Published in final edited form as:
Point Care. 2010 March 1; 9(1): 36–46. doi:10.1097/POC.0b013e3181d2d8cc.

What's the Point? How Point-of-Care STI Tests Can Impact Infected Patients

Jill Huppert, M.D., M.P.H.[1], **Elizabeth Hesse, B.S.**[1], and **Charlotte A. Gaydos, M.S., M.P.H., Dr.P.H.**[2]

[1]Division of Adoelscent Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

[2]Division of Infectious Diseases, Johns Hopkins School of Medicine, Baltimore, MD

Abstract

Point-of-care (POC) tests are an important strategy to address the epidemic of sexually transmitted infections (STIs) among both adolescents and young adults. While access to care and confidentiality are major barriers to STI care, POC tests allow the clinician to provide immediate and confidential test results and treatment. In addition, POC test results constitute a "teachable moment"; that is, an opportunity to provide immediate feedback to the patient that may impact his/her risk behaviors. This paper reviews published data and manufacturer's product literature describing current point-of-care STI tests, including studies of test performance as well as impact on treatment intervals and disease spread. It presents theoretical and proposed pitfalls and solutions of implementing POC tests in clinical settings, non-traditional settings, and home care venues. We reviewed the available STI tests according to the World Health Organization (WHO) criteria for judging POC tests: the "ASSURRED" criteria (Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment-free, Delivered).

Introduction

Point-of-care (POC) tests are an important strategy to address the epidemic of sexually transmitted infections (STIs) in the United States, especially in adolescents. The burden of STIs in the U.S.A. is greatest in adolescents and young adults and untreated women are at the greatest risk of sequelae, such as pelvic inflammatory disease, infertility, ectopic pregnancy, and chronic pelvic pain. In the usual STI testing scenario, the patient is tested and if infection is suspected based on clinical findings, given presumptive treatment. However, if persons are not treated at the visit, there is often a delay between visit and treatment, and a substantial proportion may never receive follow up at all. Clinicians must weigh the risk of delay and loss to follow up against the risks of over-treatment and antibiotic resistance. In contrast, POC tests allow the clinician to provide immediate and confidential test results and treatment. In addition, POC test results constitute a "teachable moment"; that is, an opportunity to provide immediate feedback to the patient that may impact his/her risk behaviors. For these reasons, POC STI tests may be of great importance for the care of adolescents and young adults.

Corresponding Author: Jill Huppert, MD, MPH, Cincinnati Children's Hospital Medical Center, Division of Adolescent Medicine, 3333 Burnet Avenue, ML 4000, Cincinnati, OH 45229-3039, Phone: 513-636-7042, FAX: 513-636-8844, jill.huppert@cchmc.org.

Presented in part: Society of Adolescent Medicine Annual Meeting 2009, Los Angeles, CA, Funding: NIBIB, NIH, U-54EB007958

In this article, we will review the current literature describing POC STI tests for *Chlamydia trachomatis*, *Neisseria gonorrhea*, *Trichomonas vaginalis*, and HIV. We will include studies of test performance, as well as their potential impact on treatment intervals and disease spread. In addition, we will discuss the World Health Organization's "ASSURRED" criteria (Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment-free, Delivered) for judging POC tests. We will present theoretical and proposed pitfalls, as well as solutions to implementing POC tests in clinical settings and their potential use in using non-traditional venues.

Evaluation of Currently Available POC Tests

Chlamydia

In 2007, Chlamydia was the most frequently reportable disease to the Centers for Disease Control and Prevention (CDC), with 1.18 million cases being reported.[1] Chlamydia is the most prevalent reportable STI among adolescents. Recent population surveys estimate that up to 4.7 % of women and 3.7 % of men age 18–26 are affected by Chlamydia.2 In the U.S., the estimated incidence in this age group is 1.9 million cases per year.3 Over 90% of infections are asymptomatic, which points to the need for universal screening in this age group. Thus, it is not surprising that much of prior and current research efforts have been directed at developing a sensitive point-of-care or "rapid" test for Chlamydia.

Various types of rapid tests for detecting *Chlamydia trachomatis* have been developed. Currently, these include the optical immunoassay (OIA) (Inverness [formerly Biostar], Princeton, NJ); Clearview Chlamydia (Inverness, Princeton, NJ); QuickVue (Quidel, San Diego, CA); and a new Chlamydia Rapid Test (CRT, Diagnostics for the Real World, LTD, Cambridge, UK). The first three are cleared for clinical use by the U.S. Food and Drug Administration (FDA), while the CRT is available in Europe. Two other tests, OneStep (CLIAwaived, Inc., San Diego, CA) and MICT (MagnaBioSciences, Green Cross Medical Sciences Corp, San Diego, CA), have product information on their websites but have not yet been evaluated in the literature or achieved FDA clearance.

The BioStar® OIA® CHLAYMDIA test (Inverness, Princeton, NJ) is a cartridge-based optical immunoassay test. In a study by Pate, et al. in 1998, three endocervical swabs were collected from 306 women ages 15 to 52 attending a STI clinic in Alabama. The swabs were tested using the BioStar® OIA® Chlamydia test, cell culture, direct fluorescent-antibody (DFA) assay (Syva MicroTrak; Syva Co., Palo Alto, CA.), and PCR (Roche Amplicor *Chlamydia trachomatis;* Roche, Branchburg, NJ). Chlamydia infection was defined as two or more positive test results. Based on this, 42 of 306 participants (13.7%) were positive for Chlamydia. Using this criterion, the BioStar® Chlamydia test demonstrated a sensitivity of 73.8% and a specificity of 100%.4 In addition, Bandea, et al. evaluated the Biostar® test at the Center for Disease Prevention and Control (CDC).5 They reported a sensitivity of 59.4% and a specificity of 98.4% from 261 adolescent females compared to a nucleic acid amplification test (NAAT) (Table 1). Since NAATs are now considered to be the gold standard for diagnosis of Chlamydia, older studies comparing POCs to culture as the gold standard might result in overestimation of the sensitivity, since culture is considered to be 65–85% sensitive. Thus, a reported sensitivity of 73.8% when compared to culture might have a true sensitivity and expected performance for OIA of ~48% (73.8% X 65%) when compared to a NAAT. The BioStar® test requires 20 minutes and 11 steps to complete the process. A positive result is a solid blue or purple colored reaction circle (of any intensity) that appears around the internal control dot. A negative result is when no blue- or purple-colored circle surrounds the internal control dot. It is not waived under the Clinical Laboratory Improvement Act (CLIA) and is graded as moderately complex. CLIA-waived

tests are determined to be easy to use and have little risk of an incorrect result, and can be performed in a clinic or doctor's office rather than in a laboratory.

Clearview Chlamydia (Inverness, Princeton, NJ) is another available test, called a single-reagent immunoassay test. Three published reports evaluated Clearview Chlamydia test performance. In 1991, Stratton, et al. compared Clearview to Chlamydia culture.6 Cervical swabs were collected from women attending an obstetrics/ gynecology clinic. Of 648 cervical specimens, 40 were culture positive (6.2% prevalence). Clearview Chlamydia detected 38 of 40 culture positives, and an additional 12 were positive by Clearview Chlamydia and negative by culture. Thus, Clearview Chlamydia had 95% sensitivity and 98% specificity, with positive and negative predictive values of 76% and 99.7%, respectively, compared to culture. The authors noted that Clearview was less technically demanding than other chlamydial assays. In a similar study comparing Clearview to culture, 965 women ages 14 to 82 attending gynecological clinics were included.7 Chlamydia culture was positive in 43 (4.5% prevalence). In this study, Clearview was 79% sensitive and 99.6% specific, which was similar to the performance of a commercial laboratory-based enzyme immunoassay (Chlamydiazyme, Abbott Laboratories, North Chicago, Ill.) for detecting Chlamydia. As we described for Biostar, these sensitivities also represent overestimates because culture was used as the gold standard instead of NAAT.

A more recent study by Yin, et al. compared Clearview Chlamydia to a NAAT (polymerase chain reaction, PCR) test using cervical and vaginal swabs from 1,497 women, average age 28, recruited from STI clinics.[8] Three vaginal swabs and three cervical swabs were collected from each participant. The Clearview Chlamydia test was done with the first vaginal and cervical swabs and the results were read by two research staff members. The second and third vaginal and cervical swabs were used for PCR testing (Roche Amplicor CT assay). Using cervical PCR results to define true infection, Chlamydia prevalence was 13.2% (197/1497). Clearview Chlamydia performed on cervical swabs detected more Chlamydia than with vaginal swabs. However, compared to cervical PCR, the cervical Clearview Chlamydia test was 49.7% sensitive and 97.9% specific, with a positive predictive value of 78.4%. In contrast, the vaginal swab Clearview Chlamydia test was 32.8% sensitive, 99.2% specific, and with a positive predictive value of 85.7% compared to cervical PCR.

