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A Narrative Review of Where We Are With Point-of-Care Sexually Transmitted Infection Testing in the United States

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Background: Point-of-care (POC) tests enable immediate diagnosis and targeted treatment of sexually transmitted infections (STIs), which could accelerate control of ongoing epidemics. Although older nucleic acid amplification tests have improved the accuracy of laboratory-based tests for STIs, newer POC tests can facilitate control efforts. We sought to review the performance and time to result of POC assays for STIs in the last 10 years.

Methods: The authors performed a PubMed, US National Library of Medicine, National Center for Biotechnology Information search for POC tests for STIs or sexually transmitted diseases.

Results: Diagnostic technology for POC assays for STIs has achieved high sensitivity and specificity (>90%) using recent molecular advances in the last 10 years. Three POC tests for chlamydia and gonorrhea and 2 for trichomonas have been cleared by the Food and Drug Administration and can provide rapid results during the clinical encounter. Two POC assays for syphilis are now cleared by the Food and Drug Administration. Other similar POC assays are in development. These "fast followers" have faster time to result and will extend the diagnostic armamentarium at POC.

Conclusions: New technology has improved the performance accuracy of STI POC diagnostics. Innovation in device format has resulted in accurate POC assays, which can decrease the time to result and accelerate the detection and treatment of STIs during the clinical encounter. The full implementation potential of these newer tests will depend on the ability of these tests to achieve Clinical Laboratory Improvement Amendments–waived status so they can be performed by nonlaboratorians with no previous training.

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Surveillance reports of sexually transmitted infections (STIs) in the United States have demonstrated year-on-year increases in reported cases of gonorrhea, chlamydia, and syphilis.[1] Control efforts that depend on a cohesive approach, including diagnosis and treatment of infected individuals, have failed to date. Prevention efforts are often hampered by the lack of successful screening programs for asymptomatic persons and access to testing for some symptomatic individuals. The Institute of Medicine *Hidden Epidemic* stated that the "scope, impact, and consequences of STIs are under-recognized and are of tremendous health and economic consequence in the United States."[2] Point-of-care (POC) tests, which can be performed at the clinical visit, have been hypothesized to have a positive effect on shortening the duration of the infection because patients can be treated before they leave the clinical encounter.

Sensitivity and specificity are important characteristics of the ideal POC test, especially in screening situations. Other important parameters for a POC test include cost, simplicity (automation), and time to result, which should be fast enough to affect time to treatment. Paradoxically, some older modeling studies have demonstrated that less sensitive POC tests can result in more patients being treated.[3] Unfortunately, many of the original, older POC tests were too insensitive and therefore not useful.[4–7] Clinician's and patient's attitudes toward POC tests are barriers to adoption and implementation.[8,9] Lack of Food and Drug Administration (FDA) clearance as being waived by the Clinical Laboratory Improvement Amendments (CLIA) for use by personnel who are not laboratorians is an important impediment to the use of POC tests in doctors' offices and clinics.

The World Health Organization has provided developers and users of POC diagnostics guidelines, known as ASSURED, to aid in the development and use of POC diagnostics for STIs that have true usefulness. ASSURED means that tests are *A*ffordable by those at risk for infection, *S*ensitive, *S*pecific, *U*ser-friendly (very simple to perform), *R*apid and Robust, *E*quipment-free (no complex equipment), and *D*eliverable to end-users.[10] The World Health Organization has continued to support the use of POC tests in the rapid diagnosis of treatable STIs.[4,11–13] It is important to note that new POC tests meet many of these criteria.[7,14,15]

Point-of-care test results available during the clinical encounter would allow clinicians to treat infected patients immediately and expedite appropriate precision therapy.[5,7,8] Accurate therapy can reduce empiric treatment and increase antibiotic stewardship, improve compliance/minimize loss to follow-up, decrease onward transmission, and lower the risk of sequelae.[15,16] Use of POC tests can also improve the patient experience by providing counseling opportunities.[5,15,16] Turnaround time shorter than the patient encounter is very important; once patients leave, they may be less likely to return for treatment.[17,18] The objective of this article is to review the landscape of currently available and FDA-cleared/approved POC tests for STIs in the United States (not including HIV single test assays), with additional information about acceptability and POC tests under development.

