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Horizon Scanning Technology Prioritising Summary

Rapid urine test for *Chlamydia trachomatis*

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Enquiries about the content of the report should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

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This Horizon scanning prioritising summary was prepared by Linda Mundy and Professor Janet Hiller from the National Horizon Scanning Unit, Adelaide Health Technology Assessment, Discipline of Public Health, School of Population Health and Clinical Practice, Mail Drop DX 650 545, University of Adelaide, Adelaide, SA, 5005.

PRIORITISING SUMMARY

REGISTER ID: **000429**

NAME OF TECHNOLOGY: **RAPID CHLAMYDIA TEST FOR *CHLAMYDIA TRACHOMATIS***

PURPOSE AND TARGET GROUP: **FOR THE RAPID DETECTION OF CHLAMYDIA INFECTION IN ASYMPTOMATIC SEXUALLY ACTIVE INDIVIDUALS IN URINE SAMPLES**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☐	No	
☒	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United Kingdom	✓		
Philippines	✓		

IMPACT SUMMARY:

The University of Cambridge and Diagnostics for the real World (Europe) provides *Chlamydia* Rapid Test with the aim of detecting Chlamydia trachomatis infection. The technology would be available through general practitioners or sexual health clinics for *Chlamydia* infection in asymptomatic but sexually active individuals.

BACKGROUND

Worldwide *Chlamydia trachomatis* infection is a major public health problem and one of the most common sexually transmitted bacterial infections. The majority of testing for *Chlamydia* is conducted on symptomatic cases or as a result of contact tracing, and as such remains under-diagnosed. However, approximately 40-50 per cent of males and 70-85 per cent of females infected with *Chlamydia* are symptomatic (Vajdic et al 2005). If left undetected and untreated chlamydia infection may move into the upper

genital tract causing inflammation and scarring in the reproductive tracts of both males and females. The most common complications of chlamydia infection in women include pelvic inflammatory disease (PID), urethritis, cervicitis, tubal infertility, chronic pelvic pain and ectopic pregnancy, a cause of maternal death and morbidity in the first trimester. In untreated women, 10-40 per cent of chlamydia infections may result in PID, and of these, 20 per cent will become infertile. Chlamydia infection can be transmitted to the neonate at birth, causing conjunctivitis and pneumonia (Hocking & Fairley 2003; Walleser et al 2006; Watson et al 2002).

The Rapid Chlamydia urine test requires subjects to provide a urine sample, collected using the FirstBurst urine collection device which collects the first 4-5 ml of urine. The urine is diluted with distilled water and centrifuged. The supernatant is discarded and the pellet is extracted by the sequential addition of the three kit solutions. A fraction of the extracted sample is added to a tube which contains lyophilised amplification and detection reagents. After mixing, the test strip is added to the solution and incubated at room temperature for 25 minutes (Figure 1). The test strip is embedded with a monoclonal antibody to chlamydial lipoploysaccharide. If chlamydia is present in the sample a line appears on the test strip (Nadala et al 2009).

Figure 1 The Rapid Chlamydia test, showing test strip with a result line indicating the presence of chlamydia (printed with permission Wellcome)

It has been proposed that the Rapid Chlamydia urine test will enable a test and treat regimen, with patients undergoing the test, obtaining the result and if needed receiving treatment all in the one clinic visit. Testing by polymerase chain reaction (PCR) may take hours or even days and the return rate of positive patients to clinics for treatment is approximately 65 per cent (Nadala et al 2009). Although there are other rapid chlamydia tests on the market, they lack sensitivity in comparison to PCR.

CLINICAL NEED AND BURDEN OF DISEASE

In Australia and New Zealand, the rate of chlamydia infection has been steadily increasing for a number of years, with chlamydia now the most common notifiable disease. Notification rates are likely to be an underestimate of the true rate of chlamydia infection as the majority of tests are performed on symptomatic patients (40-85% of infected individuals may be asymptomatic) or as a result of contact tracing (Vajdic et al 2005).

