BC Centre for Disease Control

Communicable Disease Control
Guidance for use of the INSTI HIV/syphilis Multiplex Test
October 2024

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1.0 BACKGROUND

This guideline provides information on the recommended use of the bioLytical INSTI Multiplex HIV-1/HIV-2/syphilis antibody test in BC. The INSTI Multiplex POC Test is the first point-of-care (POC) test or "rapid" test approved for sale and use in syphilis diagnosis in Canada. The test works by detecting antibodies to HIV-1, HIV-2 and *Treponema pallidum* (the bacterium responsible for syphilis) using a fingerprick blood sample. Results are available in under 5 minutes. POC tests can reduce the time to diagnosis, expedite linkages to care, and allow early treatment initiation.

Highlights:

- The INSTI Multiplex POC test is intended as a single-use screening test to be used by trained healthcare providers in a variety of clinical settings.
- It is intended for those at risk of HIV and/or syphilis and who face barriers to accessing mainstream care options or follow-up, or who have been traditionally underserved by routine screening programs.
- The syphilis test component has variable sensitivity depending on disease stage. It is least sensitive in very early or late-stage infection when rapid plasma reagin (RPR) titres are low or nonreactive.
- The test **cannot differentiate** between a prior syphilis infection (either untreated or adequately treated) and a new infection.
- When the INSTI Multiplex POC test is used, regardless of the result, a standard laboratory serology test for syphilis is also required.
- In select cases, it may be possible to offer immediate syphilis treatment prior to receiving confirmatory serology results.
- A positive syphilis or HIV test result by POC is reportable to public health.
- The INSTI Multiplex POC tests is not approved for self-testing.

2.0 HOW TO USE THIS GUIDELINE

The primary focus of this guideline will be the use of the INSTI Multiplex POC test for the testing of syphilis (*Treponema pallidum*) in the context of the ongoing syphilis outbreak in BC. The INSTI HIV-1/HIV-2 POC test (i.e., the HIV testing component of the Multiplex test) is currently in use in BC with separate guidance and can be used for individuals when only HIV testing is needed.

The guidance is intended for healthcare providers, sites, and organizations who may offer the INSTI Multiplex POC test. The document reviews requirements for healthcare

providers, sites and organizations, outlines recommendations for who may benefit most from POC testing, which settings may be most appropriate for POC testing use, reviews what is known about the INSTI Multiplex POC test performance, and provides algorithms for handling of test results.

Please note that this guidance does not include clinical guidance for syphilis and HIV testing generally, or for appropriate public health management of these infections. While the focus of this guidance is on the Multiplex POC test, other low-barrier testing options may be available which have unique advantages and disadvantages (e.g., dried blood spot testing), and these may need to be weighed when determining which communities or settings are best for implementing the INSTI Multiplex POC test.

3.0 HOW THIS GUIDELINE WAS DEVELOPED

The first draft of this guidance was developed by the BCCDC based on a review of the literature and guidelines from other jurisdictions, and consultation with internal sexually-transmitted and blood-borne infection (STBBI) testing leads (Clinical Prevention Services, Chee Mamuk, Public Health Laboratory) and with experts in perinatal care, pediatric and reproductive infectious diseases at PHSA. The guidance was subsequently revised based on the feedback provided by the Syphilis Testing Working Group of the BC Syphilis Outbreak Response Committee, which includes public health STBBI testing leads from FNHA, all regional Health Authorities and the Ministry of Health.

4.0 EPIDEMIOLOGY OF SYPHILIS IN BC

Cases of infectious syphilis have steadily increased in Canada and BC in the last 10 years. For comparison, in the year 2022 in BC, there were 36.9 cases of infectious syphilis per 100,000 people, up from 3.4 cases per 100,000 in 2010.(1) Initially, this increase occurred largely among Two-Spirit, Gay, Bisexual, Transgender, Queer and other men who have sex with men (2SGBTQ+ men), who continue to be disproportionately affected by syphilis. In recent years, however, the landscape of infectious syphilis has changed, with a rise in infectious syphilis cases among females and heterosexual men coupled with an increase in congenital syphilis cases.(2)

Syphilis outbreaks are mainly concentrated among people experiencing health impacts and inequities related to: (3,4)

- Social determinants of health, such as housing instability, poverty, stigma, racism and discrimination

- Overlapping epidemics (syndemics), including HIV, mental illness, substance use and the toxic drug crisis.