METHODS

The authors performed a PubMed, US National Library of Medicine, National Center for Biotechnology Information search for POC tests or rapid tests for STIs or sexually transmitted diseases (STDs), including chlamydia, gonorrhea, trichomonas, and syphilis, focusing on articles published in English in the previous 10 years. Main inclusion criteria for this narrative review included the following: being FDA cleared for use in the United States or having been submitted for clearance. Exclusion criteria included being a nonmolecular test for chlamydia, gonorrhea, and trichomonas or not FDA cleared for syphilis. There was one exception for a nonmolecular trichomonas POC test because the assay is CLIA waived. Two of the authors of this review reviewed the content of these articles. Articles that reported on the performance of POC tests with a criterion standard nucleic acid amplification tests (NAATs) comparator or that used FDA-cleared POC assays in clinical assessments were included.

RESULTS

The search returned 119 articles, of which 50 were included. Additional articles reporting other aspects of acceptability, assessments, and cost-effectiveness modeling studies for POC tests were also included.

Older available STI POC tests suffer from very poor sensitivity of about 50% to 70% or less.[5,6] Some of these published assays have been removed from the market and are of such low sensitivity that they would not meet the testing criteria in today's environment.[14] Some of these include the OIA (Inverness [formerly BioStar]), the Program for Appropriate Technology in Health (PATH) GC-Check (Seattle, WA), and OneStep (Cortez Diagnostics, Inc, Calabasas, CA).[5,6]

Currently Available POC Test Platforms for Chlamydia and Gonorrhea

GeneXpert *Chlamydia trachomatis*/*Neisseria gonorrhoeae* Platform (Xpert CT/NG)

Newer POC assays have moved to molecular NAAT assays, which are the recommended platforms for STIs by the Centers for Disease Control and Prevention[19] and have achieved commercial status and FDA clearance for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG). The first assay to use NAAT technology and achieve FDA clearance for CT/NG is the Xpert assay (Cepheid, Sunnyvale, CA).[20] This cartridge-based assay combines microfluidic technology with real-time polymerase chain reaction (PCR), extracts and amplifies the DNA, and detects the PCR amplicon in 90 minutes, but is not CLIA waived. Sensitivities and specificities for this assay range from 95.6% to 100% and 99.9% to 100%, respectively, for both female (vaginal, cervical, and urine) and male (urine) specimens[20,21] (Table 1). Lack of false-positive results with other commensal *Neisseria* species or other genital near neighbors, such as *Lactobacillus* species, *Mycoplasma* species, or *Ureaplasma* species is another important characteristic of this assay.[22,23] Although the assay requires 90 minutes, it was used successfully in an emergency department clinical trial with 254 patients, where it demonstrated that 100% of patients who had positive POC results for CT or NG were treated versus 56% in the routine NAAT test group; for uninfected patients, ~25% were unnecessarily treated in the POC test group versus 47% in the routine test group.[24] The Xpert CT/NG assay works well with rectal and oropharyngeal specimens[25,26] and has been cleared by the FDA.[27] The Xpert assay for chlamydia and gonorrhea has also been evaluated, but not FDA cleared, for pooling of ocular, vaginal, rectal, and urine specimens of samples from several patients as a cost-saving measure, but would require an additional validation by laboratories. Because most samples are usually negative and positive pools can be "deconstructed" to determine which sample(s) in the pool is positive, cost savings can potentially be achieved.[28,29]

The *io* Platform

The binx health, Limited (Trowbridge, United Kingdom, and Boston, MA) *io* platform (formerly Atlas Genetics) is the latest assay (August 2019) to receive FDA clearance. It is a molecular POC test for CT and NG.[30,31s] A pilot study for detection of CT using the assay found high sensitivity and specificity and high patient acceptability, and indicated that 70% of women preferred to self-collect vaginal swabs if a POC test was available.[32s] This POC assay is the first amplification assay to provide a sample to result in 30 minutes (including DNA extraction); this turnaround time would allow clinicians to treat infected patients before they leave most clinical encounters. The test is FDA cleared for vaginal swabs and urine samples for men, and is CLIA waived.[31s] In a multicenter clinical study with 1523 participants, 96% of patients'

