Point-of-Care Testing for Sexually Transmitted Infections

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KEYWORDS

• Sexually transmitted infections • Point-of-care • Diagnostic testing • ASSURED

KEY POINTS

- STI POC tests are available for almost all STIs.
- ASSURED/REASSURED criteria created by the WHO is directing advancements in STI POC testing.
- In high-resource areas, NAAT assays are the preferred POC diagnostic method for most STIs, excluding syphilis, and hepatitis B virus, and hepatitis C virus.
- Limitations to adequate POC testing include cost, ease-of-use, portability, turnaround time, sensitivity, and specificity of assays currently available.
- Future developments in STI diagnostics should focus on the development of POC assays for drug resistance; measuring viral loads; and detecting emerging STIs, such as BV and M genitalium.

INTRODUCTION

Leading public health organizations including the Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) recognize the importance of sexually transmitted infections (STIs) on the global public health burden and individual sexual and reproductive health.[1–5] STIs are associated with significant morbidity and mortality, with many capable of vertical transmission posing health risks to the fetus.[4] STIs have the highest prevalence in vulnerable populations (men who have sex with men, adolescents, and pregnant women), low-resource, and low-income settings.[6] Concerns for patient autonomy, discomfort, stigma, or loss of privacy often discourage these high-risk and marginalized populations from seeking care for STIs, often leading to a loss of follow-up when infections are identified.[7,8] Many factors

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contribute to the persistent infection control and surveillance problems associated with STIs, with the most commonly identified problems being a delay in diagnosis and treatment, and loss to follow-up in which the patient continues to serve as a reservoir.[7,9]

The clinical management of STIs has historically relied on syndromic testing. Many people with active STIs are asymptomatic yet are able to transmit infection. This results in the patient never seeking care or notifying their physician of any problems or histories that would lead to STI testing.[1,9] For most STIs, the likelihood of a correct diagnosis using syndromic management is low. Additionally, syndromic management approaches cannot be effectively used when performing surveillance in a large population. Effective STI prevention and control is dependent on rapid, reliable testing.

In recent years, there has been an increase in recognition of the importance of point-of-care (POC) testing for STIs. According to the CDC, POC testing is defined as rapid testing that is performed close to or near the patient bedside.[10] POC tests have the potential to improve prevention and control of STIs through rapid, same-day diagnosis and initiation of effective therapy, effectually decreasing the need for patient follow-up and reducing the likelihood of transmission and sequelae associated with STIs.[5,11] More than 20 years ago, the WHO developed and published the ASSURED (Affordable, Sensitive, Specific, User-friendly, Rapid and Robust, Equipment-free, and Deliverable) criteria as a way to guide development, standardize testing, and determine whether a POC test addresses the needs for STI diagnosis in low-resource areas.[1,3,4,8] This criterion was designed to combat the universal idea that as the accuracy of a diagnostic test increases, access and affordability of the test decrease. Recently, a renaming of the ASSURED criteria to REASSURED has been proposed with the inclusion of two additional criteria: real-time connectivity and ease of specimen collection.[12]

Since the development of the ASSURED criteria, there have been innovative advances in bacterial, viral, and protozoan STI POC testing and improvements in molecular diagnostic assays making them more accessible to low-resource areas.[5] Despite the plethora of nucleic acid amplification tests (NAAT) that are currently available in high-income, high-resource areas, these tests are often unavailable in low-resource settings including low- and middle-income countries because of cost, funding, personnel, and facility limitations ultimately preventing these populations from benefiting from these assays.[9] This article details examples of currently available POC STI tests, acknowledges tests in currently in development, and identifies areas for improvement and expansion.

TRICHOMONAS VAGINALIS

Trichomonas vaginalis (TV) is the only STI caused by a protozoan. TV is the most common nonviral STI in the United States and can infect men and women. Despite this, TV infections are underdiagnosed because of the high prevalence of asymptomatic infections and the lack of screening guidance. TV infections have been associated with negative outcomes during pregnancy including premature birth and neonatal pneumonia, and have a strong correlation with acquisition and transmission of other STIs.[13–15] Currently, in the United States, the CDC has categorized TV as a neglected parasitic infection.