In Australia, there were 73.5 per 100,000 population notifications of chlamydia infection in 1999, the first year that all states and territories reported notification data. This number has increased every year and in 2008 the notification rate was 273.8 per 100,000. The Northern Territory recorded the highest number of notifications in all years, however this is likely to be due a high number of chlamydia infections of the eye (Communicable Diseases Australia 2009). True prevalence data are difficult to obtain. An Australian systematic review identified 40 studies that used PCR to identify individuals infected with chlamydia. The mean overall prevalence of genital chlamydia infection was 4.6 per cent, 95 % CI [4.4, 4.8], which the authors considered indicated an over-sampling of high-risk groups in the included studies. Mean community-based rates were similar for non-Indigenous males and females (1.5% and 1.4%, respectively). Mean community-based rates for Indigenous men and women were 7.5 per cent (95% CI [6.4, 8.6]) and 8.7 per cent (95% CI [7.9, 9.7]), respectively. The overall mean estimate for adolescents and young adults was 3.3 per cent, 95 % CI [2.8, 3.9] (Vajdic et al 2005).

A recent Australian study reported on the medical records of women (mean age 27.7 years, range 12.2 -80.7 years) using the Melbourne Sexual Health Clinic from 2003 to 2007. All new clients to the clinic underwent a chlamydia test, regardless of their reason for visiting the clinic or whether they were symptomatic for chlamydia infection or not. Over the 5-year period, 10,498 chlamydia tests (PCR) tests were performed and an overall prevalence of 5.9 per cent (95% CI [5.5, 6.4]) was reported. Women less than 25 years had the highest rate of positive tests at 8.1 per cent. The authors report that the positive chlamydia tests are increasing by 12 per cent per year (O'Rourke et al 2009).

As reported in a previous summary[1], an Australian prevalence survey of chlamydia among young women (aged 18-35 years) was conducted in Melbourne between March 2003 and June 2004. Of the 11,001 households chosen at random, 979 women were eligible and interviewed and of these, 657 provided a urine sample. A total of six cases of chlamydia were detected (five aged 18-24 years and one aged 25-35 years), with an overall prevalence of 0.9 per cent. The prevalence was 3.7 per cent (95%CI [1.2, 8.4], n=135) in the 18-24 years group and 0.2 per cent (95%CI [0.0, 1.1], n=489)

[1] Screening for chlamydia in pharmacies

in the 25-35 years group. All women who tested positive were asymptomatic (Hocking et al 2006).

Prevalence data for New Zealand are difficult to obtain. Annual testing for chlamydia within the Waikato District Health Board region rose from approximately 18,000 tests conducted in 1998 to 23,338 tests in 2002, and remained at that level until 2006. In 1999, 7.7 per cent of tests were positive, however this rate rose to 11.3 per cent in 2005 but declined again in 2006 to 9.6 per cent (Morgan 2008). A later study again conducted in the Waikato region, reported that there were 21,104 Chlamydia tests carried out during Feb-Oct 2008. Of these, 10,847 (51.4%) tests were tests on 15-24 year olds, 82.3 per cent of whom were female. Using census data for the region, these figures represent 22.2 per cent of the region's 15-24 year olds, which was made up overwhelmingly of 37 per cent of the region's young females compared to 7.7 per cent amongst males. Overall 15.8 per cent of tests from 15-24 year olds were positive, 14.4 per cent in females and 23.0 per cent in males ($p<0.001$), with positivity double amongst Mäori (24.2% vs. 12.5%; $p<0.001$) (Morgan & Bell 2009).

New Zealand laboratory surveillance indicates an overall increase in the rate of reported chlamydia infection over time (Figure 2). In the quarter from April to June 2009, 37,678 chlamydia tests were conducted with 2,708 (7.2%) testing positive from 2,562 patients. Sixty-six per cent of all positive tests were aged 15-24 years. The Waikato region reported testing 7,379 samples for chlamydia with 768 being positive (10.4%) from the same number of patients. Seventy-five per cent of all positive tests were aged 15-24 years. Almost the same figures were reported from Bay of Plenty laboratories. The overall rate of chlamydia infection in these regions for the quarter April to June 2009 was 211.4 per 100,000 population (STI Surveillance Team 2009).