The Clearview Chlamydia test takes approximately 30 minutes to complete and requires four steps. It is not CLIA-waived and is classified as moderate complexity. Two lines (control and result line) indicate a positive result, and one line (control line only) is a negative result. The package insert also lists materials that are required to perform the test but are not provided: a heating source (Clearview Workstation), the Specimen Collection Kit for female cervical swabs, and a timer.

QuickVue® (Quidel, San Diego, CA) is also an enzyme immunoassay test. Steingrimsson, et al. and Rani, et al. investigated its effectiveness. In the first study, QuickVue and a similar test called Kodak SureCell (no longer on the market) were compared to culture or culture plus DFA (Direct ImmunoFluorescent Antibody) test. Endocervical swabs were collected from 724 women, 358 low-risk and 366 high-risk. The prevalence of infection was 11%. In comparison to the culture or culture plus DFA, QuickVue had a sensitivity of 92%, a specificity of 99.1%, a 92% predictive value of a positive, and a 99.1% predictive value of a negative. QuickVue performed effectively in both high and low risk patients and those who were symptomatic or asymptomatic.[9]

Rani, et al. compared QuickVue to NAAT testing of endocervical specimens from high and low prevalence populations.[10] One hundred women attending a genitourinary medicine clinic made up the high prevalence participants and 100 women attending a gynecology

department at a hospital constituted the low prevalence group. Two endocervical swabs were collected from each woman in both groups. For the high prevalence population (Chlamydia 16%), QuickVue was 65% sensitive and 100% specific. For the low prevalence population (Chlamydia 4%), QuickVue was 25% sensitive and 100% specific. Rani, et al. noted that for the low prevalence population, they could not recommend QuickVue because of its low sensitivity.

The QuickVue test for Chlamydia takes about seven steps and 12 minutes to perform and obtain results (based on package insert). Results are read at 10 minutes after drops of the extracted sample are in the sample well. It is a lateral flow device, and the appearance of and red test line next to the blue control line is a positive result. It is not CLIA-waived and is classified as moderately complex.

The Chlamydia Rapid Test (CRT) is a promising new POC test for Chlamydia. It is licensed for use in Europe but is not yet available in the U.S.A. This test detects chlamydial lipopolysacharide using an amplified immunoassay process. A study by Mahilum-Tapay, et al. collected vaginal swabs from 686 women ages 16–54 attending one of three clinics.[11] The CRT results were compared to NAAT (PCR of urine specimens at all clinics and strand displacement assay (SDA) of cervical specimens at two clinics). The prevalence of Chlamydia was 8.1%. CRT using vaginal swabs was 83.5 % sensitive, 98.9% specific, had a positive predictive value of 86.7%, and a negative predictive value of 98.6%. Sensitivity and specificity estimates were not different whether CRT was compared to PCR of a urine specimen or SDA of cervical swabs. In addition, self-collected vaginal swabs were as sensitive as clinician-collected vaginal swabs to detect Chlamydia (81% vs. 78%) when urine PCR was the reference test. They also found that the organism load on the swabs correlated well with the Chlamydia Rapid Test's positive visual signal. CRT of an endocervical swab was not evaluated in this study.

The CRT requires about 7 steps and 25 minutes to perform. A reaction (positive) line on the test strip along with the control indicates a positive test result. It is not FDA cleared, and would likely be considered moderately complex under CLIA rulings in the U.S.A.

Other rapid Chlamydia tests. On the Internet, references were found to two other POC Chlamydia tests that have not yet been reported in the scientific literature. The product insert for Chlamydia Dipstick Test (CLIAwaived, Inc., San Diego, CA)[12] reports it to be 97% sensitive in comparison to Direct Fluorescent Antibody (DFA) slide test. This test is no longer advertised on the manufacturer's website. Another test, MICT (MagnaBioSciences, Green Cross Medical Sciences Corp, San Diego, CA) utilizes magnetic properties to detect pathogens. This test is advertised on the company website as having clearance in Europe (CE mark), but there is no product insert or published literature yet (Table 1).[13]

In summary, the three POC enzyme immunoassay tests for Chlamydia that are available in the U.S.A. are moderately complex to perform and demonstrate disappointing sensitivity (25–65%) compared to NAAT, and are thus unlikely to be useful for clinical decision making. The CRT in use in the U.K. appears promising, and several new tests are in development.

Gonorrhea

Neisseria gonorrhoeae is one of the most prevalent sexually transmitted diseases in men and women. In 2007, there were 356,524 cases reported to the Centers for Disease Control and Prevention (CDC).14 Estimates of true incidence are approximately 700,000 new cases per year. The highest prevalence of gonorrhea is among 15–19 year-old African American females. Gonorrhea is less common than Chlamydia in adolescents, averaging about 0.42%

in females and 0.44% of males in population studies of asymptomatic young adults age 18–26.2 As with Chlamydia, a substantial number of infections occur in asymptomatic women, and infection has serious sequelae for women (PID, infertility, chronic pelvic pain, and ectopic pregnancy). Thus annual screening is recommended. Laboratory methods to make the diagnosis include culture (requires stringent conditions), gram stain (not very sensitive in women), or NAAT. Because culture performs very well in detecting gonorrhea, either culture or NAAT can be used for genital infections.15 POC tests for gonorrhea that are in development include the currently marketed optical immunoassay (OIA) (Inverness [formerly Biostar], Princeton, NJ) and two new products, PATH GC-Check (PATH, Seattle, WA) and OneStep (Cortez Diagnostics, Inc., Calabasas, CA).

The BioStar® OIA GC test was evaluated in a study by Benzaken, et al.[16] Endocervical swabs were collected from 326 high risk women, ages 18–55, at a STI clinic in Brazil. The prevalence of gonorrhea was 15% by culture. In comparison with culture, the BioStar® GC test had a sensitivity of 60% (95% confidence interval: 46.4%–73.6%); a specificity of 89.9% (86.2% to 93.6%); a positive predictive value of 55.6% (42.4% to 68.8%); and a negative predictive value of 92.6% (89.5% to 95.7%) (Table 2).

A study comparing the GC OIA test to commercial culture media, with secondary confirmation testing by LCR (Ligase Chain Reaction), reported that a total of 904 specimens were obtained from symptomatic patients at four clinical locations. Sensitivity and specificity for symptomatic male urine were 93.2 % and 97.5 respectively. Sensitivity and specificity for symptomatic female endocervical swabs were 70.7% and 99.4% respectively. Overall, PPV and NPV for males were 94.0 % and 97.2 respectively; and for females were 90.6% and 97.24%, respectively.[17,] 18

The BioStar® GC test has 9–10 steps depending on if you are using female endocervical swabs or male urine specimens. It takes approximately 20 minutes to complete. A positive result is a solid blue- or purple-colored reaction circle of any intensity that appears around the internal control dot. A negative result is when no blue- or purple-colored circle surrounds the internal control dot. It is not CLIA-waived.[19]

The PATH GC-Check® (PATH, Seattle, WA) is an immunochromatographic strip test (dipstick) that takes 15 to 20 minutes to perform. In a study by Alary, et al., samples from 1,084 female sex workers in Berlin were tested using this point of care method and compared to NAAT (Roche Amplicor CT/NG PCR).[20] The prevalence of gonorrhea among the women was 4.6%. In comparison with NAAT, the GC-Check was 70% sensitive, 97.2% specific, had a positive predictive value of 54.7%, and a negative predictive value of 98.5% when using cervical swabs. When using vaginal swabs, PATH GC-Check was 54.1% sensitive and 98.2% specific (Table 2).