TABLE 1. Performance of the GeneXpert *Chlamydia trachomatis* CT/*Neisseria gonorrhoeae* (NG) Assay

Population	Sample Type Prevalence	No. Samples	Sensitivity, n/N (95% CI)	Specificity, n/N (95% CI)	Reference
Women: OB/GYN, STD, teen, public health, FP clinics					
Chlamydia	Vaginal swab 4.6%	1713	98.7%, 78/79 (93.1%–100%)	99.4%, 1624/1634 (98.9%–99.7%)	20,21
	Endocervical swab 4.6%	1710	98.4%, 76/78 (91.0%–99.7%)	99.6%, 1625–1632 (99.1%–99.8%)	20,21
	Urine 4.8%	1718	97.6%, 80/82 (91.5%–99.7%)	99.8%, 1633/1636 (99.5%–100%)	20,21
Gonorrhea	Vaginal swab 1.3%	1713	100%, 22/22 (87.3%–100%)	99.9%, 1689/1691 (99.6%–100%)	20,21
	Endocervical swab 1.3%	1710	100%, 22/22 (87.3 –100%)	100%, 1688/1688 (99.8 –100%)	20,21
	Urine 1.3%	1718	95.6%, 22/23 (78.1 –99.9%)	99.9%, 1694/1695 (09.7 –100%)	20,21
Men: STD, teen, public health clinics					
Chlamydia	Urine 5.8%	1386	97.5%, 79/81 (91.4%–99.7%)	99.9%, 1303/1305 (99.5%–100%)	20,21
Gonorrhea	Urine 3.6%	1386	98.0%, 49/50 (89.4%–99.9%)	99.9%, 1335/1336 (99.6%–100%)	20,21

FP indicates family planning; n, number positive; N, number tested; OB/GYN, obstetrics/gynecology; STD, sexually transmitted diseases.

samples were processed on the binx *io* platform by nonlaboratorians in a POC setting. Clinical study performance for women demonstrated a 96.1% sensitivity and 99.1% specificity for CT and 100% sensitivity and 99.9% specificity for NG.[31s] For male urine, sensitivity and specificity for CT were 92.5% and 99.3%, respectively, and for NG, the sensitivity and specificity were 97.3% and 100%, respectively.[30] (Table 2).

Currently Available POC Test Platforms for Trichomonas

The GeneXpert TV Assay

The GeneXpert TV (Xpert TV) assay is also FDA cleared, but not CLIA waived, for the diagnosis of *Trichomonas vaginalis* (TV) in women and men.[33s] There were 1867 women and 4791 men who were included in the analysis. In women, the results of the Xpert TV assay were compared with patient infected status (PIS). This PIS comparator was obtained from the results of InPouch TV broth culture and the NAAT (APTIMA) for TV. The diagnostic sensitivities and specificities of the XpertTV assay for the combined female specimens (urine samples, self-collected vaginal swabs, and endocervical swabs) ranged from 99.5% to 100% and 99.4% to 99.9%, respectively. For urine samples from men, the diagnostic sensitivity and specificity were 97.2% and 99.9%, respectively, compared with PIS results of broth culture for TV and bidirectional gene sequencing of amplicons. Results for positive specimens were available in as little as 40 minutes (Table 3).

OSOM Rapid POC TV Antigen Test

The OSOM test for trichomonas is a rapid lateral flow test that has been FDA cleared and CLIA-waived for more than 10 years. It is based on the immunochromatographic detection of *Trichomonas* membrane proteins using mouse antibodies and latex beads.[34s] It has been extensively evaluated and compares very well with newer molecular amplification assays for TV.[35s,36s] Reported sensitivities range from 83% to 90%, and specificities were 100%.[35s,36s] It is simple to perform and can be accurately interpreted by untrained users. Furthermore, it has been reported to be acceptable to adolescents[37s,38s] and can easily be performed at home and in the emergency department.[39s,40s]