The historical gold standard for TV diagnostics is direct visualization of trichomonads from a genital swab or urine by microscopy, performed in the laboratory setting or at the bedside. Multiple reports show that this method has poor sensitivity (50%), and requires specialized training.[16–18] Currently, there are five diagnostic tests that are marketed for POC testing: Affirm VPIII (BD Diagnostic Systems, Sparks, MD),

GeneXpert TV (Cepheid, Sunnydale, CA), the Solana HAD Trichomonas (TV) Assay (Quidel Corporation, San Diego, CA), OSOM Trichomonas test (Sekisui Diagnostics, Burlington, MA), and the Kalon TV latex test (Kalon Biological, Surrey, UK). Of these tests currently marketed for POC TV diagnosis, the Affirm VPIII test, Solana HDA Trichomonas Assay, GeneXpert TV Assay, and OSOM Trichomonas test are Food and Drug Administration (FDA)-approved and Clinical Laboratory Improvement Amendments act (CLIA)-waived. Each of these rapid POC tests out-perform microscopy from physician-collected and self-collected samples.[9,18–21]

The Affirm VPIII microbial identification test detects and differentiates between TV, *Candida* sp, and *Gardnerella vaginalis* using nucleic acid capture and complementary DNA probes.[22] Although the ability to test for multiple organisms in a sample provides a clear clinical advantage, multiple studies show that despite the excellent specificity (99%) the VPIII test has varying sensitivities for each target (46%–92%).[21,23,24] Additionally, the Affirm VPIII test is not FDA cleared for use with specimens from men.[24]

The most sensitive assays to detect TV infections are NAAT-based. The GeneXpert TV assay is approved for vaginal, endocervical, and urine samples. The assay provides results within 45 minutes with high sensitivity (97%–99%) and specificity (>99%).[25] Although the assay speed, sensitivity, and specificity meet the ASSURED criteria, the implementation and costs of the GeneXpert system remain too expensive for many low- and middle-income countries.[26] The Solana HDA Trichomonas Assay is a rapid (35 minute) NAAT-based assay approved for vaginal swabs and female urine samples with a high sensitivity (93%–100%) and specificity (>98%).[27,28] The assay is run on the compact, benchtop Solana system and features Quidel's proprietary helicase-dependent amplification (HDA) technology that eliminates the need for a thermocycler. This HDA technology is available for other Solana infectious disease assays ultimately reducing implementation costs.

Unlike the NAAT-based tests for TV, the OSOM trichomonas test and Kalon TV latex tests use antibodies to detect TV-specific antigens that provide a rapid, easy to use bedside diagnosis without the need for additional resources, platforms, or refrigeration to perform the testing, increasing accessibility in low-resource areas and/or field-testing. The OSOM trichomonas test is a single use, low-complexity, dipstick, POC assay to detect TV with a reasonably high sensitivity (83%–90%) and specificity (98.4%–100%).[19] Importantly, compared with the traditional wet mount method, the overall costs for TV diagnosis were significantly decreased with the implementation of the OSOM test.[29] Although the Kalon TV test has also been shown to be effectively used in low-resource settings it has not been cleared for use by the United States or Europe.[16]

GONORRHEA AND CHLAMYDIA

Gonococcal infections are caused by *Neisseria gonorrhoeae* (NG) and most commonly cause urethritis in males and lower or genitourinary tract infections in females. In females, this infection can progress to cause infertility or pelvic inflammatory disease. Surveillance reports have shown an increasing trend of NG infection by 45% since 2016, and that NG infections are associated with an increased risk of acquiring or transmitting other STIs, such as *Chlamydia*, caused by *Chlamydia trachomatis* (CT).[30,31] Although NG and CT differ in infection and pathogenesis, they present with similar signs, symptoms, and potential sequelae. Because of the prevalence and similar clinical presentations, CT and NG are often included on the same POC assays.

