Accuracy of real-time polymerase chain reaction versus anaerobic culture in detection of Aggregatibacter actinomycetemcomitans and Porphyromonas gingivalis: a meta-analysis
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CRD summary
This review found that real-time polymerase chain reaction had high diagnostic accuracy for the detection of Aggregatibacter actinomycetemcomitans and Porphyromonas gingivalis. The review suffered from a number of limitations and the results presented did not support the author's conclusion. Therefore, these findings are not reliable.

Authors' objectives
To determine the accuracy of real-time polymerase chain reaction (PCR) for the detection of Aggregatibacter actinomycetemcomitans (A. actinomycetemcomitans) and Porphyromonas gingivalis (P. gingivalis).

Searching
MEDLINE via PubMed, Web of Science, National Research Register and The Cochrane Library were searched to November 2007. Reference lists of primary studies were screened and six relevant journals were hand-searched. The review was restricted to peer-reviewed published English-language studies. Search terms were reported and included a diagnostic filter.

Study selection
Studies that assessed the accuracy of real-time PCR for the detection of A. actinomycetemcomitans and/or P. gingivalis compared to the reference standard of culture were eligible for inclusion. Studies had to report sufficient data to allow calculation of sensitivity and specificity.

All included studies enrolled patients with untreated periodontitis who had not received periodontal or antibiotic treatment in the previous three to six months and assessed the number of one or more periodontal pathogens present in subgingival plaque samples. All studies used pooled subgingival samples from the deepest periodontal pocket and used dual-labelled probes with fluorescent dyes for the detection and quantification of different periodontal pathogens. Most studies used 16S-rRNA-specific primers.

Search results were assessed for relevance by a single reviewer; the author did not state how many reviewers performed the selection of studies for inclusion.

Assessment of study quality
The author did not state that they assessed validity, although some aspects of study quality were discussed in the results.

Data extraction
Data were extracted as 2x2 tables of test performance using a predefined form. Sensitivity, specificity and positive and negative likelihood ratios (LR+ and LR-) together with 95% confidence intervals (CI) were calculated for each study.

Methods of synthesis
The possibility of a threshold effect was examined graphically by plotting individual study results on a summary receiver operating characteristic (SROC) plot and statistically through assessment of the degree of heterogeneity and correlation between sensitivity and specificity. Heterogeneity was assessed using the \( \chi^2 \) and \( I^2 \) statistics. Correlation was assessed using the correlation coefficient. In the absence of a threshold effect, sensitivity and specificity were pooled; otherwise a SROC analysis was conducted and diagnostic odds ratios (DOR) were pooled. Summary likelihood ratios were presented but no details were reported on how these were calculated.

Results of the review
Five studies (n=663) were included. Only one study reported that the person interpreting the PCR results was blinded to the culture results and patient information and vice versa.
Four studies assessed the detection of *A. actinomycetemcomitans*. Sensitivity ranged from 87% to 97%; there was no evidence of heterogeneity (p=0.61, $I^2=0\%$). Specificity ranged from 67% to 77%; there was significant heterogeneity (p<0.001, $I^2=97.8\%$). The pooled LR+ was 3.24 (95% CI 0.71 to 14.65) and pooled LR- was 0.14 (95% CI 0.07 to 0.28).

Four studies assessed the detection *P. gingivalis*. Sensitivity ranged from 94% to 99% and specificity ranged from 55% to 68%; there was significant heterogeneity (p not reported) for both. The pooled LR+ was 3.02 (95% CI 0.84 to 10.82) and pooled LR- was 0.08 (95% CI 0.01 to 0.64).

**Authors’ conclusions**
Real-time PCR had high diagnostic accuracy for the detection of *A. actinomycetemcomitans* and *P. gingivalis*.

**CRD commentary**
The review addressed a clear question supported by clearly defined inclusion criteria. The literature search included a range of electronic databases, but use of a diagnostic filter meant that relevant studies may have been missed. The review was restricted to published English-language studies, so there was a possibility of language and publication bias. Appropriate steps were not taken to minimise bias and error when screening the searches; details on the process used to select full-text studies for inclusion and extract data were not reported. Given that the review included only one author and no additional reviewers were acknowledged, it seemed likely that these processes were also conducted by a single reviewer and so there was a possibility of bias and error at all stages of the review process. Study quality was not formally assessed, although details related to blinding were reported and the spectrum of patients included in the studies were described and appeared appropriate. Details on the exact methods used to pool study results were not reported and so it was unclear whether these were appropriate. There was significant heterogeneity between studies that was not investigated and so pooled estimates should be interpreted with extreme caution. The results presented suggested that PCR can be used to rule out but not rule in the pathogens assessed, although this was based on summary likelihood ratios with very wide confidence intervals, which did not support the author’s conclusion that PCR had high diagnostic accuracy. Therefore, the conclusions are not reliable.

**Implications of the review for practice and research**
**Practice:** The author stated that the choice of diagnostic test should consider factors other than diagnostic accuracy, including cost and availability.

**Research:** The author stated that controlled clinical studies were needed to evaluate real-time PCR in the treatment or monitoring of periodontally diseased patients.

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