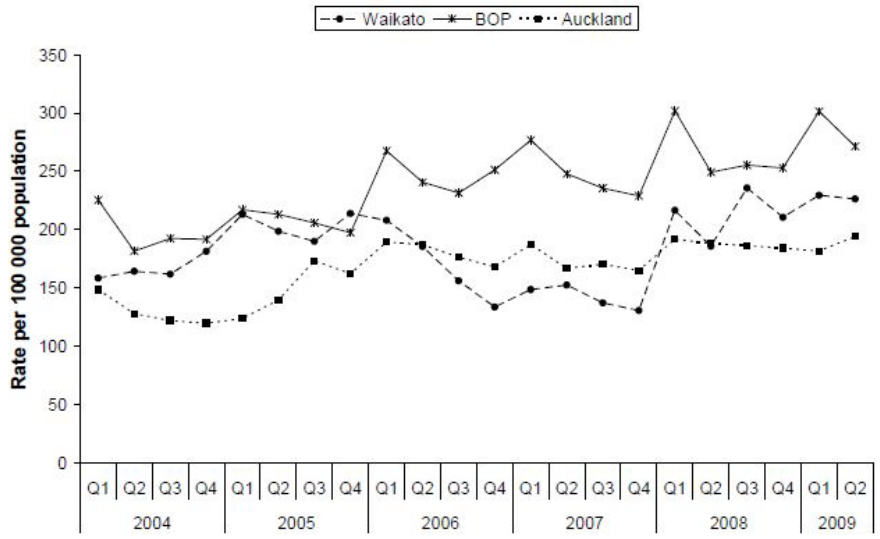

Figure 2 Rates of chlamydia infection reported via laboratory surveillance in the Waikato, Bay of Plenty and Auckland Heath Board regions (STI Surveillance Team 2009)

DIFFUSION

The Rapid Chlamydia Test is not currently available in Australia.

COMPARATORS

The gold standard diagnostic test for *Chlamydia trachomatis* currently in use in Australia and New Zealand is PCR. PCR is highly specific and sensitive, especially in comparison to culture, and will only identify *Chlamydia trachomatis* and not Chlamydia *pneumoniae* or *Chlamydia psittaci* (psittacosis) infection. The PCR test amplifies a fragment of specific DNA from the cryptic plasmid of chlamydia, and is capable of detecting only one chlamydia cell in the sample. The PCR test for *Chlamydia trachomatis* can be performed on first void urine in males and females, avoiding the need for urethral swabs, however endocervical swabs are also suitable. For swabs, a specific PCR swab specimen collection transport kit must be used (Ferguson 2005). Samples for PCR testing must be sent to a certified pathology laboratory.

SAFETY AND EFFECTIVENESS ISSUES

The Rapid Chlamydia test was first trialled in the UK for women attending a sexual health clinic (site one) or two genitourinary medicine clinics over a six-month period. All women over the age of 16 years attending the clinics were invited to attend. All participating women provided a self-collected vaginal swab and a first-void urine sample (FVU). At sites two and three, women also provided a clinician-collected vaginal swab. The majority of women attending site one were asymptomatic (98.2%) and were attending for contraception or reproductive health services. Many of the women (67%) attending sites two and three, however, reported symptoms including vaginal discharge (46%), lower abdominal pain (23%) or pelvic inflammatory disease (3%). Urine samples were divided, with one half sent for PCR chlamydia testing at an independent laboratory and the other subjected to the Rapid Chlamydia test (level III-2 diagnostic evidence). A total of 1,349 women took part in the study. The mean age of participants varied between the clinics: site 1 (n=663), mean age 18.5 years (range 16-27.4 years); site 2 (n=385) mean age 25.4 years (range 16-49.7 years) and site 3 (n=301) mean age 27.8 years (range 17.1-54.8 years).