The development of assays with reduced complexity and increased sensitivity and specificity has largely replaced nonspecific-based testing, such as leukocyte esterase, especially in high-resource areas. These assays include non-NAAT-based assays, such as BioStar OIA GC (Inverness Medical, Waltham, MA), and NAAT-based assays, such as GeneXpert CT/NG.[28,32] NAAT-based assays are the current recommended assays because of ease of use and high sensitivity and specificity.[28] GeneXpert has two assays, one for NG and one combination test for CT and NG, both of which have been FDA approved for multiple sample types including vaginal, endocervical, pharyngeal, rectal, and urine, with greater than 85% sensitivity and specificity.[33,34] The sensitivity and specificity for extragenital samples do not meet the WHO POC testing requirements.[1,12] Despite the reduced sensitivity associated with some sample types, the GeneXpert assays reduce time to treatment when compared with traditional diagnostic testing making it an optimal assay for high-resource areas.[35–42] The variety of potential sample types that the GeneXpert assays can assess increases the potential testing capabilities in many low-resource areas; however, financial and infrastructure limitations previously discussed often limit the use of the GeneXpert platform in these populations.

In addition to GeneXpert, there are two new NAAT-based POC tests available: Visby Medical Sexual Health Test (Visby Medical, San Jose, CA) and the *binx io* platform (Limited, Boston, MA).[43,44] The Visby Medical Sexual Health Test is a rapid (<30 minutes) single-use diagnostic assay that simultaneously detects CT, NG, and TV with sensitivities and specificities comparable with other NAAT and non-POC test assays (eg, Aptima Combo 2 [Hologic, San Diego, CA] and ProbeTec [Becton Dickinson, Franklin Lakes, NJ]).[28,45] The Visby test received FDA approval and CLIA-waived status in August 2021 and requires no separate instrument or reader, reducing the complication of sample preparation and result interpretation, potentially expanding accessibility for low- and middle-income settings. Currently, the Visby device is only approved for clinician and self-collected vaginal swab samples. Similarly, the *binx io* platform is a polymerase chain reaction (PCR)-based assay for the detection of CT and NG from vaginal swabs and male urine that was CE marked and FDA cleared in 2019, and CLIA-waived in 2021. Like the GeneXpert, the *io* system consists of a fully integrated, benchtop instrument that uses single-use cartridges, and provides a rapid turnaround (30 minutes). When compared with other NAAT based assays, the *io* CT/NG assay had high sensitivity and specificity for vaginal swab samples, but performed at the lower end for sensitivity specificity in male urine samples.[43,46]

The need for mobile, molecular-based CT/NG diagnostic assays, and assays to detect antimicrobial resistance in NG has been recognized and resulted in significant advancements in CT/NG POC testing.[47–49] The quantitative RT cross-priming amplification EasyNAT diagnostic system (Ustar Biotechnologies, Hangzhou, China) includes an all-in-one cartridge and a portable device for amplification and detection of CT and NG. The EasyNAT systems use a cross-priming amplification technique to amplify target sequences at a constant temperature within 80 minutes.[50] This technique reduces the amount of equipment required for analysis, and serves as a novel detection method with the potential for increased access in resource-limited areas.[51] The EasyNAT system will be optimized so that all reagents are stable at ambient air and the assay is expected to obtain CE approval in the near future.[47,49] Similarly, the ResistancePlus GC assay (SpeeDx Pty Ltd, Sydney, Australia), is the first rapid (<60 minutes) commercially available assay that simultaneously detects NG and mutations in *gyrA*, associated with resistance to ciprofloxacin.[52] To address the real-time connectivity criteria of RESSURED, a team at Johns Hopkins University has developed mobile NAAT-based assays: MobiNAAT for CT and PROMPT for NG.[53,54] These assays

use a portable, rapid, on-cartridge PCR technology to provide results within 15 minutes. The portability and ease of use with the MobiNAAT and PROMPT assay shows great potential in the future advancements of POC testing for STIs. Although neither of these tests have been approved for clinical use, in clinical trials, they have shown excellent concordance with traditional phenotypic antimicrobial resistance testing and NAAT-based testing.[53,55]

HUMAN IMMUNODEFICIENCY VIRUS (HIV)

