Testing for *Chlamydia trachomatis*: is more choice a good thing?

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Background

Chlamydia trachomatis (chlamydia) is the most common bacterial sexually transmitted infection (STI). Its incidence in the UK has risen steadily since the mid-1990s, with new diagnoses rising by 1% from 121 791 to 123 018 (from 197 to 199 per 100 000 population) between 2007 and 2008.[1] Generally the rates of chlamydia infections in other Western European countries are lower than those in the UK. Young people aged under 25 years are most likely to be infected, with 65% (80 258) of all new chlamydia diagnoses in the UK in 2008 in individuals between the ages of 16 and 24 years.[2] The incidence of re-infection among women is estimated to be 15–30% at 1 year.[3 4] Repeated infection is associated with an increased risk of complications including infertility.[5 6]

In 2003, the English Department of Health launched the National Chlamydia Screening Programme (NCSP), overseen by the Health Protection Agency. Since the NCSP's launch it has cost an estimated £100 million.[7] The NCSP enables young people (<25 years) to access screening for chlamydia in a variety of community settings including general practitioner surgeries, and sexual health and genitourinary medicine (GUM) clinics. There have also been high-profile education campaigns targeted at younger age groups, and STIs are now discussed in school-based sex education programmes.[8]

Concurrently, there has been an increase in the number of rapid, self- and point of care tests (POCTs) for many conditions including chlamydia. However, these are not yet part of routine UK health service practice in the diagnosis and management of chlamydia. This is mainly because laboratory-based nucleic acid amplification tests (NAATs) are still the most sensitive and specific tests available and the NCSP stipulates that chlamydia screening must be carried out using NAATs.[9]

Point of care testing

POCTs are tests where both sampling and analysis take place in a clinical or non-clinical setting (e.g. at home) and the result is available without reference to a laboratory. The most common technique used for POCTs for infections is an immunochromatographic test for the presence of a specific microbial antigen in the patient sample. These tests are largely based on the enzyme-linked immunosorbent assay (ELISA) principle and a positive diagnosis can be signified by a colour change, making them easy to read by non-specialist staff. Table 1 provides a summary of the advantages and disadvantages of STI POCTs.[10–12]

Compared with NAATs, where sensitivities and specificities of around 96–99% are expected, those reported for POCTs are often inferior, with sensitivities in the range of 50–60%.[10 13] In spite of this there may be public health benefits of using 'suboptimal' POCTs to enable rapid diagnosis and treatment of chlamydia in patients who have a large number of sexual partners, where there is a notable risk of onward transmission.[11] Vickerman *et al.*, for example, calculated that a gonorrhoea POCT kit would only need 47% sensitivity to show a health benefit among sex workers.[14]

Other commentators have suggested that tests with a lower accuracy can also play an important part in populations where there is a marked risk of people being lost to follow-up and at risk of not receiving treatment. Another important factor is the initial time taken by those at risk of STIs to access services; the longer the wait, the greater the potential utility of a POCT even if it does have a lower sensitivity than the reference standard NAAT.[11] However, although there are clear advantages of being able to diagnose and treat in a single visit, it does not follow that all POCTs will be beneficial. If

Table 1 Potential advantages and disadvantages of sexually transmitted infection (STI) point of care testing (POCT) strategies[10–12]

Advantages	Disadvantages
Earlier diagnosis and treatment implementation leading to improved clinical outcomes	Performance claims: limitations, validation, evaluation in the hands of users, reliability and device failure
Greater patient convenience and involvement	Specimens: appropriate sample collection, need for sample preparation prior to testing
Smaller sample and reagent volumes, may be less invasive	Quality assurance and control: adequate training, tests performed by staff from a non-analytical background
Easier access to service for those with limited mobility and for those who live in more remote areas with limited access to laboratory facilities	Operator-dependent steps: Interpretation of instructions Inappropriate, insufficient or contaminated sample Use of test outside its specification Use of damaged, inappropriately stored or out-of-date reagents Incorrect interpretation of results Lack of awareness of limitations or interferences
Elimination of specimen transportation reducing time and costs	Incompatibility with laboratory results: reference ranges and results may differ, making comparisons difficult or absent
Economic benefits with reduced number of clinic visits, reduced length of hospital stay and fewer admissions	Greater availability may encourage inappropriate or unnecessary testing
Potential for earlier diagnosis may avoid some of the costs associated with undiagnosed infections	Patient anxiety: Absence of expert explanation and discussion Misinterpretation of the meaning of positive and negative results Psychological impact
Economic benefits could accrue with over-the-counter tests, allowing part of the financial burden of diagnosing STIs to be shifted from the public to the private purse for those who choose to buy a self-test	Cost: Initial purchase Site alterations Training Maintenance Waste disposal

a clinic uses a POCT that has low sensitivity, more patients with infections will be falsely reassured by a negative test result, which could increase the number of people subsequently exposed to infection. Alternatively, if a POCT with low specificity is used it will result in a high number of false-positive results. This could lead to administration of antibiotics to people without infections, potentially increasing the rates of antibiotic resistance and hypersensitivity. False-positive test results can also be psychologically detrimental to patients.[15]