To date, the only information available on the OneStep® Strip Style Gonorrhea test (Cortez Diagnostics, Inc., Calabasas, CA) is product literature found on the company's website.[21] The test can be performed on a male urethral swab or female vaginal swab. The manufacturer tested 150 female vaginal swabs and compared results to culture. The sensitivity of the test was 98.3% and the specificity was 97.8%. The prevalence of gonorrhea in this population was 39.3%. This is unusual because vaginal swabs for gonorrhea culture have not been validated in the literature, thus the true sensitivity of this assay may be less than reported (Table 2). OneStep takes 10–20 minutes to read the results. It is a simple three step process that involves adding drops of diluents then dipping a test strip into the mixture. A negative result is when there is only one colored band on the control region. A positive result shows a pink colored band in addition to the control line.[21]

In summary, the three POC tests for gonorrhea have a wide range of sensitivities (60–98%) but promising levels of specificity (90–98%). If a higher and more consistent sensitivity can be reached, these rapid gonorrhea tests could be used clinically in the future.

Trichomoniasis

Trichomoniasis is one of the most prevalent and often undetected STIs. Accurate prevalence and incidence data are harder to find because trichomoniasis is not a reportable STI. Weinstock estimates that there were 7.4 million new cases of trichomoniasis in 2000, compared to 2.8 million new cases of Chlamydia among 15–24 year olds in the U.S.A.3 A recent cross sectional study showed that in a population of adolescents and young adults in the U.S.A., the prevalence of trichomoniasis (2.1%) is similar to Chlamydia (4.2%) and six times higher than gonorrhea (0.43%).[22] In addition, the usual testing method is direct microscopy of a saline preparation of vaginal secretions (wet mount), which has been shown to be about 50% sensitive compared to culture or NAAT.23–25 Although some women with trichomoniasis may develop vaginal symptoms, as is true for Chlamydia and gonorrhea, most cases of trichomoniasis occur in asymptomatic individuals. Because recent studies have linked trichomoniasis to HIV acquisition and shedding, there is a new urgency for better POC testing for trichomoniasis.26 These new tests include XenoStrip, OSOM, and AffirmVPIII.27

XenoStrip-*Tv*™ (Xenotope Diagnostics, Inc., San Antonio, TX) is an immunochroatogenic test device that detects *T. vaginalis* (TV) membrane proteins. Miller, et al. tested vaginal swabs collected from women during a large STI project in Peru.[28] They tested samples from 20 women with known positive culture results and 40 samples from culture negative women. When these previously frozen samples were tested with XenoStrip-*Tv*, it had 90% sensitivity and 92.5% specificity compared with culture (Table 3). Further, in a multicenter study by Kurth, et al. in Seattle and Birmingham, XenoStrip-*Tv* was also compared to culture results. Vaginal swabs were collected from 936 women total in Seattle (n=497) and Birmingham (n=439) attending STI clinics.[29] The prevalence of TV by culture was 8.7% in Seattle and 21.0% in Birmingham. Overall, XenoStrip-*Tv* was more sensitive than wet prep (78.5% vs. 72.4% [P=0.04]) but less specific (98.6% vs. 100% [P=0.001]). Test performance was not affected by vaginal symptoms or the presence of other vaginal and/or cervical infections. However, sensitivity decreased by 71% for every additional day delay until TV was first detected in cultures. Xenostrip is no longer on the market in the U.S.A. When it was available for use, it took up to 20 minutes to read and could detect the presence of 10 to 100 TV organisms in 0.5 mL of vaginal fluid (Table 3).[28]

OSOM® TV Trichomonas Rapid Test (Genzyme Diagnostics, Cambridge, MA) is also an immunochromatographic capillary flow (dipstick) assay that detects TV membrane proteins. Huppert, et al. compared the sensitivity and specificity of OSOM with wet mount and culture performed on vaginal swabs.[30] The study was conducted at seven different sites in the U.S.A., and 449 sexually active women age 18 and older participated. The overall prevalence of TV was 23.4% by composite reference standard (either wet mount or culture positive). For the vaginal swabs, OSOM was 83.3% sensitive and 98.8% specific. It performed better than wet mount, and test performance was not affected by co-infections (such as Chlamydia or gonorrhea) (Table 3).

Other studies have demonstrated the effectiveness of the OSOM test. In a 2007 study, Huppert, et al. used vaginal swabs to test 330 sexually active females ages 14–21 for trichomoniasis. The vaginal swabs were tested using wet mount, culture, OSOM, and NAAT (transcription mediated amplification, TMA).25 The prevalence of trichomoniasis in this population was 18.5% (61/330). Using latent class analysis, OSOM was shown to be 90%

sensitive and 100% specific.25 Additionally, the sensitivity of OSOM (92.5%) and TMA (97.5%) were comparable in women who had vaginal symptoms.

In a follow up to this study, Patullo, et al, performed two additional TV tests for subjects who were wet mount negative.[31] The remaining wet mount saline was used to inoculate an InPouch™TV culture, and the used wet mount swab was tested with OSOM. The most sensitive strategy to detect trichomoniasis using two tests was wet mount followed by OSOM, with a sensitivity of 86.4% (95% CI: 75.3 to 93.4%). OSOM detected TV in 67% of true positive, wet mount negative cases. In addition, the likelihood of a positive OSOM test increased with increasing time between specimen collection and testing. Therefore, the OSOM test can be delayed or performed on a used swab with no loss of sensitivity (Table 3).

One study of OSOM in a low prevalence population showed a surprisingly low sensitivity. Compared to wet mount examination, a total of 19/1,009 (2%) women had *T. vaginalis* infection, and OSOM detected 18 of these cases. The one discrepant test was tested with NAAT (TMA) and was negative, for a resolved sensitivity and specificity of 94.7 and 100%, respectively (Table 3).[32]

The OSOM TV rapid test takes five steps to complete and can be read in 10 minutes. It contains an internal control which is shown by a red control line. A negative test shows just the control line and a positive test results shows the red control line plus a blue test line. It is CLIA waived.[33]

Affirm®VPIII Microbial Identification Test (Becton Dickinson, Sparks, MD) is a test that detects *T. vaginalis*, *Candida sp*, and *Gardnerella vaginalis*. It uses synthetic nucleic acid capture probes and color development detection probes complementary to unique genetic sequences of the target organisms and takes 45 minutes to achieve results. In a study by Briselden and Hiller, five vaginal swabs were collected from 176 women attending a STI clinic in Seattle, WA.[34] The swabs were cultured for *G. vaginalis* and *T. vaginalis* and were also tested with Gram stain, wet mount, and Affirm VP, an earlier version than the currently marketed Affirm VPIII. Trichomoniasis was found in 12 of 170 specimens tested by wet mount (7%) and in 15 specimens tested by culture (9%). The sensitivity of Affirm VP when compared with culture and/or wet mount was 83% and the specificity was 100%. DeMeo, et al. compared Affirm VP to wet mount and culture resulting 615 women attending family planning clinics.[35] Trichomonas was found in 95 of the 615 specimens (15.4%). Compared to wet mount/culture, Affirm VP was 90.5% sensitive and 98% specific for trichomonas (Table 3).

A more recent study by Brown, et al. evaluated a newer version of the test, Affirm VPIII.[36] Two vaginal swabs were collected from 425 symptomatic and asymptomatic women being seen for routine OB-GYN care. One swab was evaluated using wet mount and the other using the Affirm VPIII test. Trichomonas was found in 30 participants (7% of total) by Affirm VPIII and 23 (5% of total) by wet mount. Symptomatic participants were more likely than asymptomatic women to be positive by Affirm VPIII (23% vs. 10%) and by a combination of Affirm VPIII and wet mount testing (15% vs. 1%). In a study of 535 military women, AffirmVPIII was compared to clinical diagnosis only, and the prevalence of TV was extremely low (1.5%) (Table 3).[37] Neither of these two studies reported sensitivity or specificity of the Affirm VPIII. However, product literature compares Affirm VPIII to wet mount and culture for 852 patients. The sensitivity of Affirm VPIII compared to wet mount was 91.8% and 98.1% specific. Compared to culture, Affirm VPIII was 89.2% sensitive and 99.3% specific.[38]

Affirm VPIII has not been compared directly to NAAT to detect trichomoniasis. As culture is found to be 80–90% sensitive compared to NAAT, the expected performance of Affirm VPIII would be less than that reported in the product literature. Although advertised as a POC test, the Affirm VPIII requires purchase of an analyzer and must be performed in a laboratory. It is considered a moderately complex test with numerous steps (at least 10) and requires 45 minutes for results.[38]

In summary, both Affirm and OSOM appear to detect more *T. vaginalis* infections than wet mount. The advantages of OSOM are that it is CLIA-waived and faster than the Affirm test, and it has shown to be reliable compared to NAAT diagnosis of trichomoniasis infections.

