

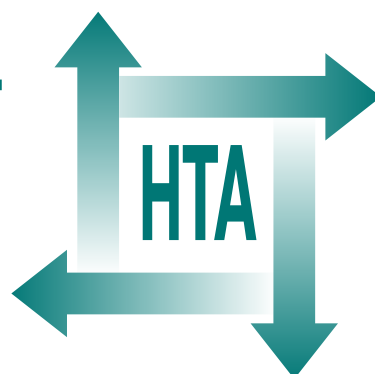
# **Systematic review of the clinical effectiveness and cost-effectiveness of rapid point-of-care tests for the detection of genital chlamydia infection in women and men**

J Hislop, Z Quayyum, G Flett,  
C Boachie, C Fraser and G Mowatt



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# 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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## Abstract

### 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

J Hislop,<sup>1\*</sup> Z Quayyum,<sup>2</sup> G Flett,<sup>3</sup> C Boachie,<sup>1</sup> C Fraser<sup>1</sup> and G Mowatt<sup>1</sup>

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**Objective:** To assess whether or not the Chlamydia Rapid Test (CRT) could improve detection of genital chlamydia, and whether it is more effective than current practice using nucleic acid amplification tests (NAATs), in terms of the number of cases of chlamydia that are detected and treated and the proportion of partners identified and treated.

**Data sources:** Eleven electronic bibliographic databases (including MEDLINE and EMBASE) were searched until November 2008, as well as relevant websites.

**Review methods:** Studies of sexually active adolescent and adult women and men suspected of having or being tested for genital chlamydia infection were considered. The tests considered were the CRT and other comparator point-of-care tests identified, using a NAAT as a reference standard. Summary sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratios for each model were reported as a median and a 95% confidence interval (CI). 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, sensitivity (95% CI) was 80% (73% to 85%) for vaginal swab specimens and 77% (59% to 89%) for first void urine (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), 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. 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.

**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, but there is currently little evidence on point-of-care methods in such settings. Robust evidence of the diagnostic accuracy of point-of-care tests for different types of samples is also still required, as are studies evaluating clinical effectiveness outcomes for these tests in comparison with NAATs.





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## List of abbreviations

CI	confidence interval	PCR	polymerase chain reaction
CRT	Chlamydia Rapid Test	PID	pelvic inflammatory disease
DCE	discrete choice experiment	POCT	point-of-care test
DFA	direct fluorescent antibody	QUADAS	Quality Assessment of Diagnostic Accuracy Studies
DOR	diagnostic odds ratio	RCT	randomised controlled trial
FVU	first void urine	RR	relative risk
GATE	Generic Appraisal Tool for Epidemiology	SDA	strand displacement amplification
GUM	genito-urinary medicine	SIGN	Scottish Intercollegiate Guidelines Network
HIV	human immunodeficiency virus	SROC	summary receiver operating characteristic
HSROC	hierarchical summary receiver operating characteristic	STI	sexually transmitted infection
ICER	incremental cost-effectiveness ratio	TMA	transcription-mediated amplification
LCR	ligase chain reaction	WMD	weighted mean difference
NAAT	nucleic acid amplification test	WTP	willingness to pay
NCSP	National Chlamydia Screening Programme		

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

### Note

Some of the point-of-care tests referenced in this report are now obsolete and it has not been possible to verify their trademark. The trademark symbols are used at first mention only for current tests for which they can be verified.





## 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.



# Chapter I

## Background

### Description of health problem

#### Introduction

Chlamydia is the most common bacterial sexually transmitted infection (STI) in the world.<sup>1</sup> In 1999, it was estimated that there were almost 92 million new infections of genital chlamydia among adults worldwide.<sup>2</sup>

Within the UK, in 2006, there were 112,473 chlamydia diagnoses made in England and Wales, and a further 17,962 made in Scotland.<sup>3</sup> Chlamydia accounts for 30% of all new STI diagnoses made in UK genito-urinary medicine (GUM) clinics<sup>3</sup> and yet it is easily treated with a single oral dose of azithromycin.<sup>4</sup>

#### Incidence, prevalence and infection epidemiology

Targeted testing, monitoring of prevalence and reaching particular risk groups are all key to ensuring effective chlamydia testing for a population. The collection of data relating to chlamydia is most robust around the specialist GUM clinics, laboratories and the National Chlamydia Screening Programme (NCSP). Data from primary care and community venues are limited, particularly for those aged over 25 years. Previous population-based studies indicate a prevalence of 2–6% for both men and women aged between 15 and 24 years old,<sup>5</sup> although some estimate prevalence to be higher<sup>6,7</sup> and recent data suggest that it could be greater than 10% among those aged between 18 and 25 years old.<sup>8</sup>

The number of cases of chlamydia diagnosed has increased markedly over recent years, but in part this may be explained by an increase in the number of tests carried out. The introduction of more sensitive nucleic acid amplification tests (NAATs) to diagnose chlamydia has also been a major contributory factor. The number and variety of testing venues have also increased to improve access to testing and, in England and Wales in 2006, 27% of all chlamydia infections were diagnosed outside a GUM clinic setting.<sup>3</sup> In

Scotland the proportion diagnosed in non-GUM clinic settings is higher (53%).<sup>9</sup>

There are still differences in the characteristics of the groups being diagnosed. For example, the ratio of new diagnoses in women compared with men is 1.6:1 in England and Wales.<sup>3</sup> The ratio in Scotland is similar (1.7:1).<sup>10</sup>

Also, with regard to age, the focus of chlamydia testing should be directed towards young people under 25 years of age (as is current practice within the NCSP), as it is recognised that young people are at most risk of chlamydia infection through a combination of their risk-taking behaviour<sup>11</sup> and biological susceptibility to infection.<sup>12</sup> There is therefore an ongoing challenge to increase testing rates among those aged less than 25 years. People below 25 years account for 12% of the total population, but accounted for 65% of all chlamydia diagnoses made in GUM clinics in 2007.<sup>13</sup>

The available diagnostic data on chlamydia also show clear geographical variation in infection rates<sup>3,8</sup> as well as variation by ethnic group (with the highest positive rates among mixed race or Black-Caribbean populations, and the lowest rates among Asian populations).<sup>3,8,13</sup>

#### Aetiology, pathology and the impact of the health problem

The natural history of chlamydia infection and the frequency of reproductive tract complications is not known.<sup>14–16</sup> This knowledge gap exists (and is unlikely to be resolved) because long-term follow-up of untreated chlamydia infection would be unethical, and diagnosed infections that are treated alter the natural history of the infection.

The sexually transmitted strains of the bacterium *Chlamydia trachomatis* (strains D–K) cause cervicitis and urethritis in women and urethritis in men, and can also cause rectal and pharyngeal infections, as well as having the potential to be transmitted in labour, causing pneumonia and eye infections in neonates.<sup>4</sup> There is clear recognition that untreated infection ascending the reproductive

tract is influenced by immunological factors and can cause tubal damage predisposing to ectopic pregnancy, tubal infertility and chronic pelvic pain.<sup>15</sup> Ascending infection in males may cause epididymitis, but the effect on future fertility is less clear.<sup>14,16</sup> This report does not consider the strains that cause the tropical STI lymphogranuloma venereum that have been responsible for outbreaks of ulcerative proctitis mainly in men who have sex with men.<sup>17</sup>

Genital tract infection with chlamydia often remains asymptomatic in at least 70% of women and 50% of men.<sup>18</sup> Current thinking is that the majority of infections clear spontaneously without any associated significant morbidity. Around 50% of infections resolve within 1 year.<sup>19</sup> Resolved infection is not thought to confer a lasting immunity, so re-infection remains a possibility.<sup>20,21</sup> Worryingly, as with other STIs, chlamydia can facilitate human immunodeficiency virus (HIV) transmission.<sup>22</sup>

Very early studies based on clinic populations considered that 30% of untreated chlamydia infections would lead to acute pelvic inflammatory disease (PID) within weeks and that complications of chlamydia infection were common, particularly in women.<sup>23</sup> More recent research suggests that the complication rate is much lower than previously believed.<sup>15</sup> There now exists uncertainty regarding the prognosis for any positive chlamydia test, but it is established that previous probability estimates for long-term sequelae associated with chlamydia infection were too high. Currently, there is significant debate about the frequency of upper reproductive tract complications following lower genital tract infection with chlamydia.<sup>14-16</sup> It should be noted, however, that most of this research has been conducted in specialist GUM clinic and hospital populations and has therefore been affected by selection bias.<sup>24</sup> Furthermore, the sound and objective diagnosis of PID is notoriously difficult.<sup>25</sup> It is also difficult to be certain that any subsequent sequelae can be directly attributed to chlamydia, particularly where time has elapsed from a diagnosis or acute infection.

Early studies suggested that the complications associated with chlamydia were common, particularly in women.<sup>23</sup> However, despite dramatic increases in the number of chlamydia tests and diagnoses, there has been no accompanying rise in PID. In fact, the number of hospital admissions for PID has fallen by 43% [figures calculated using the *International Statistical Classification of Diseases and Related Health Problems*, 10th revision

(ICD-10) codes N70–N73 inclusive] over the last decade, from 19,367 in 1998/9 to 13,502 in 2007/8.<sup>26</sup> Most PID diagnoses will be made in primary care, but the reported incidence of PID is falling in primary care settings also.<sup>3</sup> However, it is important to note that regardless of any previous overestimates of the impact of chlamydia infection, it still remains a significant cause of morbidity for women of reproductive age and has significant resource implications for health-care provision and planning.

Little is known about the psychosocial impact of a diagnosis of chlamydia infection, but there is some evidence to suggest that it creates considerable anxiety, particularly with regard to possible stigmatisation, the need to inform sexual partners of possible infection, and the risk of infertility.<sup>27,28</sup>

## Significance for the NHS

The impact of the health problem caused by chlamydia is considerable. Undiagnosed and untreated chlamydia infection is a serious public health concern, with the potential for those infected and untreated to further spread the infection, including possibly re-infecting previously treated cases.

The health-care services costs related to chlamydia include the cost of screening and the cost of treating chlamydia or complications arising from chlamydia infection described above. The complications can be grouped into female, neonatal and male sequelae.<sup>29</sup> The female sequelae include PIDs, chronic pelvic pain, ectopic pregnancy and infertility. Neonatal sequelae are conjunctivitis and pneumonia, and the male sequelae are epididymitis and urethritis. In the UK, the costs of complications of *Chlamydia trachomatis* in women were estimated as at least £50M annually in the late 1990s.<sup>30</sup> The total cost burden of chlamydia to UK health services was estimated to exceed £100M in 2002 prices.<sup>29</sup>

## Current service provision

### Management of infection

Chlamydia screening programmes operate in some countries, for example, Sweden, the USA and Canada. England introduced a NCSP in 2003<sup>31</sup> and Northern Ireland plans to introduce a similar system (the Chlamydia Testing Programme in Northern Ireland; CTPNI) in the near future. Scotland and Wales currently do not have



screening programmes in place, although targeted opportunistic testing is provided in a varied and increasing number of settings. The screening and opportunistic programmes both share an aim to reduce morbidity in individuals and achieve longer term infection control through a sustained reduction in the onward transmission of infections.

Chlamydia testing itself currently uses NAAT methods, which are laboratory dependant and therefore have an inherent processing delay between testing and advising the health provider of a positive result. Test results must be relayed to the patient tested in order for treatment and partner notification (and partner treatment) to take place. Management of confirmed chlamydia infection requires appropriate antimicrobial treatment, partner notification advice and abstinence from sexual intercourse until both the patient and any current partner(s) have been treated.

All the drug treatments available to treat chlamydia showed a cure rate of more than 90%.<sup>4</sup> It is well recognised that compliance is better with a single oral dose, and therefore azithromycin as an oral 1-g stat dose is the first choice for treating uncomplicated infection.<sup>18,32</sup> There are other regimes extending over 7 days, using ofloxacin, minocycline, lymecycline and doxycycline. Erythromycin is another alternative, but is less well tolerated and therefore has a greater likelihood of non-completion of treatment.<sup>33</sup>

Partner notification and treatment is essential to reducing re-infection rates, as the highest prevalence of chlamydia infection occurs in the partners of patients with diagnosed chlamydia infection. However, partner notification has inherent difficulties and there is evidence that it reaches only 50–60% of partners.<sup>34</sup> Indeed, in 2007/8 in England and Wales, of the 18,497 partners reported to NCSP venues, 11,596 (63%) were contacted and 7533 (40.7% of those originally reported) were eventually treated.<sup>8</sup> Current clinical recommendations are that for symptomatic patients, all partners from the 4 weeks prior to the onset of symptoms should be contacted. For asymptomatic patients, it is suggested that all partners over the preceding 6 months or the most recent sexual partner outside that time frame should be contacted.<sup>4</sup> Within the NCSP, there are additional targets to verify at least 0.6 partners per index case as treated (except within London where the standard is 0.4 partners), but recent indications suggest a decline in the proportion of programme areas achieving this rate, and it has been noted that future monitoring is required.<sup>8</sup> The latest

Scottish Intercollegiate Guidelines Network (SIGN) guideline on chlamydia also includes a key recommendation for more active management and follow-up of positive cases and contacts.<sup>18</sup>

In terms of preventing re-infection, there is only limited evidence regarding the effectiveness of follow-up and the role of test of cure (where a repeat test is carried out to confirm the absence of the infection). Routine test of cure is recommended in pregnancy and where non-compliance or re-exposure is suspected (although this should not be done using a NAAT until after 5 weeks of initiation of therapy to avoid a false-positive result due to the persistence of non-viable chlamydia organisms).<sup>4</sup>

In limiting re-infection, there is accumulating evidence that, after partners of index cases, the next highest prevalence of chlamydia is caused by the re-infection of treated index cases. One study has shown re-infection rates of between 21.1 and 29.9 per 100 people treated, depending on the original treatment setting.<sup>35</sup> It is therefore recommended that testing for re-infection be conducted at between 6 and 12 months after initial treatment.<sup>18</sup>

A follow-up interview can also serve to ensure adherence to treatment, confirm avoidance of risk of the exposure to infection and maximise the opportunity to contact all sexual partners. The success rate for partner notification has been shown in one UK study of 200 GUM clinic attendees to have significantly improved from 0.46 to 0.66 contacts per index case after specific follow-up was introduced ( $p = 0.005$ ).<sup>36</sup>

### Current service cost

Different health services' cost estimates for the UK have been reported in three recent studies.<sup>29,37,38</sup> Estimates are provided on the average costs of acute chlamydia infections and complications associated with chlamydia (*Table 1*). These cost estimates vary owing to assumptions made about the resources used. Adams and colleagues<sup>37</sup> based their estimates on the Department of Health 2004 reference costs.<sup>39</sup>

It should also be noted that aside from the index patient costs included in the table, there are also the additional costs of partner notification and treatment. It has been estimated that the average health service cost of partner notification for each index case is £11.72, and for treatment would be £32.55 at 2003 prices.<sup>34</sup>

**TABLE 1** Estimated average costs (£) of treatment of chlamydia infections and consequent illnesses

Conditions	Estimated costs (and standard deviation) at 2004 prices (£) <sup>37</sup>	Estimated unit costs at 2001 prices (£) <sup>29</sup>	Estimated unit costs at 2005 prices (£) <sup>38</sup>
Symptomatically infected and seeking treatment (men)	64 (6)		
Symptomatically infected and seeking treatment (women)	61 (5)		
Screened and treated for those infected (men and women)	31 (2)		
PIDs	137 (46)	190	3014 (HRG costs) <sup>a</sup>
Epididymitis	142 (67)	15	790
Chronic pelvic pain	–	111	
Ectopic pregnancy	762 (329)	2530	2456 (HRG costs)
Tubal factor infertility	10,798 (4279)		
Infertility	–	4540	453 (NICE guideline)
Neonatal conjunctivitis	41 (4)	8	
Neonatal pneumonia	612 (555)	303	
Neonatal complications			749 (HRG costs)

HRG, Healthcare Resource Group; NICE, National Institute for Health and Clinical Excellence; PIDs, pelvic inflammatory diseases.  
 a This cost relates to PID managed at hospitals, whilst the other two relate to the community level management.

### Variation in services and/or uncertainty about best practice

Nucleic acid amplification tests are undoubtedly the most sensitive and specific, and therefore most accurate, tests for use in practice. They have replaced the older less reliable assays, including culture and antigen detection. The high sensitivity of these tests means that specimens can be taken non-invasively, e.g. as a urine sample or from vaginal (or other) secretions. It should be noted that all NAATs currently available for use perform very well diagnostically, although there are some differences between them.<sup>40</sup> In terms of the type of NAAT method used, polymerase chain reaction (PCR) was the laboratory method used for 160,683 (48.3%) of the 332,403 chlamydia tests conducted in the NCSP in 2007/8. A further 95,966 (28.9%) were conducted using strand displacement amplification (SDA), 68,027 (20.5%) were conducted using transcription-mediated amplification (TMA), and the method for the remaining 7727 tests (2.3%) was predominantly reported as being unknown.<sup>8</sup>

These tests, although diagnostically excellent, are expensive, and the need for separate laboratory testing necessitates a return visit for treatment following a positive diagnosis. The delay causes inherent difficulties in contacting patients once

the diagnosis has been made, as well as difficulties for partner notification, and it is these latter steps that are critical to reducing the pool of infection. Therefore, there are clear advantages to developing immediate near-patient technologies for testing chlamydia, as theoretically they could have public health advantages and be more cost-effective than current practice. However, in practice, point-of-care enzyme immunoassays are not currently recommended on account of their reduced sensitivity in comparison with NAAT methods. The immediacy of a result for any new point-of-care tests (POCTs) would have to be balanced against the proportion of false-negative results (and the need for full NAAT screening for test-negative individuals would need to be determined), but finding an effective, reliable and low-cost near-patient test that gives an immediate result remains attractive to health-care providers and policy-makers.

### Relevant national guidelines, including national service frameworks

Current guidelines on the management of chlamydia infection are available from the British Association of Sexual Health and HIV.<sup>4</sup> In addition, the NCSP publishes a set of core requirements,

as standards required to be met by all screening venues performing chlamydia testing in England.<sup>32</sup> Both guidelines tend to provide uniform advice on chlamydia management, as does the SIGN guideline on the management of chlamydia infection, which was updated in March 2009.<sup>18</sup>

More information on chlamydia infection can be found in the national strategic policy work undertaken for sexual health. National sexual health policy in England is set out within the *National Strategy for Sexual Health and HIV*,<sup>41</sup> which is currently in the process of being reviewed.<sup>42</sup> Scotland has had its own national strategy and action plan in place since 2005,<sup>43</sup> and NHS Quality Improvement Scotland has also developed a set of national standards for the treatment of STIs in Scotland<sup>44</sup> (although HIV standards are taken to be equivalent to those available from the British HIV Association);<sup>45</sup> Wales<sup>46</sup> and Northern Ireland<sup>47</sup> also have their own sexual health strategies.

## Description of the technologies under assessment

### Summary of interventions

As noted above, POCTs are attractive to health-care providers and policy-makers because of their potential to deliver an immediate result, creating an opportunity for immediate treatment and discussion of partner notification and thereby reducing the pool of infection. Given the poor

sensitivity of current POCTs, for a POCT to become part of the current care pathway for testing chlamydia infection, it would have to show enhanced sensitivity, or otherwise be used only in situations where those with negative results would be retested using a NAAT method to confirm the result.

The length of treatment required for a POCT is measurable in hours, although follow-up may be required if confirmatory laboratory testing using a NAAT method is required, and this could take several days/weeks. The tests could be undertaken in the same settings as current practice, but there is the potential to expand the number of chlamydia testing venues using POCTs, as little equipment is required. Trained personnel would be needed to administer the test, provide the result, treatment and advice, and administer contact tracing to allow partner notification.

### Identification of important subgroups

Regardless of the test used, the most important subgroup with regard to chlamydia infection is those aged under 25 years, as this population is disproportionately affected by the infection.

### Current usage in the NHS

Some POCTs may not be available currently. Others may be available to buy, but it is unlikely that they are sold to the NHS, as their use is not recommended under current guidelines.



# Chapter 2

## Definition of the decision problem

### Decision problem

As described in Chapter 1, Introduction, genital chlamydia is the most common bacterial STI in the world. It creates a significant health burden for the NHS with regard to testing and treatment. However, left untreated, the health burden is potentially even greater, as the infection can cause PID, ectopic pregnancy and infertility in women and epididymo-orchitis and reactive arthritis in men.<sup>48</sup>

Current practice in detecting chlamydia involves analysing specimens in a laboratory setting, using NAATs. The delay in processing results caused by the need to send them to a laboratory for analysis means that there is the potential for positively diagnosed patients not to return for treatment and contact tracing of previous partners, as individuals receiving their test results at a later date have to make a return visit for treatment to be initiated and contacts identified.<sup>49</sup> POCTs may have lower sensitivity than the NAAT methods of current practice, but as their use would allow positively diagnosed patients to have treatment initiated during the same session in which testing was carried out, the proportion of positive cases receiving treatment would increase. Therefore, even with reduced sensitivity, POCTs could still potentially lead to the treatment of more infected people than is the case at present.

In addition, new POCTs may report improved levels of sensitivity which could make them viable alternatives to laboratory methods. One such test is the Chlamydia Rapid Test (CRT), a POCT developed by the Diagnostics Development Unit at the University of Cambridge, UK.<sup>50</sup> Whether this test represents an efficient, reliable and cost-effective alternative to current laboratory diagnosis of genital chlamydia is unclear.

### Key issues

The key issues to be addressed were:

- Can the CRT improve detection of genital chlamydia?
- Is the CRT more effective than current practice for testing and diagnosing genital chlamydia infection in terms of (i) the number of cases detected and treated, and (ii) the proportion of partners identified and treated?
- What is the incremental cost-effectiveness ratio (ICER) of the CRT (compared with current practice) for the testing and diagnosis of genital chlamydia infection?
- What are patients' own preferences with regard to chlamydia testing services?

### Care pathways

To address the above key economic issues, a care pathway was developed. The first point on this pathway is attendance at different facilities where testing is available. Patients are then faced with the choice of accepting or not accepting the offer of a test, and providing the sample for the test. It is likely that not all will accept the offer and a small proportion of those who do will be unable to provide the sample required, or the sample may not be properly collected. The group that does not accept the offer and those who cannot provide the sample will have a terminal stage in the pathway and would remain untested. The prevalence rate will be used to determine the proportion of those tested who are expected to have genital chlamydia. The sensitivity and specificity of the tests that are being compared will identify the proportion of the patients correctly or incorrectly identified. It is assumed that positive cases and any partners are treated.

## Overall aims and objectives

The aim of this review was to assess the clinical effectiveness and cost-effectiveness of the CRT, a POCT for detecting genital chlamydia infection.

The aim was addressed through:

- A systematic review of the accuracy of the CRT in the diagnosis of genital *Chlamydia trachomatis* infection.
- A systematic review of the effectiveness of the CRT in terms of the number of infected individuals diagnosed and treated.
- A systematic review of patient preferences for the organisation and outcomes of chlamydia testing services.

- Economic modelling of the cost-effectiveness of the CRT.

The specific objectives of the review were to:

- Assess the performance of the CRT in the detection of genital chlamydia infection.
- Assess the effectiveness of the CRT in identifying cases of chlamydia infection (and cases resulting in treatment), compared with current practice.
- Estimate the ICER of the CRT compared with current practice for the testing, diagnosis and treatment of genital chlamydia infection.
- Assess patients' own preferences for chlamydia testing services.

## Chapter 3

# Methods for reviewing diagnostic accuracy and clinical effectiveness

### Identification of studies

Studies were identified by searching electronic databases and relevant websites, contact with experts in the field and the scrutiny of bibliographies of retrieved papers. Highly sensitive electronic searches were conducted to identify reports of published and ongoing studies on POCTs for chlamydia. A preliminary search that included only terms related to the tests produced a small set of records, therefore no restrictions in terms of study type or publication date were used subsequently, although the results were restricted to articles written in English. The databases searched were: MEDLINE (1966 to week 3 November 2008), MEDLINE In-Process (26 November 2008), EMBASE (1980 to week 48 2008), BIOSIS (1985 to 27 November 2008), Science Citation Index (1970 to 22 November 2008), ISI Conference Proceedings (1990 to 22 November 2008), Health Management Information Consortium (October 2008) and Cochrane Controlled Trials Register (The Cochrane Library, Issue 4, 2008), as well as current research registers, Current Controlled Trials (November 2008), Clinical Trials (November 2008), CRISP (November 2008) and World Health Organization International Clinical Trials Registry (November 2008). Additional databases searched for systematic reviews and other background information included the Cochrane Database of Systematic Reviews (The Cochrane Library, Issue 4, 2008), Database of Abstracts of Reviews of Effects (November 2008) and Health Technology Assessment Database (November 2008). Recent conference proceedings were also searched. Full details of the search strategies used and websites consulted are documented in Appendix 1.

A total of 235 reports were identified (see *Table 2*). In addition, the details of 13 potentially relevant ongoing studies were noted. Reference lists of all included studies were scanned to identify additional potentially relevant studies.

### Inclusion and exclusion criteria

The types of studies considered for reporting diagnostic accuracy were:

- Randomised controlled trials (RCTs) in which people were randomised to the index and comparator test(s) and all received the reference standard test.
- Direct (head-to-head) studies in which the same group of people received the index test and/or any other comparator POCT(s), and all received the reference standard test.

In the event that there was insufficient evidence from direct or randomised studies, we considered undertaking indirect (between-study) comparisons by meta-analysing studies that compared the index test (or the identified and relevant comparators) with the reference standard test, and making comparisons between meta-analyses of the different tests. However, we were aware that this type of study design is less reliable than direct studies, as differences in diagnostic accuracy are susceptible to confounding factors between studies. Studies reporting test performance had to report the absolute numbers of true-positives, false-positives, false-negatives and true-negatives, or provide information allowing their calculation.

For assessing the CRT in terms of effectiveness outcomes, we decided to focus on RCTs unless they provided insufficient evidence, in which case we agreed to consider non-randomised comparative studies.

The participants considered for both the reviews of effectiveness and diagnostic accuracy were sexually active adolescent and adult men and women suspected of, or being tested for, genital chlamydia infection. If sufficient evidence was available, subgroup analysis was planned for high-risk participants, defined as those aged under 25 years.

TABLE 2 Search results

Database	Number retrieved
<b>Primary reports</b>	
MEDLINE (1966 to week 3 November 2008)/EMBASE (1980 to week 48 2008)/ MEDLINE In-Process (26 November 2008) multifile search (after deduplication in Ovid)	111
Science Citation Index (1970 to 22 November 2008)	77 <sup>a</sup>
BIOSIS (1985 27 November 2008)	19 <sup>a</sup>
CENTRAL (Cochrane Library, Issue 4, 2008)	4 <sup>a</sup>
Health Management Information Consortium (October 2008)	0 <sup>a</sup>
ISI Conference Proceedings (1990 to 22 November 2008)	4
Recent conference proceedings	3
Total	218
<b>Background</b>	
CDSR (The Cochrane Library, Issue 4 2008)	14
DARE (November 2008)	2
HTA Database (November 2008)	1
Total	17
<b>Total assessed for review</b>	<b>235</b>
<b>Ongoing studies</b>	
Controlled Clinical Trial	3
Clinical Trials	5
CRISP	5
WHO International Clinical Trials Registry	0
Total	13
CDSR, Cochrane Database of Systematic Reviews; CRISP, Computer Retrieval of Information on Scientific Projects; DARE, Database of Abstracts of Reviews of Effects; HMIC, Health Management Information Consortium; HTA, Health Technology Assessment; ISI, Intelligence and Security Informatics; WHO, World Health Organization.	
a The numbers retrieved from the searches in Science Citation Index, BIOSIS, HMIC and CENTRAL refer to the additional reports found after excluding those identified from the MEDLINE/EMBASE multifile search.	