Self-testing

Self-tests for STIs involve self-collection of the sample, which is sent to a laboratory for testing. These self-tests, sold in pharmacies or via the Internet, have the benefits of privacy and convenience.[16] The increased availability of such tests and their reporting systems has led to concerns over regulation standards, reliability, sparse product information and the lack of support for people who receive a positive result.[11 13 17]

Despite these concerns, the fear and stigma associated with STIs are considered important barriers to accessing local STI health services. Self- or over-the-counter tests, if well regulated and associated with good monitoring or treatment systems, may be able to contribute to reduced transmission. A good example of a self-testing strategy is the Clamelle® chlamydia test kit (developed by Actavis UK Ltd), a NAAT that can be purchased from pharmacies or the Internet. A urine sample is posted to the laboratory, with the result returned by post or obtained from the pharmacy. If a confirmed positive test is received and treatment is deemed appropriate, a sexual health consultation with the pharmacist is recommended and azithromycin 500 mg tablets supplied. This service is run jointly by Actavis UK Ltd, the National Pharmacy Association and the Gordon Laboratory Group, a private laboratory that undertakes the testing, manages the test results and the customer database.[18]

The introduction of the NCSP has also led to collaboration between some primary care trusts in England, Brook Advisory Centres and Test.me Integrated Diagnostics (the trading name of Preventx Limited) to provide a free chlamydia testing service called freetest.me. The free test kits are NAAT PCR tests, using either urine or self-taken vaginal swab samples. Visitors to the website (http://freetest.me.uk) within the participating region are offered free tests, while those outside are offered links to free local health services.[19]

New and emerging POCTs for chlamydia

During the period January to July 2009, the National Horizon Scanning Centre (http://www.haps.bham.ac.uk/publichealth/horizon/) conducted a review to identify new and emerging POCTs for a range of STIs (including chlamydia) that are intended to provide

results significantly more reliably and/or rapidly than current available options (unpublished data).

The central strategy of the review was to identify companies active in the development of POCTs and obtain information from the company of any relevant products. Five new and emerging POCTs for chlamydia were identified, all based on the immunochromatography method. Time to results ranged from 10 to 60 minutes. Samples included urine, cervical, vaginal and urethral (male) swabs. Three additional multi-tests were identified including a PCR-based biochip multiplex test (for gonorrhoea, chlamydia, herpes and trichomoniasis) that uses urine as a sample, with results in 4 hours; and two combination tests for gonorrhoea and chlamydia: (i) a nucleic acid test that uses urine or swabs and (ii) a fully automated system performing sample processing, DNA extraction and reverse transcription PCR. The time to results for these tests was 30–45 minutes.

The majority of companies contacted did not or were not able to provide clinical validity and utility data, which meant that any assessment of potential impact of these POCTs was limited. Our expert Advisory Group did, however, feel that the time to results for these POCTs may be too slow to be of practical use, as the patient contact time in primary care would have passed. One of the tests identified, the *Chlamydia* Rapid Test™ [Diagnostics for the Real World (Europe) UK, Cambridge, UK], was considered as the best chlamydia POCT recently available, with reported sensitivities and specificities of 83.5% and 98.9%, respectively.[20]

Final thoughts

The emergence of POCT for chlamydia as a viable option should be welcomed by many in primary care, family planning and GUM clinics, and there is little doubt that there is now a wide variety of choice when it comes to chlamydia testing in England. However, more choice is not necessarily wholly beneficial, particularly if the test accuracy does not meet (or exceed) the current reference standard NAAT. In an ideal world, every sexually active person would be regularly and comprehensively screened for all STIs at an adequately resourced, local health care facility. Sadly, however, this is not currently possible. The NCSP is aiming to improve the situation and raise awareness, but POCT programmes based in non-health care settings need to consider how to deliver further testing, counselling and contact tracing for those with positive tests. Additionally, as more self-tests and POCTs become commercially available and the sexual health landscape becomes more complex, it is increasingly clear that stricter regulation is required to protect consumers from substandard tests and to ensure treatment is accessible and effectiveness monitored. In 2010, the UK Parliamentary Public Accounts Committee, in a damning indictment of progress in the delivery of the NCSP, called on the Department of Health to establish national or regional arrangements for the procurement of testing kits, as well as a mechanism to measure the NCSP's impact on the level of infection.[7] The NCSP has not yet reached the coverage when models predicted that the community prevalence of chlamydia will be significantly reduced and, as a result, potential savings to the National Health Service (NHS) have not been realised. More importantly, young people continue to be unnecessarily exposed to infection.

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