Solana Trichomonas Assay

The Solana Trichomonas Assay (Quidel, San Diego, CA) is an in vitro qualitative NAAT for the detection of TV to aid in the diagnosis of trichomoniasis using the helicase-dependent amplification technology and the Solana instrument.[34s,41s] There was an earlier version of this same technology (AmpliVue; Quidel) based on a lateral flow readout using a strip-based colorimetric detection in a self-contained disposable device[42s], which evolved to better sensitivity in the Solana assay.[41s] To detect TV directly from trichomoniasis-suspected specimens, the assay targets a conserved repeat sequence of the TV genome.[41s] The assay consists of 2 major steps: (1) specimen preparation and (2) amplification and detection of target sequence specific to TV DNA using isothermal helicase-dependent amplification in the presence of target-specific fluorescence probe.[41s] Vaginal swabs and urines were obtained from 501 asymptomatic and 543 symptomatic women. The prevalence of TV was 11.5%. For swabs, Solana demonstrated high sensitivity and specificity from asymptomatic (100%/98.9%) and symptomatic (98.6%/98.5%) women, as well as for urines from asymptomatic (98.0%/98.4%) and symptomatic (92.9%/97.9%) women, compared with trichomonal wet prep and culture reference method required by the FDA (Table 3). Compared with Aptima-TV, the sensitivity/specificity values were 89.7%/99.0% for swabs and 100%/98.9% for urines.[41s] The assay requires <40 minutes but is not CLIA waived.

Currently Available POC Test Platforms for Syphilis

Syphilis Health Check POC Assay

This FDA-cleared and CLIA-waived syphilis test is a lateral-flow assay that is rapid and easy to perform.[43s] The method uses a combination of antihuman immunoglobulin gold conjugate and highly purified TP recombinant proteins to specifically detect anti-TP antibodies. The test mainly detects IgG and IgM. After FDA approval, studies found lower performance parameters.[43s,44s] The fingerstick whole blood had a sensitivity of 100% (7/7) and specificity of 95.7% (531/555) compared with consensus reference testing (rapid plasma reagin and EIA reactive), but a sensitivity of only 50% (8/16) and specificity of 95.9% (523/546) when compared with the treponemal EIA.[43s] In another analysis of the Syphilis Health Check (SHC; Diagnostics Direct, LLC, Stone Harbor, NJ) by Matthias et al., the authors reported a sensitivity of 71.4% but a lower specificity of 91.5% for the SHC performed on fingerstick whole blood compared with treponemal EIA performed on serum.[44s] Because the SHC had poor (50%) sensitivity in both fingerstick whole blood and serum compared with a treponemal EIA (Trep-Sure), which is used as an initial test in the reverse sequence algorithm, Fakile et al. concluded that positive SHC results should be confirmed with laboratory-based testing and recommended

TABLE 2. Performance of the Binx Health *io Chlamydia trachomatis* (CT)/*Neisseria gonorrhoeae* (NG) Assay

Assay	Population	Sample Type Prevalence	No. Samples	Sensitivity, n/N (95% CI)	Specificity, n/N (95% CI)	Reference
CT only	Women: adolescent health clinic	Vaginal swab 9.9%	284	92.9%, 26/28 (83.3%–100%)	98.8%, 253/256 (97.5%–100%)	[30s]
CT/NG chlamydia	Women: STI, OB/GYN, and family planning clinics	Vaginal swab 8.5%	1523	96.1%, 124/129 (91.2%–98.3%)	99.1%, 1381/1394 (98.4%–99.5%)	[30]
CT/NG gonorrhea	Women: STI, OB/GYN, and family planning clinics	Vaginal swab 3.0%	1523	100%, 45/45 (92.1%–100%)	99.9%, 1476/1478 (99.5%–100%)	[30]
CT/NG chlamydia	Men: STI clinics	Urine 13.0%	922	92.5%, 111/120 (86.4%–96.0%)	99.3%, 796/802 (98.4%–99.7%)	[30]
CT/NG gonorrhea	Men: STI clinics	Urine 8.0%	922	97.3%, 72/74 (90.7%–99.3%)	100%, 848/848 (99.5%–100%)	[30]

n indicates number positive; N, number tested; OB/GYN, obstetrics/gynecology; STI, sexually transmitted infections.