The index test considered for both the reviews of effectiveness and diagnostic accuracy was the CRT, a new 'rapid' POCT developed by the Diagnostics Development Unit at the University of Cambridge for the detection of genital chlamydia infection.

For the review of diagnostic accuracy, the reference standard test(s) considered were NAATs, including PCR, TMA, SDA and ligase chain reaction (LCR). Comparator tests considered were:

- non-POCTs (i.e. NAATs), which is equivalent to a comparison with any of the reference standard test(s) mentioned above
- other alternative rapid POCTs identified for the diagnosis of genital chlamydia infection.

For the review of effectiveness, the comparator(s) considered were tests used in current practice.

The following outcomes were considered for the review of diagnostic accuracy:

- sensitivity (the proportion of those infected who have positive test results)
- specificity (the proportion of those not infected who have negative test results)
- positive predictive value (the proportion of those with positive test results who are infected)
- negative predictive value (proportion of those with negative test results who are not infected)
- positive likelihood ratio (how many times an infected person is more likely to receive a positive test result)



- negative likelihood ratios (how many times an infected person is more likely to receive a negative test result)
- diagnostic odds ratios (DORs; the ratio of the odds of testing positive in those with infection relative to the odds of testing positive in those without infection)
- acceptability of the tests
- interpretability of the tests.

The following outcomes were considered for the review of effectiveness:

- numbers of chlamydia cases detected
- the number of infections diagnosed that are treated (including return/non-return rates for treatment in different settings and locations throughout the UK, following diagnosis using non-POCTs)
- the proportion of partners identified and treated
- acceptability of the tests
- interpretability of the tests.

The following types of report were excluded from both the reviews of effectiveness and diagnostic accuracy:

- studies published in languages other than English
- narrative reviews, editorials, letters and opinions
- animal models
- preclinical and biological studies
- case reports
- abstracts published before 2006
- reports investigating the technical aspects of a test.

## Data extraction strategy

Citations identified by the search strategy were screened by one reviewer on the basis of title and, where available, the abstract. Full-text copies of all studies deemed to be potentially relevant were obtained, and two reviewers independently assessed them for inclusion, using a full-text screening form that had been developed and piloted. Any disagreements were resolved by consensus or arbitration by a third party. Reviewers were not blinded to authors, institutions or publications. Where there was insufficient information in the published report, no attempt was made to contact the authors for clarification, owing to time constraints.

Data extraction forms were developed and piloted. One reviewer extracted details of study design, participants, tests used and outcome data, and a second reviewer checked the data extraction. Any disagreements were resolved by consensus or arbitration by a third party.

## Quality assessment strategy

Two reviewers independently assessed the quality of both the included full text and published diagnostic studies using QUADAS (Quality Assessment of Diagnostic Accuracy Studies), a quality assessment tool developed for use in systematic reviews of diagnostic studies.<sup>51</sup> QUADAS was developed through a formal consensus method and was based on empirical evidence. The original QUADAS checklist contained 14 questions. The QUADAS tool was adapted to make it more applicable to assessing the quality of studies of tests for detecting genital chlamydia infection (see Appendix 3 for an example of the modified checklist). Abstracts were not quality assessed because it was felt unlikely that they would provide sufficient information about their methods to allow for quality assessment.

Questions 1, 3–7 and 10–14 of the original checklist were retained (questions 1–11 in the modified version). Three questions in the original QUADAS tool that related to the quality of reporting rather than methodological quality were omitted from the modified version (questions 2, 8 and 9). These questions related to the description of (a) the selection criteria, (b) the execution of the index test and (c) the execution of the reference standard. Two questions were added to the modified checklist on (a) whether data on observer variation were reported and within an acceptable range and (b) whether data were presented on the subgroup of interest in this review, those under 25 years of age.

For the review of effectiveness, the intention was to assess the study quality of RCTs using a Delphi criteria list adapted from Verhagen and colleagues.<sup>52</sup> In the event that there was insufficient evidence from RCTs and a subsequent need to assess the quality of non-randomised comparative studies, it was intended to use a separate checklist to assess study quality. The checklist was adapted from several sources, including the Centre for Reviews and Dissemination's guidance for those carrying out or commissioning reviews,<sup>53</sup> Verhagen

and colleagues,<sup>52</sup> Downs and Black<sup>54</sup> and the Generic Appraisal Tool for Epidemiology (GATE).

It was intended that two reviewers would independently assess the quality of all included full-text studies for the reviews of effectiveness and diagnostic accuracy. Each question would be checked 'Yes', 'No' or 'Unclear' (with space for comments), and each item was worded so that a rating of 'Yes' was always optimal in terms of methodological quality. Any disagreements would be resolved by consensus or arbitration by a third party.

## Data analysis

For diagnostic accuracy, the results of the individual studies were tabulated and the outcomes described in Inclusion and exclusion criteria were calculated.

There are a number of different methods available for meta-analysis of diagnostic studies that allow for between-study variability. Two methods are generally accepted as the most rigorous: the hierarchical summary receiver operating characteristics (HSROCs) model<sup>55</sup> and bivariate random-effects meta-analysis.<sup>56,57</sup> The HSROC model approach was considered appropriate for this analysis.<sup>58</sup> HSROC curves were produced for each test where three or more studies reported sufficient data. Meta-analysis models were to be fitted using the HSROC model<sup>59</sup> in SAS version 9.1 using the NLMIXED function (SAS Institute Inc., Cary, NC, USA). This HSROC model takes account of the infected and non-infected sample sizes in each study, and allows estimation of random effects for the threshold and accuracy effects.<sup>55,59</sup> The summary receiver operating characteristic (SROC) curves from the HSROC models were produced and are shown on the corresponding SROC plots

along with the individual study estimates. Summary sensitivity, specificity, positive and negative likelihood ratios and DORs for each model were reported as median and 95% confidence intervals (CIs).

Sensitivity and specificity were pooled using the weighted average method,<sup>60</sup> where there was no evidence of a threshold effect. Pooled likelihood ratios and DORs were calculated using the DerSimonian and Laird random effects method.<sup>61</sup> Where a study had an empty cell, a correction of 0.5 was added to all four cells. These analyses were carried out using META-DISC software.<sup>62</sup> Heterogeneity was assessed using the  $I^2$  statistic, which describes the percentage of variability in effect estimates that is due to heterogeneity rather than sampling error. A value greater than 50% was considered to represent substantial heterogeneity.<sup>63</sup>

For the review of effectiveness, where appropriate, it was intended that meta-analysis be used to estimate a summary measure of effect for relevant outcomes. Dichotomous outcome data were to be combined using the Mantel–Haenszel relative risk (RR) method, and any continuous outcomes were to be combined using the inverse-variance weighted mean difference (WMD) method. For the estimates of RR and WMD it was planned to calculate 95% CIs and  $p$ -values, and report results using a fixed effect model. Statistical heterogeneity across studies was to be explored using chi-squared and  $I^2$  statistics, and possible reasons for heterogeneity explored using sensitivity analysis. If no obvious reasons for heterogeneity were found, it was planned to explore the implications using random effects methods. Where a quantitative synthesis was considered inappropriate or not feasible, the intention was to provide a narrative synthesis of results.

# Chapter 4

## Results of diagnostic accuracy and effectiveness

### Quantity and quality of research available

#### Number of studies identified

From the electronic searches for primary reports, 235 records were selected as possibly relevant to the reviews of diagnostic accuracy and clinical effectiveness. Following the screening of titles and abstracts, 118 of the 235 records were not considered further. The full-text reports of the remaining 117 records were obtained and assessed. Eleven met the inclusion criteria for this review, 82 were excluded and 24 were retained for background information. The main reasons for exclusion can be found in *Table 3*. Of the 11 studies that met our inclusion criteria, all met the inclusion criteria for the review of diagnostic accuracy. *Figure 1* shows a flow diagram outlining the screening process, with reasons for exclusion of full-text papers.

#### Number and type of studies included

Appendix 4 lists the 11 studies identified by the search strategy that were included in the reviews of diagnostic accuracy and effectiveness. All of these studies<sup>50,64-72</sup> met the inclusion criteria for reporting the diagnostic accuracy of POCTs, of which 10 were

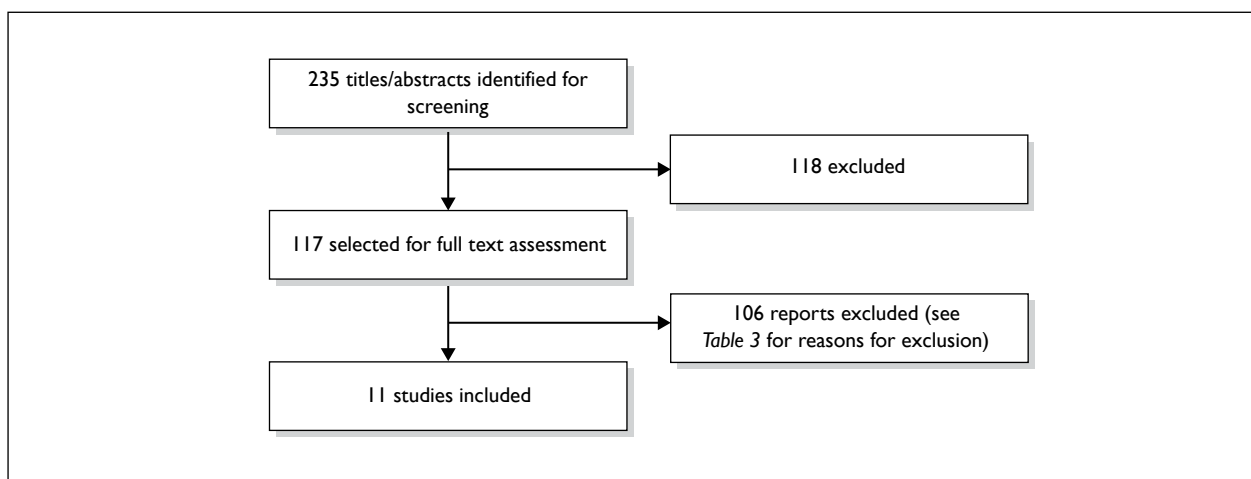
full-text papers<sup>50,64-72</sup> and one<sup>73</sup> was a conference abstract.

Three studies reported results for the CRT against a NAAT (PCR),<sup>50,65,72</sup> and a further eight reported results<sup>64,66-71,73</sup> for other POCTs, either still available on the market (as confirmed by their respective manufacturers) or possibly still available on the market (where no confirmation had been received from the manufacturer regarding whether or not the test was still available). In addition, reports of two unpublished studies were provided for this review by the Diagnostics Development Unit at the University of Cambridge, under the condition that they be treated as academic-in-confidence. Both have since been published.<sup>74,75</sup>

We did not identify any RCTs that assessed the effectiveness of POCTs compared with current practice, and therefore decided to include non-randomised comparative studies. No additional studies assessing the effectiveness of point-of-care testing compared with current practice were found.

#### Number and type of studies excluded

A list of the 82 potentially relevant studies identified by the search strategy but which



**FIGURE 1** Flow diagram outlining the screening process for the reviews of diagnostic accuracy and effectiveness.

**TABLE 3** Main reasons for exclusion of studies from reviews of diagnostic accuracy and effectiveness

Reason	Number of papers excluded from diagnostic accuracy review on this basis	Number of papers excluded from review of effectiveness on this basis
Not a diagnostic accuracy study/not a comparative study	13	25
Pre-2006 abstracts	12	12
NAAT not used/NAAT not used as reference standard	6	10
Uses an obsolete POCT	5	5
No POCT used	3	13
Not a study on chlamydia	2	3
POCT cannot distinguish between chlamydia and other infections	1	1
Not all participants received both tests	2	1
Not a study on genital chlamydia	1	1
Animal study	1	1
No outcomes of relevance/pre-specified outcomes not reported	3	3
<b>TOTAL EXCLUDED</b>	<b>49</b>	<b>75</b>
Of which were duplicates (i.e. assessed for both reviews) <sup>a</sup>	42	42
Of which were not duplicates (i.e. assessed for only one of the two reviews) <sup>a</sup>	7	33
<b>TOTAL INCLUDED</b>	<b>11</b>	<b>11</b>
<b>TOTAL ASSESSED FOR EACH REVIEW<sup>b</sup></b>	<b>60</b>	<b>86</b>

a The sum of the total number of duplicates (42) plus the number of studies excluded from only the diagnostic accuracy review (7) plus the number of studies excluded from only the review of effectiveness (33) totals the number of studies excluded (82).

b This is the sum of those in the 'TOTAL EXCLUDED' row and the 'TOTAL INCLUDED' row.

subsequently failed to meet the inclusion criteria is given in Appendix 5. These studies were excluded because they failed to meet one or more of the inclusion criteria in terms of the types of study, participants, test, reference standard or outcomes reported. Forty-two of the excluded studies had been screened and excluded from both reviews, whilst the remaining 40 had been screened only for either the diagnostic accuracy review or the effectiveness review.

### Characteristics of included studies

Appendix 6 shows the characteristics of the individual included studies. *Table 4* shows summary information for the 13 studies reporting diagnostic accuracy outcomes.<sup>50,64-75</sup>

Nine studies<sup>50,64,65,68-70,72,74,75</sup> involving 5914 participants provided details of when they took

place, with an earliest start date of September 1996 and a latest end date of May 2008. However, it should be noted that one study<sup>71</sup> was published before the earliest specified start date, although it did not actually report details of when the study took place.

Six studies, involving a total of 3788 participants took place in the UK,<sup>50,67,68,72,73,75</sup> two studies (involving 2282 participants) took place in the Philippines,<sup>65,74</sup> and one study each took place in Canada (involving 128 participants),<sup>69</sup> the Netherlands (involving 1007 participants),<sup>71</sup> the USA (involving 65 participants),<sup>70</sup> Egypt (involving 50 participants)<sup>64</sup> and China (involving 1497 participants).<sup>66</sup>

All 13 studies reported testing venues, and six studies<sup>50,65-67,74,75</sup> involving 4996 participants were held at multiple venues. Of the six UK-based studies, four studies (involving 1642 participants)

**TABLE 4** Summary information for studies included in the review of diagnostic accuracy

Characteristic	Number	Number of studies
<b>Patients</b>		
Enrolled	8904	13
Analysed	8717	
<b>Sex</b>		
Men	2156 (24.7%)	13
Women	6561 (75.3%)	
<b>Age<sup>a</sup></b>		
Median age	25.8 years	4
Age range	15–56 years	5
Not reported	–	7
<b>Symptomatic of STD infection<sup>b</sup></b>		
Shows symptoms	2104 (24.1%)	6
Asymptomatic	1701 (19.5%)	
Not reported	4912 (56.4%)	9
<b>NAAT used<sup>c</sup></b>		
PCR	8029	8
SDA	737	2
TMA	65	1
LCR	588	3
<b>Point-of-care test used<sup>c</sup></b>		
Chlamydia Rapid Test	4223	4
Clearview Chlamydia	3956	7
Chlamydia Wand/HandiLab C	331	2
QuickVue	199	1
Magic Lite Chlamydia	1007	1
SureCell Chlamydia	128	1
<b>Type of specimen used for POCT<sup>c</sup></b>		
Vaginal swab (self-collected)	2282	3
Vaginal swab (clinician-collected)	3094	4
Cervical/endocervical swab	4533	7
Urethral swab	283	1
First void urine (routine cup collection)	790	2
First void urine (using 'FirstBurst')	1745	2

STD, sexually transmitted disease.

a Six studies reported data on age, but two did not report an average figure, and another did not report a range. One reported a range in the form of age brackets only, but this was translated into a range.

b Two of the six studies reporting data on symptoms provided only this for a subset of the study population, so the remaining part of the study population is included in the 'Not reported' row.

c Some studies used more than one NAAT and/or point-of-care test and/or specimen type, and so the sum of the number of participants and studies does not equal the number of participants or studies included in the review.

included testing in at least one GUM clinic,<sup>50,67,73,75</sup> whilst three (involving 1651 participants) included a Young People's Sexual Health Centre venue.<sup>50,72,75</sup> In addition, one study (involving 395 participants) used a British Pregnancy Advisory Service Clinic,<sup>68</sup> and another (involving 100 participants) included a hospital gynaecology department venue.<sup>67</sup>

All studies reported the gender of participants. Nine studies (involving 5937 participants)<sup>50,64–68,70,73,74</sup> had exclusively female populations, whilst a further three studies (involving 1873 participants)<sup>69,72,75</sup> comprised only male participants. Therefore only one study<sup>71</sup> investigated the diagnostic accuracy of point of care testing in both genders.

In six studies providing information on patient age, four (involving 6008 participants) reported a mean or median age,<sup>50,65,66,75</sup> four (involving 4561 participants) reported specific age ranges<sup>50,64,65,75</sup> and one study (involving 395 participants)<sup>68</sup> reported the number of participants falling into different age bands (six age bands, each comprising 5 years starting at ages 15–19 years). Of the ranges reported (including the Hopwood study), participants were aged between 15 and 56 years. It should also be noted that although the age of participants was not explicitly specified in two further studies, one (involving 65 participants) had been conducted within campus venues at a university,<sup>70</sup> and the other (involving 534 participants) had been undertaken at a venue used specifically for young people under the age of 25 years, and participants had been at least 16 years of age or older.<sup>72</sup>

In six studies<sup>50,64–66,70,75</sup> reporting whether participants had symptoms or not, 3805 participants were included in the analysis, of whom 2104 (55.3%) had symptoms (including all 50 patients in one study who had been diagnosed with PID).<sup>64</sup>

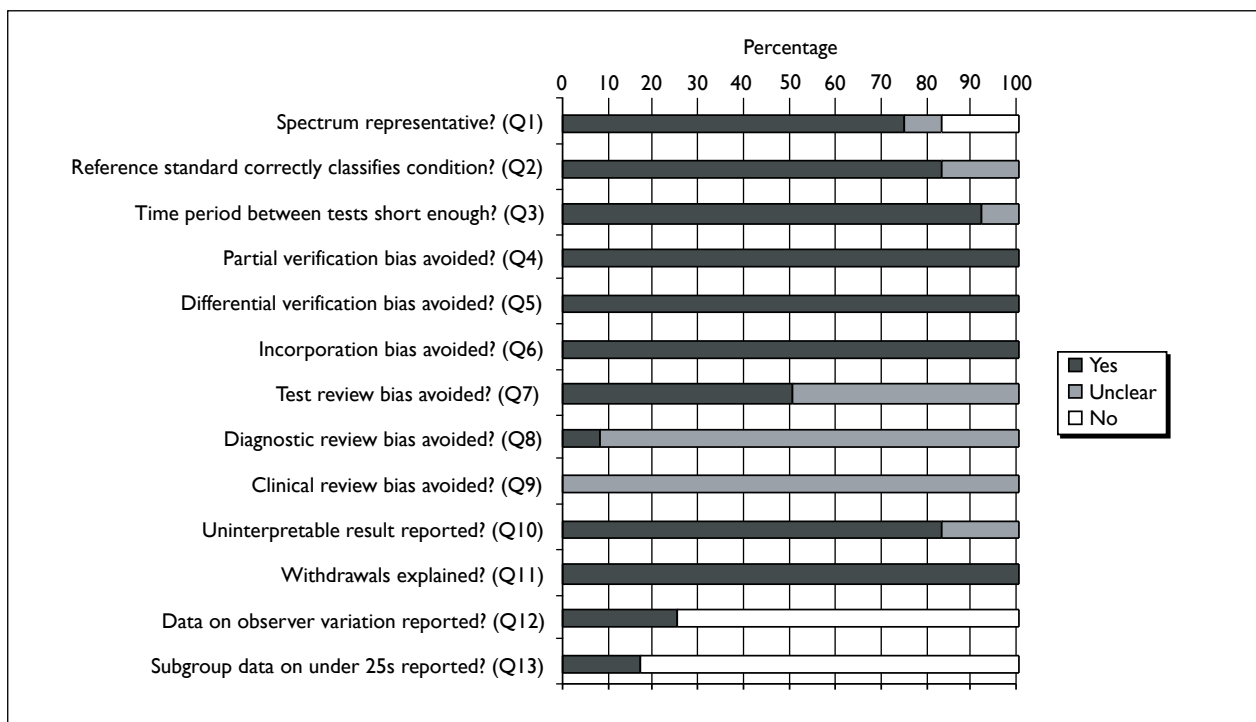
Three of the 13 studies (involving 1873 participants) used only first void urine (FVU) samples,<sup>69,72,75</sup> two (involving 431 participants) used only vaginal swab samples,<sup>73,74</sup> whilst four (involving 709 participants) used only endocervical samples.<sup>64,67,68,70</sup> A further three studies (involving 4797 participants)<sup>50,65,66</sup> collected endocervical and vaginal specimens, and one study (involving 1007 participants) collected endocervical and urethral specimens.<sup>71</sup>

Eight of the 13 studies (involving 6760 participants)<sup>64–67,71,72,74,75</sup> used PCR as the reference standard NAAT. In addition, one study (involving 1349 participants) used PCR as the reference standard but also reported data for 637 participants using SDA as the reference standard.<sup>50</sup> One study (with 100 participants) used SDA as the only reference standard.<sup>73</sup> The remaining three studies (involving 588 participants) used LCR as the reference standard test, although one (with 65 participants) also used a TMA test<sup>70</sup> and another study with 128 participants used the LCR method with additional confirmation using a direct fluorescent antibody (DFA) test.<sup>69</sup>

## Quality of the included studies

*Figure 2* summarises the quality assessment for the 12 full-text published diagnostic studies.<sup>50,64–72</sup> The results of the quality assessment of the individual studies are shown in Appendix 7.

The diagnostic studies were assessed using a modified version of the QUADAS tool containing 13 questions. In 75% (9/12) of studies the spectrum of patients who received the tests was considered to be representative of those who would receive the test in practice (question 1). For this question we considered patients to be representative if the patient population was women and/or men suspected of having or being tested for genital chlamydia. Specific population subsets (e.g. pregnant women) were not considered to be representative. In the study by Chernesky and colleagues<sup>69</sup> it was unclear whether the patient spectrum was representative, and in the studies by Hopwood and colleagues<sup>68</sup> and Shaarawy and colleagues<sup>64</sup> it was considered not to be representative. In 83.3% (10/12) of studies the reference standard NAAT was considered likely to classify correctly genital chlamydia (question 2). This was considered to be unclear in the studies by Chernesky and colleagues<sup>69</sup> and Hopwood and colleagues.<sup>68</sup> These two studies used the Abbott LCx (Abbott Laboratories, Abbott Park, IL, USA) for LCR NAAT, which was withdrawn from the market in 2002 because of reproducibility problems.<sup>76</sup> In 91.7% (11/12) of studies the time period between the POCT and reference standard was considered to be short enough to be reasonably sure that the target condition had not changed between the tests (question 3), whilst this was unclear in the study by Shaarawy and colleagues.<sup>64</sup>



**FIGURE 2** Summary of quality assessment of chlamydia diagnostic studies.

In all studies, partial verification bias was avoided as all patients who received a POCT also received a reference standard test (question 4); differential verification bias was avoided as all patients received the same reference standard (a NAAT) regardless of the index test result (question 5); and incorporation bias was avoided as the reference standard test was independent of the POCT index test (question 6). In 50% (6/12) of studies,<sup>50,65,66,70,74,75</sup> test review bias was avoided as the POCT results were interpreted without knowledge of the results of the reference standard test, whilst in the remaining six studies this was unclear (question 7). In the study by Saison and colleagues,<sup>65</sup> diagnostic review bias was avoided as the reference standard results were interpreted without knowledge of the results of the index test, whilst in the remaining 11 studies this was unclear (question 8).

In all 12 studies it was unclear whether the same clinical data were available when the POCT results were interpreted as would be available when the test was used in practice (question 9). In this context, clinical data were defined broadly to include any information relating to the patient such as age, gender, presence and severity of symptoms, and other test results. In 83.3% (10/12) of studies, either uninterpretable or intermediate test results were reported or there were none, whilst in the remaining two studies<sup>64,65</sup> this was unclear

(question 10). In all studies either withdrawals from the study were explained or there were none (question 11). In 75% (9/12) of studies, data on observer variation were not reported (question 12), the exceptions being the studies by Mahilum-Tapay and colleagues,<sup>50</sup> Nadala and colleagues<sup>75</sup> and Yin and colleagues.<sup>66</sup> Two of the 12 studies (16.7%), Mahilum-Tapay and colleagues<sup>50</sup> and Nadala and colleagues,<sup>75</sup> presented data on the specific subgroup of interest in the review, which was those under 25 years of age (question 13), as one of the venues used in both studies was a Young People's Sexual Health Centre, treating only those aged under 25 years old.

## Assessment of diagnostic accuracy

### Overview

This section reports the diagnostic accuracy of POCTs compared with a reference standard of nucleic acid amplification testing. Specimen level analysis was undertaken instead of patient level analysis, as several of the included studies conducted analysis at specimen level. Figures are included showing the sensitivity and specificity of the individual studies, SROC curves and pooled estimates with 95% CIs for sensitivity, specificity, positive and negative likelihood ratios and DORs



for each POCT for which pooled analysis could be undertaken. Results were pooled only where there were four or more studies comparing the same technique. Owing to the low number of studies, STATA's (StataCorp, College Station, TX, USA) Metandi procedure was used for the analysis instead of SAS NLMIXED, as stated in the original protocol. Metandi requires a minimum of four sets of specimens. Individual study results are given in Appendix 8.

In addition, information on the acceptability of the tests is provided in *Table 5*.

### Chlamydia Rapid Test

Two studies (involving 2478 participants) compared the accuracy of the CRT with a NAAT [PCR using the Roche AMPLICOR CT/NG Test (Hoffman-La Roche AG, Basel, Switzerland)] for detecting genital chlamydia in five sets of vaginal swab specimens.<sup>50,65</sup> This provided sufficient information to allow their inclusion in the pooled estimates for specimen level analysis. Of the five sets of vaginal swab specimens, three sets (two from the study by Saison and colleagues, and one from the study by Mahilum-Tapay and colleagues) were clinician-collected, whilst the remaining two sets from one study<sup>50</sup> were self-collected specimens taken from patients at two different testing venues (a social hygiene clinic for female sex workers, and an obstetrics and gynaecology clinic mostly attended by women for antenatal care).

