



November 2022 Volume 2 Issue 11

**CADTH Horizon Scan** 

# Rapid Syphilis Testing



Authors: Michelle Clark, Aleksandra Grobelna

ISSN: 2563-6596

**Disclaimer:** The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up to date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein are those of CADTH and do not necessarily represent the views of Canada's federal, provincial, or territorial governments or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to Requests@CADTH.ca



## **Table of Contents**

Key Messages	5
Point-of-Care Tests Can Facilitate a Faster Syphilis Diagnosis Than Standard Lab Tests	5
How It Works	5
Who Might Benefit?	6
Availability in Canada	6
What Does It Cost?	7
Current Practice	8
What Is the Evidence?	8
Safety	8
Issues to Consider	8
User Perspectives	11
Related Developments	11
Looking Ahead	
References	



List of	Ta	bl	es
---------	----	----	----

LIST OF TABLES	
Table 1: Evaluation of Point-of-Care Diagnostic Test Accuracy for the Detection of Syphilis	9
List of Figures	
Figure 1: bioLytical INSTI Multiplex HIV-1/2 Syphilis Antibody Test	7



### **Key Messages**

- This Horizon Scan summarizes available information regarding rapid point-of-care testing for the detection of *Treponema pallidum*, the bacteria that causes syphilis.
- Rapid point-of-care testing to screen people for a possible case of syphilis allows health care providers to screen people where they are, rather than relying on people's access to traditional health care settings. The rapid provision of test results can also help to guide treatment in the moment, rather than requiring additional appointments that could increase the number of people with active syphilis infections lost to follow-up.
- There are currently no point-of-care syphilis tests licensed for use by Health Canada; however, at least 1 multiplex syphilis and HIV-1/HIV-2 detection test could be licensed for use in Canada by the end of 2022.
- Based on the evidence reviewed, rapid tests for the detection of syphilis appear to be adequately sensitive and specific for screening. The use of point-of-care testing, at-home self-testing, at-home sample collection methods, and telemedicine and virtual care options may be interventions to consider as health care systems move forward and work to catch up on the screening backlog and missed tests related to the COVID-19 pandemic, and also find ways to connect with people who have previously been harder to reach.

## Point-of-Care Tests Can Facilitate a Faster Syphilis Diagnosis Than Standard Lab Tests

Traditional lab tests used to diagnose syphilis can take weeks to provide a result. Point-of-care tests can provide the user with a result in less than 20 minutes, and may help to improve uptake because they can be administered in locations outside of traditional health care settings.

## **How It Works**

Syphilis infection is confirmed by the detection of antibodies. The presence of treponemal antigens can indicate a current or past infection, so tests for treponemal antigens alone cannot confirm a current infection.<sup>1</sup> A positive treponemal test is usually confirmed with a non-treponemal test.

Point-of-care tests for syphilis are visually interpreted, rapid vertical flow immunoassays that can be performed by health care providers using a fingerstick or IV blood sample.<sup>2</sup> They can test for syphilis alone, or may include multiplex testing for both syphilis and HIV-1 and HIV-2 antibodies. Some rapid tests can return results in as little as 1 minute.<sup>3</sup> Recently, in Canadian trials, rapid multiplex tests have been used to help curb the spread of outbreaks and provide immediate access to treatment.<sup>4</sup> Currently available point-of-care tests for syphilis are only able to test for the presence of treponemal antigens and do not have the ability to detect non-treponemal antigens. Therefore, these tests are designed to be used to screen a person for a potential current syphilis infection, but additional non-treponemal testing is required to confirm the diagnosis. In harder to reach populations, the initial screening test may be



the only time a health care provider gets to see the person being tested and, in some cases, treatment may be initiated before the diagnosis is confirmed if there are concerns that a person might not return to receive the results of the confirmatory diagnostic test.