As a direct result of the harmful legacy of colonization, Indigenous people often bear a disproportionate burden of syphilis in outbreaks across Canada. The burden of syphilis on Indigenous peoples in BC is not adequately represented in syphilis surveillance data. Due to a lack of appropriate, culturally-safe information collection methods, there is a lack of information on self-reported Indigenous identity for syphilis cases in BC.

5.0 POLICY FRAMEWORK

The response to the syphilis outbreak in BC is outlined in the Syphilis Action Plan (SAP; refreshed in 2023).(1) The aim of the SAP is to stabilize the incidence of syphilis at the 2021 level (27.4 per 100,000) and to have zero cases of congenital syphilis reported in BC by 2025. Increased access to syphilis testing, including validation and implementation of POC syphilis tests, is a key activity in BC's provincial syphilis response. The testing-specific priorities in the SAP include increasing culturally appropriate and trauma-informed testing capacity and outreach to individuals who have barriers with utilizing mainstream options, expanding testing options to rural, remote, and Indigenous communities and other underserved populations, and engaging with mental health and substance use services to support testing.

This guidance acknowledges the inherent rights of Indigenous people (First Nations, Inuit and Métis people) as outlined in the 2019 Declaration on the Rights of Indigenous Peoples Act, including the right to self-determination including use of the INSTI HIV/syphilis multiplex test.(5) Indigenous people in BC often experience stigma, racism and discrimination from within the healthcare system, violence and ongoing trauma, and structural and geographic barriers to accessing health services. These are legacies of colonization and structural violence including residential schools and are further amplified through policy (e.g., centralization of health services), leading to higher rates of concurrent health issues and substance use, which have placed Indigenous peoples and communities at higher risk for experiencing an unfair proportion of adverse health events.(6) Reducing systematic barriers and harms, ensuring access to culturally safe care, and promoting Indigenous-led prevention and wellness efforts are essential in reducing the impact of syphilis on Indigenous peoples and communities. The 2020 In Plain Sight summary report highlights systemic, Indigenous-specific racism in BC healthcare leading to insufficient care for Indigenous people, including inadequate preventive care.(7) Community knowledge and published literature have well-demonstrated how these experiences contribute to increased burden of STBBI for

Indigenous people in BC.(8)

The SAP recognizes these barriers faced by Indigenous peoples, and the need to provide non-stigmatizing, culturally safe sexual health care as part of the syphilis response. The SAP also prioritizes syphilis-related strategies for other underserved populations including incarcerated individuals, 2SGBTQ+ men, immigrants and newcomers to Canada, as well as those at high risk of syphilis-related complications (such as pregnant individuals).

6.0 GENERAL REQUIREMENTS

The following sections outline the requirements for settings and healthcare providers when using the INSTI Multiplex POC test.

6.1 Setting Requirements

Settings where INSTI Multiplex POC testing is available are able to:

- Have a physical set-up that provides a safe, confidential space for testing
- Deliver INSTI Multiplex POC testing according to quality assurance standards, including staff training, quality control testing of kits, and documentation of quality assurance and test outcomes
- Offer immediate treatment for a reactive syphilis test result, when appropriate
- Support the management of complex or urgent cases when required

6.2 Healthcare Provider Requirements

Healthcare providers offering INSTI Multiplex POC testing are able to:

- Provide culturally safe and trauma-informed care
- Conduct person-led pre and post-test discussions
- Use the INSTI Multiplex POC test kit and interpret results correctly
- Offer or facilitate confirmatory testing for HIV and syphilis.
- Provide or arrange for immediate treatment of a reactive syphilis test result.
- Liaise with specialists for help with staging and treatment, or potential serious complications (e.g., neurosyphilis)
- Have knowledge of local community resources and linkages to care for those who test positive for HIV, including those specifically for Indigenous people.
- Report reactive syphilis or HIV POC test results to public health