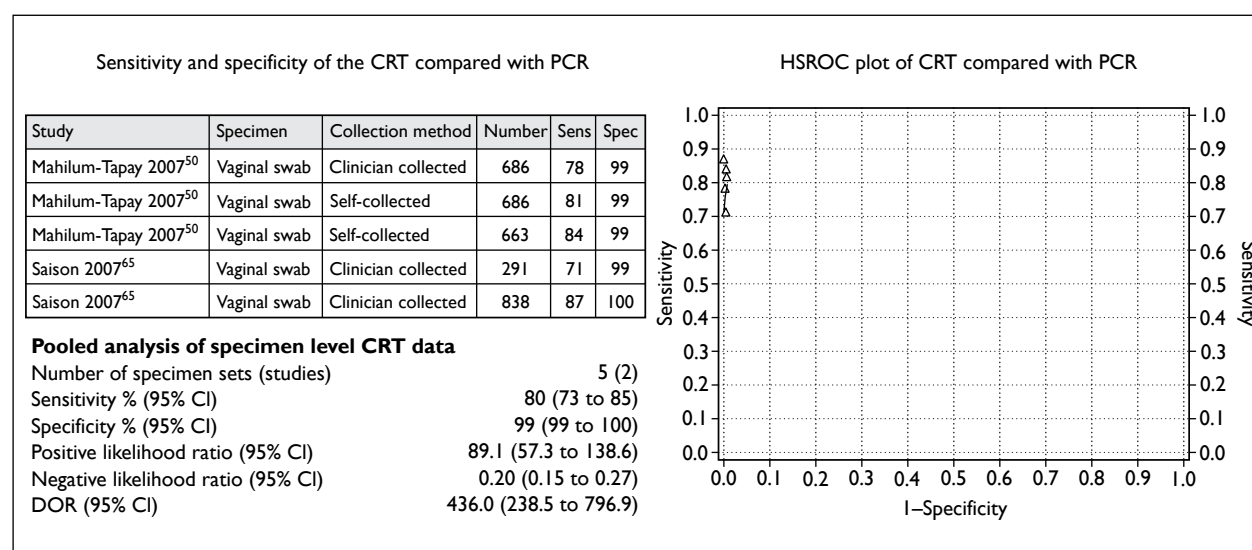
*Figure 3* shows the sensitivity and specificity of the individual studies, SROC curves and pooled

estimates for the sensitivity and specificity of the CRT for detecting genital chlamydia infection in vaginal swab specimens. The pooled sensitivity (95% CI) for the CRT was 80% (73% to 85%), whilst the pooled specificity (95% CI) was 99% (99% to 100%). The DOR (95% CI) was 436.0 (238.5 to 796.9).

Two studies (involving 1745 participants) compared the CRT with a NAAT (PCR using the Roche AMPLICOR CT/NG Test) for detecting genital chlamydia, using four sets of FVU specimens.<sup>72,75</sup> This provided sufficient information to allow their inclusion in the pooled estimates for specimen level analysis. Of the four sets of FVU specimens, three sets (two from Nadala and colleagues' 2009 study<sup>75</sup> and one from Wisniewski and colleagues' 2008 study)<sup>72</sup> used the 'FirstBurst' method of collection whilst the remaining set (from the study by Wisniewski and colleagues) used routine cup collection of urine.

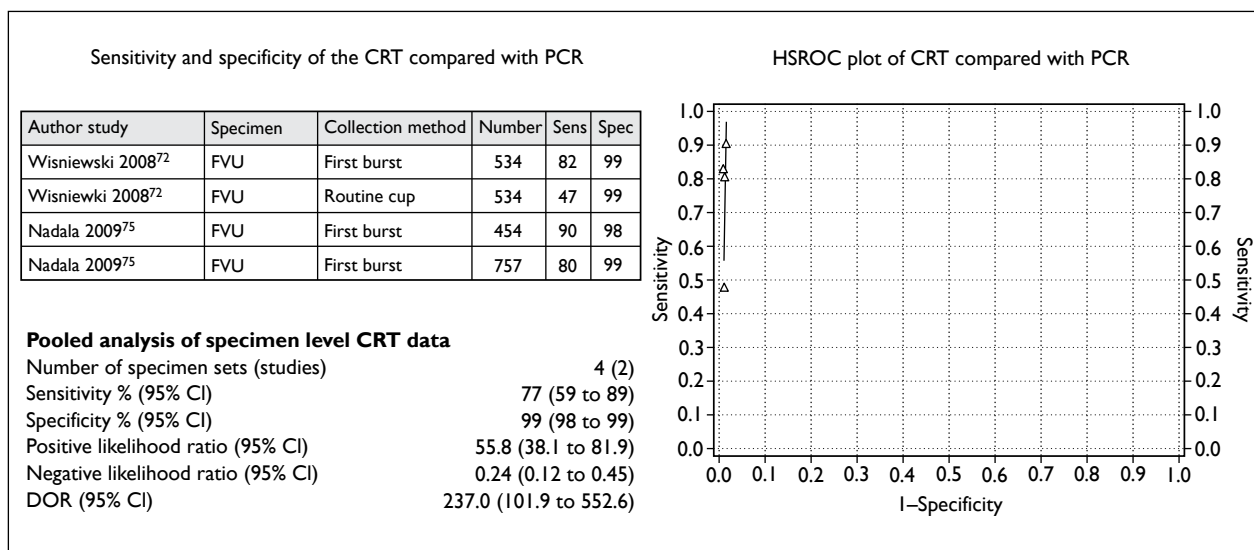
*Figure 4* shows the sensitivity and specificity for the individual studies, SROC curves and pooled estimates for the sensitivity and specificity of the CRT for the detection of genital chlamydia infection in FVU specimens. The pooled sensitivity (95% CI) for the CRT was 77% (59% to 89%), whilst the pooled specificity (95% CI) was 99% (98% to 99%). The DOR (95% CI) was 237.0 (101.9 to 552.6).

In addition to the specimens discussed above, there was one additional set of specimens from 637 participants in one study<sup>50</sup> comparing the CRT with a NAAT method. As this NAAT method was



**FIGURE 3** The Chlamydia Rapid Test (vaginal swab specimens): sensitivity, specificity, HSROC plot and pooled estimates.





**FIGURE 4** The Chlamydia Rapid Test (FVU specimens): sensitivity, specificity, HSROC plot and pooled estimates.

SDA and not PCR (as used for all other specimen sets), it was not possible to pool estimates of diagnostic accuracy for this particular comparison. Data from the study itself show that the specimens were compared using the two tests. For the POCT, the specimens were self-collected vaginal swabs taken by women attending two GUM clinics in the UK, compared with clinician collected endocervical specimens for SDA analysis. The sensitivity (95% CI) of the CRT compared with SDA was 81.6% (70.8% to 92.5%), whilst the specificity (95% CI) was 98.3% (97.2% to 99.3%).

### Clearview Chlamydia test

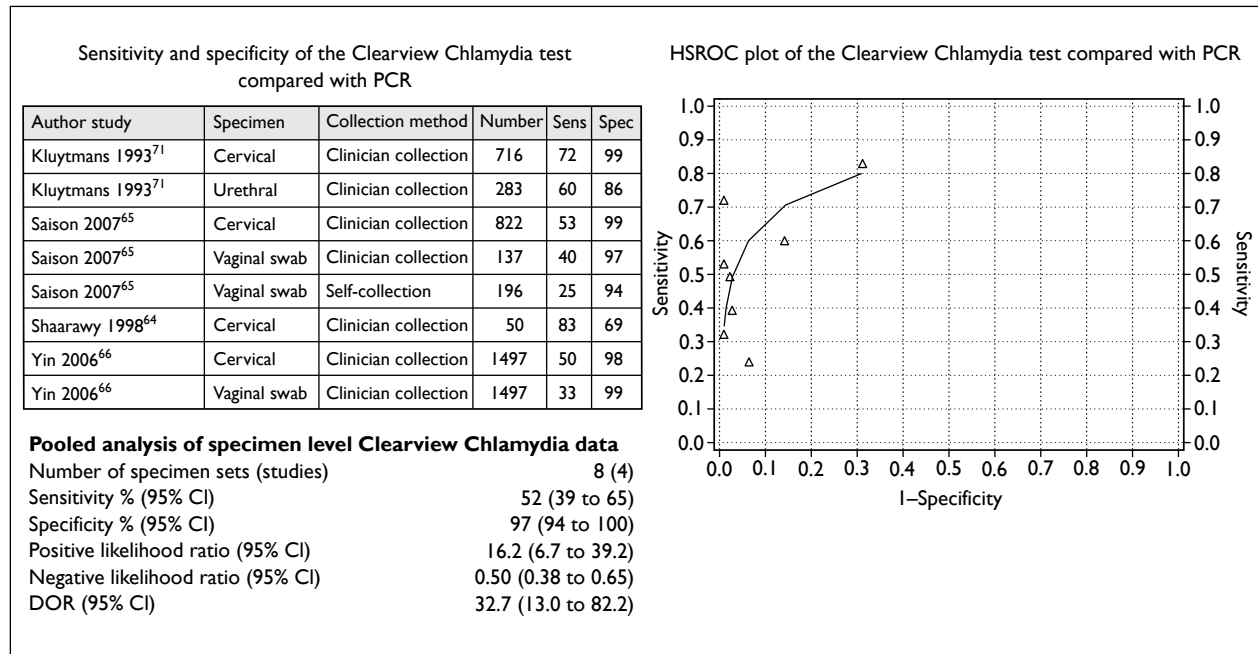
Four studies comparing the Clearview<sup>®</sup> Chlamydia test (Inverness Medical Professional Diagnostics, Princeton, NJ, USA) with a NAAT, and using eight sets of swab specimens (from a total of 3368 participants), provided sufficient information to allow their inclusion in the pooled estimates for specimen level analysis. The NAAT method reportedly used in two of the studies (involving 1547 participants) was PCR using the 'Roche AMPLICOR',<sup>64,66</sup> whilst one study involving 822 participants reported using PCR with the Roche AMPLICOR CT/NG method.<sup>65</sup> It is highly likely that these tests are the same technique and were merely reported differently (Roche Diagnostics, January 2009, personal communication). The remaining study, with 999 participants, did not specify the type of PCR method used.<sup>71</sup> Of the eight sets of swab specimens, four sets, from four different studies involving 3368 participants,<sup>64-66,71</sup> were cervical specimens. Three sets, from two different studies involving 1830 participants,<sup>65,66</sup>

were vaginal swab specimens (of which one set<sup>65</sup> was self-collected specimens whilst the remaining two sets were clinician-collected).<sup>65,66</sup> The remaining set of 283 specimens came from urethral swabs.<sup>71</sup>

Figure 5 shows the sensitivity and specificity of the individual studies, SROC curves and pooled estimates for the sensitivity and specificity of the Clearview Chlamydia test for specimen level detection of genital chlamydia infection. The pooled sensitivity (95% CI) of the test was 52% (39% to 65%), whilst the pooled specificity (95% CI) was 97% (94% to 100%). The DOR (95% CI) was 32.7 (13.0 to 82.2).

Figure 6 shows separate pooled analysis results conducted on sets of cervical swab specimens only. The pooled sensitivity (95% CI) of the Clearview test using cervical specimens was 64% (47% to 77%), whilst the pooled specificity (95% CI) was 97% (88% to 99%). The DOR (95% CI) was 59.9 (16.9 to 212.3).

In addition to the specimens available for pooled estimates, three other studies compared four sets of specimens (from a total of 588 participants) tested using the Clearview Chlamydia POCT against a NAAT.<sup>68-70</sup> The NAAT method used in three sets of specimens was the LCx assay (Abbott Laboratories),<sup>68-70</sup> although in one instance<sup>69</sup> a DFA test was used to confirm the LCx result, and data were not available separately for these comparator tests. In the remaining set of specimens, the NAAT method used was TMA [using the Gen-Probe AMP-CT test (Gen-Probe Inc., San Diego, CA, USA)]. Three sets of specimens from two studies (involving



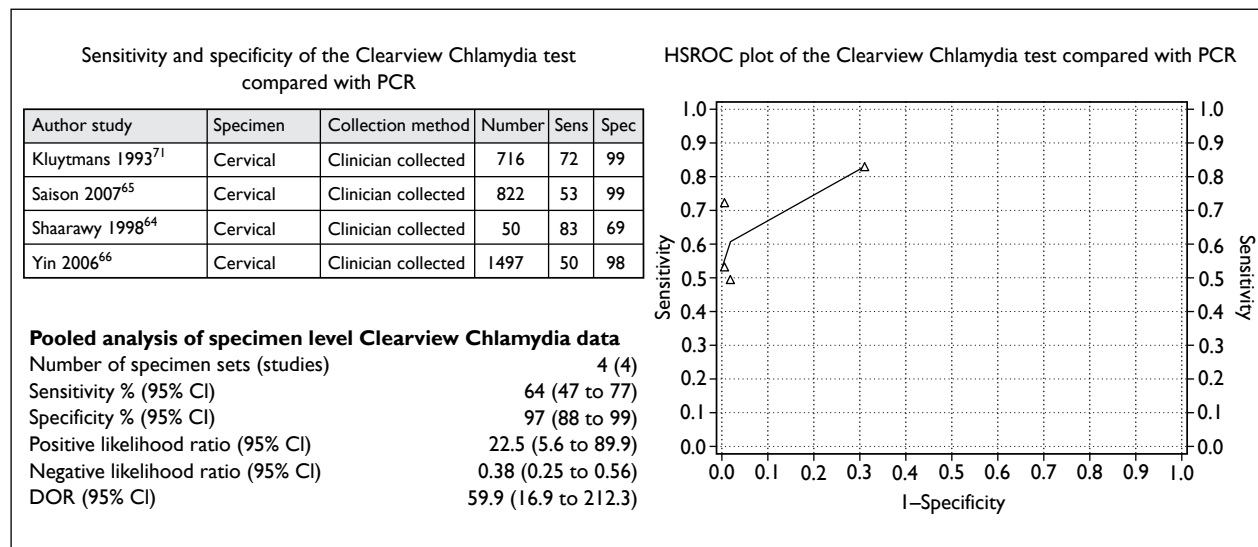
**FIGURE 5** The Clearview Chlamydia test (various types of swab specimens): sensitivity, specificity, HSROC plot and pooled estimates.

460 participants) were endocervical samples from women,<sup>68,70</sup> whilst the remaining set were FVU samples from 128 men.<sup>69</sup> There were insufficient data to enable the pooling of estimates for the diagnostic accuracy for these comparisons.

However, individual data from the studies are available, and show that 128 FVU specimens compared the diagnostic accuracy of the Clearview Chlamydia test with the LCx assay. All

the specimens were from males, but had been selected from an original sample of 762 male FVU specimens that had been submitted for testing in a private laboratory in Canada. The sensitivity of the Clearview Chlamydia test compared with the LCx assay for FVU specimens was 67.7%, whilst the specificity was 95.5%.<sup>69</sup>

In addition, two studies, one using 395 endocervical specimens from women attending a



**FIGURE 6** The Clearview Chlamydia test (cervical specimens only): sensitivity, specificity, HSROC plot and pooled estimates.

clinic of the British Pregnancy Advisory Service (BPAS) for an abortion procedure<sup>68</sup> and the other using 65 endocervical specimens from one of four outpatient obstetric and gynaecology clinics at the University of South Alabama, Mobile, AL, USA,<sup>70</sup> compared the diagnostic accuracy of the Clearview Chlamydia test with the LCx assay. The sensitivity of the Clearview Chlamydia test compared with the LCx assay for endocervical specimens in those attending the BPAS clinic for an abortion procedure was 75.0%, whilst the specificity was 99.2%.<sup>68</sup> The sensitivity for endocervical specimens in those attending the outpatient obstetric and gynaecology clinics was 50%, whilst specificity was 100%.<sup>70</sup>

Also, a set of endocervical specimens was taken from the 65 participants in the study by Lauderdale and colleagues,<sup>70</sup> to compare data from the same population of women attending one of four outpatient obstetric and gynaecology clinics at the University of South Alabama, using the Clearview Chlamydia POCT against a different NAAT as the reference standard (TMA using the Gen-Probe AMP-CT test). The sensitivity and specificity for endocervical specimens in this instance were the same as when the LCx assay was used as the reference standard (i.e. 50% and 100% respectively).

### SureScreen Chlamydia Wand

Two studies compared the diagnostic accuracy of the SureScreen Chlamydia Wand (SureScreen, Derby, UK) with a NAAT as the reference standard. There were not enough available data to allow the pooling of estimates, but data were available from the individual studies for this test (also sometimes marketed as the 'HandiLab C' test and 'SELFCheck' test). One study compared the SureScreen Chlamydia Wand with PCR using the Roche AMPLICOR CT/NG with clinician-collected vaginal swab samples of 231 women in the Philippines (in one social hygiene clinic with 131 female sex workers and one obstetric and gynaecology clinic setting with 100 women mostly attending for antenatal care). The sensitivity and specificity of the SureScreen Chlamydia Wand were 18.4% and 90.7% respectively.<sup>74</sup> Another study<sup>73</sup> compared the SureScreen Chlamydia Wand with SDA using the Becton-Dickinson ProbeTec ET™ (Becton-Dickinson, Franklin Lakes, NJ, USA), with self-collected vaginal swab specimens taken by 100 women attending a GUM clinic in the UK. The sensitivity and specificity of the SureScreen Chlamydia Wand in this case were 36.4% and 79.8% respectively.

### QuickVue Chlamydia test

One study involving 199 participants<sup>67</sup> compared the diagnostic accuracy of the QuickVue® Chlamydia test (Quidel, San Diego, CA, USA) with the PCR NAAT method of testing (Roche COBAS® AMPLICOR test) using endocervical specimens, of which 99 were taken from consecutive women attending a UK GUM clinic, and a further 100 were taken from women attending the gynaecology department of a UK hospital. The sensitivity of the QuickVue test for the GUM clinic specimens was 64.7%, whilst specificity was 100%. For the hospital gynaecology department specimens, sensitivity and specificity were 25% and 100% respectively.

### Magic Lite Chlamydia test

One study<sup>71</sup> used two sets of specimens (one urethral and one cervical) from 1007 patients to assess the diagnostic accuracy of the Magic Lite Chlamydia test at a hospital sexually transmitted disease clinic in the Netherlands, using PCR (not further specified) as the reference standard NAAT. For the 283 urethral specimens, the sensitivity and specificity of the Magic Lite were 72.1% and 99.6% respectively. For the 724 cervical specimens, the sensitivity of the Magic Lite Chlamydia test was 60.5% whilst specificity was 99.9%.

### SureCell Chlamydia test

One study with 128 participants<sup>69</sup> compared the diagnostic accuracy of the Kodak SureCell Chlamydia test with the LCx assay. A DFA test was then used to confirm the LCx result, but data were not available separately for these comparator tests. One hundred and twenty-eight selected FVU specimens from males (which were taken from an original sample of 762 specimens submitted for testing in a private laboratory in Canada) were used to compare the SureCell Chlamydia test with the LCx assay. The sensitivity of the SureCell Chlamydia test was reported as 62.9%, whilst the specificity was 100%.

### Acceptability outcomes

All additional outcomes reported by those studies included in the review of diagnostic accuracy are included below (*Table 5*). Aside from the outcome of 'number of chlamydia cases detected', five studies, involving a total of 3688 participants, provided additional information on acceptability outcomes for participants,<sup>50,66,72,73,75</sup> and one study provided information on acceptability outcomes for staff.<sup>66</sup> For study participants, the studies by Yin and colleagues,<sup>66</sup> Mahilum-Tapay and

TABLE 5 Acceptability outcomes for patients and staff

Patient outcome	Number/total (%)	Number of studies reporting outcome
<b>Willingness to wait for POCT results</b>		
< 30 minutes	1293/2378 (54.4)	Two (Mahilum-Tapay et al. <sup>50</sup> and Yin et al. <sup>66</sup> )
≤ 1 hour only	30/683 (4.4)	One (Nadala et al. <sup>75</sup> )
Between 30 minutes and 2 hours	912/2378 (38.4)	Two (Mahilum-Tapay et al. <sup>50</sup> and Yin et al. <sup>66</sup> )
≥ 1 hour	653/683 (95.6)	One (Nadala et al. <sup>75</sup> )
> 2 hours	96/881 (10.9)	One (Mahilum-Tapay et al. <sup>50</sup> )
> 1 day	63/881 (7.2)	One (Mahilum-Tapay et al. <sup>50</sup> )
<b>Preferences for collection method</b>		
Preferred 'FirstBurst' to routine cup	736/936 (78.6)	Two (Wisniewski et al. <sup>72</sup> and Nadala et al. <sup>75</sup> )
Preferred routine cup collection to 'FirstBurst'	124/687 (18.0)	One (Nadala et al. <sup>75</sup> )
Were willing to use either 'FirstBurst' or routine cup to collect FVU sample	38/687 (5.5)	One (Nadala et al. <sup>75</sup> )
Preferred a urine sample to giving a urethral swab <sup>a</sup>	619/697 (88.8)	One (Nadala et al. <sup>75</sup> )
Would have preferred to give a urethral swab <sup>a</sup>	49/697 (7.0)	One (Nadala et al. <sup>75</sup> )
Were willing to provide either a urine or a urethral swab <sup>a</sup> sample	29/697 (4.2)	One (Nadala et al. <sup>75</sup> )
Preferred self-collecting vaginal swabs to giving a urine sample	435/1068 (40.7)	One (Mahilum-Tapay et al. <sup>50</sup> )
Preferred giving a urine sample to self-collecting vaginal swabs	401/1068 (37.5)	One (Mahilum-Tapay et al. <sup>50</sup> )
No preference for either self-collecting vaginal swabs or providing a urine sample	232/1068 (21.7)	One (Mahilum-Tapay et al. <sup>50</sup> )
<b>Ease of understanding/comfort</b>		
Found instructions for urine collection easy to understand	741/759 (97.6)	One (Nadala et al. <sup>75</sup> )
Found collection of their urine easy	735/755 (97.4)	One (Nadala et al. <sup>75</sup> )
Found instructions for self-collecting vaginal swab specimens easy to understand	1813/1837 (98.7)	One (Mahilum-Tapay et al. <sup>50</sup> )
Felt comfortable self-collecting vaginal swab specimens	1039/1083 (95.9)	One (Mahilum-Tapay et al. <sup>50</sup> )
<b>Staff outcome</b>		
<b>Use of the test</b>		
Thought the kit had clear instructions from the manufacturer	13/14 (92.9)	One (Yin et al. <sup>66</sup> )
Thought the test was easy to use	12/14 (85.7)	One (Yin et al. <sup>66</sup> )
Felt the test had a 10 minutes 'hands-on' time	12/14 (85.7)	One (Yin et al. <sup>66</sup> )
Thought it was 'rapid' (i.e. <20 minutes until the result was displayed)	14/14 (100)	One (Yin et al. <sup>66</sup> )
Felt that the training on operational procedures took < 30 minutes	13/14 (92.9)	One (Yin et al. <sup>66</sup> )
a Participants were not asked to give a urethral swab for this study and may never have been required to provide one before, so this may not reflect their real-life preferences.		

colleagues<sup>50</sup> and Nadala and colleagues<sup>75</sup> reported preferences for waiting time. The studies by Mahilum-Tapay and colleagues,<sup>50</sup> Wisniewski and colleagues<sup>72</sup> and Nadala and colleagues<sup>75</sup> reported participants' preferences for providing different types of specimens, and these studies, along with the study by Kegg and colleagues,<sup>73</sup> also reported participants' views on the process of specimen collection itself.

These acceptability outcomes are listed in *Table 5*.

### Interpretability outcomes

Three of the included studies reported interpretability (or reproducibility) outcomes.<sup>50,66,75</sup> Two of these studies reported reproducibility outcomes for the CRT, by having an independent laboratory repeat testing with randomised and masked panels, using two independent operators.<sup>50,75</sup> Both found 100% concordance between the expected results and the results from independent laboratory testing. The remaining study<sup>66</sup> reported kappa statistics on the agreement of results of the Clearview test read by two independent staff. Agreement ranged from 0.94 to 1.00 for vaginal specimens and from 0.96 to 1.00 for cervical specimens, and was found to be statistically significant ( $p < 0.001$ ).<sup>66</sup>

### Review of effectiveness

Although all studies included in the diagnostic accuracy review also met the criteria for inclusion in the review of effectiveness inasmuch as they provided information on the number of chlamydia

cases detected, as the results for this outcome have been discussed above they will not be repeated here. No studies were identified that provided additional data that met the inclusion criteria for the review of effectiveness. Therefore, it was not possible to provide information on the clinical effectiveness of point-of-care testing compared with the current practice of nucleic acid amplification testing.

### Summary of results

There were 13 studies enrolling 8817 participants 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 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 POCT (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.



# Chapter 5

## Assessment of patient preferences

### Methods

The review of the preferences of patients was confined to studies that had reported willingness to pay (WTP; which may or may not have been determined using contingent valuation) or reported preferences between different relevant screening test regimens. Few relevant studies were expected to be identified but any data identified might be used to assign a value to the health benefits from a patient's perspective. Such data might then be related to cost (estimated from a NHS perspective) to provide an estimate of relative efficiency.

### Identification of studies

The review on preferences was based on electronic searches to identify reports of patient preference studies for different ways of organising chlamydia screening/testing. The searches were restricted to articles written in English, but without publication date limits. The databases searched were: MEDLINE (1966 to week 3 November 2008), MEDLINE In-Process (26 November 2008), EMBASE (1980 to week 48 2008), Science Citation Index (1970 to 1 November 2008), ISI Conference Proceedings (1990 to 22 November 2008), and Health Management Information Consortium (November 2008). Full details of the search strategies used and websites consulted are documented in Appendix 1. A total of 294 reports were identified (see *Table 6*).

One reviewer assessed these studies and found that most did not meet our inclusion criteria. Only two relevant studies<sup>77,78</sup> were identified from the search conducted.

### Summary of the review on patient preferences

#### Study selection

The review of patient preferences considered studies conducted in similar populations to those considered relevant to a UK health setting. Only economic measures of preference based on population values were considered, as such data would be most useful for priority setting. Individuals may have strong preferences not just for the outcomes of testing but also about how such a service might be organised in different settings. The studies, covering the different characteristics of screening (type of test, setting, diagnostic and long-term outcomes, etc.) and considering how patients value such characteristics and hence value alternative methods of diagnosing chlamydia, are included in this part of the review.

Ryan and Watson<sup>77</sup> conducted an experimental study to examine women's preferences for chlamydia screening, and compared the WTP estimates from two different methods: a discrete choice experiment (DCE) and a contingent valuation (using a payment card method). A total of 174 women attending family planning clinics were recruited for the study. In the DCE, the

**TABLE 6** Search results

Database	Number retrieved
<b>Patient preference</b>	
MEDLINE (1966 to week 3 November 2008)/EMBASE (1980 to week 48 2008)/MEDLINE In-Process (26 November 2008) multifile search (after deduplication in Ovid)	220
Science Citation Index (1970 to 1 November 2008)	19 <sup>a</sup>
Health Management Information Consortium (1979 to November 2008)	55 <sup>a</sup>
Total	294

<sup>a</sup> Number of additional reports found after excluding those identified from the MEDLINE/EMBASE multifile search.



women were requested to choose between sets of hypothetical scenarios that differed in terms of location of screening (family planning clinic, GUM clinic, home, GP practice), the ways in which the collection sample would be collected (full pelvic examination, perineal swab, urine test), support from providers (trained health-care provider or not) and costs (options being £0, £5, £10 and £25). These screening attributes or characteristics were derived from literature searches, policy variations and advice from family planning doctors, and can be considered to represent factors relevant to organising a screening service in the UK. The combination of different characteristics described above produced a large number of scenarios, and a fractional factorial design (generated by experimental design software) was used to reduce this down to 16 scenarios.

The payment card attempted to elicit respondents' WTP for a defined screening test: screening to be carried out at a family planning clinic, using a urine test, with a 25% risk of PID, and a trained health advisor providing support to the woman when results are obtained. Results from 130 respondents could be analysed, after incomplete questionnaires and protesters to the WTP were excluded. Results from the DCE and payment card methods could be compared for 110 women.

### Summary of contingent valuation

A general preference to be screened was observed. Mean WTP was £23.71 (95% CI £22.89 to £24.54) with the payment card method and £34.18 (95% CI £27.29 to £51.19) for the DCE. It was found that WTP was £22 (95% CI £20.92 to £27.17) for those with an annual income of less than £15,000 and £26 (95% CI £24.64 to £27.17) for those with an annual income above £15,000 (Table 7). Screening

at both the family planning clinic and GUM clinic had a positive impact on utility, whereas screening in general practice or at home reduces the utility of screening services at the family planning clinics and GUM clinics.