## Who Might Benefit?

Syphilis is a curable sexually transmitted infection (STI) caused by the bacteria *Treponema pallidum*. Syphilis is the third most reported notifiable STI in Canada, following chlamydia and gonorrhea.<sup>5</sup> In 2020, the rate of infectious syphilis in Canada was 24.7 per 100,000 population, up from 5.1 per 100,000 in 2011.<sup>5</sup> Infection rates increased in almost all provinces, but the relative increase in the Prairie provinces was particularly large, increasing by more than 400%.<sup>5</sup> Infection rates are consistently higher for those who are male, but the female infection rate in Canada increased by 773% between 2016 and 2020.<sup>5</sup> Some have attributed the rise to changes in behaviour, such as increased substance use and the increasing use of dating apps, and the corresponding increased accessibility to multiple sexual partners.<sup>4</sup>

Persistent syphilis infection can cause long-term issues like heart, brain, and nerve damage in adults. Syphilis can be passed from a pregnant parent to their unborn child and cause complications like stillbirth, premature delivery, and disability in infants. Early syphilis infection can be treated with antibiotics. Syphilis can also increase a person's risk of becoming infected with HIV. Syphilis has a long latent phase of infection before symptoms begin to show, which makes it difficult to screen for and inhibits efforts to prevent transmission and reduce infection rates. People who tend to be the most likely to become infected with syphilis are also more likely to face barriers to seeking preventive health care and attending regular health screenings. National and international efforts are under way to reduce the global incidence of syphilis by up to 90% by 2030.

People face many barriers to accessing STI screening, including syphilis testing. These barriers may include access to reliable transportation, access to a phone or the internet to make an appointment, access to a primary care provider or sexual health clinic, or other pre-existing health issues like substance use disorders.<sup>4</sup> Traditional lab-based diagnostic testing for syphilis can take a week or longer to provide results to guide patient care. This delay can lead to further spread of syphilis by those with unknown infection and can also result in loss to follow-up for people who do not return to receive their test results or obtain treatment.<sup>4</sup> Point-of-care tests allow providers to test people where they are, whether that is at a usual medical appointment, sexual health clinic, emergency department, or outreach site, and provide a preliminary test result and treatment plan immediately.<sup>4</sup>

## Availability in Canada

The tests used in recent Canadian clinical studies, the Medmira Multiplo TP/HIV and bioLytical INSTI multiplex tests (refer to Figure 1), have not received Health Canada regulatory approval. bioLytical anticipates the INSTI® Multiplex HIV-1/2 Syphilis Antibody Test will receive a class IV medical device licence from Health Canada before the end of 2022. The Medmira Multiplo TP/HIV test and the Medmira Multiplo complete syphilis (TP/nTP) antibody



test tests have received a CE mark in Europe, but are not FDA approved.<sup>2</sup> The bioLytical INSTI multiplex test has received the CE mark for the HIV component (CE mark for syphilis by self-declaration), but is not currently FDA approved.<sup>3</sup>

There is 1 standalone point-of-care syphilis test available in the US, the Syphilis Health Check assay, and 1 multiplex assay, the DPP HIV Syphilis System, authorized for use by the FDA; however, these are not available for use in Canada.<sup>8</sup>

#### What Does It Cost?

The cost of the bioLytical INSTI Multiplex HIV-1/2 Syphilis Antibody Test is anticipated to be C\$24.99.7 There is potential for these point-of-care tests to reduce costs within the Canadian health care system by removing the need for lab-based tests for screening purposes. Lab tests could be reserved for confirmation of a positive point-of-care screening test, thereby reducing the costs of lab materials and human resources required for syphilis testing.

In an economic analysis, dual screening for HIV and syphilis was shown to be more cost-effective than single rapid tests for each when examining the costs of prevention and care related to pregnancy.<sup>9</sup>

Centrel

Syphilis

MULTIPLEX HIV-1/2 Syphilis Ab Test
Intended for single use determination of HIV-1 / HIV-2 /
syphilis antibodies in whole blood, serum or EDTA plasma.

Centents

1 Membrane Unit
1 Sample Bibuent
1 Sample Bibuent
1 Colour Developer

1 Clarifying Solution
1 Pipette
1 Lancet
200818

1 Instructions for Use
1 Instructions for Use
1 Lancet
200818

Store at 15 - 30°C
200 For a noto diagnostic use only.
City Consult Instructions for Use

WACKCOMMA
Not for donor screening.

Figure 1: bioLytical INSTI Multiplex HIV-1/2 Syphilis Antibody Test

Source: Reprinted with permission from Stephanie Ritchie, bioLytical Laboratories Inc.



#### **Current Practice**

In Canada, there are 2 blood test screening algorithms used to diagnose syphilis. Most provinces use the reverse algorithm, which uses a treponemal test to screen for infection by detecting treponemal antibodies in the blood sample; and a quantitative non-treponemal test, typically a rapid plasma reagin (RPR) test, to detect non- treponemal antibodies and confirm positive treponemal test results. Treponemal tests will typically show a positive result for life once a person has had syphilis, regardless of treatment, which can lead to false-positive test results and means a positive treponemal test result should be confirmed with a non-treponemal test to accurately diagnose an active, untreated case of syphilis. These tests require time to complete and a patient will be tested, diagnosed, and treated across a number of appointments.