HIV

There is a growing epidemic of HIV among adolescent and young adults in the United States. A recent study estimated that there were 56,000 new HIV infections in the U.S.A. in 2006, which corresponds to an estimated incidence rate of 22.8 per 100,000 population.[39] Because of the urgency of diagnosis and the difficulty in achieving follow up for those who are tested, several POC tests have been developed. These include OraQuick, Reveal, Multi Spot, Uni-Gold, and Clearview. Because independent clinical trials for POC HIV tests require large sample sizes and expensive confirmatory testing, many of the studies evaluating test performance were submitted to the FDA, and thus can be found in product inserts but not very often in peer-reviewed literature.

OraQuick® Rapid HIV-1/2 Antibody Test (OraSure technologies, Bethlahem, PA) is an FDA approved rapid test that can by used with whole blood specimens, oral fluid specimens, and plasma. It is considered a CLIA-waived test when used with whole blood or oral fluids and is categorized as moderately complexity when used with plasma. For blood and plasma, a specimen loop is used to transfer the samples to the test developer solution kit. For oral samples, the absorbent pad on the end of the test device is moved along the outer surface of the upper and lower gums and then inserted into test vial. The test can be read between 20 and 40 minutes. Like a pregnancy test, two lines (control and test line) indicate a positive result and one line (control only) is read as negative.[27]

In product literature, Oraquick is reported to be 99.3% sensitive for oral specimen, 99.6% for plasma, and 99.6% with fingerstick whole blood .[40] The cited specificity for oral specimens is 99.8%, 99.9% for plasma and 100% specific for finger-stick whole blood.

In peer reviewed literature, Delaney, et al. reported four different studies to evaluate the OraQuick test using whole blood and oral specimens (Table 4).[41] Enzyme immunoassay (EIA) and Western blot were the gold standard reference. Of 12,337 participants, EIA and Western blot results detected HIV in 2.7% (327 participants). OraQuick detected 326 positives with whole blood and 324 with oral specimens, for a 99.7% sensitivity on whole blood and 99.1% sensitivity on oral specimens. It was 99.9% specific with whole blood and 99.6% specific with oral specimens.

In a recent study in 2009, Holguin, et al. evaluated the performance of OraQuick to detect antibodies in oral and sera/plasma specimens from participants from Spain and South America who were infected with different HIV-1 subtypes.[42] One hundred and fifty-six serum/plasma specimens and 139 oral specimens from people who had previously tested positive for HIV-1 by serological tests were tested with Oraquick. OraQuick detected all the positive results in the serum/plasma specimens, regardless of HIV-1 subtype, for a sensitivity of 100%. For oral specimens, it detected 136 of 139 positives, also regardless of subtype, for a sensitivity of 97.8%.

In 2009, Stekler, et al. reported a comparison of OraQuick to EIA or NAAT testing on oral or finger-stick specimens from men who have sex with men.[43] Of 14,005 specimens, 328 (2.3%) were HIV antibody positive and 36 (0.3%) were NAAT positive/antibody negative. Of the 6,811 specimens screened with OraQuick, the rapid test detected 91% of antibody positive results and 80% of positive results detected by NAAT. The specificity was 99.96% with a positive predictive value of 98.1% and a negative predictive value of 99.4%. Surprisingly, Oraquick performed less well in this high-risk screening setting than was expected.

RevealG3® Rapid HIV-1 Antibody test (MedMira, Inc., Halifax, Nova Scotia) is a POC cartridge test that is FDA cleared for use with serum or plasma. As such, it requires laboratory equipment (centrifuge) and refrigeration of reagents, rendering it moderate complexity by CLIA standards. The package insert for it describes studies evaluating the sensitivity and specificity of the test.[44] One study used 483 serum samples from known HIV-1 antibody positive patients and an additional 2,914 serum samples from high-risk individuals (total serum specimens=3397) and compared Reveal results to EIA testing and Western Blot testing. There were 606 (18%) positive HIV-1 results by Western blot. The sensitivity of the Reveal test was 605/606 (99.8%) To test the specificity of serum samples, 850 serum samples from previously screened HIV-1 antibody negative patients were added to 2,914 newly collected serum samples from high risk individuals (n= 3,764 specimens). Of these, 3,639 were deemed true negatives by Western blot. Reveal detected 3,608 of these true negatives for a specificity of 99.1% (Table 5).

In addition to testing of serum samples, the performance of Reveal was examined for plasma samples in product literature.[44] In the first study, plasma samples were collected from 397 patients who were positive for HIV-1 and 107 from clinically-diagnosed AIDS patients (n= 504 specimens). Of these, 499 were positive for HIV by Western blot. Reveal detected 498 of 499 for a sensitivity of 99.8%. To determine specificity, 1,000 known negative samples plus 2,011 samples from unscreened people from low risk population made up a sample size of 3,011. Using Western blot to define a true negative, Reveal detected 2,970 out of 3011 true negatives for a specificity of 98.6% (Table 5).[44] Reveal G3 is FDA-cleared and rated as moderate complexity.

Multispot® HIV-1/HIV-2 Rapid Test (Bio-Rad Laboratories, Redmond, WA) is another HIV rapid test. Like Reveal, it is FDA cleared for serum or plasma, requires equipment, and is moderately complex. According to the company's product sheet,45 Multispot has 100% sensitivity for HIV-1 and HIV-2 compared to Western blot, and the specificity is 99.93% in fresh serum and 99.91% in fresh plasma. In the published literature, Phillips, et al.,46 Multispot was tested on 241 serum samples, 172 of which were Western blot positive and repeatedly reactive on EIA (prevalence of 71%). Multispot detected all positive and negative infections correctly, for a specificity of 100% and a sensitivity of 100%, regardless of HIV-1 subtype. Holguín, et al.evaluated the performance of three rapid HIV tests, including Multispot.47 One hundred and eleven plasma specimens were collected from African immigrants attending three HIV clinics in Spain. Of these, 81 were known positives and 30 known negatives based on EIA results and Western blot (prevalence of 73%). Again, Multispot was 100% sensitive and 100% specific, detecting all positive and negative cases of HIV-1 non-B subtypes. Multispot was also 92.7% specific for HIV-2. In a recent study by O'Connell, et al., frozen serum samples from 248 known positive (by EIA reactivity and Western blot) subjects were tested using Multispot.48 Multispot was able to detect all positive cases, for a sensitivity of 100% (Table 4).

Multispot can be used with fresh or frozen serum or plasma. It is FDA approved and is classified as CLIA moderately complex. It requires 10 steps and takes approximately nine

minutes to complete. A negative result is when only the control spot appears (a purple spot in the top left corner). One, two, or three extra spots in addition to the control spot indicate a positive result and the spots indicate if it is HIV-1 or HIV-2. If there is no control spot at all, the test is invalid.[45]

Uni-Gold™ Recombigen® HIV test (Trinity Biotech PLC, Dublin, Ireland). According to the package insert,[49] in a study with 1032 Western blot positive specimens, Uni-Gold detected all positive results when tested using the serum, plasma, and whole blood portions of the sample sets. Thus, the sensitivity was 100%. Two studies on the package insert evaluated specificity in both low- and high-risk groups. In the first study, of 1,000 EIA-negative samples from a low risk population only 2 serum/plasma and 3 whole blood samples tested false positive using Uni-Gold, for specificities of 99.8% for serum or plasma; and 99.7% for whole blood. Similar results were obtained using 968 EIA-negative samples from a high risk population. Uni-Gold showed specificities in a high risk population of 99.7% for serum and 99.8% for plasma or whole blood.

In contrast to other studies, Uni-Gold has been tested as an HIV screening tool. Eller, et al. tested 940 whole blood samples from patients at a Ugandan blood bank.[50] There were 10 EIA HIV positive samples, for a prevalence of 1.06%. Uni-Gold detected all positive results, for a sensitivity of 100%, and yielded 8 false positive results, for a specificity of 99.1% (Table 4).