### Discrete choice experiment

Watson and colleagues<sup>78</sup> used a DCE to examine how the characteristics of a screening programme for chlamydia affected the value of the screening programme. For the 16 profiles in the choice set, patients were asked to answer whether they would or would not accept the screening. The total respondents to the DCE survey were 149 women out of the 175 who were recruited, and these respondents generated 2142 observations for the experiments. The respondents from the family planning clinics valued the screening for chlamydia, on average at £15.23. The study also provided the estimates of marginal WTP. It was found that a less invasive screening test increased WTP by £7.09 from the average of £15.23, and more invasive tests would reduce WTP by £3.51 for a perineal swab, and by £3.58 when pelvic examination was used. The most preferred screening location was family planning clinics and this choice would increase the average WTP by £5.32, whilst a home location would reduce WTP by £4.14. The GUM clinic as location did not have any significant effect on patients' WTP. The support from a trained health-care professional after receiving the results would increase the average WTP by £4.26.<sup>78</sup> Predicted uptake of urine testing at family planning clinics with support was 91%, and 87% at a GUM clinic. In a sensitivity analysis it was found that respondents aged below 25 years and having casual relationships had less preference for screening and have obtained less utility from screening.

TABLE 7 Willingness-to-pay estimates

	Payment card method (all income groups)	Payment card method (<£15,000) (n=59)	Payment card method (>£15,000) (n=58)	Discrete choice experiment (n=130)
Mean WTP	£23.71	£22.20	£25.90	£34.18
95% confidence interval	£22.89 to £24.54	£20.92 to £23.48	£24.64 to £27.17	£27.29 to £51.19

From Ryan and Watson 2008,<sup>77</sup> with permission of John Wiley & Sons Ltd.



### **Relationship between planned and actual behaviour**

Comparison of the stated intention and actual behaviour suggested that 77% of those providing payment card responses behaved in the same way as they intended when they were actually offered the test. In the case of the discrete choice experiment respondents, 81% behaved in the same way as predicted. The hypothetical response patterns were significantly different among the respondents for both the payment card methods

and the DCEs, and the findings from the Ryan and Watson<sup>77</sup> study suggest that in both cases the hypothetical data overestimated the actual screening test uptake.

The review suggests that, from a patient's point of view, the preferable location for testing would be a family planning clinic. The method of sample collection would ideally be non-invasive and, out of the methods of sampling considered, a urine sample would be favoured most.



# Chapter 6

## Assessment of cost-effectiveness

The principal research question addressed is: 'what testing strategies, using the new CRT, for detecting genital chlamydia infection will increase the number of infections effectively treated in index patients and contacts, and be cost-effective compared with current detection practice?'

### Methods

#### Relevant patient population

The cost-effectiveness and cost-consequence analyses were based on a cohort modelling approach that reflects the prevalence of chlamydia in a population of people presenting or a specified subgroup presenting for testing. The time horizon of the model covers only the period of initial diagnosis and subsequent treatment for chlamydia infection. The model also includes another short-term element: the identification of contacts for those tested as positive. As the time horizon is short (< 1 year), no discounting of costs or effects was necessary.

The target population considered is sexually active adolescent and adult men and women suspected of having or being tested for chlamydia infection. Where data were available, the following subgroups would have been considered: those aged under 25 years old; men who have sex with men; sex workers; and high-risk African populations. Given the lack of data, separate models were not constructed for these groups. However, by changing the pre-test probability of the prevalence of chlamydia, the effect of the screening for these groups might be considered.

#### Screening options to be evaluated

A decision analytic model was developed to compare the CRT to other relevant POCTs and one non-POCT (current practice assumed to involve NAATs). This model displays the logical sequence of the clinical decision problem.

Based on the results of the systematic review of test performance (see Chapter 4), the use of the best two POCTs in terms of diagnostic performance (and quantity of evidence available)

were considered within the model. The two POCTs considered for the decision model were Clearview and the CRT. For the decision model, the test performance (and cost) of the comparator test(s) considered is PCR, which is the most frequently used NAAT in current practice.

The setting considered for the reviews of test performance and effectiveness is a family planning clinic. This has not been explored in a sensitivity analysis as no data are available to assess how parameter estimates might change as the setting varies.

#### Screening and treatment pathway: the model

The different strategies were compared in terms of the number of chlamydia cases detected, diagnosed and treated in index patients and contacts, and the costs of the different strategies used to detect chlamydia. The model compares three basic strategies: screening A (the Clearview POCT); screening B (CRT POCT); and screening C (current practice – PCR – see *Figure 7*).

The model describes the pathway of individuals covering the period of offer of screening, testing and the costs and consequences of any subsequent short-term outcomes. The structure of the economic model is based on care pathways developed in consultation with our expert advisors, and describes alternative ways in which a service for chlamydia testing may be organised.

The decision model for the three screening options is also used to identify the costs and consequences of contact tracing (*Figure 7*). For illustrative purposes, the structure for only one test is shown. The structure for the other tests would be identical.

#### The assumed pathway of the model

When a test is offered in a particular setting, a proportion of the target population is assumed to accept the offer. Of those who do not take up the offer of testing, some will have chlamydia that remains undetected. The health service incurs the costs of offering the test, i.e. the cost of inviting the

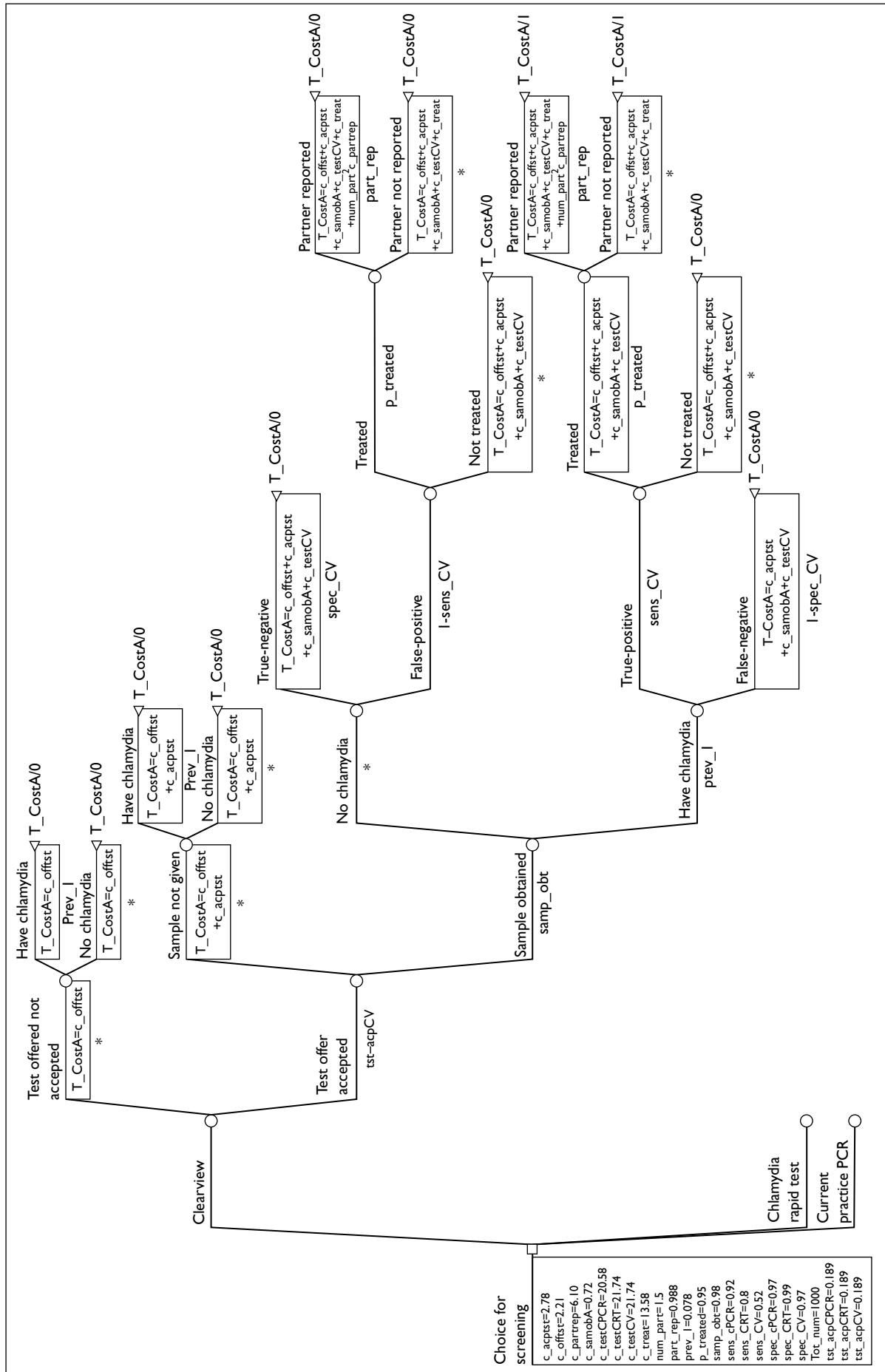


FIGURE 7 Pathway of the patient.

target population to receive the test. Of those who do decide to take up the test, it is possible that a proportion may not be able, or willing, to provide a suitable sample for testing. Those for whom samples were not obtained remain undiagnosed and untreated. For those who do provide a sample, some will test positive and some negative. The proportion of people in each group will depend upon the prevalence of infection and the diagnostic performance of the test. Those with a positive result, which might have been a true- or a false-positive result, are expected to be treated and their partners are notified. The model assumes that all those who test negative (true or false) are not treated, and for these people no contact tracing is performed. The model also assumes that a certain proportion of partners of those who test positive are contacted.

### Data requirements for the model

Effectiveness, as included in the model, is largely influenced by the performance of the test, i.e. the sensitivity and specificity of the different types of the test and also the type of setting. These factors may result in different levels of acceptance and proportions of those in the different risk groups presenting for testing.

Effectiveness within the model was measured in terms of the absolute numbers of true-positives, false-positives, false-negatives (and other positive cases missed) and true-negatives detected. We have also considered the two other different measures of outcome: (1) cases of chlamydia correctly diagnosed and treated and the index patients' partners notified and (2) correct diagnosis with those with chlamydia treated and the index patients' partners notified. In this latter situation, testing is considered to be effective if it could also correctly identify true-negatives.

The diagnostic performance of the tests was based upon the data reported in Chapter 4. We used simple equations to determine the true-positive and true-negative rates:

False-positive rate = 1 – specificity of the test

True-positive rate = 1 – false-positive rate

False-negative rate = 1 – sensitivity of the test

True-negative rate = 1 – false-negative rate

### Resource use, cost data and unit costs

Cost information is derived by combining information on resource use with information on the unit costs for the different POCTs and comparators in different settings (GUM clinics, chlamydia screening clinics/programmes, GP surgery, pharmacies) where the testing will be conducted and diagnosed. Data were obtained from the manufacturers of the different tests, the literature (e.g. the ClaSS studies<sup>5</sup>) and expert opinion. Costs include resource material costs incurred in offering the test (e.g. the time of personnel in a clinical setting, the costs of education leaflets, the cost of kits and other supplies, laboratory personnel time, treatment and partner notification). The model assumes a pre-test probability of presence of chlamydia which is the prevalence rate of the age group of 15–24 years old. *Table 8* gives a list of the parameters and their associated values that were used in the model.

### Assumptions

In addition to those parameters taken from other studies, assumptions had to be made for some other parameters. For the numbers of partners per index case, a number of different figures are found in different studies. The number of partners per index case was an assumption based on expert opinion, from a small unpublished survey. In many economic evaluations of chlamydia screening, a 100% rate of partner notification was assumed. We have used a value of 98%. However, there are reports (e.g. *NCSP Five Years: 5th annual report of the National Chlamydia Screening Programme*<sup>8</sup>) suggesting that only 63% of partners might be contacted. A second assumption related to the cost of testing using the CRT was that the cost of testing using the CRT would be same as, or close to, the cost using Clearview Chlamydia kit. We took the market price (March 2009) of this kit.<sup>80</sup>

### Model analysis

The analysis compares the cost-effectiveness of testing of two POCTs with a current practice option. The results of the analysis are presented as the costs and the number of true cases (i.e. true-positive) detected and treated with partners notified. The difference in costs and effectiveness is also compared with the effectiveness and measured in terms of true cases (including true-negative) identified. The cost-effectiveness analysis is based on health service provider (the NHS) perspectives.

TABLE 8 Model parameters, values and data sources

Parameters	Description	Value	Value used for sensitivity analysis		Source
			Low	High	
<b>Uptake of screening and prevalence</b>					
tst_acpCPCR	Proportion accepting test offer for current practice (PCR)	0.189	0.16	0.233	Low <i>et al.</i> <sup>5</sup>
tst_acpCRT	Proportion accepting the offer of test B (CRT)	0.189	0.16	0.25	Same uptake used for PCR (from Low <i>et al.</i> <sup>5</sup> )
tst_acpCV	Proportion accepting the offer of test A (Clearview)	0.189	0.16	0.25	Same uptake used for PCR (from Low <i>et al.</i> <sup>5</sup> )
Prev_l	Prevalence in the population group	0.078	0.069	0.091	NHS Vital Signs <sup>79</sup>
num_part	Average number of partners	1.5	1.3	2	Assumption
part_rep	Percentage of partners reported	0.988	0.968	0.991	Assumption
p_treated	Proportion of index patient treated	0.95	0.65	1	Assumption
samp_obt	Sample obtained	0.98	0.97	1	Assumption
<b>Cost parameters</b>					
c_acptst	Cost of accepting test	£2.78	£2.00	£5.00	Adams <i>et al.</i> <sup>6</sup>
c_offtst	Cost of offering test	£2.21	£1.80	£2.50	Adams <i>et al.</i> <sup>6</sup>
c_partrep	Cost of partner notifications	£6.10	£3.06	£8.10	Adams <i>et al.</i> <sup>6</sup>
c_samobA	Cost of sample obtained	£0.72	£0.70	£0.75	Low <i>et al.</i> <sup>5</sup>
c_testCPCR	Cost of current practice (PCR)	£20.56	£19.50	£21.50	Low <i>et al.</i> <sup>5</sup>
c_testCRT	Cost of screening test (CRT)	£21.74	£20.50	£22.50	Low <i>et al.</i> <sup>5</sup> and cost of test kit price assumed to same as Clearview
c_testCV	Cost of screening test (Clearview)	£21.74	£20.50	£22.50	Low <i>et al.</i> <sup>5,80</sup>
c_treat	Cost of treating patient – drugs+	£13.58	£12.50	£14.80	Low <i>et al.</i> <sup>5</sup>
T_CostA	Total cost of test A (Clearview)				Estimates derived within the model
T_CostB	Total cost of test B (CRT)				Estimates derived within the model
T_CostC	Total cost of current practice				Estimates derived within the model
<b>Sensitivity and specificity</b>					
sens_cPCR	Sensitivity of current practice	0.92	0.89	0.96	Roberts <sup>38</sup>
sens_CRT	Sensitivity of test B (CRT)	0.8	0.73	0.85	From the review, Chapter 4
sens_CV	Sensitivity of test A (Clearview)	0.52	0.39	0.65	From the review, Chapter 4
spec_cPCR	Specificity of current practice (PCR)	0.97	0.96	1	Roberts <sup>38</sup>
spec_CRT	Specificity of test B (CRT)	0.99	0.99	1	From the review
spec_CV	Specificity of test A (Clearview)	0.97	0.94	1	From the review
Tot_num	Total cohort	1000			

### Sensitivity analysis

The sensitivity of the findings was tested using one-way sensitivity analysis to examine the impact of varying key assumptions and/or values of the following parameters:

1. The proportion of patients taking the test (accepting the offer) in order to capture the likely difference in preferences of different settings which may also vary among different risk groups of the population.
2. The pre-test prevalence of chlamydia.
3. Sensitivity analysis in relation to the sensitivity and specificity of different POCTs.
4. Sensitivity analysis in relation to the changes in the costs of the screening test.
5. The rates showing the details of these sensitivity analyses are reported in Sensitivity analysis (see page 34).

## Results

### Cost-consequences analysis

Current practice performed better in terms of the number of true-positives identified, and hence the number of true-positives treated compared with the POCTs. It also resulted in fewer false-negatives and hence missed fewer people with

chlamydia. The current practice and the Clearview test would result in a similar number of false-positives (who would then receive unnecessary treatment and have contacts treated needlessly). Among the two POCTs, the CRT performed better in terms identifying more true-positives, fewer false-negatives, more true-negatives, more partners of true-positive cases notified and fewer partners notified among those falsely identified as positive (*Table 9*).

### Cost-effectiveness analysis

The results of the cost-effectiveness analysis using the two different outcome measures are shown in *Table 10*. If effectiveness is measured in terms of the number of true-positives identified and treated and their partners notified, then current practice performs better than the two POCTs considered in our model.

If effectiveness is measured in terms of the number of people correctly diagnosed by the test (i.e. true-positives and true-negatives), including notifying the partners of the true-positives and treating the positive cases where necessary, then the CRT performs better than current practice with a marginal increase in costs.

**TABLE 9** Performance of the different test strategies<sup>a</sup>

	Current practice (PCR)-C	Clearview (POCT)-A	Chlamydia Rapid Test (CRT-POCT)-B
Number of false-positives	5.123	5.123	1.708
Number of false-negatives	1.156	6.934	2.889
Number of false-positives treated	4.867	4.867	1.622
Number of true-positives	13.291	7.5125	11.558
Number of true-negatives	165.649	165.649	169.065
Number of true-positives treated	12.627	7.137	10.979
Number of partners reported for true-positives	18.712	10.577	16.272
Number of partners reported for false-positives	7.213	7.123	2.404
Total costs of offering, screening and treating index patients and their partners	7070	7170	7180

a Numbers refer to number of events in a cohort of 1000 people offered testing and assuming a prevalence of chlamydia in this cohort of 7.8%

**TABLE 10** Costs, effectiveness and cost-effectiveness of three screening tests for a population cohort of 1000

	Total costs (£) <sup>a</sup>	Total effectiveness <sup>b</sup>	ICER
<b>Effectiveness measured as number of true-positive cases identified and treated and their partners notified</b>			
Current practice (PCR)	7070	12.63	
Clearview (POCT)	7170	7.14	Dominated
Chlamydia Rapid Test (CRT-POCT)	7180	10.98	Dominated
<b>Effectiveness measured as number of cases correctly identified and treated if necessary and partners of positive cases notified</b>			
Current practice (PCR)	7070	178.27	
Clearview (POCT)	7170	172.79	Dominated
Chlamydia Rapid Test (CRT-POCT)	7180	180.05	62.18
a Total cost of offering testing to 1000 people.			
b Total number of cases out of a cohort of 1000 people.			

## Sensitivity analysis

The sensitivity analyses are conducted with respect to the outcome defined as the number of cases of chlamydia correctly identified and treated, and partners notified. A summary of the sensitivity analyses is given in *Table 11*.

### Change in the uptake of the test offer

The current practice of using PCR will remain cost-effective even if the rate of acceptance of the offer of the test is increased for all the three tests reported in *Table 8*. If we assume that the acceptance rate for PCR and Clearview was 18.9% and that the acceptance for the CRT was 22.75%, the sensitivity analysis suggests that the CRT would be more effective but more costly than PCR and that the incremental cost per case of chlamydia correctly identified and treated and partners traced was £906.

### Sensitivity of pre-test prevalence

One-way sensitivity analysis also suggests that at both the high and low pre-test prevalence rate of chlamydia (low = 6.9%, high = 9.1%), the current practice of using PCR for screening is less costly and more effective (i.e. it is dominant).

### Change in sensitivity of the point-of-care tests

Similarly, the lower and higher values for sensitivity and specificity (see *Table 8*) were considered in a sensitivity analysis. In none of these analyses would the conclusion change from that based on the base-case analysis (results shown in *Table 11*).

Sensitivity analysis using higher and lower levels of sensitivity and specificity of the POCTs does not change the relative cost-effectiveness against PCR.

There are two different assumptions used for the sensitivity of costs, in one instance we lowered the cost of all tests to £19.50 and in another we kept the cost of testing for PCR unchanged at £20.56. We found the results were sensitive to changes.

The model used is only deterministic. It is important to show the changes in the value of the parameters simultaneously, and a probabilistic model needs to be used.

## Discussion

The cost-effectiveness study compared two POCTs and one non-POCT. In our analysis we provided the estimates of the total costs of screening for a cohort of 1000 men and women aged 16–24 years. Our findings suggest that the current types of screening using PCR would identify more true-positive cases than the other two POCTs, namely CRT and Clearview. The CRT performs better than Clearview in identifying more true-positives, fewer false-negatives and more true-negatives, and is the more effective POCT. The current practice of using PCR would be the least costly method of detecting chlamydia at a total cost for the cohort of £7070. Furthermore, it was the most effective method – 12.63 people per 1000 offered the test (and assuming a prevalence of chlamydia of 7.8%) would be correctly treated and their partners contacted.



TABLE 11 Sensitivity analysis

Parameters' value and strategies	Values of the parameters	Total costs	Effectiveness <sup>a</sup>	ICER
<b>Acceptance rate of the test offer</b>				
Current practice (PCR)	22.3%	£7880	14.9	
Clearview (CV)	25%	£8710	9.44	Dominated
Chlamydia Rapid Test (CRT)	25%	£8730	14.52	Dominated
<b>Keeping the acceptance rate fixed at 18.9% for PCR and CV, changing CRT's to 22.75%</b>				
Current practice (PCR)	18.9%	£7010	12.63	
Clearview (CV)	18.9%	£7130	7.14	Dominated
Chlamydia Rapid Test (CRT)	22.75%	£8730	14.52	906.69
<b>Pre-test prevalence=0.069 (6.9%)</b>				
Current practice (PCR)	6.9%	£6990	11.17	
Clearview (CV)	6.9%	£7110	6.31	Dominated
Chlamydia Rapid Test (CRT)	6.9%	£7120	9.71	Dominated
<b>Pre-test prevalence=0.091(9.1%)</b>				
Current practice (PCR)	9.1%	£7050	14.73	
Clearview (CV)	9.1%	£7150	8.32	Dominated
Chlamydia Rapid Test (CRT)	9.1%	£7170	12.81	Dominated
<b>Costs of tests at lower value of £19.50</b>				
Clearview (CV)		£6752	7.14	22.58
Chlamydia Rapid Test (CRT)		£6766	10.98	3.65
Current practice (PCR)		£6876	12.63	66.66
<b>Costs of the POCTs reduced to £19.50 keeping PCR unchanged at £20.56</b>				
Clearview (CV)		£6752	7.14	
Chlamydia Rapid Test (CRT)		£6766	10.98	3.65
Current practice (PCR)		£7072	12.63	185.45
Sensitivity of Chlamydia Rapid Test=0.85	0.85			
Current practice (PCR)		£7070	12.63	
Clearview (CV)		£7170	7.14	Dominated
Chlamydia Rapid Test (CRT)		£7200	11.67	Dominated
Specificity of Chlamydia Rapid Test=1.00	1.00			
Current practice (PCR)		£7070	12.63	
Chlamydia Rapid Test (CRT)		£7180	10.98	Dominated
Clearview (CV)		£7170	7.14	Dominated
Sensitivity of Clearview=0.65	0.65			
Current practice (PCR)		£7070	12.63	
Chlamydia Rapid Test (CRT)		£7180	10.98	Dominated
Clearview (CV)		£7210	8.92	Dominated
Specificity of Clearview=1.00	1.00			
Current practice (PCR)		£7060	7.14	
Chlamydia Rapid Test (CRT)		£7070	12.63	2.74
Chlamydia Rapid Test (CRT)		£7180	10.98	Dominated

a Total number of cases out of a cohort of 1000 people.

The CRT POCT may be worth considering over current practice when the acceptance of offer for the CRT tests by the patients visiting a chlamydia screening facility is higher at 22.75% (the base-case uptake rate of testing for CRT was 18.9% and the uptake rates for the other tests were kept at 18.9%). Such a situation might arise if the POCT was deemed to be more acceptable to patients because it was more convenient (in terms of location of testing and speed of obtaining a result).

The results were also (as might be expected) sensitive to reductions in the cost of the POCT, and the Clearview test has a higher ICER.

### **Limitations of the analysis**

The short-time horizon has led to a focus on diagnostic outcomes, the likelihood of receiving treatment and contact tracing. The impact on health has not been considered nor has the effect of testing on the overall burden of the infection. It might be expected however that the more effective test in terms of the outcomes modelled would be the test that results in the highest health gain and the greatest reduction in the prevalence of infection in the population.

The analysis conducted has been deterministic in nature but has been supplemented by various sensitivity analyses. Ideally, further sensitivity analysis might be useful to explore more fully threshold values for key parameters. However, the sensitivity analysis conducted has highlighted some of the key areas for further investigation (e.g. uptake rates and costs of the tests).

Ideally, we would have liked to incorporate patient preferences into our model. Unfortunately few data are available and what data there were, were not suitable for incorporation into the model. Nevertheless, the results of the DCE suggest that family planning clinics are the preferred facility for screening, and less invasive techniques are favoured. However, no information was elicited to show if a POCT would be preferred or not. Ideally, further research investigating preferences for setting, diagnostic accuracy and waiting time for results could be performed. A DCE comparing variation in these attributes would be useful because, as we reported earlier, people have a preference for a short waiting time for the result, but we do not know how this might be traded off against diagnostic performance or other characteristics of the service by people receiving the test.

## Chapter 7

# Assessment of factors relevant to the NHS and other parties

### Factors relevant to the NHS

There is currently insufficient evidence to suggest that using POCTs within the NHS would increase the overall number of cases of chlamydia detected. Tests used in current practice (i.e. NAATs) have been shown to have greater sensitivity and specificity than POCTs. This loss in diagnostic performance might be offset if POCTs increased the likelihood that individuals would come forward for testing (because the whole process of detecting and if necessary treating chlamydia was perceived as being less onerous) and/or that once tested individuals are more likely to receive treatment as required. There is an absence of evidence to suggest that either of these two changes is likely to occur. This suggests that there will still be a considerable amount of undiagnosed chlamydia infections which will result in a continuing burden on the NHS to manage patients who experience complications.

The use of POCTs would also increase the number of people incorrectly diagnosed as having chlamydia. There will be costs incurred of counselling and treating these people as well as of subsequent contact tracing.

Given the burden of chlamydia in the community, it is unlikely that the introduction of a point-of-care service would allow any reduction in the scale of existing testing services. Therefore, the introduction of POCTs will result in a net increase in costs. Nevertheless, for the NHS, any improvement in uptake rates would be beneficial, particularly where certain population groups are disproportionately affected by chlamydia as a result of the current low uptake of testing. This would potentially reduce the number of complications arising from undiagnosed chlamydia infection that require NHS treatment. The introduction of point-of-care testing in settings where uptake rates are low may require the provision of testing at a wider range of venues than is currently available. The NHS would incur the additional costs of such increased provision (e.g. capital costs, training health professionals to undertake the tests, providing immediate treatment and advice, and

immediate contact tracing of the partners of each index case) and it is likely that different venues would incur different costs depending on the extent of uptake at each type of venue. However, in order to provide a service that is as accessible as possible, the NHS would be required to meet these costs.

The results of the economic evaluation suggested point-of-care testing may be more cost-effective than current practice if the cost of the POCT is reduced. Given the potential market power of the NHS the cost may be reduced if any economies of scale in purchasing the test can be realised.

New or improved technology that results in greater sensitivity of point-of-care tests would be of benefit to the NHS, but currently there is insufficient evidence to support the widespread adoption of POCTs as an alternative to current practice.