TABLE 3. Performance of the GeneXpert *Trichomonas vaginalis* (TV) Assay and Solana TV Assay

Assay	Population	Sample Type Prevalence	No. Samples	Sensitivity, n/N (95% CI)	Specificity, n/N (95% CI)	Reference
GeneXpert TV	Women: academic medical centers, STD, FP, public health, clinical trial clinics	Vaginal swab 10.8%	1791	98.4%, 186/193 (92.7%–98.5%)	98.9%, 1604/1622 (98.3%–99.3%)	33s
		Endocervical swab 9.8%	1799	98.9%, 175/177 (96.0%–99.9%)	99.6%, 1625/1632 (99.1%–99.8%)	33s
		Urine 10.2%	1793	98.4%, 180/183 (95.3%–99.7%)	99.7%, 1605/1610 (99.3%–99.9%)	33s
	Men: academic medical centers, STD, FP, public health, clinical trial clinics	Urine 2.7%	4611	89.6%, 112/125* (83.0%–93.8%)	99.3%, 4455/4486† (99.0%–99.5%)	33s

Assay	Population	Sample Type Prevalence	No. Samples	Sensitivity (95% CI)	Specificity (95% CI)	Reference
Solana	Women	Vaginal swab 11.5%	1044	Compared with wet mount/culture: 99.2% (95.4%–99.9%) Compared with NAAT: 89.7% (83.5%–93.9%)	Compared with wet mount/culture: 98.6% (97.6%–99.2%) Compared with NAAT: 99.0% (98.1%–99.5%)	41s
	Women	Urine 11.5%	1044	100% (96.9%–100%)	98.9% 98.0%–99.4%	41s

*Results from secondary sequencing: 9 of 13 false-negatives were *T. vaginalis* negative and 4 of 13 were *T. vaginalis* positive.
†Results from secondary sequencing: 27 of 31 false-positives were *T. vaginalis* positive and 4 of 31 were *T. vaginalis* negative.
FP, family planning; n, number positive; N, number tested; NAAT, nucleic acid amplification tests; STD, sexually transmitted diseases.

adequate training of persons performing SHC testing and ongoing quality assurance.[43s]

Dual Path Platform POC Test for HIV and Syphilis Serology

The Dual Path Platform (DPP) HIV Syphilis Assay (Chembio Diagnostics Systems, Medford, NY) (Fig. 1) is an in vitro single-use, visual and qualitative immunochromagraphic, DPP lateral flow immunoassay for the simultaneous detection of *Treponema pallidum* and HIV antibodies in fingerstick whole blood, venous whole blood, and plasma.[45s] The assay was FDA cleared on October 2, 2020, and has room temperature storage (2°C–25°C, or 36°F to 77°F) with a 24-month shelf life.[46s,47s] Leon et al. assessed early laboratory performance of the DPP assay in 450 previously characterized serum specimens comparing the results obtained by visual interpretation with those with a small, battery-powered, electronic reader.[48s] In this study, sensitivity and specificity using visual interpretation or the electronic reader for HIV antibody detection were reported as 100% and 98.7%, respectively.[48s] For visual *T. pallidum* antibody detection, the test sensitivity was 94.7% and the specificity was 100.0%; with the electronic reader, the sensitivity was 94.7% and the specificity was 99.7%.[48s] Data from the FDA trial from 2762 individuals from 10 geographically distinct study sites within the United States demonstrated >99% sensitivity and specificity for HIV and positive percent agreement for *T. pallidum* of 94.7% for capillary fingerstick blood, 96.5% for serum, and 96.8% for plasma with negative percent agreement ranging from 93.8% to 95.3% (Table 4).[46s]