7.0 POTENTIAL BENEFITS AND HARMS OF POC TESTING

7.1 Potential benefits

- High acceptability for POC testing among populations affected by STBBI, including 2SGBTQ+ men, pregnant persons, incarcerated populations, although this may depend on the setting and healthcare provider.(9–12)
- May increase access to testing among underserved populations, such as those facing discrimination or stigma when accessing mainstream care options, and those in rural or remote locations.(9,10)
- Having access to a variety of testing options including POC testing promotes self-determination for Indigenous peoples, especially in rural and remote communities with barriers to health care.(8)
- Impact on treatment and transmission: faster turnaround time for results facilitates timely clinical decision-making and expedites linkages to care. Rapid access to treatment has the potential to reduce the risk of onward transmission.(11)
- Facilitate initial and ongoing engagement with sexual healthcare.
- Use as an alternative when venipuncture is not preferred, available or has been unsuccessful.

7.2 Potential harms

- May lead to decreased uptake of testing for other STBBI (e.g., serology for hepatitis C testing).(11)
- May lead to increased anxiety for individuals waiting for confirmatory test results
- Potential for false positive or false negative results.

8.0 RECOMMENDED USE OF THE INSTI MULTIPLEX POC TEST

8.1 General

The INSTI Multiplex POC test is intended for use by trained healthcare providers in a variety of settings including medical facilities, physician or nurse practitioner offices, emergency care settings, and community settings. It is not approved as a self-test, nor for donor screening.(12)

These recommended uses are not exhaustive or prescriptive, and the clinical judgement of healthcare providers remains important. Sites where POC testing will be available are

subject to the syphilis testing-related priorities of Health Authorities and Indigenous (First Nations, Inuit and Métis) communities in BC.

8.2 Priority Populations

POC testing may be offered to individuals at risk of HIV and/or syphilis and who have or may have one or more of the following criteria:

- Face barriers to engaging in follow-up for test results or care
- Have limited access to health services
- Have difficulty engaging in care options due to barriers such as stigma, discrimination or racism in healthcare settings

Examples of individuals who may benefit from POC testing include persons who use substances, persons who engage in transactional sex, persons experiencing unstable housing, persons experiencing or who have recently experienced incarceration, transgender and non-binary persons, and 2SGBTQ+ men.

8.3 Priority Sites

Sites or settings (e.g., facility-based, community sites or outreach programs) where POC testing may be most indicated include:

- Rural, remote and Indigenous communities
- Sites where time to access or acquire serology testing or results is prolonged
- Sites operating in areas of a new syphilis outbreak*
- Sites which may be the only point of contact with the healthcare system for some people (certain community sites or emergency departments, as examples)
- Community sites offering mental health and substance use services
- Sites offering community prenatal, abortion or contraception services to underserved populations

*Syphilis POC may be less useful in areas or populations experiencing longer-term outbreaks, as the test cannot distinguish between a prior infection (whether treated or untreated) and a new infection.

8.4 Testing during pregnancy

Special consideration should be given to **prenatal and labouring** people. POC testing may be beneficial at sites offering prenatal and obstetrical services, for pregnant people with limited prenatal care, those with no prenatal syphilis test results available, those

with ongoing risk of acquisition of syphilis in their pregnancy despite a previous negative results, or those facing barriers to engaging in follow-up or routine care.

8.5 Scenarios in which testing is not recommended

- Individual provides a verbal history of prior, treated syphilis or prior positive syphilis serology (if testing for syphilis)
- Individuals with sufficient existing access to testing and timely results are a lower priority for the INSTI Multiplex POC Test for syphilis (e.g. already connected with health care services or providers that offer standard syphilis serology without prolonged time to results being available).