Although prevention and early detection are essential for any STI, it is especially important for HIV because of the nature of the infection and potential sequelae. The CDC recommends HIV testing at least once in individuals age 13 to 64, and annual testing for high-risk individuals.[56–58] POC testing for HIV allows for early appropriate initiation of antiretroviral therapy, treatment monitoring, and prevention of opportunistic infections.[59,60] Over the last two decades, numerous easily accessible antibody-based rapid HIV diagnostic tests have been FDA approved, including POC tests and over-the-counter assays, such as the OraQuick In-Home HIV Test (OraSure Technologies, Bethlehem, PA) and the INSTI HIV-1/HIV-2 Antibody Test (Biolytical Laboratories Inc, BC, Canada).[59] Current POC testing options for HIV use a variety of sample types including whole blood, plasma, urine, and oral fluid that allows for improved testing opportunities in patients who prefer less invasive options for sample collection.[59,61] Antibody-based POC diagnostic assays have a high specificity (98%–100%) and sensitivity (>98%) in seroconverted patients. However, in HIV, the window following initial infection and before seroconversion can last up to 12 weeks, during which antibody-based assays cannot detect infection.[60,62] Current, fourth-generation POC tests seek to address the need for earlier diagnosis through the detection of anti-HIV antibodies and the structural viral protein, p24, increasing sensitivity and decreasing the postexposure latency window.[62] Examples of these tests including the Alere HIV Combo Test (Alere Diagnostics, Charlottesville, VA) and the GS HIV Combo Ag/Ab EIA (Bio-Rad Laboratories, Hercules, CA). Despite the shorter window to detection, sensitivity of the assay in patients before seroconversion still remains low (2%–80%).[62]

As with other STI POC tests, NAATs currently have the highest sensitivity and specificity (both >99.9%).[63,64] POC tests to determine HIV viral load are not yet commercially available, requiring samples to be shipped to laboratories for testing.[65,66] Recently, the GeneXpert HIV-1 Quant was evaluated in clinical studies and will likely be added to the growing list of available GeneXpert POC assays.[67] An ideal POC test for HIV viral load would have a limit of detection of less than 1000 copies/mL, give results in less than 1 hour, be easy to use, and inexpensive to perform.[68] The development of POC HIV viral load assays that meet the REASSURED criteria and assays to detect mutations related to drug resistance would be a great advantage to effectively treating HIV infections and preventing transmission.[69]

Additional assays that assist with monitoring HIV infection include monitoring the CD4 T-cell count with less than 200 CD4 cells/mm^3 (normal: 500–1500 cells/mm^3) defining the development of AIDS, and a need for prophylaxis against HIV-associated opportunistic infections.[70] Much like NAATs, traditional CD4 testing requires considerable capital investment and complex training to implement and maintain, impeding their use in resource-limited settings.[71,72] POC CD4 assays, such as PIMA CD4 (Abbott Diagnostics, Charlottesville, VA) and Vitisect CD4 test for advanced HIV (Omega Diagnostics Group, Alva, Scotland) have varying sensitivity (60%–98%), specificity (77%–89%), and diagnostic cutoffs (200–350 cells/

mm^3). A study evaluating CD4 assays in Uganda showed acceptable sensitivity and specificity for monitoring disease progression with HIV.[73] Recently, antibody-based combination POC tests that detect HIV and other STIs from a single sample have been developed. These combination assays include HIV, hepatitis B (HBV), hepatitis C (HCV), and syphilis and are also available over the counter.[74–76] The Miriad Rapid HBc/HIV/HCV Antibody Test POU+ (MedMira, Halifax, Nova Scotia) is one such immunochromatographic assay that uses whole blood, plasma, or serum to detect HBc antibodies, HIV1/2 antibodies, and HCV antibodies within 15 minutes. Similarly, the Dual Path Platform (DPP) HIV Syphilis Assay (Chembio Diagnostics Systems, Medford, NY) is an immunochromatographic lateral flow assay for antibodies against syphilis and HIV from a single finger stick. The assay was cleared by the FDA in 2020 and can be stored at room temperature with a shelf-life of 24 months making it ideal for clinics, emergency departments, and field-testing.[77] The development of these assays focuses on screening high-risk populations for multiple STIs on using one sample on one assay.[78]

With all HIV POC tests, counseling, screening strategies, and follow-up confirmatory testing is necessary and should be performed based on local epidemiology and individual risk factors of the relevant patient population. Screening strategies using multiplex assays should be implemented based on local epidemiology of infection and individual risk factors of the patient.[78] Confirmatory tests are almost never POC, because they require a higher specificity or different methods than what is currently available for POC.[60,62,79] Regardless, the benefits of HIV POC testing outweigh the complications as a useful and practical tool to screen high-risk patients and provide a rapid preliminary diagnosis.[79] The development of quantitative HIV POC tests, POC assays to detect mutations related to HIV drug resistance, and further multiplex POC tests that include HIV would be a great advantage to effectively treat HIV infections and prevent transmission.[69]