Although there may be circumstances in which the benefit of treponemal tests alone for diagnosis (instead of screening) may outweigh the risk of overtreatment, WHO recommends that all positive point-of-care tests for syphilis be confirmed using a standard laboratory test.<sup>1</sup>

#### What Is the Evidence?

As demonstrated in a variety of controlled lab evaluation studies <sup>12-14</sup> field evaluations, <sup>15,16</sup> and systematic reviews and meta-analyses, <sup>9,17,18</sup> rapid tests for the detection of syphilis appear to be adequately sensitive and specific for screening. A summary of diagnostic accuracy for a variety of point-of-care syphilis and syphilis/HIV multiplex tests is provided in <u>Table 1</u>. The current commercially available tests are only able to detect treponemal antibodies and cannot distinguish between an active and a prior treated syphilis infection. Positive results therefore require confirmation with a non-treponemal lab test to diagnose a current case of syphilis.

## Safety

No information was identified regarding safety issues related to the use of rapid, point-of-care syphilis testing.

## **Issues to Consider**

People with a suspected case of syphilis through point-of-care testing will still require follow-up with a health care provider to receive their confirmatory diagnostic tests results and complete treatment. The implementation of point-of-care testing for syphilis can help to reduce the time to diagnosis and also reduce the number of patients lost to follow-up by allowing health care providers to initiate treatment based on the person's screening test result rather than waiting weeks to receive the confirmation of diagnosis to begin treatment.



Table 1: Evaluation of Point-of-Care Diagnostic Test Accuracy for the Detection of Syphilis

Test name	Study setting	Number of samples or participants	Overall sensitivity (95% CI)	Overall specificity (95% CI)
restrianc		sang et al. (2022) <sup>12</sup> (lab stu	, ,	(30% 61)
Reveal Rapid TP Antibody Test	Controlled lab and samples with known serological status	Sensitivity = 40 samples Specificity = 100 samples	95.0%	83.3%
DPP Syphilis Screen and Confirm Test	Controlled lab and samples with known serological status	Sensitivity = 40 samples Specificity = 100 samples	87.5%	98.3%
	Angel	-Miller et al. (2021)19 (SR a	nd MA)	
ACON Syphilis Test	Field conditions (1 study)	1,439 participants	1.00 (0.74 to 1.00)	0.99 (0.98 to 0.99)
SD Bioline HIV/Syphilis DuoTest	Field conditions (1 study)	401 participants	0.92 (0.78 to 0.98)	0.93 (0.90 to 0.96)
Determine Test	Field conditions (1 study)	198 participants	0.97 (0.83 to 1.00)	1.00 (0.98 to 1.00)
ICS Test	Field conditions (1 study)	684 participants	0.94 (0.89 to 0.98)	0.93 (0.90 to 0.95)
Qualpro Syphicheck- WB	Field conditions (1 study)	1,617 participants	0.71 (0.62 to 0.79)	0.98 (0.97 to 0.98)
Syphilis Health Check	Field conditions (3 studies)	3,008 participants	0.87 (0.80 to 0.92) 0.75 (0.59 to 0.87) 0.77 (0.46 to 0.95)	0.93 (0.91 to 0.95) 0.95 (0.94 to 0.96) 0.99 (0.98 to 0.99)
SD Bioline Test	Field conditions (2 studies)	1,649 participants	0.67 (0.52 to 0.79) 0.92 (0.62 to 100.0)	0.98 (0.95 to 0.99) 0.99 (0.98 to 0.99)
Serodia	Field conditions (1 study)	198 participants	0.87 (0.70 to 0.96)	1.00 (0.98 to 1.00)
Visitect Syphilis Test	Field conditions (1 study)	506 participants	0.79 (0.63 to 0.90)	1.00 (0.99 to 1.00)
Bristow et al. (2020) <sup>18</sup> (SR and MA)				
Syphilis Health Check	Controlled lab studies (5 studies)	NR	98.5% (92.1 to 100)	95.9% (81.5 to 100)
Syphilis Health Check	Prospective studies (10 studies)	NR	87.7% (71.8 to 97.2)	96.7% (91.9 to 99.2)