### Factors relevant to other parties

Given that NAATs have been shown to be superior to POCTs in terms of diagnostic accuracy, changing practice within the NHS to diagnose chlamydia using POCTs may (because of the number of false-positives) cause physical and psychological distress to patients and their partners. POCTs may be a more acceptable method of testing as they offer the opportunity to get a result quickly (the available evidence suggests that most people would be willing to wait for a period of up to 2 hours for a test result) and hence avoid the need to make a further visit to receive treatment and perform contact tracing if necessary. The net impact of these two factors on the health of, and the costs incurred by, individuals is uncertain.

The use of POCTs may provide advantages to individuals (and their partners) in terms of earlier detection and treatment of the infection. This would rely on an increase in uptake of testing, which might be facilitated if point-of-care testing can be provided in venues that are more acceptable to potential clients.



# Chapter 8

## Discussion

### Statement of principal findings

#### Review of test performance – pooled estimates

Most studies compared Clearview Chlamydia with PCR as the NAAT reference standard. Studies comparing the CRT with PCR, and those comparing Clearview Chlamydia with PCR were included in the pooled estimates (meta-analyses) using a HSROC model.

In terms of methodological quality, most populations in the studies included in the analysis<sup>50,64–72</sup> were considered representative of those who would receive the test in practice. Two studies considered specific population groups (e.g. pregnant women, women receiving hospital treatment for PID)<sup>64,68</sup> and one reported an unspecified population.<sup>69</sup> All NAATs were considered to be able to correctly classify chlamydia, except LCx, which was used in two studies<sup>68,69</sup> but withdrawn from the market in 2002 because of reproducibility problems.<sup>76,81</sup> None of the quality assessed studies presented data on the specific subgroup of interest (those aged under 25 years).

A summary of the results of the pooled estimates is shown in *Table 12*.

There was sufficient evidence available to pool estimates for the diagnostic accuracy of the CRT for both vaginal swab and FVU samples. For vaginal swabs, there was insufficient evidence to separate the pooled analysis by whether swabs were self- or clinician-collected, although the study by Mahilum-Tapay and colleagues,<sup>50</sup> included in the diagnostic accuracy analysis, had compared these swab collection methods (using 686 self-collected and 686 clinician-collected specimens) and found no statistically significant difference between them ( $p = 0.096$ ).<sup>50</sup> For FVU samples, there was also insufficient evidence to allow separation of the pooled analysis of routine cup collected urine and urine collected using the 'FirstBurst' device. The study by Wisniewski and colleagues<sup>72</sup> compared these collection methods (using 534 specimens collected using 'FirstBurst' and 534

specimens collected using routine cup collection), and reported that more cases of chlamydia were identified using the 'FirstBurst' device. This result was statistically significant ( $p = 0.0015$ )<sup>72</sup> and should be taken into account when considering the results of the diagnostic accuracy of the CRT when compared with PCR testing.

The pooled sensitivity (95% CI) of the CRT compared with PCR was 80% (73% to 85%) using vaginal swab samples and 77% (59% to 89%) when using FVU samples. Specificity (95% CI) was also similar at 99% (99% to 100%) using vaginal swab samples and 99% (98% to 99%) using FVU samples. DORs (95% CI) were also higher for vaginal swab samples at 436.0 (238.5 to 796.9) than for FVU samples at 237.0 (101.9 to 552.6). Although the reduced sensitivity of the CRT using FVU specimens might be explained by the difference in the method of specimen collection ('FirstBurst' versus routine cup collection), the CIs for the POCTs compared with the reference standard overlap for the sensitivity, specificity and DOR. Such indirect comparisons are difficult to interpret but these data suggest that there is no evidence of a difference in sensitivity between vaginal swab and FVU specimens.

For the Clearview Chlamydia test estimates, we originally pooled those studies containing comparisons with PCR as the reference standard, using vaginal, cervical or urethral swab specimens. This provided a sensitivity (95% CI) estimate of 52% (39% to 65%), a specificity (95% CI) estimate of 97% (94% to 100%) and a DOR (95% CI) of 32.7 (13.0 to 82.2). However, the resulting HSROC plot (see *Figure 5*) indicated that type of specimen can make a difference to the diagnostic accuracy results. Therefore, the results of the Clearview Chlamydia test compared with PCR using cervical samples were reported separately from those comparing Clearview Chlamydia with PCR using vaginal or urethral samples. There were insufficient comparisons available to conduct pooled analysis of the results using vaginal swabs (separately from the results using urethral and cervical specimens), and this was also true for urethral samples (as there was only one comparison available comparing the Clearview Chlamydia test using urethral samples

TABLE 12 Summary of pooled estimates for diagnostic accuracy

POCT	Type of point-of-care specimen included	Type of NAAT test used	Number of specimen sets included (number of studies from which specimens came)	Number of participants included (number of specimens included)	Sensitivity % (95% CI)	Specificity % (95% CI)	DOR (95% CI)
Chlamydia Rapid Test	Vaginal	PCR	5 (2)	2478 (3164)	80 (73 to 85)	99 (99 to 100)	436.0 (238.5 to 796.9)
Chlamydia Rapid Test	FVU	PCR	4 (2)	1745 (2279)	77 (59 to 89)	99 (98 to 99)	237.0 (101.9 to 552.6)
Clearview Chlamydia	Vaginal, cervical and urethral	PCR	8 (4)	3368 (5198)	52 (39 to 65)	97 (94 to 100)	32.7 (13.0 to 82.2)
Clearview Chlamydia	Cervical	PCR	4 (4)	3085 (3085)	64 (47 to 77)	97 (88 to 99)	59.9 (16.9 to 212.3)

with PCR testing). When the estimates were pooled for the Clearview Chlamydia test using cervical specimens only, sensitivity (95% CI) increased to 64% (44% to 77%), specificity (95% CI) was slightly reduced at 97% (88% to 99%) and the DOR (95% CI) increased to 59.9 (16.9 to 212.3). It should be noted that the study by Shaarawy and colleagues,<sup>64</sup> which had a much smaller sample size than the other specimen sets, had much reduced specificity compared with the other three studies. It is likely that the small sample size accounted for this relatively low specificity.

The Clearview Chlamydia test is meant for use only in women, although the Clearview Chlamydia MF test can also be used with male FVU specimens.<sup>82</sup> This may explain the reduced sensitivity and specificity of the test when vaginal swab specimens are used instead of cervical swab specimens.<sup>65,66</sup> Use with a clinician-collected urethral swab<sup>71</sup> did not appear to compromise diagnostic accuracy, although the test is not validated for this type of sample.<sup>82,83</sup>

No studies were identified that directly compared the diagnostic accuracy of the CRT with Clearview Chlamydia. Evidence that one test is superior to the other can only be inferred from the indirect comparison of the results of each test compared with the reference standard. For the pooled estimates of Clearview Chlamydia's sensitivity using cervical, vaginal and urethral swab specimens combined, the upper 95% CI for the Clearview Chlamydia test did not overlap with the lower 95% CI for the CRT using vaginal swab specimens, suggesting that the CRT might be a more sensitive test. However, when only cervical specimens were pooled, the CIs overlapped. For specificity, overlap in the CIs was present (regardless of whether the pooled results for the Clearview Chlamydia test were based upon combined or cervical only specimens) when Clearview Chlamydia results were compared with CRT results (using either vaginal swab or FVU samples).

Diagnostic odds ratios for the pooled analysis of Clearview Chlamydia using combined (vaginal, cervical and urethral) specimen types had an upper 95% CI that did not overlap with the lower 95% CI for either the pooled analysis of the CRT using vaginal swab samples or the pooled analysis of the CRT using FVU samples. The pooled analysis of Clearview Chlamydia using cervical only specimens had an upper 95% CI that did not overlap with the lower 95% CI for the pooled analysis of the CRT using vaginal swab samples.

Interpretation of these results therefore largely depends on the emphasis placed on the value of the DOR as a measure of diagnostic accuracy. The DOR is used to summarise diagnostic accuracy into a single value, but compared with values of sensitivity and/or specificity, it is less directly interpretable from a clinical point of view. Given the limited number of studies eligible for inclusion in this review and the limited amount of data that could be used in the pooled analysis, the DOR results should be interpreted with caution, as there is currently insufficient evidence to determine whether the CRT (using either vaginal swab or FVU specimens) performs better than the Clearview Chlamydia test (using cervical specimens) as a POCT for detecting genital chlamydia. Further research is required to determine which test is more accurate in diagnosing chlamydia infection.

### Review of test performance – data that were not pooled

A summary of the results of data that could not be pooled is shown in *Table 13*.

The study by Mahilum-Tapay and colleagues<sup>50</sup> provides one additional set of self-collected vaginal swab specimens that could not be included in the pooled analysis for the CRT because a different reference standard (SDA) was used. The study did investigate if there was any significant difference depending on whether the SDA or PCR nucleic acid amplification method was used, and found that there was no evidence of a difference ( $p = 0.317$ ).<sup>50</sup> The sensitivity and specificity of self-collected vaginal swabs using the CRT compared with SDA, as reported by Mahilum-Tapay and colleagues,<sup>50</sup> lay within the CIs of the pooled analysis (see above) for vaginal swab specimens using the CRT compared with PCR testing.

Data from studies by Chernesky and colleagues,<sup>69</sup> Hopwood and colleagues<sup>68</sup> and Lauderdale and colleagues<sup>70</sup> provided four additional sets of specimens on the diagnostic accuracy of Clearview Chlamydia. One set used FVU samples from men,<sup>69</sup> whilst the remaining three sets used cervical specimens from women.<sup>68,70</sup> One of the cervical specimen sets<sup>70</sup> was compared with the TMA method as the NAAT reference standard, whilst the remaining sets used the LCx assay which was withdrawn in 2002 following concerns over its reproducibility.<sup>76,81</sup> The sensitivity of the cervical specimen sets ranged from 50% to 75%, whilst specificity ranged from 99.2% to 100%. For sensitivity, these results are within the CIs for the pooled analysis of the sensitivity of the Clearview

**TABLE 13** Summary of the results for studies not pooled in the analysis of diagnostic accuracy

POCT	Type of point-of-care specimen included	Type of NAAT test used	Number of specimen sets included (from number of studies)	Number of participants included (number of specimens included)	Sensitivity	Specificity
Chlamydia Rapid Test	Vaginal	SDA	1 (1)	637 (637)	81.6%	98.3%
Clearview Chlamydia	FVU	LCR	1 (1)	128 (128)	67.7%	95.5%
Clearview Chlamydia	Cervical	LCR	1 (1)	395 (395)	75.0%	99.2%
Clearview Chlamydia	Cervical	LCR	1 (1)	65 (65)	50.0%	100%
Clearview Chlamydia	Cervical	TMA	1 (1)	65 (65)	50.0%	100%
Chlamydia Wand/ HandiLab C	Vaginal	SDA	1 (1)	100 (100)	36.4%	79.8%
Chlamydia Wand/ HandiLab C	Vaginal	PCR	1 (1)	231 (231)	18.4%	90.7%
QuickVue Chlamydia	Cervical	PCR	1 (1)	99 (99)	64.7%	100%
QuickVue Chlamydia	Cervical	PCR	1 (1)	100 (100)	25.0%	100%
Magic Lite Chlamydia	Urethral	PCR	1 (1)	283 (283)	72.1%	99.6%
Magic Lite Chlamydia	Cervical	PCR	1 (1)	724	60.5%	99.9%
SureCell Chlamydia	FVU	LCR	1	128	62.9%	100%

Chlamydia test using cervical samples alone. However, the specificities cited by these individual studies are higher than the pooled result. This is perhaps explained by low specificity in the Shaarawy study<sup>64</sup> included in the pooled estimates.

There are no FVU samples eligible for inclusion in the pooled analysis of Clearview Chlamydia results using all specimen types. The sensitivity of the study comparing Clearview Chlamydia using FVU specimens, with the LCx assay (with a DFA test as confirmation)<sup>69</sup> at 67.7% was above the upper 95% CI limit of the pooled estimate for all specimen types (65%). However, the specificity was within the 95% CI for the pooled estimate, and both sensitivity and specificity were within the 95% CI limits for the pooled estimates of Clearview Chlamydia using cervical specimens compared with PCR. These results could indicate that using Clearview Chlamydia with an FVU sample may, like cervical samples, be more sensitive than using the test with vaginal swab specimens. More evidence, however, is needed to be able to draw reliable conclusions. Furthermore, it should be noted that

the study in question was the first to analyse use of the Clearview Chlamydia test with FVU specimens, using modifications to the original test (meant only for cervical specimens) and not the Clearview Chlamydia MF test which is validated for use with FVU specimens.<sup>69,83</sup>

In addition to the two POCTs for which pooled analysis could be undertaken, results were available for another four POCTs. The Magic Lite test using urethral specimens reported the highest sensitivity (72.1%) compared with PCR as the reference standard, in the study by Kluytmans and colleagues.<sup>71</sup> The test with the lowest reported sensitivity was the Surescreen Chlamydia wand (18.4%), where PCR was again the reference standard, in the study by Michel and colleagues.<sup>74</sup> The highest specificity reported was 100% for the QuickVue Chlamydia test (using both the GUM clinic and hospital gynaecology department venues) compared with PCR, in the study by Rani and colleagues,<sup>67</sup> and the SureCell Chlamydia test, using the LCx as the reference standard, in the study by Chernesky and colleagues.<sup>69</sup> The lowest



specificity reported (79.8%) used the Surescreen Chlamydia wand compared with PCR as the reference standard, in the study by Kegg and colleagues.<sup>73</sup>

## Review of effectiveness

The comparative effectiveness of point-of-care testing with current practice in terms of the number of cases detected, treated and the number of partners identified, notified, tested and treated was not possible because of a lack of available evidence. This review found no RCTs or non-randomised studies comparing any of the identified POCTs with current practice using NAATs, for any of these outcomes. Therefore, it was not possible to determine whether or not the CRT was more effective than current practice for testing and diagnosing genital chlamydia infection in terms of the number of cases detected and treated, and the proportion of partners notified and treated. Further research is required to evaluate the practical use of point-of-care testing compared with laboratory testing methods currently in use throughout the NHS. The need for this research on non-diagnostic outcomes is particularly important because the relevance of point-of-care testing methods to diagnose chlamydia in clinical practice extends beyond their diagnostic accuracy, owing to what Gift and colleagues<sup>49</sup> referred to as 'the rapid test paradox', whereby the non-return rate of positively infected patients (from the time of being tested to the time of requested attendance for treatment after a delay caused by waiting for a laboratory-based diagnosis) exceeds any relative diagnostic superiority, in terms of sensitivity and specificity, of the laboratory-based testing method over a POCT. In this way, even with poorer diagnostic accuracy, more positive cases could potentially be treated using the POCT than with a laboratory-based method,<sup>84</sup> as treatment of the patient would take place immediately and contact tracing of sexual partners could also begin without delay.

## Acceptability outcomes and patient preferences

Five studies provided information on the acceptability of the tests used,<sup>50,66,72,73,75</sup> but no more than two studies reported data on the same outcome using the same criteria (e.g. cut-offs for waiting time categories), and the methods used for collecting acceptability data were not well reported by any of the studies.

The data collected showed that the majority of those surveyed would be willing to wait for up to 2 hours for the results of a POCT. Results also suggested that the vast majority (over 90% in each instance) were comfortable collecting either vaginal swab or urine samples for testing, and found instructions for collection of these specimens easy to understand. In terms of preferred type of specimen to provide (urine sample or urethral swab), most (88.8%, 619/697) would prefer to provide a urine sample. For cup collection methods, both studies comparing preference between the new 'FirstBurst' method and routine cup collection found that most participants (78.6%, 736/936) preferred the 'FirstBurst' method. Between providing a vaginal swab specimen or a urine specimen, there was no clear method favoured by most participants, but 40.7% (435/1068) would prefer to provide a self-collected vaginal swab, whilst 37.6% (401/1068) would prefer to provide a urine sample and the remaining 21.7% (232/1068) had no preference.

Acceptability outcomes for staff were only available from the study by Yin and colleagues,<sup>66</sup> questioning 14 staff members on use of the Clearview Chlamydia test. Most responded that the test had clear instructions from the manufacturer, was easy to use, took around 10 minutes of 'hands-on' time to perform, gave a 'rapid' result in less than 20 minutes and required less than 30 minutes of training time.

There is a need for more research to be conducted on the acceptability of POCTs to both patients and staff, to provide more robust evidence of the acceptability of these tests, particularly in comparison with current practice.

The results of the DCE suggest that, in terms of patients' own preferences for chlamydia testing services, family planning clinics are preferred as a facility for screening, and less invasive techniques are favoured. Further research investigating preferences for setting, type of tests, diagnostic accuracy and waiting time for results is needed. A DCE comparing variation in these attributes would be useful to consider how patients might trade off these attributes against poorer diagnostic performance of a test providing a faster result (e.g. POCTs). Such information would also be useful for improving the economic model to incorporate patient preferences, as those data available were sparse and not suitable for incorporation into the economic model for this review.

Three studies reported interpretability or reproducibility outcomes.<sup>50,66,75</sup> For both POCTs, reproducibility and/or interpretability outcomes were good. There was 100% concordance between the expected results and the results generated at an independent laboratory by two operators using randomised masked panels in both the studies by Mahilum-Tapay and colleagues<sup>50</sup> and Nadala and colleagues.<sup>75</sup> The study by Yin and colleagues<sup>66</sup> found statistically significant agreement between the results of the Clearview Chlamydia test, when interpreted by two different members of staff ( $p < 0.001$ ). These results indicate that the interpretability of both the CRT and the Clearview Chlamydia test is good, although the fact that only three of the 13 included studies reported any interpretability outcomes suggests that further data on this would be beneficial.

### Cost-effectiveness

The cost-effectiveness analysis compared two POCTs (the CRT and Clearview Chlamydia) and one NAAT method (PCR testing) in a setting where screening would generally be offered. In the analysis, the estimates of the total costs of screening a cohort of 1000 men and women aged 16–24 years were provided. The findings suggest that the current methods of testing using PCR would identify more true-positive cases than either of the POCTs. The CRT performs better than Clearview Chlamydia in identifying more true-positives, fewer false-negatives and more true-negatives, and is the more effective POCT. The current practice of using PCR would be the least costly method of detecting chlamydia, at a total cost for the cohort of £7070, and it would result in the most people correctly treated and their partners contacted (12.63 people per 1000 who are offered the test assuming a prevalence of chlamydia of 7.8%). Therefore no incremental cost-effectiveness of the CRT was found when compared with current practice.

Nevertheless, the CRT may still be worth considering (compared with current practice), if the acceptance rate of the offer of testing using this method could be increased. For example, if acceptance rate of the offer was 22.75% or greater (the base-case uptake rate of the testing for CRT was 18.9% and the uptake rates for the other tests was kept at 18.9%) then the CRT would be more effective but more costly than current practice. A judgement would be required as to whether the extra effectiveness would be worth the extra cost. Such a situation might arise if the POCT was deemed to be more acceptable to patients, for example if it was more convenient to them

(in terms of location of testing and the speed in obtaining a result).

The results were also (as might be expected) sensitive to reductions in the cost of the POCT. This showed that increases in uptake rates and reductions in cost could make the CRT worthwhile, although results were not sensitive to changes in diagnostic accuracy for the levels used in the analysis. The sensitivity analysis conducted has highlighted some of the key areas for further investigation, including prevalence and uptake rates. These are discussed in Strengths and limitations of the assessment.

### Strengths and limitations of the assessment

In terms of strengths of the research, a NAAT method was used as the reference standard, and the results for only people who received both the POCT and the reference standard were included in the pooled estimates. The use of point-of-care testing in a variety of different settings (e.g. GUM clinics, hospital obstetric and gynaecology venues, social hygiene clinics for female sex workers and sexual health centres providing contraceptive advice) was considered. The manufacturers of the CRT were contacted for information on any ongoing studies, and provided 'in confidence' reports of two studies awaiting publication. This provided sufficient information for pooled estimate analysis of the diagnostic accuracy of the CRT for more than one type of specimen (i.e. vaginal swab and FVU samples).

In terms of limitations, non-English studies were excluded, as were abstracts published prior to 2006. Most (nine of the 13) included studies had entirely female populations, and therefore may not be relevant to evaluating POCTs in male populations. Also, although age group is considered important in terms of risk, not all studies reported the age groups of participants and, of those who did, most did not report any information by age group. Therefore, subgroup analysis could not be performed on the high-risk age group (18–24 years), for the review of diagnostic accuracy.

It has been assumed that all the strains of chlamydia identified in Chapter 1 – Aetiology, pathology and the impact of the health problem – are equally detected by NAATs. It has also been assumed that all cases of chlamydia are of equal importance, but it is possible that some untreated positive cases clear spontaneously.

No comparative studies were identified that reported effectiveness outcomes for the POCTs under consideration (for example, the number of cases detected and treated and the number of partners notified and treated). Therefore, it was not possible to undertake a review of effectiveness. It was also not possible to consider the public health implications of effectiveness, e.g. re-infection, which is of particular relevance to high-risk populations (i.e. those aged less than 25 years). In addition, methods used in evaluating the acceptability and interpretability of POCTs within diagnostic accuracy studies were poorly reported, and few DCE studies were eligible for inclusion in this review.

For the economic evaluation, the short time horizon has led to a focus on diagnostic outcomes of test performance, likelihood of receiving treatment and contact tracing. The impact on health has not been considered nor has the effect of testing on the overall burden of the infection. It is possible that a herd immunity from chlamydia could occur if the vast majority of a population is tested and treated regularly, preventing the overall spread of infection. However, it is more likely that re-infection would create a longer term burden on services. It might be expected, however, that the more effective test in terms of the outcomes modelled would be the test that results in the highest health gain and the greatest reduction in the prevalence of infection in the population.

The focus of this review is point-of-care testing; therefore, other possible options for providing chlamydia testing services through altering the current NAAT service were not examined. Several alternatives could be considered, for example reducing transport times between the testing centre and the laboratory, reducing laboratory processing times, and undertaking dual testing of chlamydia alongside testing for gonorrhoea. However, it is likely that enhancing the way in which chlamydia testing services are currently provided would incur capital costs and also require additional staff.

The analysis conducted has been deterministic in nature but has been supplemented by various sensitivity analyses. Ideally, further sensitivity analysis might be useful to explore threshold values for key parameters more fully. For example, the cost estimates for testing are applicable to venues where testing is currently carried out, but further investigation on the implications on cost of conducting testing in each of these different venues could improve the model. It was not possible to include these parameters in the sensitivity analysis because of the lack of evidence on uptake rates at different testing venues.

However, the sensitivity analysis conducted has highlighted this and other key areas for further investigation (e.g. uptake rates, prevalence and costs of the tests).

## Uncertainties

The dearth of available evidence hinders the interpretability of results. For the diagnostic accuracy review there is insufficient evidence available to conclude whether or not the CRT is a POCT with enhanced diagnostic capabilities compared with other POCTs. There were insufficient comparative studies available to conduct a review of effectiveness. For the review of patient preferences, there were few data available that were suitable enough to allow preferences to be incorporated into the economic model. For the economic evaluation, the impact of different methods of chlamydia testing on patients' health has not been considered, nor has the effect of different testing methods on the overall burden of infection.

The withdrawal of the LCx assay in 2002 because of reproducibility issues<sup>76,81</sup> means that the diagnostic accuracy results for studies using this method as the reference standard should be interpreted with caution (although in any event there were insufficient comparable specimen sets for pooled analysis using this test as the reference standard).



# Chapter 9

## Conclusions

### Implications for service provision

In terms of diagnostic accuracy, the sensitivity of the CRT was higher than that of the Clearview Chlamydia test, but the sensitivity of POCTs was inferior to the current reference standard of NAAT testing for detecting genital chlamydia infection, and there was insufficient evidence available to suggest a clear difference in the performance of the point-of-care methods. However, both POCTs reported levels of specificity that were similar to the current reference standard, suggesting that all tests are effective in ruling out the presence of infection in uninfected patients. In addition, as things stand, NAAT methods currently used for diagnosing chlamydia remain the most cost-effective for service providers.

Nevertheless, even with relatively poorer diagnostic accuracy than in NAATs, POCTs could potentially still treat more infected people in instances where non-return rates for treatment using laboratory-based testing methods are particularly high or, as suggested by the economic evaluation, where uptake rates are increased by using the CRT method. However, this review found no comparative studies that had compared outcomes other than diagnostic accuracy for POCTs against NAATs. Until there is more robust evidence on the clinical effectiveness of POCTs beyond their diagnostic accuracy, service providers would need to provide point-of-care testing as a preliminary adjunct to existing laboratory testing with NAATs, and not as a replacement for current service provision for chlamydia diagnosis.

There is a very limited amount of evidence on the acceptability of POCTs, but the results suggest that most patients find these methods of testing acceptable. Evidence from a selective sample shows that women preferred having chlamydia testing services provided in family planning clinics, and preferred less invasive techniques for specimen collection. If services accommodate these preferences as far as possible, there is potentially an opportunity to increase uptake rates for testing. Further research is needed to determine whether

increasing uptake rates would make point-of-care testing a viable alternative to current practice.

### Suggested research priorities

This review did not identify any studies comparing point-of-care testing with NAATs that reported effectiveness outcomes, therefore research on this subject is required. Until this is done, the extent to which the ability of POCTs to provide an immediate result compensates for reduced diagnostic accuracy will not be known.

Research on uptake rates using point-of-care testing would be beneficial as there is evidence to suggest that if the CRT can improve uptake rates for testing, it could become more cost-effective than current practice using NAATs. A DCE would be useful for this type of research, as it is a research method that could predict uptake rates for a particular service, based on the preferences elicited from respondents. Further research on patients' preferences, and the extent to which they find point-of-care testing acceptable, would also be necessary to evaluate this type of testing, and could perhaps also be used in instances where the cost-effectiveness of point-of-care testing is being considered.

Further studies are needed to confirm the relative diagnostic accuracy of the CRT compared with other POCTs, as there is currently not enough evidence available (from clinically similar sets of specimens) to allow a robust comparison of POCTs and NAATs.

The evidence on the long-term effects of undiagnosed chlamydia infection is confusing, as it is now estimated that the early evidence overestimated the proportion of infected patients who develop long-term complications from infection. There is a need to precisely determine the correct scale of the problem, as the potential for future ill-health resulting from undiagnosed chlamydia is what provides the rationale for prioritising research on effective testing.





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### Contribution of authors

Jenni Hislop (Research Fellow) screened the search results, assessed full text studies for inclusion,

undertook data extraction and quality assessment, drafted the chapters on diagnostic accuracy and clinical effectiveness, and co-ordinated the review. Zahidul Quayyum (Research Fellow) drafted the chapters on patient preferences and cost-effectiveness, supervised by Luke Vale (Professor of Health Technology Assessment). Gillian Flett (Clinical Lead for Sexual Health, NHS Grampian) drafted the background chapter with assistance from Jenni Hislop and Zahidul Quayyum. Charles Boachie (Statistician) drafted the data analysis section of the review and conducted the statistical analysis. Gillian Flett provided expert advice on clinical aspects of the review. Cynthia Fraser (Information Officer) developed and ran the search strategies, obtained papers and formatted the references. Graham Mowatt (Senior Research Fellow) screened full-text papers, checked data extraction, undertook quality assessment and drafted quality assessment results and tables. All authors assisted in preparing the manuscript, reading and commenting on drafts and reading the final draft.