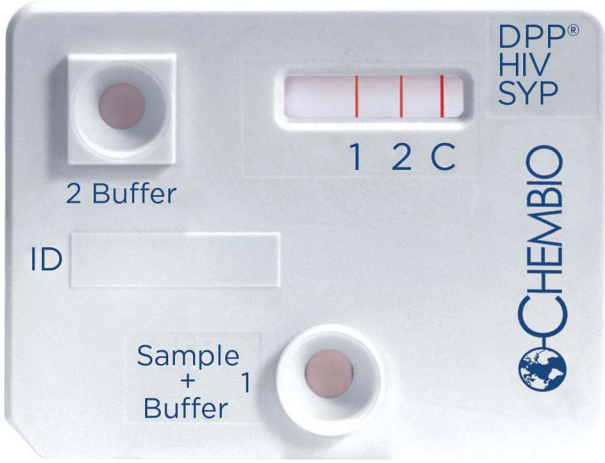

Figure 1. Chembio Dual Path Platform (DPP) assay for detection of syphilis and HIV.

STI POC Tests in Clinical Trials and Under Development

Visby Medical Sexual Health Test Assay (Formerly Click)

The Visby Medical Sexual Health Test assay (formerly Click) is an innovative single-use, rapid NAAT for the detection of NG, CT, and TV infections that can be performed at the POC, without complex instrumentation (Fig. 2), and gives results in less than 30 minutes.[49s] The data from the trial, which has been submitted to the FDA for approval, recruited women 14 years or older at 10 clinical sites for a cross-sectional, single-visit study to provide self-collected vaginal swab for testing with the investigational device compared with the PIS. This PIS comparator was derived from clinician-collected vaginal specimens based on concordance of Aptima Combo2 CT/NG and TV with the BD ProbetecTM NG/CT and TV assays. Discordant samples were adjudicated with the BD MAX CT/GC/TV as a tiebreaker. The primary outcome was sensitivity and specificity for the detection of NG, CT, and TV with 95% confidence intervals (95% CIs). Subgroup analyses included outcomes by symptomatic status.[49s] The study reported

TABLE 4. Chembio Trial Data Results for HIV and Syphilis Treponemal Performance

HIV Performance		
Matrix	**Sensitivity % (Ratio; 95% CI)**	**Sensitivity % (Ratio; 95% CI)**
Capillary (fingerstrick) whole blood	99.4% (635/639; 98.4%–99.8%)	99.6% (1352/1357; 99.1%–99.8%)
Venous whole blood	99.5% (635/638; 98.6%–99.8%)	99.5% (1352/1359; 98.9%–99.8%)
Plasma	99.3% (405/408; 97.9%–99.7%)	99.6% (902/906; 98.9%–99.8%)
Treponemal Test Line Performance		
Matrix	**Sensitivity Percent Agreement (Ratio; 95% CI)**	**Sensitivity Percent Agreement (Ratio; 95% CI)**
Capillary (fingerstrick) whole blood	94.7% (108/114; 89.0%–97.6%)	95.5% (1116/1169; 94.2%–96.6%)
Venous whole blood	96.5% (110/114; 91.3%–98.6%)	94.3% (1100/1116; 92.9%–95.5%)
Plasma	96.8% (60/62; 89.0%–99.1%)	93.9% (1034/1101; 92.3%–95.2%)

results for 1457 CT, 1468 NG, and 1449 TV specimens.[49s] The observed sensitivities were as follows: CT, 97.6% (95% CI, 93.2%–99.2%); NG, 97.4% (95% CI, 86.5%–99.5%); and TV, 99.2% (95% CI, 95.5%–99.9%). Observed specificities were as follows: CT, 98.3% (95% CI, 97.5%–98.9%); NG, 99.4% (95% CI, 98.9%–99.7%); and TV, 96.9% (95% CI, 95.8%–97.7%; Table 5).

