. One prospective study enrolled children who presented with thyroid nodules.

Two reviewers independently assessed studies for inclusion. Disagreement was resolved through referral to a third reviewer. An expert in the field excluded studies judged to have poor external validity or poor methodological quality.

Assessment of study quality
Two reviewers independently assessed study quality using the QUADAS tool. Summary scores were estimated by summing the number of QUADAS items fulfilled by each study. Disagreements were resolved through consensus.

Data extraction
Data were extracted to enable calculation of sensitivity, specificity, accuracy and positive and negative predictive values. Where possible raw data were extracted and used to calculate these measures.

Calculations were done independently by two reviewers; it was unclear how other data were extracted.

Methods of synthesis
Summary sensitivity and specificity, together with 95% confidence intervals (CIs), were estimated using the bivariate random-effects model. These data were used to estimate summary positive and negative likelihood ratios and accuracy. Positive and negative predictive values based on a pre-test probability of 20% were estimated. A summary receiver operating characteristic (SROC) analysis was conducted to estimate the area under the SROC curve (AUC). Sensitivity analysis was conducted by exclusion of each study individually from the meta-analysis.

Results of the review
Twelve studies (n=643) were included in the review. All studies fulfilled QUADAS criteria for reference standard, time between index test and reference standard, independence of the reference standard, blinding of the index test results to the reference standard, availability of clinical information, reporting of withdrawals and reporting of...
uninterpretable/intermediate results. None of the studies fulfilled items for reporting of reference standard execution. Only one study reported that the reference standard was interpreted blind to the index test. Eight studies included an appropriate patient spectrum and there was a possibility of differential and/or partial verification bias in all but two studies.

Sensitivity ranged from 64% to 100%. Summary sensitivity was 94% (95% CI 86% to 100%). Specificity ranged from 57% to 97%. Summary specificity was 81% (95% CI 72% to 91%). Exclusion of individual studies did not impact on results. The SROC plot suggested substantial heterogeneity between studies.

**Authors’ conclusions**

There was good evidence that FNA biopsy of thyroid nodules was a sensitive test in the paediatric population and may be a useful tool for excluding malignancy in young patients.

**CRD commentary**

The review addressed a clear question and inclusion criteria were defined. However, the authors stated that an expert excluded studies based on external validity and quality; this is not a systematic approach and may have introduced bias into the review, although it was unclear how many (if any) studies were excluded on this basis. The literature search included some relevant sources, but use of a diagnostic filter, restriction to English-language studies and lack of an explicit search for unpublished studies meant that relevant studies may have been missed. Appropriate steps were taken to minimise bias and errors during the review process. Study quality was assessed using appropriate criteria and the results were clearly presented, but were not considered in the synthesis. Very few details on the participants in the included studies were reported, which made it difficult to determine the generalisability of the findings. Sophisticated methods were used to pool data; however, heterogeneity was not formally assessed or investigated.

Limitations in the review including the possibility of missing studies and failure to investigate heterogeneity together with the small number, size and variable quality of the included studies mean that the authors' conclusions are unlikely to be reliable.

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

**Practice:** The authors stated that FNA biopsy of thyroid nodules may be a useful tool for excluding malignancy in young patients

**Research:** The authors stated that future prospective studies are needed to evaluate this further.

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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.