SYPHILIS

Syphilis is an infection caused by *Treponema pallidum* (TP) and is categorized based on disease pathology and progression: primary (chancre), secondary (maculopapular rash), latent (asymptomatic), and tertiary (any organ can be affected). There are approximately 6 million new cases of syphilis each year, with a 52% increase from 2016 in the United States alone.[30] POC tests currently available have low specificity (<90%), leading to overtreatment. Consequently, these tests are underused for screening purposes, especially pregnant women where it is essential for preventing congenital syphilis.[3] Differentiation between past and present syphilis infection requires multiple tests, with the most sensitive reporting a high false positivity rate and the most specific tests unable to differentiate previous and active infection.[80]

Currently, all available POC diagnostic tests for syphilis rely on the detection of antibodies against the organism (antitreponemal [AT]) or against the products of cellular damage that occurs during infection (nontreponemal [NT]). Antibody-based POC tests for syphilis use immunochromatographic methods and is performed on whole blood, plasma, or serum, providing a result within 30 minutes.[81] POC NT tests are temperature stable, easy to perform, and require minimal instrumentation.[82] These tests include Alere Determine syphilis TP and SD Bioline Syphilis (Abbott Diagnostics, Abbott Park, IL), Syphicheck (Qualpro Diagnostics, Goa, India), and Visitect Syphilis (Omega Diagnostics Ltd, Scotland, UK). The most common NT test type is the rapid plasma reagin test for anticardiolipin (reagin) antibodies. NT tests can result in false-positive results because of production of antireagin antibodies in various nonsyphilis

conditions, such as lupus or malaria. False-negative results can occur because of excess antibody overloading the test antigen (termed the prozone effect).[3] In contrast, AT antibody tests have a high sensitivity but cannot distinguish between active and past infection.[3] Available AT tests have similar sensitivity (96%–100%) and specificity (84%– 99%).[83–87] Newer AT assays, such as the BioPoint TP-IgA (Nanjing BioPoint Diagnostics, Nanjing, China), detect TP-specific IgA antibodies that are more sensitive and specific than traditional IgM or IgG detection during active infection.[87]

The most popular syphilis POC assays consist of combination tests that detect AT and NT antibodies, aiding in diagnosing and differentiating active from previous infections. The DPP Syphilis Screen and Confirm Test (Chembio Diagnostics) detects AT and NT antibodies, providing results in less than 15 minutes.[87] The sensitivity and specificity of the NT portion of the DPP does not meet ASSURED criteria, and a recent clinical study showed that DPP did not reduce the number of women overtreated for syphilis.[82] Syphilis testing that can differentiate past and present infection while maintaining high sensitivity may reduce overtreatment and increase screening initiatives.[81] The current POC syphilis testing options cost more than traditional laboratory-based testing. However, the overall cost-benefit associated with reduce infection transmission, and the decrease in disability-adjusted life-years support the value of using and improving syphilis POC testing.[88]

HUMAN PAPILLOMA VIRUS

Human papilloma virus (HPV) includes more than 200 strains, 14 of which are associated with STIs and increased risk for developing cervical cancer.[89] Most HPV testing is performed in high-complexity laboratories, uses highly trained personnel, and has slow turnaround times, and therefore is not sustainable in low-resource areas.[90] In 2020 the WHO launched a global strategy for the elimination of HPV-related cervical cancer, to advance the development and evaluation of HPV screening and treatment approaches.[91,92] There are currently no POC HPV assays that meet the WHO ASSURED criteria. However, two assays are currently available: the Truenat HPV-HR assay (Molbio, Goa, India) and the GeneXpert HPV assay, which indicate the realization of a clinical need for POC HPV testing. Truenat is a portable chip-based test that consists of a sample-processing device and a reverse transcriptase (RT)-PCR analyzer that detects high-risk HPV strains 16, 18, 31, and 45 in cervical samples in less than 1 hour with high sensitivity (86%–99%) and specificity (97%–99%).[93] The Truenat is rechargeable with an 8-hour battery life increasing potential for diagnosis in low-resource areas. The GeneXpert assay detects HPV 16, 18, and 45 using the Xpert RT-PCR cartridge technology.[94] In clinical studies, the GeneXpert had a 90% correlation with traditional testing.[94,95] The sensitivity and specificity of the GeneXpert varied based on the strain of HPV, self- or clinician-collection of sample, overall viral load in the sample, and the cervical intraepithelial neoplasia grade, with increasing specificity as the grade increased.[94,95] With limited POC options available, there is considerable opportunity for improvement in new cost-effective technology and assays that include additional high-risk strains, and improved turnaround times for HPV POC diagnosis.

