The accuracy and efficacy of screening tests for Chlamydia trachomatis: a systematic review

Authors' objectives
To determine which of the available diagnostic tests for Chlamydia trachomatis is the most accurate and effective when used in young, asymptomatic, sexually active populations.

Searching
Studies published from 1990 onwards were sought in MEDLINE, CINAHL and EMBASE. Relevant (unspecified) journals were handsearched. Additional articles were sought through internet searches and by scanning the bibliographies of included studies and contacting experts in the field.

Study selection
Study designs of evaluations included in the review
All study designs were eligible for inclusion. Only comparative diagnostic accuracy studies were identified.

Specific interventions included in the review
Studies of any method for detecting urogenital infection with chlamydia were eligible for inclusion. The diagnostic tests examined were: nucleic acid amplification techniques (polymerase chain reaction and ligase chain reaction, PCR and LCR respectively), gene probes, enzyme immunoassay, direct immunofluorescence and the leukocyte esterase test. Sampling techniques were also reviewed.

Reference standard test against which the new test was compared
No inclusion criteria were specified for the reference standard. All tests evaluated were compared with culture or an expanded reference standard of two non-culture tests (used where the index tests performed better than culture). The sensitivity of culture was calculated by comparing it with two non-culture techniques.

Participants included in the review
All participants in the included studies were required to be sexually active young men or women with no symptoms of chlamydia infection. The participants in the included studies were aged from 14 to 40 years. The majority of the included studies (21 out of 30) were conducted in all female populations. Where reported, the prevalence of Chlamydia trachomatis in the included studies ranged from 1.03 to 15%.

Outcomes assessed in the review
No inclusion criteria were specified for the diagnostic outcome measures. The review reported the sensitivity, specificity and odds ratio (OR), with 95% confidence interval (CI), for each data set included (some studies evaluated more than one test or sampling method and therefore reported multiple data sets).

How were decisions on the relevance of primary studies made?
One reviewer examined titles and abstracts on three occasions to determine whether studies were potentially relevant (conducted in asymptomatic populations). These articles were then further evaluated, against the inclusion criteria, by two reviewers.

Assessment of study quality
The methodological quality of the included studies was assessed using criteria published by Irwig et al. These considered: the use of a recognised reference standard; blind and independent interpretation of the reference; the inclusion of consecutive patients; verification of negative test results; and description of techniques. The maximum Irwig score is 10; studies with a score of less than 5 were considered poor and were excluded. Reviewers assessing study quality were not blinded to authorship. No further details of how study quality was assessed, or how many reviewers performed the quality assessment, were reported.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Sensitivity and specificity values, for each included study, were calculated from the data reported in the individual studies.

Methods of synthesis
How were the studies combined?
The diagnostic accuracy results were plotted, by index test type, in receiver operating characteristic curve (ROC) space (sensitivity versus 1 minus the specificity). An OR (defined as the likelihood of a false-negative result in the index test divided by the likelihood of a false-negative result in the reference standard) was calculated, along with the 95% CI, for each data set. Pooled estimates of OR, with 95% CIs, were calculated separately for urine and cervical samples for each test. The mean sensitivity values for each test were plotted for urine and cervical samples.

How were differences between studies investigated?
The authors did not report a method for assessing between-study heterogeneity.

Results of the review
Thirty studies involving approximately 31,000 participants (the participant numbers were not reported for two studies) were included in the review.

Two studies were excluded from the review solely on the basis of a quality score of less than 5.

The meta-analysis showed that DNA-based tests detected more cases of asymptomatic chlamydial infections than conventional non-culture tests. The ORs showed a statistically significantly lower rate of false-negative results with urine LCR (0.33, 95% CI: 0.13, 0.80) and cervix PCR (0.26, 95% CI: 0.12, 0.56) than with the reference standard. The ORs showed no significant differences between the false-negative rates with urine PCR (0.84, 95% CI: 0.37, 1.89), urine gene probe (0.44, 95% CI: 0.15, 1.26), cervix gene probe (1.16, 95% CI: 0.25, 5.47), urine enzyme immunoassay (1.86, 95% CI: 0.39, 8.75) and cervix direct immunofluorescence (1.05, 95% CI: 0.09, 12.93) and the reference standard. The OR revealed a significantly higher rate of false-negative results for cervix enzyme immunoassay than the reference standard (4.10, 95% CI: 1.15, 14.59).

Authors' conclusions
Nucleic acid amplification tests using noninvasive samples such as urine are more effective at detecting asymptomatic chlamydial infection than conventional tests, but there are few data to relate a positive result with clinical outcome.

CRD commentary
This review stated a clear objective. Broad inclusion criteria were generally used, and this approach seems appropriate to the topic. The relevant study population was clearly defined by the inclusion criteria. Several relevant sources were searched for published articles, and experts in the field were contacted to elicit additional information; it is therefore likely that the majority of the available data were identified. Published criteria, appropriate to diagnostic accuracy studies, were used to assess the methodological quality of the included studies and the results were summarised in the article. A minimum threshold summary quality score was used as an inclusion criterion for the review; the inclusion of all relevant studies, with an assessment of the impact of individual components of methodological quality on diagnostic accuracy, might have been a more informative approach. The review methodology was poorly reported, making it impossible to assess the extent to which biases might have been introduced by the review process itself.

The reporting of the tests and reference standards used in the included studies was lacking in detail. Though data were analysed in subgroups according to test and sampling method, no assessment of between-study heterogeneity was
reported. The lack of detail of the included studies and the methods used to pool them makes it difficult to assess the appropriateness of pooling. There was also some inconsistency between the text and figures in terms of the reported study results. The heterogeneity evident in the forest plots casts some doubt on the validity of the approach used. The plot in ROC space showed similar evidence of between-study heterogeneity in pooled subgroups, though the data points were very difficult to distinguish. The authors' conclusions are phrased in definite terms and should be treated with considerable caution given the limitations outlined above. The conclusions refer in part to data relating a positive result with clinical outcome; such data do not appear to form part of the review.

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

**Practice**: The authors stated that, in order to be efficient, a programme of screening for chlamydia must detect as many cases as possible and nucleic acid amplification methods with urine samples are currently the best option.

**Research**: The authors stated that new techniques are constantly being introduced and further reviews will be required as peer-reviewed papers evaluating these are published.

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