9.0 TEST PERFORMANCE

In Canada, one multi-center trial in Alberta studied the diagnostic test performance of the INSTI Multiplex POC Test in multiple settings, including urban STI clinics, urgent care centers, correctional centers, and a First Nations community.(13) The HIV test component demonstrated high sensitivity (100%) and specificity (99.6%) in this study. The syphilis component had a lower sensitivity overall (76.7%), although sensitivity increased at higher RPR values (97.9% for an RPR titre greater than or equal to 1:8). The syphilis test component may therefore fail to detect infections with a low RPR titre (e.g. very early infection; late latent stage).(14) The syphilis test specificity was 99.8%. This field performance of the syphilis component is similar to a community-based study of the INSTI Multiplex POC Test in Los Angeles and New York.(15)

Table 1: Performance metrics from an Alberta validation study of the INSTI Multiplex HIV/Syphilis POC test.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV	FP (%)
HIV	100 (86.2-100.0)	99.6 (99.1-99.8)	82.8 (65.5-92.4)	100 (99.7-100)	0.37*
Syphilis *(overall, any RPR value)*	76.7 (72.7-80.2)	99.8 (99.2-99.9)	95.5 (98.1–99.9)	88.4 (86.3-90.3)	0.3**

Syphilis *(RPR non-reactive)*	28.4 (20.8–37.5)	99.8 (99.2–99.9)	93.9 (80.4–98.3)	91.8 (89.9–93.4)	Not reported
Syphilis *(RPR, 1:1 to 1:4 dilutions)*	78.6 (71.3-84.5)	99.8 (99.2–99.9)	98.3 (93.9–99.5)	96.6 (95.2-97.6)	Not reported
Syphilis *(RPR ≥1:8 dilution)*	97.9 (95.1-99.1)	99.8 (99.2-99.9)	99.1 (96.9-99.8)	99.4 (98.7-99.8)	Not reported

PPV = positive predictive value, NPV = negative predictive value, FP = false positives
*False positive HIV results are more likely among populations with a low prevalence of HIV.
**Study population had a high baseline prevalence of positive syphilis serology. The proportion of false positives would likely be higher in sites with lower baseline prevalence.

Table 2: Performance Limitations of the INSTI Multiplex POC Test.

	Expected Window period*	Cases with potential for false positives:	Cases with potential for false negatives:
HIV	3-12 weeks	Rare false positives reported	Individuals on long-term antiretroviral therapy, with hypogammaglobulinemia, or elevated hemoglobin
Syphilis	Up to 12 weeks	May occur in patients with hepatitis A, B or C infections** [13]	Late-latent Infection (when RPR is very low or nonreactive) May occur in patients with hepatitis A, B or C infections [13]**

* Based on window periods of standard serologic tests.
** May occur although likely rare according to the product monograph (e.g., < 5% of serum samples from patients with Hepatitis A, Hepatitis B, and Hepatitis C infection yielded false positive results on the INSTI Multiplex POC test). Syphilis POC testing should still be offered to patients with a history of these infections, if indicated.

10.0 INTERPRETATION OF TEST RESULTS AND FOLLOW-UP

The figure on the next page provides guidance for the recommended uses, interpretation and follow up of syphilis and HIV test results obtained using the INSTI Multiplex POC test.

Prior to using the test, where possible and appropriate, offer and provide a comprehensive sexual health assessment that includes: a sexual health history, physical assessment, standard laboratory serological testing, and pre and post test discussions.