HERPES SIMPLEX VIRUS

Herpes simplex virus 1 and 2 (HSV-1/2) is one of the most common STIs, with an estimated 12% of the US population being positive for HSV-2 antibodies.[96] HSV-1/2 is a noncurable STI with asymptomatic latency and risk of reactivation. HSV-1/2 presentation is often atypical or subclinical and diagnosis often relies on the presentation

of lesions. As with other STIs, the rapid and effective diagnosis of HSV can drastically reduce transmission because of effective treatment and counseling.[97] Currently, the detection of live virus or nucleic acids from lesions is the preferred diagnostic method but relies on symptomatic presentation for adequate sample collection and diagnosis.

Antibody-based POC HSV testing is performed for large population surveillance on samples from asymptomatic patients to determine exposure and infection status. Various lateral-flow assays to detect anti-HSV antibodies are available with high sensitivity (>80%) and specificity (>90%); however, the only commercially available FDA-approved microfluidic antibody-based HSV POC test is the HSV-2 UniGold (Trinity Biotech Plc, Bray, Ireland).[98] This assay uses a portable device to detect HSV-2 gG2 antibodies in approximately 15 minutes.[98] In seroconverted patients, HSV serology is highly sensitive (85%–100%) and specific (97%–100%) when compared with traditional immunoblot testing for HSV-1/2.[97,98] Serology testing can indicate a chronic infection, but it can miss a primary infection, and cannot determine the cause of genital lesions. Therefore, viral detection methods (NAAT, antigen, culture) are needed to diagnose acute infections.[99]

Currently the NAAT-based AmpliVue HSV 1 + 2 and Solana HSV 1 + 2/VZV (Quidel) are the only POC assays available that are performed on swabs from mucosal and genital lesions. The Solana assay is able to differentiate lesions caused by varicella-zoster virus, HSV-1, or HSV-2 with a high sensitivity (91%–100%) and specificity (94%–98%).[98] With the limited number of POC HSV tests available, there is a need to expand and improve these assays to detect and differentiate HSV-1/2 in acute and chronic infection.

BACTERIAL VAGINOSIS

Bacterial vaginosis (BV) is a polymicrobial infection caused by dysregulation of the vaginal microbiome. Although BV is not traditionally considered an STI, epidemiologic and microbiologic studies suggest that sexual transmission is essential to the development of BV.[2,100,101] Historically, BV has been diagnosed at the bedside using Amsel criteria: visual attributes (color and consistency) of the vaginal discharge, presence of amines (measured by whiff test), vaginal pH, and microscopic detection of clue cells in vaginal fluid.[102] Amsel criteria has a low sensitivity and specificity; and vaginal microbial dysregulation can occur without these visible signs or symptoms, resulting in an increased risk of STI acquisition, and preterm birth.[2,103,104] Sensitive and specific POC testing for BV allows for appropriate initiation of therapy, and counseling.[105]

Currently available POC tests for BV detect nonspecific antigens, bacterial species that are correlated with BV but not causative, or vaginal environmental changes. As such, they perform better than traditional syndromic testing yet maintain a low sensitivity and specificity. These tests include OSOM BV Blue Test (Sekisui Diagnostics), which detects sialidase produced by *G vaginalis*, and FemExam pH and Amines TestCard (Litmus Concepts, Santa Clara, CA), which detects abnormal vaginal pH and amines in vaginal secretions and identifies nonspecific antigens or vaginal environment alterations associated with BV. Likewise, assays to detect BV-associated vaginal inflammation (eg, increased interleukin-1β and IP-10) are currently in development. Although nonspecific for BV, preliminary studies show that this detection of vaginal inflammation has increased sensitivity when compared with Amsel criteria, 77% and 19%, respectively.[103] Detection of vaginal inflammation before the development of more severe BV symptoms may decrease time to diagnosis, initiation of treatment, and incidence of transmission.