Uni-Gold™ Recombigen® HIV test (Trinity Biotech plc, Dublin, Ireland) is FDA approved and available for use in the United States. It can be used with whole blood, serum, or plasma. It is CLIA-waived for use with whole blood and considered moderately complex when used with serum or plasma. It is easy to conduct and takes about 10 steps.[49] To perform, a sample of whole blood, serum, or plasma is collected with a pipette and one drop is added on the sample port on the test device. Then four drops of the wash solution from the dropper bottle is added to the sample port. Results appear after 10 minutes. Like the OraQuick, a positive result is two lines (control and test line) and a negative result is one line (control line only).27

In the package insert for Clearview® HIV 1/2 STAT-PAK (Inverness, Princeton, NJ), reports data demonstrating the product's sensitivity and specificity.[51] For a sample of 1,389 specimens (613 known positives and 776 from high risk individuals), 647 were determined to be true HIV-1 positives by Western blot and/or FDA approved NAAT assay (prevalence of 47%). The sensitivity of Clearview was 99.7%. In a sample of 203 true HIV-2 positives only (from serum/plasma specimens), the sensitivity was 100%. To determine specificity, 1,431 specimens from high- and low-risk populations for HIV-1 were confirmed as true negative by Western blot, IFA, or NAAT. The specificity of Clearview was 99.9%.

Clearview HIV 1/2 STAT-PAK is a simple, two-step procedure used for whole blood (finger stick or venipuncture), serum, or plasma. It is FDA approved, CLIA-waived for use with whole blood, and classified as moderately complex for serum and plasma. Results are available in 15 minutes. This assay detects HIV-1 and HIV-2 for a complete picture in one test, and a minimal sample size of 5 μL reduces sample handling and exposure risk; it is less invasive for the patient.[51]

A recent modification of this test is the Clearview Complete HIV 1/ 2 test, a single-use, self contained, closed system for the collection processing and analysis of a whole blood, serum or plasma sample for the detection of HIV-1 and HIV-2 antibodies. According to the package insert, Clearview Complete was tested against the same samples and yielded the same results as those described above for Clearview StatPak.[52] The added advantage of this system is its self-contained nature, which reduces the risk of exposure to healthcare workers.

In summary, the documented sensitivities and specificities of these various rapid HIV tests are exceptional. Of concern, however, is that published sensitivities may be less in clinical screening settings than expected, and antibody tests may miss early HIV infection that would be detected by NAAT, as was evidenced in Steckler's work.[43] It is important for rapid HIV tests to be not only noninvasive (such as with oral specimens) and fast to encourage use and acceptance, but also easy to read for clinicians. In this respect, the Multispot might not be best for a fast-paced clinical setting where there is not much time for interpretation and where physicians need something very simple to read.

The World Health Organization (*WHO*) *and ASSURED criteria*

The ideal screening test for STIs would be 100% sensitive and 100% specific. However, few tests are perfect. The World Health Organization (WHO) launched a STI Diagnostics Initiative (SDI) in 1990.[53] The current priorities of this initiative are to improve the detection of Chlamydia (screening of a high risk population), gonorrhea (supporting syndromic management in high and low disease prevalence settings), and syphilis (specifically the screening of pregnant women). In conjunction, the initiative promoted the development and evaluation of STI diagnostics that meet specific criteria known by the acronym "ASSURED." ASSURED stands for : ***A****ffordable* by those at risk of infection; ***S****ensitive* – few false negatives; ***S****pecific* – few false positives; ***U****ser-friendly* – simple to perform (three to four steps required with minimal training necessary); ***R****apid and Robust* – to enable treatment at first visit (rapid) and does not require refrigerated storage (robust); ***E****quipment-free* – easily collected non-invasive specimens (e.g., saliva, urine); ***D****elivered* – to end users.[54] Based on these guidelines, we developed a scoring system for each criterion, assigning a higher value to indicate a better match. Thus we rated *affordability* (cost to purchase a single test) as 0 (over $25), 1 ($11–24), 2 ($3-$10), or 3 (under $2). Sensitivity and specificity were each scored as 0 (under 65%), 1 (66–85%), 2 (83–94%), or 3(over 95%). *User-friendly* scores related to CLIA designation: 0 (moderate complexity) or 1 (waived). *Rapid and robust* was scored as 0 (over 20 minutes to perform and/or refrigeration required) or 1 (under 20 minutes to perform and requires no refrigeration). *Equipment-free* was scored on invasiveness of testing: 0 (major invasive sample, such as blood draw or pelvic exam), 1 (minor invasive sample, such as finger stick), or 2 (non-invasive sample such as oral swab, vaginal swab, or urine test). *Delivered* was determined by FDA clearance and availability for purchase in the U.S.A, rated as 0 (Not FDA cleared/ available) or 1 (FDA cleared/ available for sale). Criteria scores were summed (range 0–15). In Table 6, we offer our opinion as to how well currently available POC tests would fare if judged by the ASSURED criteria using this scoring system.

Rationale behind POC tests for STIs

The ASSURED criteria also emphasize the benefits of point-of-care testing. Point-of-care testing allows for a quick and non-invasive ways to detect infection. Non-invasive tests are tests that don't require a pelvic exam, such as self obtained vaginal swabs, oral swabs, or urine tests. Some patients find the pelvic exam uncomfortable, and some providers who care for young adults lack the resources and experience to perform a pelvic exam.[55] In fact, when participants were asked about acceptability of self-collecting vaginal swabs to be used for rapid testing (in this case, for Chlamydia), 95.9% felt comfortable collecting self-swabs.[11] In addition, rapid point-of-care STI tests allow the patient to have confidential notification and immediate treatment. This decreases the potential for disease spread and the provider can offer immediate counseling on risk reduction actions such as abstinence and condoms use.

While an ideal POC test has near 100% sensitivity, this level of performance has not yet been achieved for most STIs (the exception is HIV). However, disease spread can be reduced even without perfect sensitivity. This crucial aspect of point-of-care testing was

highlighted by Gift, et al.[56] Their analyses showed that a POC test that was 65% sensitive treated more Chlamydia positive cases than the PCR alone if the return for treatment rate was less than 65%. Further, Gift, et al. discovered that, "a two-test algorithm of the rapid test followed by a PCR test on those initially testing negative identified and treated the greatest number of chlamydial infections and was the most cost-effective at all prevalences above 9%." The most important conclusion that can be drawn from the Gift, et al. study is that in situations where it is difficult to get patients to return for results and treatment, such as with adolescents, an imperfect POC test can help detect and treat a great portion of infections.

Patients like getting same day results and are willing to wait for these results. Over 99% participants in the study by Yin, et al. indicated they were willing to wait up to two hours for rapid Chlamydia test results.[8] Benzaken, et al. also measured patient acceptability for a rapid gonorrhea test, and 98.8% of participants said they would be willing to wait up to an hour for test results.[16] In reality, however, Bandea, et al. found that 6.8% of patients would not wait more than 20 minutes for a POC Chlamydia test.[5]

Point-of-care tests can also be used in series to increase sensitivity of testing. The study by Pattullo, et al. describes a stepwise algorithm to improve detection of trichomoniasis. In this case, the inexpensive first test (wet mount) was 58% sensitive; adding a POC TV test after a negative wet mount increased sensitivity to 86%; and adding culture if the rapid test was negative increased sensitivity to 94%.[31] A similar algorithm could be applied to other STIs.

Barriers to use of POC tests in clinical settings

Barriers to use for POC tests in clinical settings include patient acceptability, clinician knowledge and acceptance, cost, and technology requirements. Patient acceptability of POC tests is just beginning to be explored. Although patients might be comfortable collecting self-swabs, they might not trust the results of the POC test as much as they would a standard testing method such as NAAT testing of samples from a pelvic exam or urine specimen.[57] Clinicians may sometimes fail to adopt new technologies and prefer testing methods they are comfortable with and are considered the "gold standard" (i.e., wet mount for trichomoniasis and NAAT for Chlamydia). There can be a wide variation in the time between product development and adoption of new technology, which depends not only on the costs of the new technology but also on how well information and support is distributed over the network of potential users.[58] Knowledge alone is not enough to ensure diffusion. A good example of the gap between knowledge and practice is the imperfect uptake of annual Chlamydia screening. Despite strong recommendations by scientific groups such as the CDC since 1993, in 2007 less than 50% of eligible women were screened for Chlamydia.[59–61] Therefore, while developers work at "building a better POC test" that meets most of the ASSURED criteria, additional work will be required to ensure that these products are "delivered" to the end uses and don't languish on the shelves.