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# Appendix I

## Search strategies

### Clinical effectiveness

**MEDLINE (1966 – Week 3 November 2008), EMBASE (1980 – Week 48 2008), Medline In-Process (26 November 2008)**

**Ovid multifile search URL: gateway.ovid.com/athens**

1. chlamydia infection/use mesz
2. chlamydiae/use emez
3. chlamydia/use mesz
4. chlamydia trachomatis/
5. chlamydia.tw.
6. or/1–5
7. “Point-of-Care Systems”/use mesz
8. “Point of Care Testing”/use emez
9. point of care.tw.
10. poct?.tw.
11. near patient?.tw.
12. (rapid adj1 test\$.tw.
13. (clearview or surecell or quickvue or biostar or oia or handilab or nptgold or insticheck).tw.
14. or/7–13
15. 6 and 14
16. limit 15 to english language
17. remove duplicates from 16

**Science Citation Index (1970 – 22 November 2008)**

**BIOSIS (1985 – 27 November 2008)**

**ISI Proceedings (1990 – 22 November 2008)**

**Web of Knowledge URL: wok.mimas.ac.uk/**

- #1 TS=chlamydia AND Language=(English)
- #2 TS=point of care AND Language=(English)
- #3 TS=poct\* AND Language=(English)
- #4 TS=(rapid SAME test\*) AND Language=(English)
- #5 TS=(clearview OR surecell or quickvue or biostar or oia or handilab or nptgold or insticheck) AND Language=(English)
- #6 #2 or #3 or #4 or #5 AND Language=(English)
- #7 #1 and #6 AND Language=(English) and TA=humans

### Cochrane Library Issue 4, 2008

**URL: www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME**

- #1 MeSH descriptor Chlamydia Infections, this term only
- #2 MeSH descriptor Chlamydia, this term only
- #3 MeSH descriptor Chlamydia trachomatis, this term only
- #4 (chlamydia)
- #5 (#1 OR #2 OR #3 OR #4)
- #6 MeSH descriptor Point-of-Care Systems, this term only
- #7 (point of care) or (poct\*)
- #8 “near patient\*” or (rapid NEAR/3 test\*)
- #9 (clearview) or (surecell) or (quickvue) or (biostar) or (oia)
- #10 (handilab) or (nptgold or insticheck)
- #11 (#6 OR #7 OR #8 OR #9 OR #10)
- #12 (#5 AND #11)

### DARE and HTA Databases (November 2008)

**Centre for Reviews and Dissemination**

**URL: www.york.ac.uk/inst/crd**

- #1 MeSH Chlamydia
- #2 MeSH Chlamydia Infections
- #3 MeSH Chlamydia trachomatis
- #4 chlamydia
- #5 #1 OR #2 OR #3 OR #4
- #6 MeSH Health Services Administration EXPLODE 1 2
- #7 MeSH Point-of-Care Systems
- #8 “point of care”
- #9 “near patient\*”
- #10 poct\*
- #11 “rapid test\*”
- #12 clearview OR surecell OR quickvue OR biostar
- #13 oia OR handilab OR nptgold or insticheck
- #14 #7 or #8 or #9 or #10 or #11 or #12 or #13
- #15 #5 and #14

**Health Management Information Consortium (1979 – October 2008)**  
**Ovid Gateway URL: gateway.ovid.com/athens**

1. chlamydia infections/
2. chlamydia.tw.
3. 1 or 2
4. point of care.tw.
5. poct\*.tw.
6. near patient\*.tw.
7. (rapid adj1 test\*).tw.
8. (clearview or surecell or quickvue or biostar or oia or handilab or nptgold).tw.
9. or/4–8
10. 3 and 9

**Clinical Trials (November 2008)**  
**URL: clinicaltrials.gov/ct/gui/c/r**  
 “chlamydia infections”:Topic

**Current Controlled Trials (November 2008)**  
**URL: www.controlled-trials.com/**  
 Chlamydia AND test%

**World Health Organization International Clinical Trials Registry Platform (November 2008)**  
**URL: www.who.int/ictrp/en/**  
 chlamydia:Condition

**Computer Retrieval of Information on Scientific Projects (November 2008)**  
**URL: crisp.cit.nih.gov/**  
 Chlamydia AND test\*

**Conference proceedings**  
**European Society of Clinical Microbiology and Infectious Diseases**  
 16th European Congress, Copenhagen, Denmark, 2–5 April 2005

16th European Congress, Nice, France, 1–4 April 2006

17th European Congress, Munich, Germany, 31 March–3 April 2007

18th European Congress, Barcelona, Spain, 19–22 April 2008

**American Association for Clinical Chemistry**  
 Annual meeting, Orlando, FL, USA, 25–28 July 2005

Annual meeting, Chicago, IL, USA, 23–27 July 2006

Annual meeting, San Diego, CA, USA, 15–19 July 2007

Annual meeting, Washington, DC, USA, 27–31 July 2008

**International Society for Sexually Transmitted Diseases Research**  
 16th Biennial meeting, Amsterdam, the Netherlands, 11–13 July 2005

17th Biennial meeting, Seattle, WA, USA, 30 July–1 August 2007

**British Association for Sexual Health and HIV**  
 Spring Meeting, Blackpool, UK, 2–4 May 2006

Spring Meeting, Nottingham, UK, 17–19 May 2007

**Patient preferences**  
**MEDLINE (1966 – Week 3 November 2008), EMBASE (1980 – Week 48 2008), Medline In-Process (1 December 2008)**  
**Ovid multifile search URL: gateway.ovid.com/athens**

1. chlamydia infection/use mesz
2. chlamydiasis/use emez
3. chlamydia/use mesz
4. chlamydia trachomatis/
5. chlamydia.tw.
6. or/1–5
7. “Point-of-Care Systems”/use mesz
8. “Point of Care Testing”/use emez
9. point of care.tw.
10. poct?.tw.
11. near patient?.tw.
12. (rapid adj1 test\$.tw.
13. (clearview or surecell or quickvue or biostar or oia or handilab or nptgold).tw.
14. mass screening/
15. screen\$.tw.
16. (opportun\$adj3 test\$.tw.
17. or/7–16
18. 6 and 17
19. patient satisfaction/
20. patient attitude/use emez
21. attitude/use mesz
22. decision making/
23. choice behavior/



24. willing\$to pay.tw.
25. willing\$to wait.tw.
26. (discrete adj3 choice\$.tw.
27. standard gamble.tw.
28. contingennt valu\$.tw
29. ((preference\$or opinion\$or choice\$) adj3 (elicit\$or measure\$or obtain\$or technique\$)).tw.
30. rating scale/
31. questionnaires/
32. (hui or hui1 or hui2 or hui3).tw.
33. (health adj3 (utilit\$or disutili\$)).tw.
34. or/19–32
35. 18 and 33
36. limit 34 to english language

### Science Citation Index (1970 – 1 November 2008)

Web of Knowledge URL: [wok.mimas.ac.uk/](http://wok.mimas.ac.uk/)

- #1 TS=chlamydia AND Language=(English)
- #2 TS=point of care AND Language=(English)
- #3 TS=poct AND Language=(English)
- #4 TS=(rapid SAME test\*) AND Language=(English)
- #5 TS=(clearview or surecell or quickvue or biostar or oia or handilab or nptgold or insticheck) AND Language=(English)
- #6 1,312 TS=(chlamydia and screen\*) AND Language=(English)
- #7 TS=(opportun\* SAME test\*) AND Language=(English)
- #8 #1 and (#2 or #3 or #4 or #5 or #6 or #7) AND Language=(English)
- #9 TS=willing\* to pay AND Language=(English)
- #10 TS=willing\* to wait AND Language=(English)
- #11 TS=standard gamble AND Language=(English)
- #12 TS=(discrete SAME choice) AND Language=(English)
- #13 TS=((preference\* SAME elicit\*) or (preference\* SAME measure\*) or (preference\* SAME obtain\*) or (preference\* SAME technique\*)) AND Language=(English)
- #14 TS=((opinion\* SAME elicit\*) or (opinion\* SAME measure\*) or (opinion\* SAME obtain\*) or (opinion\* SAME technique\*)) AND Language=(English)
- #15 TS=((elicit\* SAME elicit\*) or (elicit\* SAME measure\*) or (elicit\* SAME obtain\*) or (elicit\* SAME technique\*)) AND Language=(English)

- #16 TS=((choice\* SAME elicit\*) or (choice\* SAME measure\*) or (choice\* SAME obtain\*) or (choice\* SAME technique\*)) AND Language=(English)
- #17 TS=(utilit\* or disutilit\*) AND Language=(English)
- #18 #8 and (#9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17) AND Language=(English) AND Document Type=(Article)

**Health Management Information Consortium (1979 – November 2008)**  
Ovid multifile search URL: [gateway.ovid.com/athens](http://gateway.ovid.com/athens)

1. chlamydia infections/
2. chlamydia.tw.
3. 1 or 2
4. point of care.tw
5. poct\*.tw
6. near patient\*.tw.
7. (rapid adj1 test\*).tw.
8. (clearview or surecell or quickvue or biostar or oia or handilab or nptgold).tw.
9. mass screening/
10. screen\*.tw
11. (opportun\* adj3 test\*).tw
12. or/4–11
13. 3 and 12

### Economic evaluation

**NHS Economic Evaluation Database (November 2008)**

**Health Technology Assessment Database (November 2008)**

**Centre for Reviews and Dissemination URL: [www.york.ac.uk/inst/crd](http://www.york.ac.uk/inst/crd)**

- #1 MeSH Chlamydia
- #2 MeSH Chlamydia Infections
- #3 MeSH Chlamydia trachomatis
- #4 chlamydia
- #5 #1 OR #2 OR #3 OR #4

### IDEAS (November 2008)

RePeC URL: [ideas.repec.org/](http://ideas.repec.org/)  
chlamydia

### Websites consulted (accessed January 2009)

Australia and New Zealand Horizon Scanning Network  
URL: [www.horizonscanning.gov.au/](http://www.horizonscanning.gov.au/)

Biostar OIA Chlamydia, Inverness Medical  
Professional Diagnostics  
URL: [www.invernessmedicalpd.com/poc/products/oia\\_chlamydia.html](http://www.invernessmedicalpd.com/poc/products/oia_chlamydia.html)

British Association for Sexual Health and HIV  
URL: [www.bashh.org/](http://www.bashh.org/)

Clearview Chlamydia, Inverness Medical  
Professional Diagnostics  
URL: [www.invernessmedicalpd.com/poc/products/clr\\_chlamydia.html](http://www.invernessmedicalpd.com/poc/products/clr_chlamydia.html)

Department of Health  
URL: [www.dh.gov.uk/en/index.htm](http://www.dh.gov.uk/en/index.htm)

Enigma Diagnostics  
URL: [www.enigmadiagnostics.com/](http://www.enigmadiagnostics.com/)

HandiLab, Zonca Incorporated  
URL: [www.zondaincusa.com/index2.php?id=spproducts](http://www.zondaincusa.com/index2.php?id=spproducts)

Health Protection Agency (HPA)  
URL: [www.hpa.org.uk/](http://www.hpa.org.uk/)

Medicines and Healthcare products Regulatory  
Agency  
URL: [www.mhra.gov.uk/](http://www.mhra.gov.uk/)

National Chlamydia Screening Programme  
URL: [www.chlamydia-screening.nhs.uk/](http://www.chlamydia-screening.nhs.uk/)

National Institute for Health and Clinical  
Excellence  
URL: [www.nice.org.uk/nice-web/Cat.asp?c=20](http://www.nice.org.uk/nice-web/Cat.asp?c=20)

NHS Quality Improvement Scotland  
URL: [www.nhshealthquality.org/nhsqis/](http://www.nhshealthquality.org/nhsqis/)

Quickvue Chlamydia, bioMérieux UK Ltd  
URL: [www.quickvue.co.uk/en/gbr/contact.html](http://www.quickvue.co.uk/en/gbr/contact.html)

Scottish Intercollegiate Guideline Network  
URL: [www.sign.ac.uk/](http://www.sign.ac.uk/)

US National Institute of Health: Sexually  
Transmitted Diseases  
URL: [health.nih.gov/result.asp/588](http://health.nih.gov/result.asp/588)

US Agency for Healthcare Research and Quality  
URL: [www.ahrq.gov/](http://www.ahrq.gov/)

# **Appendix 2**

## Data extraction form – diagnostic accuracy

**Point-of-care Testing for Chlamydia Infection**  
**Data extraction – Diagnostic accuracy**

Reviewer ID:

Date:

**Administration details for study:**

**Study ID:**

**Study design:**

**Multicentre study:**

Yes. Number of centres \_\_\_\_\_

No

- RCT

All patients randomised to index vs comparator. All also receive the reference standard

- Direct (head to head)

comparison. All patients receive index test, comparator and reference standard

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**Country/countries:**

**Setting** (e.g. primary care, GUM clinic, community health point):

**Duration of study:**

**Funding details** government / private / manufacturer / other (specify):

**Study start/end dates:**

**Additional info:**

**Length of follow-up:**

**Aim of study:**

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**Comparisons:**

- *Chlamydia* Rapid test vs other POCT comparator and reference standard

Specify index test

Specify comparator

Specify reference standard used

- *Chlamydia* Rapid test vs NAAT comparator (i.e. the reference standard)

Specify index test

Specify reference standard used

**Outcomes reported:**

Test performance results

Data provided for relevant subgroup:

Acceptability of the test to patients/healthcare staff (delete as appropriate)

Those aged <25 years old

Men who have sex with men (MSM)

Sex workers

Interpretability of the test

High-risk African populations

**Inclusion criteria:**

**Exclusion criteria:**

**Characteristics of participants:**

	Index test	Comparator 1	Comparator 2	All
Enrolled				
Received tests				
Received reference standard				
Analysed				
Number of uninterpretable tests				
Lost to follow-up				
Age (mean/median, SD/IQR range)				
Sex	F: M:	F: M:	F: M:	F: M:
% aged < 25				
% MSM				
% sex workers				
% other high risk groups (please specify)				

**Additional information on participants:**

**Characteristics of the tests:****Index test:** *Chlamydia* Rapid Test**Manufacturer, country:****Number of samples taken per patient:****Time taken till test result available:****Sample(s) obtained by:** Voided urine Urethral swab Endocervical swab Vaginal swab (self taken) Vaginal swab (taken by practitioner)

Other (specify)

**Setting where sample was collected:** General practitioner GUM clinic Family planning centre Acute care Other community health point. Please specify (e.g. pharmacy, youth club)**Positive test result defined as:****Additional information on test:**

**Comparator test 1:**

**Manufacturer, country:**

**Type of test:**

**Time taken till test result available:**

- POCT
- NAAT
- Other (please specify)

**Number of samples taken per patient:**

**Sample(s) obtained by:**

**Setting where sample was collected:**

- |   |  |
|---|--|
| <input type="checkbox"/> Voided urine                         | <input type="checkbox"/> General practitioner  |
| <input type="checkbox"/> Urethral swab                        | <input type="checkbox"/> GUM clinic  |
| <input type="checkbox"/> Endocervical swab                    | <input type="checkbox"/> Family planning centre  |
| <input type="checkbox"/> Vaginal swab (self taken)            | <input type="checkbox"/> Acute care  |
| <input type="checkbox"/> Vaginal swab (taken by practitioner) | <input type="checkbox"/> Other community health point. Please specify (e.g<br>pharmacy, youth club): |
| Other (specify)   |  |

**Positive test result defined as:**

**Additional information on test:**



**Characteristics of the tests:****Comparator test 2:****Manufacturer, country:****Type of test:****Time taken till test result available:** POCT NAAT Other (please specify)**Number of samples taken per patient:****Sample(s) obtained by:****Setting where sample was collected:** Voided urine General practitioner Urethral swab GUM clinic Endocervical swab Family planning centre Vaginal swab (self taken) Acute care Vaginal swab (taken by practitioner) Other community health point. Please specify (e.g pharmacy, youth club):

Other (specify)

**Positive test result defined as:****Additional information on test:****Reference standard test:****Manufacturer, country:****Type of NAAT:****Time taken till test result available:** Polymerase chain reaction (PCR) Ligase chain reaction (LCR) Strand displacement amplification (SDA)**Time interval between index test and reference standard test:** Transcription mediated amplification (TMA)

**Number of samples taken per patient:**

**Sample(s) obtained by:**

- Voided urine
- Urethral swab
- Endocervical swab
- Vaginal swab (self taken)
- Vaginal swab (taken by practitioner)
- Other (specify) \_\_\_\_\_

**Setting where sample was collected:**

- General practitioner
- GUM clinic
- Family planning centre
- Acute care
- Other community health point. Please specify (e.g pharmacy, youth club) \_\_\_\_\_

Positive test result defined as:

Additional information on test:

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**Results:**

	Index test	Comparator 1	Comparator 2	Reference standard
<b>N in analysis</b>				
<b>True-positives</b>				
<b>False-positives</b>				
<b>True-negatives</b>				
<b>False-negatives</b>				
<b>Sensitivity</b>				

Specificity

Positive LR

Negative LR

PPV

NPV

Diagnostic odds  
ratio

Additional information on results (e.g. contradictory results resolved by...):

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**Adverse events:**

General information on adverse events:

Adverse events reported	Index test	Comparator 1	Comparator 2	Reference standard
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Acceptability and interpretability of tests:

Additional study information:

# **Appendix 3**

## **Quality assessment checklist – diagnostic accuracy**

**HTA on Point-of-care Testing for Chlamydia Infection**  
**Quality assessment tool – Diagnostic accuracy studies (QUADAS Tool)**

Assessor initials:

Date assessed:

Study ID:

Item		Yes	No	Unclear
1.	Was the spectrum of patients representative of the patients who will receive the test in practice?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2.	Is the reference standard likely to correctly classify the target condition?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.	Is the time period between the reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4.	Did the whole sample or a random selection of the sample receive verification using a reference standard of diagnosis?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5.	Did patients receive the same reference standard regardless of the index test result?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6.	Was the reference standard independent of the index test (i.e. the index test did not form part of the reference standard)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7.	Were the index test results interpreted without knowledge of the results of the reference standard?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8.	Were the reference standard results interpreted without knowledge of the results of the index test?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9.	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10.	Were uninterpretable/intermediate/test results reported?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11.	Were withdrawals from the study explained?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12.	Were data on observer variation reported and within an acceptable range?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13.	Were data presented for appropriate sub-groups of patients (e.g. high risk groups)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

# Appendix 4

## List of included studies

### Charnesky et al. 1999

Charnesky M, Jang D, Krepel J, Sellors J, Mahony J. Impact of reference standard sensitivity on accuracy of rapid antigen detection assays and a leukocyte esterase dipstick for diagnosis of *Chlamydia trachomatis* infection in first-void urine specimens from men. *J Clin Microbiol* 1999;**37**:2777–80.

### Hopwood et al. 2001

Hopwood J, Mallinson H, Gleave T. Evaluation of near patient testing for *Chlamydia trachomatis* in a pregnancy termination service. *J Fam Plann Reprod Health Care* 2001;**27**:127–30.

### Kegg and Roberts 2006

Kegg S, Roberts C. Evaluation of a rapid self-administered test for *Chlamydia trachomatis*: caveat emptor. *Int J STD AIDS* 2006;**17**(Suppl. 1):39–40.

### Kluytmans et al. 1993

Kluytmans JA, Goessens WH, Mouton JW, Rijsoort-Vos JH, Niesters HG, Quint WG, et al. Evaluation of Clearview and Magic Lite tests, polymerase chain reaction, and cell culture for detection of *Chlamydia trachomatis* in urogenital specimens. *J Clin Microbiol* 1993;**31**:3204–10.

### Lauderdale et al. 1999

Lauderdale TL, Landers L, Thorneycroft I, Chapin K. Comparison of the PACE 2 assay, two amplification assays, and Clearview EIA for detection of *Chlamydia trachomatis* in female endocervical and urine specimens. *J Clin Microbiol* 1999;**37**:2223–9.

### Mahilum-Tapay et al. 2007

Mahilum-Tapay L, Laitila V, Wawrzyniak JJ, Lee HH, Alexander S, Ison C, et al. New point of care Chlamydia Rapid Test – bridging the gap between diagnosis and treatment: performance evaluation study. *BMJ* 2007;**335**:1190–4.

### Michel et al. 2009

Michel CE, Saison FG, Joshi H, Mahilum-Tapay LM, Lee HH. Pitfalls of internet-accessible diagnostic tests:

inadequate performance of a CE-marked *Chlamydia* test for home use. *Sex Transm Infect* 2009;**85**:187–9.

### Nadala et al. 2009

Nadala EC, Goh BT, Magbanua JP, Barber P, Swain A, Alexander S, et al. Performance evaluation of a new rapid urine test for chlamydia in men: prospective cohort study. *BMJ* 2009;**339**:b2655

### Rani et al. 2002

Rani R, Corbitt G, Killough R, Curless E. Is there any role for rapid tests for *Chlamydia trachomatis*? *Int J STD AIDS* 2002;**13**:22–4.

### Saison et al. 2007

Saison F, Mahilum-Tapay L, Michel CE, Buttress ND, Nadala EC, Jr., Magbanua JP, et al. Prevalence of *Chlamydia trachomatis* infection among low- and high-risk Filipino women and performance of *Chlamydia* rapid tests in resource-limited settings. *J Clin Microbiol* 2007;**45**:4011–17.

### Shaarawy 1998

Shaarawy M. *Chlamydia trachomatis* infection in pelvic inflammatory disease (PID) prevalence and comparative methodology. *Clin Lab* 1998;**44**:285–90.

### Wisniewski et al. 2008

Wisniewski CA, White JA, Michel CE, Mahilum-Tapay L, Magbanua JP, Nadala EC, Jr., et al. Optimal method of collection of first-void urine for diagnosis of *Chlamydia trachomatis* infection in men. *J Clin Microbiol* 2008;**46**:1466–9.

### Yin et al. 2006

Yin YP, Peeling RW, Chen XS, Gong KL, Zhou H, Gu WM, et al. Clinic-based evaluation of Clearview Chlamydia MF for detection of *Chlamydia trachomatis* in vaginal and cervical specimens from women at high risk in China. *Sex Transm Infect* 2006;**82**(Suppl. 5):v33–7.





## Appendix 5

### List of excluded studies

Study	Reason for exclusion from review	
	Diagnostic accuracy	Effectiveness
Alary M, Gbenafa-Agossa C, Aina G, Ndour M, Labbe AC, Fortin D, et al. Evaluation of a rapid point-of-care test for the detection of gonococcal infection among female sex workers in Benin. <i>Sex Transm Infect</i> 2006; <b>82</b> :V29–32.	Not a study on chlamydia	Not applicable
Andersen B, Gundgaard J, Kretzschmar M, Olsen J, Welte R, Oster-Gaard L. Prediction of costs, effectiveness, and disease control of a population-based program using home sampling for diagnosis of urogenital <i>Chlamydia trachomatis</i> infections (Structured abstract). <i>Sex Transm Dis</i> 2006; <b>33</b> :407–15.	Not applicable	No POCT used
Blanding J, Aarnaes S, Darrow V, De La Maza L, Peterson E. The evaluation of the chlamydia optical immunoassay (OIA) for the direct detection of <i>Chlamydia</i> in cervical specimens. <i>Interscience Conference on Antimicrobial Agents and Chemotherapy</i> 1995; <b>35</b> .	Pre-2006 abstract	Pre-2006 abstract
Bowden FJ. Reappraising the value of urine leukocyte esterase testing in the age of nucleic acid amplification. <i>Sex Transm Dis</i> 1998; <b>25</b> :322–6.	POCT cannot distinguish between chlamydia and other infections	POCT cannot distinguish between chlamydia and other infections
Braverman PK, Schwarz DF, Mph M, Deforest A, Hodinka RL, McGowan KL, et al. Use of ligase chain reaction for laboratory identification of <i>Chlamydia trachomatis</i> and <i>Neisseria gonorrhoeae</i> in adolescent women. <i>J Ped Adoles Gynecol</i> 2002; <b>15</b> :37–41.	No POCT used	No POCT used
Carder C, Mercey D, Benn P. <i>Chlamydia trachomatis</i> . <i>Sex Transm Infect</i> 2006; <b>82</b> (Suppl. 4):iv10–12.	Not a diagnostic accuracy study	Not a comparative study
Coleman P, Varitek V, Mushahwar IK, Marchlewicz B, Safford J, Hansen J, et al. Testpack Chlamydia, a new rapid assay for the direct detection of <i>Chlamydia trachomatis</i> . <i>J Clin Microbiol</i> 1989; <b>27</b> :2811–14.	NAAT not used as reference standard	No NAAT used
de Vries R, van Bergen JE, de Jong-van den Berg, Postma MJ. Systematic screening for <i>Chlamydia trachomatis</i> : estimating cost-effectiveness using dynamic modeling and Dutch data. <i>Value in Health</i> 2006; <b>9</b> :1–11.	Not applicable	Not a comparative study
Dean GL. Near-patient testing will not improve the control of sexually transmitted infections. <i>Sex Transm Infect</i> 2006; <b>82</b> :509–12.	Not applicable	Not a comparative study
Dean D, Ferrero D, McCarthy M. Comparison of performance and cost-effectiveness of direct fluorescent-antibody, ligase chain reaction, and PCR assays for verification of chlamydial enzyme immunoassay results for populations with a low to moderate prevalence of <i>Chlamydia trachomatis</i> infection. <i>J Clin Microbiol</i> 1998; <b>36</b> :94–9.	Not all participants received both tests	No outcomes of relevance
Diallo MO, Ghys PD, Vuylsteke B, Ettiegné-Traore V, Gnaore E, Soroh D, et al. Evaluation of simple diagnostic algorithms for <i>Neisseria gonorrhoeae</i> and <i>Chlamydia trachomatis</i> cervical infections in female sex workers in Abidjan, Cote d'Ivoire. <i>Sex Transm Infect</i> 1998; <b>74</b> :S106–111.	No POCT used	Not a comparative study
Ferris DG, Petry LJ, Fischer PM. Sensitivity of rapid antigen-detection tests for <i>Chlamydia trachomatis</i> screening. <i>JAMA</i> 1995; <b>273</b> :917–18.	Not a diagnostic accuracy study	Not a comparative study
Forward KR. The impact of switching to polymerase chain reaction for the diagnosis of <i>Chlamydia trachomatis</i> infections in women. <i>Can J Pub Health</i> 2003; <b>94</b> :229–32.	Not all participants received both tests	Not all participants received both tests