There was no significant difference between vaginal swab collection methods when compared to PCR. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for self-collected swabs was 81.5, 98.7, 84.6 and 98.4 per cent, respectively. The sensitivity, specificity, PPV and NPV for clinician-collected swabs for the same women was 77.8, 99.2, 89.4 and 98.1 per cent, respectively. The difference in performance of the Rapid Chlamydia test between self- and clinician-collected vaginal swabs was not significant (p=0.096). When self-collected swabs from all centres were compared to the gold standard PCR, the

sensitivity, specificity, PPV and NPV values were 82.7, 98.8, 85.8 and 98.5 per cent, respectively. When only the *asymptomatic* subjects from all three sites were considered, the Rapid Chlamydia test had an overall sensitivity of 80.5 per cent when compared to PCR. It is unclear from the study why a vaginal swab was the preferred method of testing as opposed to testing of the urine sample. The majority of women (95.9%) were comfortable collecting their own vaginal swab. Self-collected swabs were the preferred method of sample collection for 40.7 per cent of women, with 37.5 per cent preferring a urine sample. The remaining 27.7 per cent of women did not express a preference. Seventy-five per cent of women were prepared to wait between 30 minutes and two hours for test results, with only 6.9 per cent preferring to wait less than 30 minutes (Mahilum-Tapay et al 2007).

In order to reduce or slow the steadily increasing rate of chlamydia infection in the population, it has been suggested that more widespread and systematic testing and treatment of males would reduce the infective pool and prevent transmission to females. Therefore a test which makes it quicker and easier to test males via a urine sample rather than a painful urethral swab may be advantageous. Males over 16 years (n=1,002) were recruited over a 12-month period at two of the sites described in the above study (one sexual health clinic, one genitourinary clinic) (level III-2 diagnostic evidence).

To optimise the urine collection method, participants were randomised to provide two urine samples using two different methods. One group provided a urine sample using the FirstBurst collection device, then after a two hour interval the second sample was collected using a conventional cup. The second group reversed the order of sample taking. The FirstBurst collection device, regardless of whether the sample was taken first or second, provided a sample with a significantly higher bacterial load when compared to the conventional cup device ($p<0.0001$). To further analyse the optimal collection mode, 31 chlamydia positive males provided a urine sample using the FirstBurst collection device and fractionation system, which allowed four distinct fractions from the one urine void. The importance of collecting the first fraction for chlamydia testing, and thus optimising bacterial load, is emphasised by the results. The first fraction (4.6ml) contained a mean bacterial load of 38,561 plasmids/ml with the number decreasing significantly with the second, third and fourth fractions yielding 5,219, 1,669 and 270 plasmids/ml.

The performance of the Rapid Chlamydia test using both FirstBurst and cup urine specimens were compared to the gold standard PCR in 534 randomly collected samples. PCR detected chlamydia infection in 34 of the FirstBurst urine samples (positivity rate 6.4%) and in 33 of the cup collected samples (6.2%). The Rapid Chlamydia test had a sensitivity of 82 per cent when the FirstBurst sample was used compared to a sensitivity of 47 per cent for the cup collected samples. The overall

specificity of the Rapid Chlamydia test was high at 98.8 per cent (Wisniewski et al 2008).

Having established the optimal collection conditions for urine samples from males (collecting the first 4-5ml of a urine sample using the FirstBurst collection device), Nadala et al (2009) enrolled 1,277 young males (>16 years) attending the same two clinics described by Wisniewski et al (2008) (level III-2 diagnostic evidence). The majority of men attending site one were asymptomatic and were attending for contraception or reproductive health services. However, 62 per cent of subjects (467/749) enrolled at site two reported symptoms including urethral discharge (21%) and painful or difficult urination (23%). In addition, three per cent of participants were attending the clinic after being identified via contact tracing. Of those eligible, 1,211 provided a usable urine sample. Samples were tested for the presence of chlamydia using the Rapid Chlamydia test and the reference standard, PCR. Twenty participants were identified as positive for chlamydia infection by PCR at site one (4%) and 90 (12%) at site two. The overall sensitivity and specificity of the Rapid Chlamydia test was 81.8 and 98.5 per cent, respectively (Table 1).