Potential uses in non-clinical settings

In addition to the clinical context, POC tests have numerous potential uses in non-clinical settings such as schools, specifically outreach programs at schools that have medical supervision available, and homes, where the test can be purchased over-the-counter and performed without medical supervision. In the future, POC tests could be ordered on the Internet and delivered in the mail to maintain complete confidentiality for the user. Internet delivered tests are useful for detecting infections in the community.[62] However, steps must be taken to ensure the quality of tests that are available via the internet. One study showed that an approved internet home Chlamydia test in the U.K. was less that 20% sensitive compared to NAAT.[63]

Future Directions

Several reliable point-of-care tests are now on the market for clinical use for HIV and trichomoniasis. Available tests for Chlamydia have disappointing sensitivity, while tests for gonorrhea show promise in early studies. In the future, new POC tests need to meet ASSURED criteria, including adequate sensitivity and specificity and a simple and rapid format, if the goal is to have clinicians adopt these new tests in busy clinical settings. Patients need to be educated on the benefits of POC tests and encouraged to wait for the results. If POC tests are used in non-clinical settings, measures will have to be in place to assure follow up of results. If POC tests become available over the Internet or over-the-counter, patients, especially adolescents, may require additional incentives that encourage them to seek care after testing themselves. For example, Shew, et al. showed that many adolescents who use a home pregnancy test do not seek medical attention after the test—although presumably they are at continued risk for pregnancy, not to mention STIs.[64] Also, in an Internet study by Gaydos, only one-third of requested kits were returned for testing.[62] If kits had contained a home test, it is unclear if some women would have failed to test themselves or neglected to get follow up care.

“What’s the point?”

There are many critical points about point-of-care STI testing that argue for continued development and implementation of these tools. First, we must guard against the dissemination of inaccurate tests that will decrease clinician and patient acceptance of other new tests. If we are armed with POC tests that meet ASSURRED criteria, we can rapidly offer accurate and efficient tests to patients so that effective and immediate care can be offered. This will reduce the risks of disease sequelae in the individual patient, and transmission to partners can be prevented. Inexpensive and non-invasive tests will increase the likelihood that more people will be tested by a POC test than a traditional test. Thus, even imperfectly sensitive POC tests can be expected to dramatically impact the epidemic of STIs that exists in the U.S.A. today.

References

1. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance, 2007, Chlamydia. Atlanta, GA: U.S. Department of Health and Human Services; 2008. p. 27-36.ed.
2. Miller WC, Ford CA, Morris M, et al. Prevalence of chlamydial and gonococcal infections among young adults in the United States. JAMA 2004 May 12;291(18):2229–2236. [PubMed: 15138245]
3. Weinstock H, Berman S, Cates W Jr. Sexually transmitted diseases among American youth: incidence and prevalence estimates,2000. Perspect Sex Reprod Health 2004 Jan-Feb;36(1):6–10. [PubMed: 14982671]
4. Pate MS, Dixon PB, Hardy K, et al. Evaluation of the Biostar Chlamydia OIA assay with specimens from women attending a sexually transmitted disease clinic. J Clin Microbiol 1998 Aug;36(8): 2183–2186. [PubMed: 9665987]
5. Bandea CI, Koumans EH, Sawyer MK, et al. Evaluation of the rapid BioStar optical immunoassay for detection of Chlamydia trachomatis in adolescent women. J Clin Microbiol 2009 Jan;47(1):215–216. [PubMed: 19005149]
6. Stratton NJ, Hirsch L, Harris F, et al. Evaluation of the rapid CLEARVIEW Chlamydia test for direct detection of chlamydiae from cervical specimens. J Clin Microbiol 1991 Jul;29(7):1551–1553. [PubMed: 1885755]
7. Skulnick M, Small GW, Simor AE, et al. Comparison of the Clearview Chlamydia test, Chlamydiazyme, and cell culture for detection of Chlamydia trachomatis in women with a low prevalence of infection. J Clin Microbiol 1991 Sep;29(9):2086–2088. [PubMed: 1774342]

8. Yin YP, Peeling RW, Chen XS, 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 Dec;82:v33–V37. [PubMed: 17121763]
9. Steingrimsson O, Pawlak C, Van Der Pol B, et al. Multicenter comparative evaluation of two rapid immunoassay methods for the detection of Chlamydia trachomatis antigen in endocervical specimens. Clin Microbiol Infect 1997 Feb;3(6):663–667. [PubMed: 11864210]
10. Rani R, Corbitt G, Killough R, et al. Is there any role for rapid tests for Chlamydia trachomatis? Int J STD AIDS 2002 Jan;13(1):22–24. [PubMed: 11802925]
11. Mahilum-Tapay L, Laitila V, Wawrzyniak JJ, et al. New point of care Chlamydia Rapid Test--bridging the gap between diagnosis and treatment: performance evaluation study. BMJ 2007 Dec 8;335(7631):1190–1194. [PubMed: 18055487]
12. CLIAwaived I. One-step Chlamydia dipstick test (product insert). 2001. http://www.cliawaived.com/web/items/pdf/CHLA1004insert.pdf, 2009
13. MagnaBioSciences L. MagnaBioSciences: A quantim design company. 2000. http://www.magnabiosciences.com/clinicalDiagnostics.html, 2009
14. Centers for Disease Control and Prevention. Sexually transmitted disease surveillance, 2007, Gonorrhea. Atlanta, GA: U.S. Department of Health and Human Services; 2008. p. 37-43.ed.
15. Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2006, Clinical Prevention and Guidance. Atlanta, GA: U. S. Department of Health and Human Services; 2006 Aug 4.
16. Benzaken AS, Galban EG, Antunes W, et al. Diagnosis of gonococcal infection in high risk women using a rapid test. Sex Transm Infect 2006 Dec;82:v26–v28. [PubMed: 17118954]
17. Food and Drug Administration. 510(k) Summary: Chlamydia OIA Assasy. 2003 [Accessed 2009]. http://www.accessdata.fda.gov/cdrh_docs/pdf2/k023947.pdf
18. Theodore, M.; Hook, E.; Mableton, S., et al. Use of Thermo Biostar Optical Immunoassay (OIA) as a point-of-care assay for *Chlamydia trachomatic* and *Neisseria gonorrhoeae* in sexually transmitted disease clinics; Paper presented at: International Society for STD Research 14th Annual Meeting; Berlin: 2001.
19. Inverness Medical I. BioStar OIA GC. Package insert. [Accessed August 31, 2009]. Available at: http://rapiddiagnostictesting.com/PDF%20Files/OIA_GC_Brochure_02476.04.pdf
20. Alary M, Gbenafa-Agossa C, Aina G, et al. Evaluation of a rapid point-of-care test for the detection of gonococcal infection among female sex workers in Benin. Sex Transm Infect 2006 Dec;82:v29–v32. [PubMed: 17215275]
21. Cortez-Diagnostics. OneStep RapiDip Gonorrhea InstaTest (product insert). 2006. http://www.rapidtest.com/Gonorrhea_176512.pdf
22. Miller WC, Zenilman JM. Epidemiology of chlamydial infection, gonorrhea, and trichomoniasis in the United States--2005. Infect Dis Clin North Am 2005 Jun;19(2):281–296. [PubMed: 15963872]
23. Madico G, Quinn TC, Rompalo A, et al. Diagnosis of Trichomonas vaginalis infection by PCR using vaginal swab samples. J Clin Microbiol 1998;36(11):3205–3210. [PubMed: 9774566]
24. Wendel KA, Erbelding EJ, Gaydos CA, et al. Trichomonas vaginalis polymerase chain reaction compared with standard diagnostic and therapeutic protocols for detection and treatment of vaginal trichomoniasis. Clin Infect Dis 2002;35(5):576–580. [PubMed: 12173132]
25. Huppert JS, Mortensen JE, Reed JL, et al. Rapid antigen testing compares favorably with transcription-mediated amplification assay for the detection of Trichomonas vaginalis in young women. Clin Infect Dis 2007 Jul 15;45(2):194–198. [PubMed: 17578778]
26. Van Der Pol B, Kwok C, Pierre-Louis B, et al. Trichomonas vaginalis infection and human immunodeficiency virus acquisition in African women. J Infect Dis 2008 Feb 15;197(4):548–554. [PubMed: 18275275]
27. Gaydos CA. Rapid tests for sexually transmitted diseases. Curr Infect Dis Rep 2006 Mar;8(2):115–124. [PubMed: 16524548]
28. Miller GA, Klausner JD, Coates TJ, et al. Assessment of a rapid antigen detection system for Trichomonas vaginalis infection. Clin Diagn Lab Immunol 2003 Nov;10(6):1157–1158. [PubMed: 14607884]