Direct detection of BV-associated organisms is more specific than detection of vaginal inflammation biomarkers. The colorimetric BD Affirm VPIII directly detects *G vaginalis*, TV, and *Candida* spp through DNA hybridization technology.[101,106–108] Like the Affirm VPIII, the GeneXpert MVP assay was recently granted 501(k) clearance, and also differentiates BV from TV and *Candida* infections.[109] Utility of the GeneXpert MVP is disputed because it only detects *Atopobium* spp, BV-associated bacterium 2, and *Megasphaera* spp for BV diagnosis, without consideration for the overall bacterial community or other BV-associated organisms, such as *G vaginalis* and *Mycoplasma genitalium*.[110,111] *M genitalium* is an emerging STI that has been recognized as a cause of vaginal inflammation and potential contributor to the development of BV.[104,112–114] Currently, there are no POC tests for the detection of *M genitalium*. The development of rapid POC testing for BV and vaginitis is important for effective STI screening and decreasing pregnancy complications that can arise because of microbiome dysregulation and vaginal inflammation.

SEXUALLY TRANSMITTED INFECTION AT-HOME, SELF-TESTING

At-home, self-testing for STIs provide patients with privacy, confidentiality, convenience, and speed that traditional testing and POCs cannot provide. Additionally, at-home self-testing reduces barriers to health care access and burden on medical systems and personnel that already face staffing shortages. Popularity of at-home test kits has grown since the beginning of the COVID-19 pandemic, and many public health departments and hospital systems now partner with at-home STI testing companies to increase access to STI testing while limiting the burden on clinical staff.[115] Such companies as Binx Health, Inc (Boston, MA), CVS Health (Woonsocket, RI), Everlywell (Austin, TX), and LetsGetChecked (New York, NY) provide sample collection kits and prepaid shipping materials addressed to CLIA-certified and CAP-accredited laboratories for testing.[116,117] Patients follow the package instructions to self-collect urine or swab samples, ship samples with provided materials to the partner laboratory, and receive results less than a week after samples are received by the laboratory. Testing kits are available for HIV, chlamydia, gonorrhea, syphilis, and hepatitis. For those kits provided through a partnership with health departments, positive STI test results are accompanied with connections to in-person follow-up with a health care professional.

Since their introduction nearly a decade ago, multiple reviews have indicated that the availability of STI self-testing has expanded the potential for testing populations with limited access to in-person physician care, and for syphilis and HIV, with similar reliability as traditional POC tests.[118,119] Because of this expanded potential for testing and patient autonomy, in 2019, the WHO issued a report advocating for STI self-testing and proposing adaptions to the established STI testing methods.[120] Soon after this report, the COVID-19 pandemic limited access to in-person clinical STI testing, and laboratories began evaluating the accuracy and reliability of off-label at-home specimen self-collection for STI POC tests, resulting in the implementation of protocol adaptions for tests that were typically performed on physician-collected samples.[121] The increase in demand for at-home STI testing and self-sampling has facilitated the collection and review of implementation-and-use data for these at-home methods, addressing the benefits and issues throughout the United Kingdom and United States.[121,122] At-home testing introduces many of the same risks as traditional, non-POC STI testing, such as lack of follow-up treatment or care. Emphasizing the attrition between testing and follow-up care, reviews of patients who use pharmacy-based infectious disease testing suggest that only 30% to 40% of patients using these services

notify a primary care provider.[123,124] Additionally, at home and self-testing for STIs limit community and public health surveillance data; increase the likelihood of unintended, unnecessary, or incorrect use, which subsequently increase the return of incorrect test results; and limit connection to necessary risk counseling or partner notification. Few FDA-approved, CLIA-waived at-home tests are available in which collection and testing are performed at home. These tests have been discussed in previous sections of this article because they related to specific STIs.

