Systematic review: noninvasive testing for Chlamydia trachomatis and Neisseria gonorrhoeae

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CRD summary
This review compared the diagnostic accuracy of three nucleic acid amplification tests (using urine samples) for Chlamydia trachomatis and Neisseria gonorrhoeae. The authors concluded that accuracy results in tests for the first condition equate favourably to traditional sampling methods. More research is needed for the second condition. Limitations in the review process mean that the reliability of the authors' conclusions is unclear.

Authors' objectives
To compare the diagnostic accuracy of nucleic acid amplification tests for Chlamydia trachomatis and Neisseria gonorrhoeae in urine specimens according to the type of assay, sample collection site, presence of symptoms, disease prevalence and reference standard characteristics.

Searching
MEDLINE was searched from 1 January 1991 to 31 December 2004; the search terms were reported. In addition, reference lists were checked scanned and relevant journals were handsearched (to January 2005).

Study selection
Study designs of evaluations included in the review
There were no explicit inclusion criteria for the study designs. The designs of the included studies were not reported.

Specific interventions included in the review
Studies comparing polymerase chain reaction (PCR), transcription-mediated amplification (TMA) or strand displacement amplification (SDA) assays with an appropriate reference standard were eligible for inclusion. Studies were included if they compared data from the same assay on both a urine sample and a traditional sample (taken from the cervix or urethra). Non-commercially available tests were excluded, as were data from studies only of urine samples.

Reference standard test against which the new test was compared
To be eligible for inclusion, the reference standard tests had to meet two criteria: the collection of samples had to be from a minimum of 2 anatomic sites (including the cervix in women and the urethra in men), and the test required confirmation by culture or by a least one additional nucleic acid amplification test that differed from the test being evaluated. A wide variety of reference standards (in terms of the number and type of test used, and the number of anatomic sites sampled) were included.

Participants included in the review
There were no specific inclusion criteria for the participants. The included studies comprised symptomatic and asymptomatic men and women, under the age of 30 years, who were seeking evaluation mainly at sexually transmitted disease clinics. The samples originated from North America, Europe, Africa and Australia.

Outcomes assessed in the review
The primary outcome measures used were those relating to test performance (i.e. sensitivity, specificity, and positive and negative likelihood ratios). Studies were only included if they presented outcome data separately according to gender.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
The validity was assessed according to whether the study sample was clearly defined and not known to have the condition; whether the reference standard was clearly defined and applied independently of the index test; whether all the participants were subjected to the same evaluation; and whether the reference standard was clearly defined. The authors did not state how many reviewers performed the validity assessment.

Data extraction
Two authors independently extracted the data from eligible articles. Data on accuracy were collected in order to calculate the sensitivity, specificity, and positive and negative likelihood ratios.

Methods of synthesis
How were the studies combined?
Summary estimates were calculated for the sensitivity and specificity, along with corresponding 95% confidence intervals (CIs), using the random-effects model of DerSimonian and Laird. Separate summary estimates were calculated for each type of assay, while a separate analysis was conducted for noninvasive methods (urine samples) and for traditional methods (from the cervix or urethra).

How were differences between studies investigated?
Statistical heterogeneity between some of the studies was noted, but the methods and results of this analysis were not reported. An additional subgroup analysis was carried out on the PCR test for Chlamydia, in relation to disease prevalence and definition of the reference standard.

Results of the review
Twenty-nine studies were included in the analysis. The overall number of participants was 20,536.

Tests for Chlamydia trachomatis in women.

The pooled sensitivities and specificities of the PCR test (14 studies) were, respectively, 83.3% (95% CI: 77.7, 88.9) and 99.5% (95% CI: 99.3, 99.8) for urine samples and 85.5% (95% CI: 80.3, 90.6) and 99.6% (95% CI: 99.4, 99.8) for cervical samples. The TMA test (4 studies) had pooled sensitivities and specificities of 92.5% (95% CI: 88.0, 97.0) and 98.6% (95% CI: 97.7, 99.6), respectively, for urine samples and 96.7% (95% CI: 93.0, 100) and 99.1% (95% CI: 98.2, 100) for cervical samples. Studies of the SDA test (2 studies) showed pooled sensitivities and specificities of 79.9% (95% CI: 73.3, 86.4) and 99.1% (95% CI: 97.7, 100), respectively, for urine samples and 93.6% (95% CI: 91.2, 96.1) and 97.9% (95% CI: 97.3, 98.5) for cervical samples.

Tests for Chlamydia trachomatis in men.