MobiNAAT Platform

This PCR assay is a stand-alone, rapid, portable, sample-to-answer platform. The test is carried out in an inexpensive, disposable cartridge, which contains all of the necessary reagents for nucleic acid extraction and amplification.[50s,51s] In the small cartridge, a droplet magnetofluidics process transports the nucleic acid–carrying particles through a multistep process terminating with nucleic acid amplification and detection. The MobiNAAT platform has been previously evaluated for detection of CT[50s,51s] and quantification of hepatitis C viral load[52s] and showed excellent concordance with criterion standard tests. A 15-minute multiplex assay for the detection of NG and determination of ciprofloxacin susceptibility has been recently developed and is currently undergoing clinical validation. A pilot study conducted at 2 public STD clinics in Baltimore, MD, using prospectively collected penile-meatal swabs found 100% concordance between the MobiNAAT results and the criterion-standard NAAT results.[53s]

Novel Microdevices LLC (Baltimore, MD)

Another prototype assay in clinical evaluation is the Novel Dx platform.[54s] The Novel Dx technology used a rapid, portable, and microfluidic molecular diagnostic automation instrument, and a self-contained single-use, test-specific cartridge. The Novel Dx assay for CT and NG takes 30 minutes to complete and is designed for use at the POC. Analytical sensitivity of the real-time LAMP CT/NG assay was 5 cells/test for CT and 25 cells/test for NG. Preliminary analysis of vaginal swabs and urine samples demonstrated promising results.

Twist Diagnostics (Cambridge, United Kingdom)

A prototype recombinase polymerase amplification assay has been evaluated as a POC test for gonorrhea and chlamydia in a prospective, multicenter study of symptomatic and asymptomatic patients for vaginal swabs and urine samples at 3 sexual health clinics.[55s] For male urine, gonorrhea prevalence was 3.1% (12/392); the sensitivity and specificity were 100%. However, for females, only 3 samples were positive from urine and vaginal swabs. Although the detection part of the assay can be completed in 15 minutes, a processing step of desalting using a chromatography device was required for urines, thus increasing the time of the whole assay beyond a true POC test.[55s]

DISCUSSION

In the past decade, diagnostic technology for STIs has rapidly expanded with excellent performance and many fast followers. This review addresses recent advances of some new POCs that are FDA cleared, as well as some preliminary performance data on a few assays in advanced development, but not FDA cleared. Some of these newer assays using amplification technology platforms show increased sensitivity and specificity and offer the possibility of providing results to patients within the time frame of the clinical encounter. To achieve their fullest potential, STI POC diagnostics will need to achieve FDA CLIA waiver status, so they can be performed outside of the laboratory setting by professional health care workers who are not laboratorians.[56s]

Modeling studies can provide information about the impact of POC test use on controlling future STI prevalence. One modeling study demonstrated that a POC test with a sensitivity of 95% could hypothetically reduce the prevalence of gonorrhea from 7.1% to 5.7% under baseline screening coverage of 44% per year.[57s] If

Figure 2. Visby POC PCR assay demonstrating a positive result for gonorrhea.

TABLE 5. Test Performance of Visby Medical Sexual Health Test by Organism in an Evaluation of a Rapid Point-of-Care Molecular Test for the Detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* From Self-Collected Vaginal Swabs

			Patient Infected Status Designation					
			Positive	Negative	Total	Sensitivity	Specificity	Overall Accuracy
	Organism	Click Device Result	n	n	n	(95% CI*)	(95% CI*)	(95% CI*)
Symptomatic and asymptomatic combined	CT (n = 1457)	Positive	122	22	144	97.6 (93.2–99.2)	98.3 (97.5–98.9)	98.3 (97.5–98.8)
		Negative	3	1310	1313			
		Total	125	1332	1457			
	NG (n = 1468)	Positive	37	8	45	97.4 (86.5–99.5)	99.4 (98.8–99.7)	99.2 (95.5–99.9)
		Negative	1	1422	1423			
		Total	38	1430	1468			
	TV (n = 1449)	Positive	121	41	162	99.4 (98.9–99.7)	96.9 (95.8–97.7)	97.1 (96.1–97.8)
		Negative	1	1286	1287			
		Total	122	1327	1449			

*As determined by patient-infected status designation. The denominator for estimates is based on subjects in the evaluable population for the specified organism (n).

95% CI indicates 95% Wilson confidence interval.