Table 1 Performance of the Rapid Chlamydia test compared to PCR

Site	Sensitivity (%) [95 % CI]	Specificity (%) [95 % CI]	PPV (%) [95 % CI]	NPV (%) [95 % CI]
1 (n=454)	90.0 [68.3, 98.8]	98.2 [96.4, 99.2]	69.2 [48.2, 85.7]	99.5 [98.3, 99.9]
2 (n=757)	80.0 [70.2, 87.7]	98.7 [97.4, 99.4]	88.9 [80.0, 94.8]	97.3 [95.8, 98.4]
Total (n=1211)	81.8 [73.3, 88.5]	98.5 [97.5, 99.1]	84.1 [75.8, 90.5]	98.2 [97.2, 98.9]

The authors reported a significant difference between the PPV and NPV values obtained at the two sites (p=0.009 and p=0.028, respectively), which may reflect differences in prevalence of chlamydia infection between the two sites. The likelihood ratios of a positive and negative result from the chlamydia test from both sites and sites combined are summarised in Table 2.

Table 2 Positive and negative likelihood ratios for test results with Rapid Chlamydia test

Site	Positive	Negative
1 (n=454)	50.0	0.102
2 (n=757)	61.5	0.202
Total (n=1211)	54.5	0.185
Adjusted total (range)	43.1 (15.0-55.1)	0.184 (0.177-0.477)

Of the 20 participants found to be positive for chlamydia at site one, 18 (90%) were asymptomatic at presentation. At site two, 28 (31%) of those found to be positive had

no symptoms. Of these *asymptomatic* men, 16/18 (89%) and 20/28 (71%) tested positive for chlamydia using the Rapid Chlamydia test, giving an overall test sensitivity of 78 per cent (36/46) for asymptomatic men. The combined sensitivity for symptomatic men testing positive at both sites was higher at 84 per cent.

The majority of participants preferred giving a urine sample (89%), with seven per cent preferring a swab and four per cent willing to provide either. However as participants were not asked to provide a swab, this preference may not be valid. The majority of subjects (96%) indicated that they were willing to wait an hour or more for test results with only four per cent unwilling to wait an hour.

COST IMPACT

The Wellcome Trust were contacted via email for pricing information, however no reply was received by the evaluators. In the previous summary in 2006, which described the use of a dipstick assay for trachoma using the same principles, Diagnostics for the Real World aimed to have a two-tiered price range. Developing countries would be able to access the FirstBurst Trachoma test for approximately 70 cents per dipstick test, however prices would be higher in developed countries such as Australia (personal communication University of Cambridge, May 2006).

The fee for the MBS item number 69316, which covers the detection of chlamydia by any method, is $28.85.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

The Rapid Chlamydia urine test may be of benefit to rural and remote communities that do not have access to pathology laboratory testing. Although samples for PCR testing can be transported from these communities to regional centres the turnaround time for results is extended. The Rapid Chlamydia urine test enables a rapid diagnosis and a treatment regimen may be put in place immediately without a return visit.

SUMMARY OF FINDINGS

Initial studies with the Rapid Chlamydia test combined with either the FirstBurst collection device or vaginal swabs for women, appears to have good sensitivity and specificity for the rapid detection of chlamydia, depending on the prevalence of chlamydia in the tested population. The Rapid test has the advantage that results can be given to the patient within a short time frame and if found to be positive, patients can be given immediate treatment. The targeting and testing of young males may be an effective way in which to reduce the infective pool and to halt the increase in chlamydia infection rates.

HealthPACT action:

The rapid Chlamydia test may be of use in rural and remote areas and in public hospital settings. Whether or not this test may be useful for screening populations remains to be ascertained. However, based on initial promising results from studies, the rapid increase in infection rates and the need to reduce the number of new chlamydia infections in the population by identifying asymptomatic individuals HealthPACT have recommended that this technology be monitored for further information in 12-months time.

Number of included Studies

Total number of studies	3
Level III-2 diagnostic evidence	3

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SEARCH CRITERIA TO BE USED:

Chlamydia Infections
Patient Satisfaction
Polymerase Chain Reaction
Urinalysis
Chlamydia trachomatis
Bacterial/analysis
Point-of-Care Systems