Rapid point-of-care tests for the detection of genital chlamydia infection

Systematic review of the clinical effectiveness and cost-effectiveness of rapid point-of-care tests for the detection of genital chlamydia infection in women and men

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Executive summary

Health Technology Assessment 2010; Vol. 14: No. 29
DOI: 10.3310/hta14290

Health Technology Assessment
NIHR HTA programme
www.hta.ac.uk

Executive summary

Background

Chlamydia is the most common sexually-transmitted infection in the world. Left untreated, chlamydia can cause epididymitis and urethritis in men, and cervicitis and urethritis in women, as well as potentially creating future fertility problems for women (e.g. ectopic pregnancy, pelvic inflammatory disease and tubal infertility). Yet, 50% of infected men and 70% of infected women do not experience symptoms of the infection.

Throughout the UK, testing for chlamydia involves the use of nucleic acid amplification tests (NAATs). These tests are very accurate, but are laboratory dependent, creating a delay between testing and receipt of diagnosis, caused by the time it takes to transport the test sample to the laboratory and process the result. This delay is problematic, as a number of infected patients will not return for treatment, following their positive diagnosis.

Point-of-care testing methods can provide results within hours after the tests are carried out, which could allow infected patients to be treated immediately, as well as allowing the immediate identification of recent sexual partners who should also be tested. Currently, point-of-care methods are not recommended for use in the NHS because they are less accurate than methods used in current practice, but if new point-of-care tests reported improved accuracy or increased the uptake of testing, they could potentially become an effective alternative to laboratory testing. The Chlamydia Rapid Test (CRT) is a point-of-care test that has reported improved accuracy.

Objectives

The objective of this review was to assess whether or not the CRT could improve detection of genital chlamydia, and whether it is more effective than current practice using NAATs, in terms of the number of cases of chlamydia that are detected and treated, and the proportion of partners identified and treated.

This review also sought to establish the incremental cost-effectiveness of the CRT (compared with current practice), and patients' own preferences for chlamydia testing services.

Methods

Electronic searches were undertaken to identify published and unpublished reports. Electronic databases searched included MEDLINE, EMBASE, BIOSIS and CENTRAL. The most recent search was conducted in November 2008. The types of studies considered were randomised controlled trials (RCTs) for the reviews of diagnostic accuracy and effectiveness, direct head-to-head studies for the review of diagnostic accuracy, and non-randomised comparative studies if there was an insufficient number of RCTs identified for the review of effectiveness. Participants were sexually active adolescent and adult women and men, suspected of having or being tested for genital chlamydia infection. The tests considered were the CRT and other comparator point-of-care tests identified, using a NAAT as a reference standard.

One reviewer screened the titles and abstracts of all reports identified by the search strategy. Two reviewers independently assessed all full-text reports of potentially relevant studies. One reviewer extracted data from the included full-text studies, which were checked by the second reviewer. For the diagnostic accuracy review, two reviewers independently assessed the quality of all included studies using a modified version of the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) instrument. For the effectiveness review, modified checklists adapted from Verhagen and colleagues (1998) were to be used for RCTs and non-randomised studies.

The results of the individual studies were tabulated, and sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratios (DORs) calculated. Hierarchical summary receiver operating characteristic (HSROC) curves were produced for each test where sufficient data for analysis were reported. Meta-analysis models were fitted using HSROC models. Summary sensitivity, specificity, positive and negative likelihood ratios, and DORs for each model were reported as a median and a 95% confidence interval (CI). For

studies reporting effectiveness outcomes, meta-analysis was to be used to estimate a summary measure of effect, with dichotomous outcome data combined using relative risk using a fixed effect model in the absence of statistical heterogeneity.

A review of the preferences of patients was also conducted and was confined to studies that had reported willingness to pay or reported preferences between different relevant screening test regimens. Only economic measures of preference based on population values were considered, as such data would be most useful for priority setting. Only two studies were identified. A discrete choice experiment suggested that family planning clinics were preferred as a facility for screening, and less invasive techniques were favoured.

For cost-effectiveness analysis, a simple decision model was used to show that patients attend different screening facilities and are faced with the choice of accepting or not accepting the test offer and providing the sample for the test. Most who attend accept the offer, and a small proportion of those who do attend would not be able to provide the sample required and remain unscreened. The prevalence rate has been used to determine the proportion of those tested who are expected to have chlamydia. The sensitivity and specificity of the tests that are being compared identify the proportion of the patients correctly or incorrectly identified in the model. It is assumed that a significant proportion of positive cases and their partners are treated. Effectiveness was measured in terms of the absolute numbers of true-positives, false-positives, false-negatives (and other positive cases missed) and true-negatives detected. Costs were considered from the health service's perspective. Incremental cost-effectiveness ratios were used to examine the relative cost-effectiveness, and values of the major parameters of the models were varied in a sensitivity analysis.