Study	Reason for exclusion from review	
	Diagnostic accuracy	Effectiveness
Gift TL, Walsh C, Haddix A, Irwin KL. A cost-effectiveness evaluation of testing and treatment of <i>Chlamydia trachomatis</i> infection among asymptomatic women infected with <i>Neisseria gonorrhoeae</i> . <i>Sex Transm Dis</i> 2002; <b>29</b> :542–51.	Not applicable	No POCT used
Gift TL, Pate MS, Hook EW, III, Kassler WJ. The rapid test paradox: when fewer cases detected lead to more cases treated: a decision analysis of tests for <i>Chlamydia trachomatis</i> . <i>Sex Transm Dis</i> 1999; <b>26</b> :232–40.	Not a diagnostic accuracy study	Not a comparative study
Gilbert G. Chlamydia rapid test as accurate as conventional testing. <i>J Natl Med Assoc</i> 2008; <b>100</b> :459–60.	Not a diagnostic accuracy study	Not a comparative study
Goeree R, Jang D, Blackhouse G, Chong S, Mahony J, Sellors J, et al. Cost-effectiveness of screening swab or urine specimens for <i>Chlamydia trachomatis</i> from young Canadian women in Ontario. <i>Sex Transm Dis</i> 2001; <b>28</b> :701–9.	Not applicable	Not a comparative study
Groody E, Leszczynski J, Hendricks K, Spesard J. IXth International Conference on Aids and the IVth Std World Congress. <i>Evaluation of Testpack Chlamydia, Kodak SureCell Chlamydia and Clearview Chlamydia across multiple clinical studies</i> . IXth International Conference on AIDS in affiliation with the IVth STD World Congress, 1993.	Pre-2006 abstract	Not applicable
Greer L, Wendel GD, Jr. Rapid diagnostic methods in sexually transmitted infections. <i>Infect Dis Clin North Am</i> 2008; <b>22</b> :601–17.	Not a diagnostic accuracy study	Not applicable
Heath CB, Heath JM. <i>Chlamydia trachomatis</i> infection update. <i>Am Fam Physician</i> 1995; <b>52</b> :1455–61.	Not applicable	Not a comparative study
Herring A, Ballard R, Mabey D, Peeling RW. Evaluation of rapid diagnostic tests: chlamydia and gonorrhoea. <i>Nature Rev Microbiol</i> 2006; <b>6</b> :S41–8.	Not applicable	Not a comparative study
Hesterberg LK. An overview of rapid immunoassays. <i>Lab Med</i> 1996; <b>27</b> :41–6.	Not applicable	Not a comparative study
Hobbs FD, Delaney BC, Fitzmaurice DA, Wilson S, Hyde CJ, Thorpe GH, et al. A review of near patient testing in primary care. <i>Health Technol Assess</i> 1997; <b>1</b> (5).	Not applicable	Not a comparative study
Hogan DR, Baltussen R, Hayashi C, Lauer JA, Salomon JA. Cost effective analysis of strategies to combat HIV/AIDS in developing countries (Structured abstract). <i>BMJ</i> 2005; <b>331</b> :1431–5.	Not applicable	Not about chlamydia
Hossain A. Rapid diagnosis of <i>Chlamydia trachomatis</i> infections by a monoclonal-antibody direct immunofluorescence test. <i>J Trop Med Hyg</i> 1987; <b>90</b> :307–10.	No NAAT used	No NAAT used
Howell MR, Mckee KT, Gaydos JC, Quinn TC, Gaydos CA. Point-of-entry screening for <i>C. trachomatis</i> in female army recruits: who derives the cost savings? <i>Am J Prev Med</i> 2000; <b>19</b> :160–6.	Not applicable	No POCT used
Howell MR, Gaydos JC, Mckee KT, Quinn TC, Gaydos CA. Control of <i>Chlamydia trachomatis</i> infections in female army recruits: cost-effective screening and treatment in training cohorts to prevent pelvic inflammatory disease. <i>Sex Transm Dis</i> 1999; <b>26</b> :519–26.	Not applicable	No POCT used
Howell MR, Kassler WJ, Haddix A. Partner notification to prevent pelvic inflammatory disease in women: cost-effectiveness of two strategies. <i>Sex Transm Dis</i> 1997; <b>24</b> :287–92.	Not applicable	Not a comparative study
Jones HE, Altini L, de Kock A, Young T, van de Wijgert JH. Home-based versus clinic-based self-sampling and testing for sexually transmitted infections in Gugulethu, South Africa: randomised controlled trial. <i>Sex Transm Infect</i> 2007; <b>83</b> :552–7.	Not applicable	No POCT used
Khare VK, Consonni R, Martin DC, Winfield AC. Use of algorithmic pathways to develop quality, cost-effective clinical care. <i>J Am Assoc Gynecol Laparosc</i> 1995; <b>2</b> :169–74.	Not applicable	Not about chlamydia

Study	Reason for exclusion from review	
	Diagnostic accuracy	Effectiveness
Kubo R, Kaneko T, Nomura A, Kouda M, Matsuzaki H, Murahashi I. Comparison of new simple immunochromatography test and conventional assay for detecting chlamydia in urine specimens. <i>Gen Meet Am Soc Microbiol</i> 1998; <b>98</b> .	Pre-2006 abstract	Pre-2006 abstract
Landers L, Lauderdale T, Thorneycroft I, Chapin K. Comparison of PACE and amplified <i>Chlamydia trachomatis</i> (Amp CT) assays, ligase chain reaction (LCx) and clearview EIA for CT. <i>Gen Meet Am Soc Microbiol</i> 1998; <b>98</b> .	Pre-2006 abstract	Pre-2006 abstract
Lewis DA. The burden of asymptomatic sexually transmitted infections among men in Carletonville, South Africa: Implications for syndromic management. <i>Sex Transm Infect</i> 2008; <b>84</b> :371–6.	Not applicable	No POCT used
Lippman SA, Jones HE, Luppi CG, Pinho AA, Veras MA, van de Wijert JH. Home-based self-sampling and self-testing for sexually transmitted infections: acceptable and feasible alternatives to provider-based screening in low-income women in São Paulo, Brazil. <i>Sex Transm Dis</i> 2007; <b>34</b> :421–8.	Not applicable	No POCT used
Mabey D. Rapid and simple point of care diagnostics for STIs. <i>Sex Transm Infect</i> 2001; <b>77</b> :397–8.	Not a diagnostic accuracy study	Not a comparative study
Magbanua JP, Goh BT, Michel CE, Aguirre-Andreasen A, Alexander S, Ushiro-Lumb I, et al. <i>Chlamydia trachomatis</i> variant not detected by plasmid based nucleic acid amplification tests: molecular characterisation and failure of single dose azithromycin. <i>Sex Transm Infect</i> 2007; <b>83</b> :339–43.	Not a diagnostic accuracy study	Not a comparative study
Machungo F, Zanconato G, Persson K, Lind I, Jorgensen B, Herrmann B, et al. Syphilis, gonorrhoea and chlamydial infection among women undergoing legal or illegal abortion in Maputo. <i>Int J STD AIDS</i> 2002; <b>13</b> :326–30.	Not applicable	No NAAT used
Marions L, Rotzen-Ostlund M, Grillner L, Edgardh K, Tiveljung-Lindell A, Wikstrom A, et al. High occurrence of a new variant of <i>Chlamydia trachomatis</i> escaping diagnostic tests among STI clinic patients in Stockholm, Sweden. <i>Sex Transm Dis</i> 2008; <b>35</b> :61–4.	No point-of-care test used	Not applicable
Martin JL, Alexander SY, Selwood TS, Cross GF. Use of the polymerase chain reaction for the detection of <i>Chlamydia trachomatis</i> in clinical specimens and its comparison to commercially available tests. <i>Genitourin Med</i> 1995; <b>71</b> :169–71.	No outcomes of relevance	No outcomes of relevance
Matthews R, Wise R, Radcliffe K, Temple C, Sheard P, Davidson I. Evaluation of a new prototype rapid immunoassay (Clearview Chlamydia) for the detection of <i>Chlamydia trachomatis</i> in male urine samples and female endocervical swabs. <i>Gen Meet Am Soc Microbiol</i> 1995; <b>95</b> .	Pre-2006 abstract	Pre-2006 abstract
Matthews R, Ridgway G, Carder C, Hooki E, Pate M, Gleason B, et al. Evaluation of a new rapid immunoassay (Clearview™ Chlamydia) for the detection of <i>Chlamydia trachomatis</i> in male urine samples and female endocervical swabs. <i>Gen Meet Am Soc Microbiol</i> 1996; <b>96</b> .	Pre-2006 abstract	Pre-2006 abstract
Noguchi M, Okamoto T, Aoyama N, Hieda S, Yabushita H, Nakanishi M. Rapid diagnosis of <i>Chlamydia trachomatis</i> infection in obstetrics and gynecology – evaluation of chlamydia test pack. <i>Curr Ther Res Clin Exp</i> 1989; <b>46</b> :462–70.	No NAAT used	No NAAT used
Nyari T, Woodward M, Kovacs L. Should all sexually active young women in Hungary be screened for <i>Chlamydia trachomatis</i> . <i>Eur J Obstet Gynecol Reprod Biol</i> 2003; <b>106</b> :55–9.	Not applicable	No NAAT used
Pate MS, Dixon PB, Hardy K, Crosby M, Hook EW, III. Evaluation of the Biostar Chlamydia OIA assay with specimens from women attending a sexually transmitted disease clinic. <i>J Clin Microbiol</i> 1998; <b>36</b> :2183–6.	Uses an obsolete POCT	Uses an obsolete POCT
Philips DR, McCarthy O, Pakianathan MR, Sadiq ST. A computer based non-urine, non-swab simple point of care diagnostic test for <i>Chlamydia trachomatis</i> . <i>Sex Transm Infect</i> 2006; <b>82</b> :A11.	Not a diagnostic accuracy study	No NAAT used

Study	Reason for exclusion from review	
	Diagnostic accuracy	Effectiveness
Pittrof R, McLellan J. Test Not Talk screening for asymptomatic men. <i>Int J STD AIDS</i> 2007; <b>18</b> :274–5.	Not applicable	Not a comparative study
Postma MJ, Welte R, van den Hoek JA, van Doornum GJ, Coutinho RA, Jager JC. Opportunistic screening for genital infections with <i>Chlamydia trachomatis</i> in sexually active population of Amsterdam. II: Cost-effectiveness analysis of screening women. <i>Ned Tijdschr Geneesk</i> 1999; <b>143</b> :677–81.	Not applicable	No POCT used
Reichart CA, Moncada J, Schachter J, Koshakow M, Sedmak G, Reising S, et al. Multicenter Evaluation of Clearview Chlamydia for Detection of <i>Chlamydia trachomatis</i> in Women. <i>Interscience Conference on Antimicrobial Agents and Chemotherapy</i> 1992; <b>32</b> .	Pre-2006 abstract	Pre-2006 abstract
Romoren M, Hussein F, Steen TW, Velauthapillai M, Sundby J, Hjortdahl P, et al. Costs and health consequences of chlamydia management strategies among pregnant women in sub-Saharan Africa. <i>Sex Transm Infect</i> 2007; <b>83</b> :558–66.	Not applicable	No NAAT used
Romoren M. Chlamydia and gonorrhea in pregnancy: effectiveness of diagnosis and treatment in Botswana. <i>Sex Transm Infect</i> 2004; <b>80</b> :395–400.	Not applicable	No NAAT used
Sahin-Hodoglugil NN, Woods R, Pettifor A, Walsh J. A comparison of cost-effectiveness of three protocols for diagnosis and treatment of gonococcal and chlamydial infections in women in Africa. <i>Sex Transm Dis</i> 2003; <b>30</b> :455–69.	Not applicable	No POCT used
Schachter J. We must be realistic in evaluating rapid diagnostic tests. <i>Sex Transm Dis</i> 1999; <b>26</b> :241–2.	Not a diagnostic accuracy study	Not a comparative study
Schubiner HH, LeBar WD, Joseph S, Taylor C, Jemal C. Evaluation of two rapid tests for the diagnosis of <i>Chlamydia trachomatis</i> genital infections. <i>Eur J Clin Microbiol Infect Dis</i> 1992; <b>11</b> :553–6. [Erratum appears in <i>Eur J Clin Microbiol Infect Dis</i> 1992; <b>11</b> :872].	Not applicable	No NAAT used
Schubiner H, Taylor C, Ritchie J, Jemal C, Lebar W, Herschman B. Comparison of two membrane enzyme immunoassays for the detection of <i>Chlamydia trachomatis</i> in clinical samples. <i>Ann Meet Am Soc Microbiol</i> 1990; <b>90</b> .	Not applicable	Pre-2006 abstract
Sharma M, Nayak N, Malhotra S, Kumar B, Hemal A. Chlamydiazyme test for rapid detection of <i>Chlamydia trachomatis</i> . <i>Ind J Med Res A-Infect Dis</i> 1989; <b>89</b> :87–91.	No NAAT used	No NAAT used
Skidmore S, Randall S, Mallinson H. Testing for <i>Chlamydia trachomatis</i> : self-test or laboratory-based diagnosis? <i>J Fam Plan Reprod Health Care</i> 2007; <b>33</b> :231–2.	Not a diagnostic accuracy study	Not a comparative study
Sloan NL, Winikoff B, Haberland N, Coggins C, Elias C. Screening and syndromic approaches to identify gonorrhoea and chlamydial infection among women. <i>Stud Fam Plan 31(1)</i> 2000:55–68.	No NAAT used	Not applicable
Steingrimsson O, Olafsson J, Dolphin L, Pals-Dottir R, Davidsson S, Pawlak C, et al. Clinical evaluation of two immunoassay methods for the rapid detection of <i>Chlamydia trachomatis</i> antigen in endocervical specimens from high risk female patients. <i>Gen Meet Am Soc Microbiol</i> 1995; <b>95</b> .	Pre-2006 abstract	Pre-2006 abstract
Stratton N, Hirsch L, Harris F, Condon F, De La MAZA, Peterson EM. Evaluation of the Rapid Clearview Test for the direct detection of <i>Chlamydia</i> from cervical specimens. <i>Gen Meet Am Soc Microbiol</i> 1991; <b>91</b> .	No NAAT used	Not applicable
Svanas G, Boisen M, Brien J, Cox C, Frisch L, Hopkins D, et al. Thermo BioStar™ rapid immunoassays for <i>Chlamydia trachomatis</i> (CT) and <i>Neisseria gonorrhoeae</i> (GC) from a single male or female specimen. <i>Int J STD AIDS</i> 2001; <b>12</b> .	Pre-2006 abstract	Pre-2006 abstract
Swain GR, McDonald RA, Pfister JR, Gradus MS, Sedmak GV, Singh A. Decision analysis: point-of-care <i>Chlamydia</i> testing vs. laboratory-based methods. <i>Clin Med Res</i> 2004; <b>2</b> :29–35.	Uses an obsolete POCT	Uses an obsolete POCT

Study	Reason for exclusion from review	
	Diagnostic accuracy	Effectiveness
Tao G, Abban BK, Gift TL, Chen G, Irwin KL. Applying a mixed-integer program to model re-screening women who test positive for <i>C. trachomatis</i> infection (Structured abstract). <i>Health Care Manag Sci</i> 2004; <b>7</b> :135–44.	Not applicable	No POCT used
Taylor-Robinson D. The value of nonculture techniques for diagnosis of <i>Chlamydia trachomatis</i> infections – making the best of a bad job. <i>Eur J Clin Microbiol Infect Dis</i> 1992; <b>11</b> :499–503.	Not a diagnostic accuracy study	Not a comparative study
Theodore M, Hook E, Mableton S, Whittington W, Gaydos C. Use of Thermo BioStar™ optical immunoassay (OIA®) as a point of care assay for <i>Chlamydia trachomatis</i> (CT) and <i>Neisseria gonorrhoeae</i> (GC) in sexually transmitted disease clinics. <i>Int J STD AIDS</i> 2001; <b>12</b> .	Pre-2006 abstract	Pre-2006 abstract
Thomas BJ, MacLeod EJ, Taylor-Robinson D. Evaluation of sensitivity of 10 diagnostic assays for <i>Chlamydia trachomatis</i> by use of a simple laboratory procedure. <i>J Clin Pathol</i> 1993; <b>46</b> :408–10.	No outcomes of relevance	No outcomes of relevance
Thomas BJ, MacLeod EJ, Taylor-Robinson D. Evaluation of sensitivity of 10 diagnostic assays for <i>Chlamydia trachomatis</i> by use of a simple laboratory procedure. <i>J Clin Pathol</i> 1993; <b>46</b> :912–14.	No outcomes of relevance	Not applicable
Tison DL. Evaluation of the Kodak SureCell Chlamydia Test Kit for the Direct Detection of <i>Chlamydia trachomatis</i> . <i>Genl Meet Am Soc Microbiol</i> 1991; <b>91</b> .	Pre-2006 abstract	Pre-2006 abstract
Veringa EM. Detection of <i>Chlamydia trachomatis</i> in clinical specimens. Comparison of culture, direct antigen detection, DNA probe hybridization and PCR. <i>J Microbiol Methods</i> 1994; <b>19</b> :117–25.	Uses an obsolete POCT	Uses an obsolete POCT
Vickerman P, Watts C, Alary M, Mabey D, Peeling RW. Sensitivity requirements for the point of care diagnosis of <i>Chlamydia trachomatis</i> and <i>Neisseria gonorrhoeae</i> in women. <i>Sex Transm Infect</i> 2003; <b>79</b> :363–7.	Not applicable	Not a comparative study
Wang LY, Burstein GR, Cohen DA. An economic evaluation of a school-based sexually transmitted disease screening program. <i>Sex Transm Dis</i> 2002; <b>29</b> :737–45.	Not applicable	Not a comparative study
Wang LY, Davis M, Robin L, Collins J, Coyle K, Baumler E. Economic evaluation of Safer Choices: a school-based human immunodeficiency virus, other sexually transmitted diseases, and pregnancy prevention program. <i>Arch Pediatr Adolesc Med</i> 2000; <b>154</b> :1017–24.	Not applicable	Not about chlamydia
Warszawski J, Meyer L, Weber P. CLEARVIEW <i>Chlamydia</i> test for detection of chlamydiae in cervical specimens. <i>J Clin Microbiol</i> 1992; <b>30</b> :2216.	Not a diagnostic accuracy study	Not a comparative study
Wells A. Evaluation of the BioStar <i>Chlamydia</i> OIA assay for <i>Chlamydia trachomatis</i> in an outpatient setting. <i>Interscience Conference on Antimicrobial Agents and Chemotherapy</i> 1995; <b>35</b> .	Pre-2006 abstract	Pre-2006 abstract
Welte R, Kretzschmar M, Leidl R, Van den HA, Jager JC, Postma MJ. Cost-effectiveness of screening programs for <i>Chlamydia trachomatis</i> : a population-based dynamic approach. <i>Sex Transm Dis</i> 2000; <b>27</b> :518–29.	Not applicable	No POCT used
Widjaja S, Cohen S, Brady WE, O'reilly K, Susanto, Wibowo A et al. Evaluation of a rapid assay for detection of <i>Chlamydia trachomatis</i> infections in outpatient clinics in South Kalimantan, Indonesia. <i>J Clin Microbiol</i> 1999; <b>37</b> :4183–5.	Uses an obsolete POCT	Uses an obsolete POCT
Wilsmore AJ, Davidson I. 'Clearview' rapid test compared with other methods to diagnose chlamydial infection. <i>Vet Rec</i> 1991; <b>128</b> :503–4.	Animal study	Animal study
Witkin SS, Bongiovanni AM, Inglis SR. Detection of endocervical anti- <i>Chlamydia trachomatis</i> immunoglobulin A in pregnant women by a rapid, 6-minute enzyme-linked immunosorbent assay: Comparison with PCR and chlamydial antigen detection methods. <i>J Clin Microbiol</i> 1997; <b>35</b> :1781–3.	Uses an obsolete POCT	Uses an obsolete POCT

Study	Reason for exclusion from review	
	Diagnostic accuracy	Effectiveness
You JH, Wong WC, Sin CW, Woo J. The cost-effectiveness of an outreach clinical model in the management and prevention of gonorrhoea and chlamydia among Chinese female sex workers in Hong Kong (Structured abstract). <i>Sex Transm Dis</i> 2006; <b>33</b> :220–7.	Not applicable	No POCT used
Point of care testing opportunities: <i>Chlamydia</i> screening. <i>Pharm J</i> 2007; <b>279</b> :506.	Not applicable	Not a comparative study
Adelaide Health Technology Assessment on behalf of National Horizon Scanning Unit (HealthPACT and MSAC). <i>Rapid point-of-care test for the detection of chlamydia; horizon scanning prioritising summary – volume 13 (Brief record)</i> . Adelaide: Adelaide Health Technology Assessment (AHTA) on behalf of National Horizon Scanning Unit (HealthPACT and MSAC) 2006.	Not genital chlamydia	Not genital chlamydia
Kaye D. New rapid test developed to detect chlamydia. <i>Clin Infect Dis</i> 2004; <b>38</b> :iv.	Not a diagnostic accuracy study	Not a comparative study
Point-of-care tests should be quick and cheap. <i>Pharm J</i> 2002; <b>269</b> :185.	Not about chlamydia	Not a comparative study



## Appendix 6

### Characteristics of the included studies

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
<p>Study: Chernesky <i>et al.</i><sup>69</sup></p> <p>Year: 1999</p> <p>Time period: 1997 (not specified further)</p> <p>Country: Canada</p>	<p>Enrolled: 128</p> <p>Analysed: 128 (100%)</p> <p>Gender: male 128 (100%); female 0 (0%)</p> <p>Age (mean, SD): not specified</p> <p>Baseline characteristics (e.g. symptoms, etc.): not specified</p> <p>Venue: private laboratory in Toronto, Ontario</p> <p>Setting (prevalence): 43% (sample of positive samples from the private laboratory were chosen for this study)</p>	<p>POCT used: Clearview Chlamydia by Unipath (now Inverness Medical)</p> <p>Specimen type for POCT: FVU</p> <p>POCT used: SureCell Chlamydia by Kodak</p> <p>Specimen type for POCT: FVU</p> <p>NAAT reference standard: LCR using LCx assay by Abbott, confirmed with DFA staining (not specified further)</p> <p>Specimen type for NAAT: FVU</p>	<p>Unit of analysis: specimen</p> <p><i>Using Clearview:</i></p> <p>Sensitivity (%): 42/62 (67.7)</p> <p>Specificity (%): 63/66 (95.5)</p> <p>Positive predictive value (%): 42/45 (93.3)</p> <p>Negative predictive value (%): 63/83 (75.9)</p> <p>Positive likelihood ratio: 14.90</p> <p>Negative likelihood ratio: 0.34</p> <p><i>Using SureCell:</i></p> <p>Sensitivity (%): 39/62 (62.9)</p> <p>Specificity (%): 66/66 (100)</p> <p>Positive predictive value (%): 39/39 (100)</p> <p>Negative predictive value (%): 66/89 (74.2)</p> <p>Positive likelihood ratio: –</p> <p>Negative likelihood ratio: 0.37</p>
<p>Study: Hopwood <i>et al.</i><sup>68</sup></p> <p>Year: 2001</p> <p>Time period: February – March 2000 (2 months)</p> <p>Country: England (UK)</p>	<p>Enrolled: 400</p> <p>Analysed: 395 (98.8%)</p> <p>Gender: male 0 (0%); female 395 (100%)</p> <p>Age (mean, SD): age groups provided for 378 participants, of which:</p> <p>15–19 years old – 89/378 (23.5%)</p> <p>20–24 years old – 119/378 (31.5%)</p> <p>25–29 years old – 65/378 (17.2%)</p> <p>30–34 years old – 67/378 (17.7%)</p> <p>35–39 years old – 29/378 (7.7%)</p> <p>40–44 years old – 9/378 (2.4%)</p> <p>Baseline characteristics (e.g. symptoms, etc.): all participants were pregnant women undergoing a termination of pregnancy procedure.</p> <p>Venue: British Pregnancy Advisory Service clinic</p> <p>Setting (prevalence): not specified</p>	<p>POCT used: Clearview Chlamydia MF by Unipath (now Inverness Medical)</p> <p>Specimen Type for POCT: endocervical swab</p> <p>NAAT reference standard: LCR using LCx assay by Abbott Laboratories</p> <p>Specimen type for NAAT: endocervical swab</p>	<p>Unit of analysis: specimen/patient</p> <p>Sensitivity (%): 24/32 (75.0)</p> <p>Specificity (%): 360/363 (99.2)</p> <p>Positive predictive value (%): 24/27 (88.9)</p> <p>Negative predictive value (%): 360/368 (97.8)</p> <p>Positive likelihood ratio: 90.75</p> <p>Negative likelihood ratio: 0.25</p> <p>Additional outcomes:</p> <p>270/397 (68.0%) asked for their results to be sent to their home address</p> <p>23/397 (5.8%) asked for their results to be sent to another address</p> <p>104/397 (26%) were 'harder to reach', of which:</p> <p>15/397 (3.8%) gave a contact telephone number</p> <p>80/397 (20.2%) wanted to simply telephone the clinic to find out their results</p> <p>9/397 (2.3%) wanted to be contacted at various other places</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
Study: Kegg and Roberts <sup>73</sup> Year: 2006 Time period: not specified Country: England, UK	Enrolled: 100 Analysed: 100 (100%) Gender: male 0 (0%); female 100 (100%) Age (mean, SD): not specified Baseline characteristics (e.g. symptoms, etc.): not specified Venue: GUM clinic Setting (prevalence): not specified	POCT used: Chlamydia Wand by Surescreen Specimen type: Vaginal swab (self-collected) NAAT reference standard: SDA by Becton Dickinson ProbeTec Specimen type: cervical	Unit of analysis: specimen/patient Sensitivity (%): 4/11 (36.4) Specificity (%): 71/89 (79.8) Positive predictive value (%): 4/22 (18.2) Negative predictive value (%): 71/78 (91.0) Positive likelihood ratio: 1.80 Negative likelihood ratio: 0.80  Additional outcomes: 'Our experienced nursing staff encountered significant difficulties in manipulating the test device and is [sic] interpreting the colour change denoting a positive result'
Study: Kluytmans et al. <sup>71</sup> Year: 1993 Time period: not specified Country: the Netherlands	Enrolled: 1007 Analysed: Magic Lite test – 1007/1007 (100%); Clearview Chlamydia test – 999/1007 (99.2%) Gender: male 283/1007 (28.1%); female 724/1007 (71.9%) Age (mean, SD): not specified Baseline characteristics (e.g. symptoms, etc.): not specified Venue: sexually transmitted disease clinic based in a hospital (University Hospital Rotterdam) Setting (prevalence): not specified	POCT used: Clearview Chlamydia by Unipath (now Inverness Medical) Specimen type: urethral (for men); cervical (for women) POCT used: Magic Lite by CIBA Corning (now part of Novartis/Chiron) NAAT reference standard: PCR (not specified further) Specimen type: urethral (for men); cervical (for women)	Unit of analysis: specimen <i>Using Clearview:</i> Sensitivity (%): women 31/43 (72.1); men: 26/44 (59.1) Specificity (%): women 667/673 (99.1); men 206/239 (86.2) Positive predictive value (%): women 31/37 (83.8); men 26/60 (43.3) Negative predictive value (%): women 667/679 (98.2); men 206/223 (92.4) Positive likelihood ratio: women 80.86; men 4.28 Negative likelihood ratio: women 0.28; men 0.47 <i>Using Magic Lite:</i> Sensitivity (%): women 26/43 (60.5); men 31/44 (70.5) Specificity (%): women 680/681 (99.9); men 239/239 (100) Positive predictive value (%): women 26/27 (96.3); men 31/32 (96.9) Negative predictive value (%): women 680/697 (97.6); men 239/251 (95.2) Positive likelihood ratio: women 411.77; men – Negative likelihood ratio: women 0.40; men 0.30 Additional outcomes: –



Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
<p>Study: Lauderdale <i>et al.</i><sup>70</sup></p> <p>Year: 1999</p> <p>Time period: June 1997 to November 1997 (6 months)</p> <p>Country: USA</p>	<p>Enrolled: 68</p> <p>Analysed: 65</p> <p>Gender: male 0 (0%); female 68 (100%)</p> <p>Age (mean, SD): not specified (but likely university students)</p> <p>Baseline characteristics (e.g. symptoms etc): 87% asymptomatic ('had no STD related symptoms')</p> <p>Venue: Local OB-GYN outpatient clinics at the University of South Alabama, Mobile, AL</p> <p>Setting (prevalence): 'low to moderate' prevalence of between 3.0% and 6.5%</p>	<p>POCT used: Clearview enzyme immunoassay by Wampole (now made by Inverness Medical)</p> <p>Specimen type: endocervical</p> <p>NAAT reference standard: TMA using AMP CT assay by Gen-Probe</p> <p>Specimen type: endocervical</p> <p>NAAT reference standard: LCR using LCx assay by Abbott Laboratories</p> <p>Specimen type: endocervical</p>	<p>Unit of analysis: specimen</p> <p>Using either LCR or TMA as reference standard (results identical):</p> <p>Sensitivity (%): 5/10 (50)</p> <p>Specificity (%): 55/55 (100)</p> <p>Positive predictive value (%): 5/5 (100)</p> <p>Negative predictive value (%): 55/60 (91.7)</p> <p>Positive likelihood ratio: –</p> <p>Negative likelihood ratio: 0.50</p> <p>Additional outcomes: –</p>
<p>Study: Mahilum-Tapay <i>et al.</i><sup>50</sup></p> <p>Year: 2007</p> <p>Time period: November 2005 to March 2006 (5 months)</p> <p>Country: England, UK</p>	<p>Enrolled: 1458</p> <p>Analysed: 1349 (using PCR as reference standard); 637 (using SDA as reference standard)</p> <p>Gender: male 0 (0%); female 1349 (100%)</p> <p>Age (mean, SD): ranged from 16 to 54 years:</p> <p>At site 1: 18.5 years (16.0–27.4 years)</p> <p>At site 2: 25.4 years (16.0–49.7 years)</p> <p>At site 3: 27.8 years (17.1–54.8 years)</p> <p>Baseline characteristics (e.g. symptoms, etc.): Of the 662 attending GUM clinic venues, 441/662 (66.6%) had symptoms. However, 'most' were asymptomatic at the Young People's Sexual Health Centre venue</p> <p>Venue: One Sexual Health Centre for Young People (providing contraceptive advice etc) as 'Site 1' – 663; and two GUM clinics, as 'Site 2' and 'Site 3' – 686</p> <p>Setting (prevalence): not specified</p>	<p>POCT used: Chlamydia Rapid Test</p> <p>Specimen type: vaginal swabs (both self-collected and clinician-collected)</p> <p>NAAT reference standard: PCR using AMPLICOR CT/NG by Roche, and SDA (not further specified)</p> <p>Specimen type: FVU (for PCR samples) and endocervical swabs (for SDA samples)</p>	<p>Unit of analysis: specimen</p> <p>Using clinician-collected vaginal swabs at sites 2 and 3 (with PCR as reference standard):</p> <p>Sensitivity (%): 42/54 (77.8)</p> <p>Specificity (%): 627/632 (99.2)</p> <p>Positive predictive value (%): 42/47 (89.4)</p> <p>Negative predictive value (%): 627/632 (98.1)</p> <p>Positive likelihood ratio: 98.31</p> <p>Negative likelihood ratio: 0.22</p> <p>Using self-collected vaginal swabs at sites 2 and 3 (with PCR as reference standard):</p> <p>Sensitivity (%): 44/54 (81.5)</p> <p>Specificity (%): 624/632 (98.7)</p> <p>Positive predictive value (%): 44/52 (84.6)</p> <p>Negative predictive value (%): 624/632 (98.4)</p> <p>Positive likelihood ratio: 64.37</p> <p>Negative likelihood ratio: 0.19</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
			<p><i>Using self-collected vaginal swabs at site 1 (with PCR as reference standard):</i></p> <p>Sensitivity (%): 47/56 (83.9)            Specificity (%): 600/607 (98.8)            Positive predictive value (%): 47/54 (87.0)            Negative predictive value (%): 600/609 (98.5)            Positive likelihood ratio: 72.78            Negative likelihood ratio: 0.16</p> <p><i>Using self-collected vaginal swabs (total for all sites as listed above), with PCR as reference standard:</i></p> <p>Sensitivity (%): 91/110 (82.7)            Specificity (%): 1224/1239 (98.8)            Positive predictive value (%): 91/106 (85.8)            Negative predictive value (%): 1224/1243 (98.5)            Positive likelihood ratio: 68.92            Negative likelihood ratio: 0.18</p> <p><i>Using self-collected vaginal swabs at sites 2 and 3 (with SDA as reference standard):</i></p> <p>Sensitivity (%): 40/49 (81.6)            Specificity (%): 578/588 (98.3)            Positive predictive value (%): 40/50 (80.0)            Negative predictive value (%): 578/587 (98.5)            Positive likelihood ratio: 48.00            Negative likelihood ratio: 0.19</p> <p>Additional outcomes:            1083/1349 (80.3%) of participants completed a questionnaire after testing            1072/1078 (99.4%) found instructions easy to understand            1039/1083 (95.9%) felt comfortable collecting their own vaginal swab specimens            435/1068 (40.7%) preferred self-collected vaginal swabs            401/1068 (37.5%) preferred giving a urine sample</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
<p>Study: Michel <i>et al.</i><sup>74</sup>  Year: 2009  Time period: not specified  Country: the Philippines</p>	<p>Enrolled: 231  Analysed: 231  Gender: male 0 (0%), female 231 (100%)  Age (mean, SD): not specified  Baseline characteristics (e.g. symptoms, etc.): most of the Social Hygiene Clinic participants were commercial sex workers who attended the clinic for a weekly health check, whereas participants at the OB-GYN clinic were mostly pregnant women attending for antenatal care  Venue: Social Hygiene Clinic 131/231 (56.7%), OB-GYN Clinic 100/231 (43.3%)  Setting (prevalence): not specified</p>	<p>POCT used: Handilab C test, also known as 'SureScreen' and 'SELFCheck'  Specimen type: vaginal swab  NAAT reference standard: PCR using AMPLICOR CT/NG by Roche  Specimen type: vaginal swab</p>	<p>232/1068 (21.7%) had no preference for type of sample they preferred (there was no significant difference between sites <math>p=0.069</math>)  61/881 (6.9%) were willing to wait less than 30 minutes for their results  661/881 (75.0%) were willing to wait between 30 minutes and 2 hours for their results  96/881 (10.9%) were willing to wait more than 2 hours for their results  63/881 (7.2%) were willing to wait more than 1 day for their results</p> <p>Unit of analysis: specimen/patient  For Social Hygiene Clinic setting:  Sensitivity (%): 6/30 (20.0)  Specificity (%): 89/101 (88.1)  Positive predictive value (%): 6/18 (33.3)  Negative predictive value (%): 89/113 (78.8%)  Positive likelihood ratio: 1.68  Negative likelihood ratio: 0.91  For OB-GYN setting:  Sensitivity (%): 1/8 (12.5)  Specificity (%): 86/92 (93.5)  Positive predictive value (%): 1/7 (14.3)  Negative predictive value (%): 86/93 (92.5)  Positive likelihood ratio: 1.92  Negative likelihood ratio: 0.94  For both settings combined:  Sensitivity (%): 7/38 (18.4)  Specificity (%): 175/193 (90.7)  Positive predictive value (%): 7/25 (28.0)  Negative predictive value (%): 175/206 (85.0)  Positive likelihood ratio: 1.98  Negative likelihood ratio: 0.90  Additional outcomes: not specified</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
<p>Study: Nadala <i>et al.</i><sup>75</sup>  Year: 2009  Time Period: March to November 2007  Country: England, UK</p>	<p>Enrolled: 1277  Analysed: 1211  Gender: male 1211 (100%), female 0 (0%)  Age (mean, SD):  Baseline characteristics (e.g. symptoms, etc.): At site 1 (Sexual Health Centre), most participants were attending for contraception/advice and were asymptomatic. At site 2 (GUM Clinic) 62% (467/469) were symptomatic. 21% (155/741) had urethral discharge, 23% (169/744) had dysuria. 2.6% (20/757) of participants attended with contact slips  Venue: site 1 was a Sexual Health Centre. Site 2 was a GUM clinic. There were significant differences in the negative and positive predictive values of the Chlamydia Rapid Test between the two sites (<math>p=0.0089</math> and <math>p=0.0283</math> respectively)  Setting (prevalence): not specified</p>	<p>POCT used: Chlamydia Rapid Test  Specimen type: first void urine using the 'FirstBurst' collection method  NAAT reference standard: PCR using AMPLICOR CT/NG by Roche  Specimen type: first void urine collected using routine cup collection</p>	<p>Unit of analysis: specimen/patient  For site 1 (Sexual Health Centre):  Sensitivity (%): 18/20 (90.0)  Specificity (%): 426/434 (98.2)  Positive predictive value (%): 18/26 (69.2)  Negative predictive value (%): 426/428 (99.5)  Positive likelihood ratio: 50.0  Negative likelihood ratio: 0.10  For site 2 (GUM clinic):  Sensitivity (%): 72/90 (80.0)  Specificity (%): 658/667 (98.7)  Positive predictive value (%): 72/81 (88.9)  Negative predictive value (%): 658/676 (97.3)  Positive likelihood ratio: 61.5  Negative likelihood ratio: 0.20  For both settings combined:  Sensitivity (%): 90/110 (81.8)  Specificity (%): 1084/1101 (98.5)  Positive predictive value (%): 90/107 (84.1)  Negative predictive value (%): 1084/1104 (98.2)  Positive likelihood ratio: 54.5  Negative likelihood ratio: 0.19  Additional outcomes:  'A concordance of 100% was found between the expected results and the results generated from randomised and masked panels by two independent operators performing the Chlamydia Rapid Test'</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
			<p>Of the 20 attending with contact slips, 30% (6/20) tested positive using PCR and 25% (5/20) tested positive using the Chlamydia Rapid Test. At site 1, 18/20 (90%) of PCR positive participants were without genitourinary symptoms at time of recruitment to the study. At site 2, 31.1% (28/90) were without symptoms. The CRT picked up 16/18 (88.9%) of these participants at site 1, and 20/28 (71.4%) at site 2, giving the CRT a sensitivity of 78.3% for asymptomatic men, and 84.4% for symptomatic men</p> <p>812 participants were offered a questionnaire, of which 767 (94.5%) responded (though not to all questions). Of them: 97.6% (741/759) of respondents found the instructions easy to understand</p> <p>97.4% (735/755) found collection of their urine easy</p> <p>88.8% (619/697) of respondents preferred to give a urine sample</p> <p>7.0% (49/697) would have preferred to give a urethral swab<sup>a</sup></p> <p>4.2% (29/697) were willing to provide either sample</p> <p>76.4% (525/687) of respondents preferred the FirstBurst device</p> <p>18.0% (124/687) preferred the urine cup</p> <p>5.5% (38/687) were willing to use either device</p> <p>95.6% (653/683) of respondents indicated that they were willing to wait 1 hour or more</p> <p>4.4% (30/683) indicated that they would not wait more than 1 hour</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
<p>Study: Rani <i>et al.</i><sup>67</sup>  Year: 2002  Time period: not specified  Country: England, UK</p>	<p>Enrolled: 200  Analysed: 199  Gender: male 0 (0%); female 200 (100%)  Age (mean, SD): not specified  Baseline characteristics (e.g. symptoms, etc.): not specified  Venue: one GUM clinic and the Gynaecology Department of hospital  Setting (prevalence): GUM clinic considered 'high prevalence' and Gynaecology Department considered 'low prevalence' but no further detail</p>	<p>POCT used: QuickVue Chlamydia (Quidel)  Specimen type: endocervical  NAAT reference standard: PCR using the COBAS Amplicor by Roche  Specimen type: endocervical</p>	<p>Unit of analysis: specimen/patient  For GUM Clinic setting:  Sensitivity (%): 11/17 (62.5)  Specificity (%): 83/83 (100)  Positive predictive value (%): 11/11 (100)  Negative predictive value (%): 83/89 (93.3)  Positive likelihood ratio: –  Negative likelihood ratio: 0.38  For Gynaecology Department setting:  Sensitivity (%): 1/4 (25.0)  Specificity (%): 96/96 (100)  Positive predictive value (%): 1/1 (100)  Negative predictive value (%): 96/99 (97.0)  Positive likelihood ratio: –  Negative likelihood ratio: 0.75  Additional outcomes: –</p>
<p>Study: Saison <i>et al.</i><sup>65</sup>  Year: 2007  Time period: August 2002 to March 2006 (six 2- to 3-week periods within these dates for data collection at the Social Hygiene Clinic; 6 months within these dates for data collection at the OB-GYN clinic)  Country: the Philippines</p>	<p>Enrolled: 2322  Analysed: 822 (using Clearview); 1129 (using the Chlamydia Rapid Test)  Gender: male 0 (0%); female 2322 (100%)  Age (mean, SD): given for 782 attendees at the Social Hygiene Clinic, where the median (range) was 25.8 years (18–56 years)  Baseline characteristics (e.g. symptoms, etc.): 219/782 (28%) had symptoms  Venue: a Social Hygiene Clinic for Female Sex Workers and an OB-GYN Clinic at a Medical Centre  Setting (prevalence): for female sex workers, the prevalence range was estimated to be between 27% and 36%. The OB-GYN setting was considered 'low-risk'</p>	<p>POCT used: Chlamydia Rapid Test  Specimen type: vaginal swabs (×2)  POCT used: Clearview Chlamydia MF by Inverness Medical  Specimen type: vaginal (×2) and endocervical (×1)  NAAT reference standard: PCR using the AMPLICOR CT/NG by Roche  Specimen type: vaginal (×4) and endocervical (×1)</p>	<p>Unit of analysis: specimen  Using Clearview at SHC setting, with endocervical swabs:  Sensitivity (%): 85/159 (53.5)  Specificity (%): 657/663 (99.1)  Positive predictive value (%): 85/91 (93.4)  Negative predictive value (%): 657/731 (89.9)  Positive likelihood ratio: 59.07  Negative likelihood ratio: 0.47  Using Clearview at the SHC setting with clinician-collected vaginal swabs:  Sensitivity (%): 10/25 (40.0)  Specificity (%): 109/112 (97.3)  Positive predictive value (%): 10/13 (76.9)  Negative predictive value (%): 109/124 (87.9)  Positive likelihood ratio: 14.93  Negative likelihood ratio: 0.62</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
<p>Study: Shaarawy<sup>64</sup>  Year: 1998  Time period:  September 1996 to  December 1996 (4  months)  Country: Egypt</p>	<p>Enrolled: 50  Analysed: 50  Gender: male 0 (0%); female 50 (100%)  Age (mean, SD): ranged from 25 to 35 years old  Baseline characteristics (e.g. symptoms, etc.): all participants had pelvic inflammatory disease  Venue: the OB-GYN department of a hospital  Setting (prevalence): not specified</p>	<p>POCT used: Clearview  Specimen type: cervical  NAAT reference standard: PCR using AMPLICOR by Roche  Specimen type: cervical</p>	<p><i>Using Clearview at the SHC setting with self-collected vaginal swabs:</i>  Sensitivity (%): 9/36 (25.0)  Specificity (%): 150/160 (93.8)  Positive predictive value (%): 9/19 (47.4)  Negative predictive value (%): 150/177 (84.7)  Positive likelihood ratio: 4.00  Negative likelihood ratio: 0.80</p> <p><i>Using the Chlamydia Rapid Test at the SHC setting with clinician-collected vaginal swabs:</i>  Sensitivity (%): 66/93 (71.0)  Specificity (%): 196/198 (99.0)  Positive predictive value (%): 66/68 (97.1)  Negative predictive value (%): 196/223 (87.9)  Positive likelihood ratio: 70.26  Negative likelihood ratio: 0.29</p> <p><i>Using the Chlamydia Rapid Test at the OB-GYN clinic with clinician-collected vaginal swabs:</i>  Sensitivity (%): 46/53 (86.8)  Specificity (%): 782/785 (99.6)  Positive predictive value (%): 46/49 (93.9)  Negative predictive value (%): 782/789 (99.1)  Positive likelihood ratio: 227.11  Negative likelihood ratio: 0.13</p> <p>Additional outcomes: –</p> <p>Unit of analysis: specimen/patient  Sensitivity (%): 15/18 (83.3)  Specificity (%): 22/32 (68.8)  Positive predictive value (%): 15/25 (60.0)  Negative predictive value (%): 22/25 (88.0)  Positive likelihood ratio: 2.67  Negative likelihood ratio: 0.24  Additional outcomes: –</p>

Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
<p>Study: Wisniewski <i>et al.</i><sup>72</sup></p> <p>Year: 2008</p> <p>Time period: September 2005 to December 2006 (4 months)</p> <p>Country: England, UK</p>	<p>Enrolled: 534</p> <p>Analysed: 534</p> <p>Gender: male 534 (100%); female 0 (0%)</p> <p>Age (mean, SD): greater than 16 years old (not further specified)</p> <p>Baseline characteristics (e.g. symptoms, etc.): not specified</p> <p>Venue: Young People's Sexual Health Centre</p> <p>Setting (prevalence): not specified</p>	<p>POCT used: Chlamydia Rapid Test</p> <p>Specimen type: FVU (using routine cup collection and the 'FirstBurst' device)</p> <p>NAAT reference standard: PCR using the AMPLICOR CT/NG by Roche</p> <p>Specimen type: FVU</p>	<p>Unit of analysis: specimen</p> <p><i>Using the 'FirstBurst' device:</i></p> <p>Sensitivity (%): 28/34 (82.4)</p> <p>Specificity (%): 494/500 (98.8)</p> <p>Positive predictive value (%): 28/34 (82.4)</p> <p>Negative predictive value (%): 494/500 (98.8)</p> <p>Positive likelihood ratio: 68.63</p> <p>Negative likelihood ratio: 0.18</p> <p><i>Using routine urine cup collection:</i></p> <p>Sensitivity (%): 16/34 (47.1)</p> <p>Specificity (%): 494/500 (98.8)</p> <p>Positive predictive value (%): 16/22 (72.7)</p> <p>Negative predictive value (%): 494/512 (96.5)</p> <p>Positive likelihood ratio: 39.22</p> <p>Negative likelihood ratio: 0.54</p> <p>Additional outcomes: –</p>
<p>Study: Yin <i>et al.</i><sup>66</sup></p> <p>Year: 2006</p> <p>Time period: not specified</p> <p>Country: China</p>	<p>Enrolled: 1500</p> <p>Analysed: 1497</p> <p>Gender: male 0 (0%); female 1500 (100%)</p> <p>Age (mean, SD): 28 years (median)</p> <p>Baseline characteristics (e.g. symptoms, etc.): 920/1497 (61.5%) had symptoms</p> <p>Venue: sexually transmitted disease clinics, female re-education centres and sex entertainment venues in six cities in China</p> <p>Setting (prevalence): not specified</p>	<p>POCT used: Clearview Chlamydia MF by Unipath (now made by Inverness Medical)</p> <p>Specimen type: vaginal and cervical specimens</p> <p>NAAT reference standard: PCR using AMPLICOR by Roche</p> <p>Specimen type: vaginal and cervical specimens</p>	<p>Unit of analysis: specimen</p> <p><i>Using cervical specimens:</i></p> <p>Sensitivity (%): 98/197 (49.7)</p> <p>Specificity (%): 1273/1300 (97.9)</p> <p>Positive predictive value (%): 98/125 (78.4)</p> <p>Negative predictive value (%): 1273/1300 (92.8)</p> <p>Positive likelihood ratio: 23.95</p> <p>Negative likelihood ratio: 0.51</p> <p><i>Using vaginal specimens:</i></p> <p>Sensitivity (%): 66/201 (32.8)</p> <p>Specificity (%): 1285/1296 (99.2)</p> <p>Positive predictive value (%): 66/77 (85.7)</p> <p>Negative predictive value (%): 1285/1296 (90.5)</p> <p>Positive likelihood ratio: 38.69</p> <p>Negative likelihood ratio: 0.68</p> <p>Additional outcomes:</p> <p>'The vast majority of the patients (99.1%) were willing to wait up to two hours for the result, of whom 83.1% preferred waiting for 30 min'</p>



Study ID	Participants	Intervention test(s) and comparator	Outcomes summary
			<p>14 staff members were surveyed, of which:</p> <p>13/14 (92.9%) recognised that the kit provided very clear manufacturers' instructions</p> <p>12/14 (85.7%) felt the test had a 10-minute 'hands on' time</p> <p>12/14 (85.7%) felt the test was very easy to use</p> <p>14/14 (100%) thought it was quick (&lt; 20 minutes) to display the results</p> <p>13/14 (92.9%) thought the training of operational procedures took ≤ 30 minutes</p>
<p>OB-GYN, obstetrics and gynecology; SHC, Sexual Health Clinic.</p> <p>a Participants were not asked to give a urethral swab; therefore for those individuals who have not experienced urethral swabbing, their expressed specimen preference may not be valid.</p>			



## Appendix 7

### Quality assessment results for the individual full text, published chlamydia diagnostic studies

Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
Chernesky et al., <sup>69</sup> 1999	?	?	+	+	+	+	?	?	?	+	+	-	-
Hopwood et al., <sup>68</sup> 1991	-	?	+	+	+	+	?	?	?	+	+	-	-
Kluytmans et al., <sup>71</sup> 1993	+	+	+	+	+	+	?	?	?	+	+	-	-
Lauderdale et al., <sup>70</sup> 1999	+	+	+	+	+	+	+	?	?	+	+	-	-
Mahilum-Tapay et al., <sup>50</sup> 2007	+	+	+	+	+	+	+	?	?	+	+	+	+
Michel et al., <sup>74</sup> 2009	+	+	+	+	+	+	+	?	?	+	+	-	-
Nadala et al., <sup>75</sup> 2009	+	+	+	+	+	+	+	?	?	+	+	+	+
Rani et al., <sup>67</sup> 2002	+	+	+	+	+	+	?	?	?	+	+	-	-
Saison et al., <sup>65</sup> 2007	+	+	+	+	+	+	+	+	?	?	+	-	-
Shaarawy, <sup>64</sup> 1998	-	+	?	+	+	+	?	?	?	?	+	-	-
Wisniewski et al., <sup>72</sup> 2008	+	+	+	+	+	+	?	?	?	+	+	-	-
Yin et al., <sup>66</sup> 2006	+	+	+	+	+	+	+	?	?	+	+	+	-

+ , yes to the question; - , no to the question; ? , unclear.



# **Appendix 8**

## **Test accuracy results for the individual studies**

Study	POCT	Type of specimen	Method of collection	NAAT method	Specimens analysed	Sensitivity	Specificity	PPV	NPV	Positive LR	Negative LR
Chernesky et al., <sup>69</sup> 1999	Clearview	FVU	Self-collected	LCR	128	67.7%	95.5%	93.3%	75.9%	14.90	0.34
Chernesky et al., <sup>69</sup> 1999	SureCell	FVU	Self-collected	LCR	128	62.9%	100.0%	100.0%	74.2%	–	0.37
Hopwood et al., <sup>68</sup> 2001	Clearview	Endocervical	Clinician-collected	LCR	395	75.0%	99.2%	88.9%	97.8%	90.75	0.25
Kegg and Roberts, <sup>73</sup> 2006	Chlamydia Wand	Vaginal	Self-collected	SDA	100	36.4%	79.8%	18.2%	91.0%	1.80	0.80
Kluytmans et al., <sup>71</sup> 1993	Clearview	Cervical	Clinician-collected	PCR	716	72.1%	99.1%	83.8%	98.2%	80.86	0.28
Kluytmans et al., <sup>71</sup> 1993	Clearview	Urethral	Clinician-collected	PCR	283	59.1%	86.2%	43.3%	92.4%	4.28	0.47
Kluytmans et al., <sup>71</sup> 1993	Magic Lite	Cervical	Clinician-collected	PCR	724	60.5%	99.9%	96.3%	97.6%	411.77	0.40
Kluytmans et al., <sup>71</sup> 1993	Magic Lite	Urethral	Clinician-collected	PCR	283	70.5%	100.0%	96.9%	95.2%	–	0.30
Lauderdale et al., <sup>70</sup> 1999	Clearview	Endocervical	Clinician-collected	LCR	65	50.0%	100.0%	100.0%	91.7%	–	0.50
Lauderdale et al., <sup>70</sup> 1999	Clearview	Endocervical	Clinician-collected	TMA	65	50.0%	100.0%	100.0%	91.7%	–	0.50
Mahilum-Tapay et al., <sup>50</sup> 2007	Chlamydia Rapid Test	Vaginal	Clinician-collected	PCR	686	77.8%	99.2%	89.4%	98.1%	98.31	0.22
Mahilum-Tapay et al., <sup>50</sup> 2007	Chlamydia Rapid Test	Vaginal	Self-collected	PCR	686	81.5%	98.7%	84.6%	98.4%	64.37	0.19
Mahilum-Tapay et al., <sup>50</sup> 2007	Chlamydia Rapid Test	Vaginal	Self-collected	PCR	663	83.9%	98.8%	87.0%	98.5%	72.78	0.16
Mahilum-Tapay et al., <sup>50</sup> 2007	Chlamydia Rapid Test	Vaginal	Self-collected	SDA	637	81.6%	98.3%	80.0%	98.5%	48.00	0.19
Michel et al., <sup>74</sup> 2009	Chlamydia Wand	Vaginal	Clinician-collected	PCR	131	20.0%	88.1%	33.3%	78.8%	1.68	0.91

Study	POCT	Type of specimen	Method of collection	NAAT method	Specimens analysed	Sensitivity	Specificity	PPV	NPV	Positive LR	Negative LR
Michel <i>et al.</i> , <sup>74</sup> 2009	Chlamydia Wand	Vaginal	Clinician-collected	PCR	100	12.5%	93.5%	14.3%	92.5%	1.92	0.94
Nadala <i>et al.</i> , <sup>75</sup> 2009	Chlamydia Rapid Test	FVU	Self-collected	PCR	454	90.0%	98.2%	69.2%	99.5%	48.83	0.10
Nadala <i>et al.</i> , <sup>75</sup> 2009	Chlamydia Rapid Test	FVU	Self-collected	PCR	757	80.0%	98.7%	88.9%	97.3%	59.29	0.20
Rani <i>et al.</i> , <sup>67</sup> 2002	QuickVue	Endocervical	Clinician-collected	PCR	99	62.5%	100.0%	100.0%	93.3%	–	0.38
Rani <i>et al.</i> , <sup>67</sup> 2002	QuickVue	Endocervical	Clinician-collected	PCR	100	25.0%	100.0%	100.0%	97.0%	–	0.75
Saison <i>et al.</i> , <sup>65</sup> 2007	Clearview	Endocervical	Clinician-collected	PCR	822	53.5%	99.1%	93.4%	89.9%	59.07	0.47
Saison <i>et al.</i> , <sup>65</sup> 2007	Clearview	Vaginal	Clinician-collected	PCR	137	40.0%	97.3%	76.9%	87.9%	14.93	0.62
Saison <i>et al.</i> , <sup>65</sup> 2007	Clearview	Vaginal	Self-collected	PCR	196	25.0%	93.8%	47.4%	84.7%	4.00	0.80
Saison <i>et al.</i> , <sup>65</sup> 2007	Chlamydia Rapid Test	Vaginal	Clinician-collected	PCR	291	71.0%	99.0%	97.1%	87.9%	70.26	0.29
Saison <i>et al.</i> , <sup>65</sup> 2007	Chlamydia Rapid Test	Vaginal	Clinician-collected	PCR	838	86.8%	99.6%	93.9%	99.1%	227.11	0.13
Shaarawy, <sup>64</sup> 1998	Clearview	Endocervical	Clinician-collected	PCR	50	83.3%	68.8%	60.0%	88.0%	2.67	0.24
Wisniewski <i>et al.</i> , <sup>72</sup> 2008	Chlamydia Rapid Test	FVU	FirstBurst	PCR	534	82.4%	98.8%	82.4%	98.8%	68.63	0.18
Wisniewski <i>et al.</i> , <sup>72</sup> 2008	Chlamydia Rapid Test	FVU	Routine Cup	PCR	534	47.1%	98.8%	72.7%	96.5%	39.22	0.54
Yin <i>et al.</i> , <sup>66</sup> 2006	Clearview	Endocervical	Clinician-collected	PCR	1497	49.7%	97.9%	78.4%	92.8%	23.95	0.51
Yin <i>et al.</i> , <sup>66</sup> 2006	Clearview	Vaginal	Clinician-collected	PCR	1497	32.8%	99.2%	85.7%	90.5%	38.69	0.68

LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.





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