11.0 ADDITIONAL RESOURCES

Resources and information about POC testing for HIV can be found at the website of the BC Point of Care HIV Testing Program:

- http://www.bccdc.ca/our-services/programs/point-of-care-rapid-hiv-testing

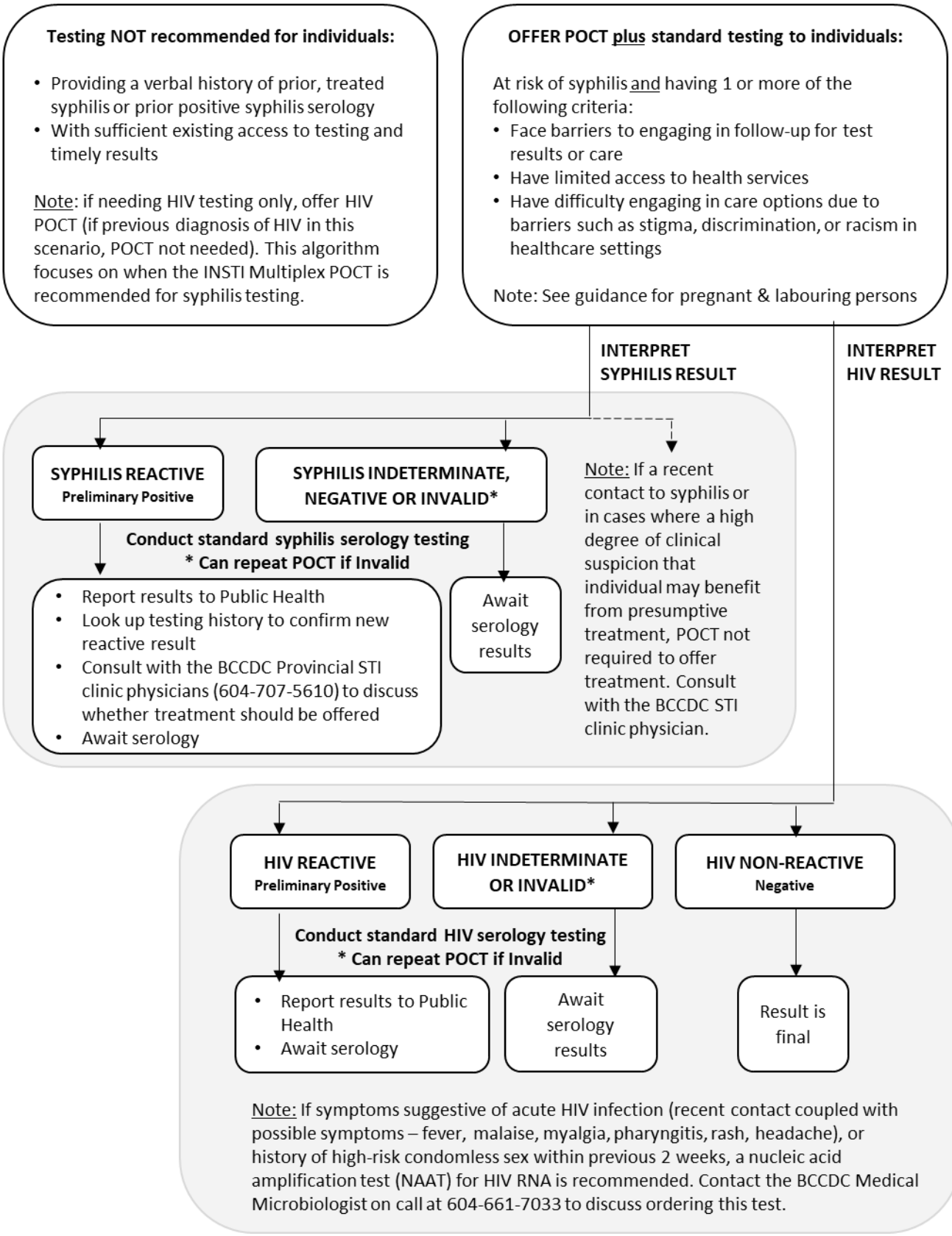
For the BC guideline to syphilis testing in pregnancy:

- https://www.psbchealthhub.ca/search?keyword=syphilis

For BC guidelines related to HIV testing, follow-up and prevention:

- http://www.bccdc.ca/resource-gallery/Documents/Communicable-Disease-Manual/Chapter%205%20-%20STI/HIV_Guidelines_Testing_FollowUp_Prevention.pdf

Figure: Interpretation of the INSTI Multiplex POC Test



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