29. Kurth A, Whittington WL, Golden MR, et al. Performance of a new, rapid assay for detection of *Trichomonas vaginalis*. J Clin Microbiol 2004 Jul;42(7):2940–2943. [PubMed: 15243042]
30. Huppert JS, Batteiger BE, Braslins P, et al. Use of an immunochromatographic assay for rapid detection of Trichomonas vaginalis in vaginal specimens. J Clin Microbiol 2005 Feb;43(2):684–687. [PubMed: 15695664]
31. Pattullo L, Griffeth S, Ding L, et al. Stepwise diagnosis of Trichomonas vaginalis infection in adolescent women. J Clin Microbiol 2009 Jan;47(1):59–63. [PubMed: 18987174]
32. Campbell L, Woods V, Lloyd T, et al. Evaluation of the OSOM Trichomonas rapid test versus wet preparation examination for detection of Trichomonas vaginalis vaginitis in specimens from women with a low prevalence of infection. J Clin Microbiol 2008 Oct;46(10):3467–3469. [PubMed: 18685008]
33. Genzyme Diagnostics. OSOM *Trichomonas* rapid test (product insert): Genzyme Corporation.
34. Briselden AM, Hillier SL. Evaluation of affirm VP Microbial Identification Test for Gardnerella vaginalis and Trichomonas vaginalis. J Clin Microbiol 1994 Jan;32(1):148–152. [PubMed: 8126171]
35. DeMeo LR, Draper DL, McGregor JA, et al. Evaluation of a deoxyribonucleic acid probe for the detection of Trichomonas vaginalis in vaginal secretions. Am J Obstet Gynecol 1996 Apr;174(4):1339–1342. [PubMed: 8623867]
36. Brown HL, Fuller DD, Jasper LT, et al. Clinical evaluation of Affirm VPIII in the detection and identification of Trichomonas vaginalis, Gardnerella vaginalis, and Candida species in vaginitis/vaginosis. Infect Dis Obstet Gynecol 2004;12(1):17–21. [PubMed: 15460191]
37. Lowe NK, Neal JL, Ryan-Wenger NA. Accuracy of the clinical diagnosis of vaginitis compared with a DNA probe laboratory standard. Obstet Gynecol 2009 Jan;113(1):89–95. [PubMed: 19104364]
38. Becton Dickinson. Affirm VPIII Microbial Identification System. 2003
39. Hall HI, Song R, Rhodes P, et al. Estimation of HIV incidence in the United States. JAMA 2008 Aug 6;300(5):520–529. [PubMed: 18677024]
40. OraSure. OraQuick ADVANCE Rapid HIV-1/2 Antibody Test (product insert). 2007 [Accessed August 31 2009]. <http://www.orasure.com/docs/pdfs/products/oraquick_advance/OraQuick-Advance-Package-Insert-English.pdf> 2009
41. Delaney KP, Branson BM, Uniyal A, et al. Performance of an oral fluid rapid HIV-1/2 test: experience from four CDC studies. AIDS 2006 Aug 1;20(12):1655–1660. [PubMed: 16868447]
42. Holguín A, Gutierrez M, Portocarrero N, et al. Performance of OraQuick Advance Rapid HIV-1/2 Antibody Test for detection of antibodies in oral fluid and serum/plasma in HIV-1+ subjects carrying different HIV-1 subtypes and recombinant variants. J Clin Virol 2009 Jun;45(2):150–152. [PubMed: 19451023]
43. Stekler JD, Swenson PD, Coombs RW, et al. HIV testing in a high-incidence population: is antibody testing alone good enough? Clin Infect Dis 2009 Aug 1;49(3):444–453. [PubMed: 19538088]
44. Reveal® G3 Rapid HIV-1 Antibody Test (product insert). 2009. <http://www.medmira.com/images/Reveal%20PDFs/g3_insert.pdf>
45. BioRad. Multispot HIV-1/HIV-2 Rapid Test (product insert). 2009. http://www.bio-rad.com/prd/en/US/adirect/biorad?cmd=BRCatgProductDetail&isFromSearch=true&entryPoint=adirect&catID=18a8dae4-1f7f-4b49-b25e–fadf83b3411&vertical=CDG&messageType=BRCatgProductDetail, 2009
46. Phillips S, Granade TC, Pau CP, et al. Diagnosis of human immunodeficiency virus type 1 infection with different subtypes using rapid tests. Clin Diagn Lab Immunol 2000 Jul;7(4):698–699. [PubMed: 10882675]
47. Holguín A. Evaluation of three rapid tests for detection of antibodies to HIV-1 non-B subtypes. J Virol Methods 2004 Jan;115(1):105–107. [PubMed: 14656467]
48. O'Connell RJ, Agan BK, Anderson SA, et al. Sensitivity of the Multispot HIV-1/HIV-2 rapid test using samples from human immunodeficiency virus type 1-positive individuals with various levels

of exposure to highly active antiretroviral therapy. J Clin Microbiol 2006 May;44(5):1831–1833. [PubMed: 16672414]

49. Trinity-Bioech. Uni-Gold™ Recombigen® HIV (product insert). 2004 [Accessed August 31 2009]. http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/PremarketApprovalsPMAs/ucm093428.pdf 2009
50. Eller LA, Eller MA, Ouma BJ, et al. Large-scale human immunodeficiency virus rapid test evaluation in a low-prevalence Ugandan blood bank population. J Clin Microbiol 2007 Oct; 45(10):3281–3285. [PubMed: 17699650]
51. Inverness_Medical. Clearview HIV 1/2 Stat-Pak (product insert). 2009 [Accessed August 31 2009]. http://www.invernessmedicalpd.com/point_of_care/hiv%e2%81%84stds/clearview%c2%ae_hiv_stat-pak.aspx 2009
52. Inverness_Medical. Clearview Complete HIV 1/2 (product insert). 2009 [Accessed August 31 2009]. http://www.invernessmedicalpd.com/point_of_care/hiv⁄stds/clearview®_complete_hiv.aspx 2009
53. World Health Organization. From Bench to Bedside: Setting a path for the translation of improved sexually transmitted infections diagnostics into health care delivery in the developing world *Sexually transmitted diseases diagnostics initiative 2001*. 2009. www.who.int/std_diagnostics/about_SDI/priorities.htm
54. Peeling RW, Holmes KK, Mabey D, et al. Rapid tests for sexually transmitted infections (STIs): the way forward. Sex Transm Infect 2006 Dec;82:v1–v6. [PubMed: 17151023]
55. Ginsburg K, Slap G. Unique needs of the teen in the health care setting. Curr Opin Pediatr 1996;8(4):333–337. [PubMed: 8954263]
56. Gift TL, Pate MS, Hook EW 3rd, et al. The rapid test paradox: when fewer cases detected lead to more cases treated: a decision analysis of tests for Chlamydia trachomatis. Sex Transm Dis 1999 Apr;26(4):232–240. [PubMed: 10225593]
57. Kahn JA, Bernstein DI, Rosenthal SL, et al. Acceptability of human papillomavirus self testing in female adolescents. Sex Transm Infect 2005 Oct;81(5):408–414. [PubMed: 16199741]
58. Rogers, E. Inovativeness and adopter categories. In: Rogers, E., editor. Diffusion of Innovations. 5th ed. New York, NY: The Free Press; 2003. p. 267-300.
59. Huppert JS, Goodman E, Khoury J, et al. Sexually transmitted infection testing and screening in hospital-based primary care visits by women. Obstet Gynecol 2005 Feb;105(2):390–396. [PubMed: 15684170]
60. Tao G, Tian LH, Peterman TA. Estimating Chlamydia screening rates by using reported sexually transmitted disease tests for sexually active women aged 16 to 25 years in the United States. Sex Transm Dis 2007 Mar;34(3):180–182. [PubMed: 16865052]
61. National Committee for Quality Assurance. Chlamydia screening. The State of Health Care Quality 2008 2008:39–40. National Committee for Quality Assurance.
62. Gaydos CA, Dwyer K, Barnes M, et al. Internet-based screening for Chlamydia trachomatis to reach non-clinic populations with mailed self-administered vaginal swabs. Sex Transm Dis 2006 Jul;33(7):451–457. [PubMed: 16652069]
63. Michel CE, Saison FG, Joshi H, et al. Pitfalls of internet-accessible diagnostic tests: inadequate performance of a CE-marked Chlamydia test for home use. Sex Transm Infect 2009 Jun;85(3): 187–189. [PubMed: 19398434]
64. Shew ML, Hellerstedt WL, Sieving RE, et al. Prevalence of home pregnancy testing among adolescents. Am J Public Health 2000 Jun;90(6):974–976. [PubMed: 10846519]

Table 1

Comparison of published test characteristics for POC Chlamydia tests in women.