Results

Thirteen studies enrolling 8817 participants were included in the analysis. In the pooled estimates for the CRT, two studies compared five separate sets of vaginal swab specimens, and a further two studies compared four sets of first void urine (FVU) specimens. The sensitivity (95% CI) of the CRT was 80% (73% to 85%) for vaginal swab specimens and 77% (59% to 89%) for FVU specimens. Specificity was 99% (99% to 100%) for vaginal swab specimens and 99% (98% to 99%) for FVU specimens.

In the pooled estimates for a comparator point-of-care test (Clearview Chlamydia), four studies compared eight separate sets of vaginal, cervical and urethral specimens. For cervical specimens alone, there were four sets of specimens from the four studies. The sensitivity (95% CI) was 52% (39% to 65%) for vaginal, cervical and urethral swab specimens combined, and 64% (47% to 77%) for cervical specimens alone. Specificity was 97% (94% to 100%) for vaginal, cervical and urethral swab specimens combined, and 97% (88% to 99%) for cervical specimens alone.

No studies were identified comparing non-diagnostic clinical effectiveness outcomes for point-of-care tests compared with NAATs, for example the number of cases detected and treated, and the number of partners contacted and treated.

The results of the economic evaluation showed that for a hypothetical cohort of 1000 people, using the current practice of polymerase chain reaction testing would result in 12.63 people who were offered testing being correctly treated and having their sexual partners contacted, at a cost of £7070 (for the whole cohort). For the CRT, the number being correctly treated would be 10.98, at a cost of £7180. For the Clearview Chlamydia test, the number correctly treated would be 7.14, at a cost of £7170. Both point-of-care tests were therefore more costly and less effective than current practice.

An increase in uptake rates, improvement in diagnostic performance and reductions in cost would all potentially make the CRT worthwhile, but it is unclear whether changes of sufficient magnitude are feasible.

Patient preferences indicated that those being tested preferred for treatment to be provided in a family planning clinic setting, preferred less invasive methods of specimen collection (e.g. FVU), and preferred having a trained health-care advisor present for support. If services accommodate these preferences as far as possible, there is potentially an opportunity to increase uptake rates for testing.

Discussion

There was insufficient evidence to suggest that the CRT could improve detection of genital chlamydia infection compared with current practice, as there were insufficient comparisons available to allow robust conclusions to be drawn from the analysis. In addition, as no comparative studies were

identified reporting non-diagnostic outcomes, it was not possible to conduct the review of clinical effectiveness to determine whether the CRT could detect and treat more people than methods currently in use. Current practice was found to be less costly and more effective, although there were circumstances under which point-of-care testing could become a viable alternative (i.e. if uptake rates for testing were increased using this point-of-care method). Patients' preferences for the provision of chlamydia services favoured non-invasive testing methods, provided in a family planning setting. Robust evidence on patient preferences for point-of-care testing was not available, although where reported in the diagnostic accuracy studies, participants found these tests to be very acceptable.

Conclusions

The limited evidence available suggests that NAATs are still the most accurate and cost-effective method for diagnosing chlamydia infection. There may be circumstances in which point-of-care tests could be provided in addition to existing NAAT services (e.g. where this might increase uptake rates or reduce non-return rates for treatment), but there is currently little evidence on point-of-care methods in such settings. Research on this would be useful, along with research on the acceptability of point-of-care testing. Robust evidence of the diagnostic accuracy of point-of-care tests for different types of samples is also still required, as are studies comparing clinical effectiveness outcomes for these tests in comparison with NAATs.

Publication

Hislop J, Quayyum Z, Flett G, Boachie C, Fraser C, Mowatt G. Systematic review of the clinical effectiveness and cost-effectiveness of rapid point-of-care tests for the detection of genital chlamydia infection in women and men. *Health Technol Assess* 2010;**14**(29).

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The Health Technology Assessment (HTA) programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA programme then commissions the research by competitive tender.

Second, the HTA programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this issue of the journal was commissioned by the HTA programme as project number 08/54/01. The contractual start date was in December 2008. The draft report began editorial review in April 2009 and was accepted for publication in August 2009. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA programme or the Department of Health.

ISSN 1366-5278

Published by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk), on behalf of NETSCC, HTA.

Printed on acid-free paper in the UK by Henry Ling Ltd, The Dorset Press, Dorchester.