The pooled sensitivities and specificities of the PCR test (12 studies) were, respectively, 84.0% (95% CI: 78.5, 89.4) and 99.3% (95% CI: 98.9, 99.7) for urine samples and 87.5% (95% CI: 82.4, 92.5) and 99.2% (95% CI: 98.8, 99.6) for urethral samples. From 2 studies of the TMA test, the pooled sensitivities and specificities were 87.7% (95% CI: 80.1, 95.2) and 99.4% (95% CI: 98.7, 100), respectively, for urine samples and 95.9% (95% CI: 91.3, 100) and 99.4% (95% CI: 98.7, 100) for urethral samples. In the only study focusing on the SDA test, the sensitivity and specificity were 93.1% (95% CI: 87.7, 96.7) and 93.8% (95% CI: 90.7, 95.1), respectively, for urine samples and 92.4% (95% CI: 86.8, 96.2) and 96.3% (95% CI: 94.3, 97.8) for urethral samples.

Tests for Neisseria gonorrhoeae in women.

In 4 studies of the PCR test, the pooled sensitivities and specificities were 55.6% (95% CI: 36.3, 74.9) and 98.7% (95% CI: 97.5, 99.9), respectively, for urine samples and 94.2% (95% CI: 90.5, 98.0) and 99.2% (95% CI: 98.4, 100) for cervical samples. In the only study of the TMA test, the sensitivity and specificity were 91.3% (95% CI: 85.0, 95.6) and 99.3% (95% CI: 98.6, 99.6), respectively, for urine samples and 99.2% (95% CI: 95.7, 100) and 98.7% (95% CI: 98.0, 99.3) for cervical samples. In the study of SDA, the sensitivity and specificity were 84.9% (95% CI: 75.6, 91.7) and 99.4% (95% CI: 98.9, 99.8), respectively, for urine samples and 96.5% (95% CI: 90.1, 99.3) and 99.5% (95% CI: 99.0,
Tests for Neisseria gonorrhoeae in men.

Studies of the PCR test (4 studies) showed pooled sensitivities and specificities of 90.4% (95% CI: 87.9, 92.9) and 99.7% (95% CI: 99.4, 100), respectively, for urine samples and 96.1% (95% CI: 94.4, 97.7) and 99.0% (95% CI: 98.2, 99.8) for urethral samples.

The results of the subgroup analysis showed that sensitivity was unchanged with variations in the prevalence of infection or presence of symptoms. However, sensitivity varied according to the reference standard used.

The above results suggested that the sensitivity and specificity of tests for Chlamydia trachomatis conducted on urine samples (i.e. using a noninvasive method) were almost identical to those obtained by traditional invasive techniques. This finding applied to both men and women and did not vary with the presence or absence of clinical symptoms. In women, the diagnostic accuracy of the PCR test for Neisseria gonorrhoeae was significantly lower when the noninvasive technique was adopted. Although no major differences in diagnostic accuracy were observed in the other two tests, the results were obtained only from a single study in each case. The trend for men showed that the two techniques had similar sensitivities and specificities, but more data are needed to draw a conclusion.

Cost information
Some references to cost-effectiveness data were made, although no specific details were supplied.

Authors' conclusions
Nucleic amplification tests for Chlamydia trachomatis on urine samples are of near equal diagnostic accuracy to traditional invasive techniques conducted on cervical or urethral samples. All three of the studied tests can be used for the detection of Neisseria gonorrhoeae, although the sensitivity of the PCR test is not high enough to recommend its routine use with urine samples in women.

CRD commentary
The objective of the review was clearly defined in terms of the interventions under investigation. Although the search strategy was inclusive of all languages, the restriction to one database with no reference to unpublished material meant that relevant studies might have been missed. The design of the included studies was not reported and, although based on published criteria which addressed items relevant to diagnostic tests, the procedure and results for the validity assessment were not supplied. The review also lacked detail on how the studies were selected for inclusion.

Adequate details of the primary studies were reported. However, it was unclear whether the pooling of sensitivities and specificities was appropriate as the heterogeneity tests were not described in full. Given these limitations, the extent to which the authors' conclusions are reliable is unclear.

Implications of the review for practice and research
Practice: The authors stated that noninvasive testing is a potentially effective method for use in non-clinical settings and, given its perceived acceptability over traditional methods, might serve as an effective way to capture a wider population.

Research: The authors stated that more research is needed to make definitive conclusions about urine testing for Neisseria gonorrhoeae in men and women.

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