Test	Author (year)	Number	Prevalence (% positive)	Reference standard	Sensitivity %	Specificity %
BioStar® OIA® CHLAYMDIA test	Pate, et al. (1998)	306	13.7%	Culture DFA, PCR	73.8	100
	Bandea, et al (2009)	261	Not stated	Two NAAT Assays Culture	59.4 78.6	98.4 97.2
Clearview® Chlamydia	Stratton, et al (1991)	648	6.2%	Culture	95	98
	Skulnick, et al (1991)	965	4.5%	Culture	79	99.6
	Yin, et al. (2006)	1497	13.2%	NAAT (PCR) cervical swabs vaginal swabs	49.7 32.8	97.9 99.2
QuickVue®	Steingrimsson, et al. (1997)	724	11%	Culture or culture plus DFA	92%	99.1
	Rani, et al (2002)	100	16%	NAAT	65	100
		100	4%	NAAT	25	100
Chlamydia Rapid Test (CRT)	Mahilum-Tapay, et al. (2007)	686	8.1%	NAAT	83.5	98.9

Table 2

Comparison of published test characteristics for POC gonorrhea tests in women.

Test	Author	N	Prevalence (% positive)	Reference standard	Sensitivity	Specificity
BioStar® OIA® GC test	Benzaken et al. (2006)	326	15%	Culture	60%	89.9%
PATH GC-Check®	Avary, et al (2006)	1,084	4.6%	NAAT (Roche Amplicor CT/NG PCR)	70 % (cervical swabs) 54.1% (vaginal swabs)	97.2% (cervical swabs) 98.2% (vaginal swabs)
OneStep®	Product literature	1,050	39.3%	Culture	98.3%	97.8%

Table 3

Comparison of POC Trichomonas tests in women. Sensitivity estimates are relative to NAAT gold standard. Published comparisons are referenced.

Test	Author	N	Prevalence (% positive)	Reference standard	Sensitivity	Specificity
XenoStrip Tv™	Miller, et al (2003)	60	(33%)	Culture	90%	92.5%
	Kurth, et al (2004)	936	14.42%	Culture	78.5%	98.6%
OSOM® TV	Huppert, et al(2005)	449	23.4%	Wet mount and culture	83.3%	98.8%
	Huppert, et al. (2007)	330	18.5%	wet mount, culture, and NAAT (TMA)	90%	100%
	Campbell, et al. (2008)	1,009	2%	Wet mount	94.7%	100%
Affirm®VPIII	Briselden and Hiller (1994)	176	7% by wet mount 9% by culture	Wet mount and culture	83%	100%
	DeMeo, et al. (1996)	615	15.4%	Wet mount and culture	90.5%	98%
	Product literature	852	13%	Wet mount	91.8%	98.1%
				Culture	89.2%	99.3%
	Brown, et al (2004)	425	7% by Affirm VPIII 5% by wet mount	Wet mount	Not stated	Not stated
	Lowe, et al. (2009)	535	1.5%	Clinical diagnosis	too small to assess	too small to assess

Table 4

Comparison of POC HIV tests published in peer reviewed medical literature. Sensitivity estimates are relative to the reference standard.

Test	Author	Number of samples	Prevalence (% positive)	Reference standard	Specimen type	Sensitivity	Specificity
OraQuick	Delaney, et al (2006)	12,337	2.7%	Enzyme Immunoassay (EIA) and Western blot	Whole blood	99.7%	99.9%
					Oral	99.1%	99.6%
	Holguín, et al (2009)	156	100%	EIA Western Blot	Serum/plasma	100%	
					Oral	97.8%	
	Stekler, et al (2009)	6,964	2.7%	EIA	Oral or Whole blood	91%	99.96%
				NAAT	Oral or Whole blood	80%	99.96%
Multispot	Phillips, et al (2000)	241	71%	Western blot and EIA	Serum	100%	100%
	Holguín, et al (2004) *f HIV-1 non-B subtypes **for HIV-2	111	73%	Western blot and EIA	Plasma	100%	100%*
						N/A	92.7%**
	O'Connell, et al (2006)	248	100%	Western blot and EIA	Previously frozen serum	100%	Not stated
Uni-Gold	Eller, et al. (2007)	940	1.06%	EIA	Whole blood	100%	99.1%

Table 5

Comparison of POC HIV tests product literature. Sensitivity estimates are relative to EIA/Western Blot gold standard.

Test	Number of specimens*	Specimen Type	Sensitivity % (95% CI)	Specificity % (95% CI)	CLIA Classification
OraQuick ADVANCE Rapid HIV-1/2 Antibody Test	>3,700	Oral fluid	99.3 (98.4−99.7)	99.8 (99.6−99.9)	Waived
	>1,100	Whole Blood	99.6 (98.5−99.9)	100 (99.7−100)	Waived
	>1,400	Plasma	99.0 (98.9−99.8)	99.9 (99.6−99.9)	Moderate
Uni-Gold Recombigen HIV	>1,000	Whole Blood	100 (99.5−100)	99.7 (99.0−100)	Waived
	>1,000	Serum/Plasma	100 (99.5−100)	99.8 (99.3−100)	Moderate
Reveal G-3 Rapid HIV-1 Antibody Test	>3,300	Serum	99.8 (99.2−100)	99.1 (98.8−99.4)	Moderate
	>500	Plasma	99.8 (99.0−100)	98.6 (98.4−98.8)	Moderate
MultiSpot HIV-1/HIV-2 Rapid Test		Serum	100 (99.94−100)	99.93 (99.79−100)	Moderate
		Plasma	100 (99.94−100)	99.9 (99.77−100)	Moderate
Clearview HIV 1/2 STAT-PAK or Clearview COMPLETE* HIV 1/2	>1,300	Whole Blood	99.7 (98.9−100)	99.9 (99.6−100)	Waived
	>1,300	Serum/Plasma	99.7 (98.9−100)	99.9 (99.6−100)	Moderate

* Exact number of specimens varies for sensitivity and specificity estimates; see text for details.

Table 6

Score currently available STI tests on ASSURED criteria.

STI	Test	Affordable	Sensitive	Specific	User-friendly	Rapid and Robust	Equipment-free	Delivered	Total ASSURED Score
HIV	***OraQuick ADVANCE***	0	3	3	1	1	2	1	11
	Uni-Gold Recombigen	1	3	3	1	1	1	1	11
	Reveal	NA	3	3	0	0	1	1	8
	Multispot	NA	3	3	0	0	1	1	8
	Clearview Stat-Pak	0	3	3	1	1	1	1	10
Trichomoniasis	***Wet Mount***	3	0	3	0	1	1	1	9
	OSOM	1	2	3	1	1	2	1	11
	Affirm VPIII	2*	1	3	0	0	0	1	7
Chlamydia	***BioStar***	NA	0	3	0	0	0	1	4
	Clearview	NA	0	3	0	0	0	1	4
	Quikvue	NA	0	3	0	0	0	1	4
	CRT	1	1	3	0	0	2	0	7
Gonorrhea	***BioStar***	NA	0	3	0	0	0	1	4
	PATH	NA	1	3	0	1	1	0	6

*After initial outlay of>$10,000 for machinery.

NA -prices not available on the website

Explanation of Scores. Total score is the sum (range 0–15):

Affordability (cost to purchase a single test): 0 (over $25), 1 ($11–24), 2 ($3-$10), or 3 (under $2).

Sensitivity and **S**pecificity: 0 (under 65%), 1 (66–85%), 2 (83–94%), or 3 (over 95%).

User-friendly: 0 (moderate complexity) or 1 (waived).

Rapid and **R**obust: 0 (over 20 minutes to perform and/or refrigeration required) or 1 (under 20 minutes to perform and requires no refrigeration).

Equipment–free: 0 (major invasive sample, such as blood draw or pelvic exam), 1 (minor invasive sample, such as finger prick), or 2 (non-invasive sample such as oral, vaginal swab or urine test).

Delivered: 0 (Not FDA cleared/ available) or 1 (FDA cleared/ available for sale).