Table adapted from Ref. 49s.

screening coverage were increased to 60% per year, prevalence could be reduced to 3.6%.[57s] Similarly, another modeling study for chlamydia predicted that POC tests could improve chlamydia prevention efforts if test performance characteristics could be greatly improved.[58s] A POC test with 99% sensitivity could prevent up to 12,700 cases of pelvic inflammatory disease cases per year, if 100% were treated immediately with a baseline lost to follow up of 20% and 3-week treatment delay.[58s]

Another parameter of importance in introducing POC tests is their ability to be cost-saving or cost-effective. One study in United Kingdom estimated resource use for POC versus standard testing and treatment of CT and NG in genitourinary medicine clinics.[59s] The cost for sexual health screening per patient was predicted to be able to reduce cost by £16 for symptomatic patients and by £6 for standalone CT/NG screening.[59s] Turner et al. concluded that use of a POC test for CT/NG was more effective and less expensive, demonstrating that replacing standard laboratory tests for CT/NG with a POC test would be cost-saving.[60s] The authors also estimated that using POC tests could prevent 95,000 inappropriate treatments, 189 cases of pelvic inflammatory disease, and 17,561 forward transmissions, annually.[60s]

The importance of the acceptability for actual use of POC tests by clinicians and patients cannot be overstated.[16–18] Perceptions of an ideal POC test for STIs and what qualities are most important to making a POC test desirable for clinicians have been studied.[8,61s,62s] One survey using forced choice modeling for "build your own POC test" indicated clinicians preferred the new POCT to have a sensitivity of 90% to 99%, a cost of $20, a specificity of 99%, and a turnaround time of 5 minutes.[61s]

There are many challenges and barriers to the implementation of POC tests for detection of STIs in clinical encounters. There are logistical issues required to change clinic workflow and reimbursement for ordering routine laboratory tests versus performing POC tests in the clinic. Funds for an instrument and consumables must also be budgeted. If the assay is CLIA waived, the clinical practice must obtain a CLIA license to provide the test. Training of operators and maintenance of proficiency of staff must also be performed.[15] The development of quality control protocols and incorporation into the active clinical work flow must be considered. Quality control measures for the performance of POC tests will need to be carefully monitored to ensure that recommendations regarding positive and negative controls are met. Quality control for physician's office or clinic testing is especially important to ensure fastidious technique to avoid amplicon contamination.[15] Additional challenges include development of methods to link POC test results to electronic medical records and reporting notifiable diseases to public health agencies directly from POC tests performed in venues like doctors' offices, pharmacies,[63s] and emergency departments.[24] To maintain surveillance systems, reporting via "cloud-linked" systems will need to be developed, especially for venues like urgent care centers.[64s]

The time it takes to perform the POC tests in a clinic relative to automated laboratory methods is an important consideration. Although performing a POC test in a clinic may take a longer assay time for a person than the time for adding another test in a laboratory to an automated robotic system, the most significant time outcome may be the minutes or hours in time to correct treatment of results. A detailed time-in-motion study of 6 clinical staff for 4 weeks for a POC test for trichomonas reported that time of the POC test was a median of 2 minutes, 13 seconds compared with a laboratory time median of 1 minute, 4 seconds.[65s] The order to result time of the POC was 24 minutes (range, 2–57 minutes; time to correct treatment, 12 minutes, 9 seconds), whereas the comparison NAAT laboratory test result to treatment was 45 hours, 22 minutes (range, 1 hour, 47 minutes to 70 hours, 1 minute).[65s] Thus, the small increase in hands on time for the POC test allowed the patient to receive treatment in approximately 12 minutes compared with about 3 days for patients who received telephone calls and prescriptions.

Given the emerging specter of antimicrobial resistance, POC tests that can accurately diagnose antibiotic susceptibility will be important additions to the diagnostic armamentarium, particularly with gonorrhea and *Mycoplasma genitalium*. These are beyond this scoping review but are currently under development.[15,66s–68s] Lastly, POC tests for low-resource settings need to be developed and implemented to decrease the burden of STIs in these settings. Frugal innovation that curbs cost while maintaining the performance of molecular tests will be needed for adoption, but lower cost of goods should be an important development aspiration to increase adoption in all settings.[69s]

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