THE FUTURE OF SEXUALLY TRANSMITTED INFECTION POINT-OF-CARE TESTING

Incorporating POC testing for STIs into the clinical setting enables clinicians to provide a definitive diagnosis and initiate appropriate treatment, all within the same visit. Some POC testing even allows for implementation of large, on-site community screening in high-risk populations.[1] However, important inhibiting factors for the use of many POC tests for STIs exist: cost; available resources; and regulatory agencies, such as the FDA, WHO, and CLIA, which determine who is qualified to perform the test and whether a test meets quality standards.[27,28] Low sensitivity and specificity of current STI POC tests prove to be additional barriers to clinical implementation.[125] Since the establishment of the ASSURED criteria and the global initiative for STI POC testing, advancements in technology have improved on the sensitivity, specificity, cost, ease of use, sample processing, and result turnaround times (often <15 minutes), yet as discussed throughout, there remains significant room for improvements. Ideal POC STI tests are stored at room temperature, provide results in less than 1 hour, and do not need high-skilled laboratory scientists to perform the test.[126]

Although many new and in-development POC tests for STIs achieve the ASSURED criteria, limitations in current testing exist. NAATs remain the most specific and sensitive STI tests, most of which do not meet ASSURED criteria because of cost and complexity.[127–129] Improvements in NAAT testing should include the development of portable multiplex platforms that do not require a consistent power source. Further reductions in the turnaround times and implementation costs are needed for NAATs. Conversely, immunochromatographic paper-based assays, which are cheap and easy to use, have revolutionized POC testing in developing countries. However, these assays often have less than optimal sensitivities and/or specificity for STI/s, especially when the microbial burden is low.[1,9] Importantly, improvements in all STI POC assays should consider the limitations that exist in the areas or populations where STI prevalence is high, such as the lack of financial means or infrastructural resources in developing countries.

Given the documented increase and growing concern for antimicrobial resistance in STIs, such as NG and HIV, it is paramount that new POC tests be developed to detect resistance to first-line antimicrobial therapy. Potential effects of these combination detection-resistance POC tests include improved patient outcomes, reduced transmission after initiation of treatment, and ultimately reduction of the emergence of antimicrobial resistance in STIs that currently poses a serious health risk.

In addition to detecting antimicrobial resistance, POC tests for STIs are in need of improved detection in nonstandard STI disease presentation or nonstandard sample types, such as those collected from extragenital infections. Expansions in approved sample types that POC tests can screen increases the detection, ultimately reducing the potential damage or transmission related to STI infections. STIs frequently cause extragenital infections including the mouth, throat, and rectum, yet most STI POC tests are not approved for extragenital specimens. This limits the utility of the POC assays and neglects the needs of patients, often in marginalized groups, that experience

these nonstandard presentations. Adding to this, most POC STI tests currently available do not include the option for self-collected samples. Self-collection promotes patient autonomy and empowers individuals to take control of their health care. Likewise, it also encourages providers to complete STI screening by eliminating additional time associated with clinician collection.[130–134] Self-collection of specimens with appropriate instruction has been an effective method for specimen collection with accurate results and has shown to increase uptake of screening for STIs in vulnerable populations. POC tests for STIs that allow for expanded sample-type screening including extragenital and self-collected samples have potential to increase the detection and treatment of otherwise damaging, transmissible STIs.

Importantly, considerations for the needs or perceptions of patients and providers, and the clinic workflow, and available resources must guide future advancements in POC testing for STIs.[1,28] The goal of all advancements in POC testing for STIs is to facilitate increased use of POC assays by the physicians; improve patient satisfaction; and increase clinical diagnostic compliance, accuracy, and treatment of STIs. POC testing, even with lower than optimal sensitivity and specificity, can significantly improve treatment and infection prevention efforts by reducing patient attrition between sample collection treatment initiation when compared with traditional methods of syndromic-based testing.[9,11,135] These improvements can be expanded as advancements in STI POC testing options continue to be made.

CLINICS CARE POINTS

- STI POC tests are available for almost all STIs.
- ASSURED/REASSURED criteria created by the WHO is directing advancements in STI POC testing.
- In high-resource areas, NAAT assays are the preferred POC diagnostic method for most STIs, excluding syphilis, and hepatitis B virus, and hepatitis C virus.
- Limitations to adequate POC testing include cost, ease-of-use, portability, turnaround time, sensitivity, and specificity of assays currently available.
- Future developments in STI diagnostics should focus on the development of POC assays for drug resistance; measuring viral loads; and detecting emerging STIs, such as BV and *M genitalium*.

DISCLOSURE

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