Test name	Study setting	Number of samples or participants	Overall sensitivity (95% CI)	Overall specificity (95% CI)
Stafylis et at. (2019) <sup>15</sup> (field evaluation)				
INSTI Multiplex HIV-1/ HIV-1/Syphilis Antibody Test	4 outpatient clinics of the AIDS Health Foundation	274 participants	56.8 (44.7 to 68.2)	98.5 (95.7 to 99.7)
	Van Den I	Heuvel et al. (2019)13 (lab e	valuation)	
SD Bioline HIV/Syphilis Duo	Controlled lab and WHO specimen reference panel	400 specimens	100 (98.2 to 100)	99.5 (97.2 to 100)
DPP HIV/Syphilis Assay	Controlled lab and WHO specimen reference panel	400 specimens	100 (98.2 to 100)	96.0 (92.3 to 98.3)
Muliplo Rapid TP/HIV Antibody Test	Controlled lab and WHO specimen reference panel	400 specimens	99.5 (97.2 to 100)	99.5 (97.2 to 100)
INSTI Multiplex HIV-1/ HIV-1/Syphilis Antibody Test	Controlled lab and WHO specimen reference panel	400 specimens	99.5 (97.2 to 100)	88.0 (89.1 to 96.5)
	Obafer	ni et al. (2019)16 (field eval	uation)	
Syphilis Health Check	6 outreach sites	690 MSM with no prior history of syphilis	90.0 (55.5 to 99.5)	98.5 (97.3 to 99.3)
	Pere	ira et al (2018)14 (lab evalua	ation)	
Syphilis Health Check	Controlled lab and samples with known serological status compared with treponemal tests alone	1,406 archived human serum samples	88.7 (86.2 to 90.0)	93.1 (90.0 to 94.9)
Syphilis Health Check	Controlled lab and samples with known serological status compared with lab test panel consensus	1,406 archived human serum samples	95.7 (93.6 to 97.2)	93.2 (91.0 to 95.1)
Gliddon et al. (2017) <sup>9</sup> (SR and MA)				
SD BIOLINE HIV/ Syphilis Duo Test	Manufacturer's studies (syphilis component only)	NR	89% to 100%	91% to 100%
MedMira Multiplo Rapid TP/HIV Antibody Test	Manufacturer's studies (syphilis component only)	NR	81% to 95%	93% to 100%
Chembio DPP HIV/ Syphilis Assay	Manufacturer's studies (syphilis component only)	NR	46% to 97%	100%



Test name	Study setting	Number of samples or participants	Overall sensitivity (95% CI)	Overall specificity (95% CI)
Chembio DPP HIV/ Syphilis Assay	Lab setting	NR	93% to 100%	NR
Chembio DPP HIV/ Syphilis Assay	Field settings	NR	91% to 100%	NR

CI = confidence interval; DPP = dual path platform; ICS = immunochromatographic strip; MA = meta-analysis; MSM = men who have sex with men; NR = not reported; SR = systematic review; TP = treponemal.

## **User Perspectives**

Qualitative evaluations of the use of rapid tests for the detection of syphilis, and particularly dual tests with HIV detection, found that users were generally positive about their experience with the tests. The short time to receive the results and the need for a single finger prick sample to run both tests were important characteristics that users liked. Rapid tests used in settings outside of traditional medical care settings, like mobile outreach programs, provided a discrete, easy to access, and effective way for people to be screened. Users in 1 study indicated that they would be more likely to be tested regularly if a mobile clinic continued to be offered.

## **Related Developments**

Following the most recent Canadian trials of the combined syphilis and HIV-1/HIV-2 tests, further trials are ongoing in Saskatchewan.<sup>4</sup> The trial will start at clinics and pharmacies in Regina, and will potentially expand to include Indigenous communities.<sup>4</sup> bioLytical is working toward introducing a self-test version of the INSTI Multiplex HIV-1/2 Syphilis Antibody Test in the first quarter of 2023.<sup>7</sup>The Stopping Syphilis Transmission in Arctic Communities Through Rapid Diagnostic Testing (STAR) study began in January 2020 and will continue through the end of 2022.<sup>21</sup> Its aim is to evaluate the clinical and epidemiological impact of using the Chembio DPP Syphilis Screen and Confirm Test, a rapid test that can detect both treponemal and non-treponemal antibodies and provide a confirmed diagnosis at the point of care, in the context of ongoing transmission in Nunavut and Nunavik.<sup>21</sup> The test is not currently available for use in Canada and was obtained for use in the study through Health Canada's Special Access Program.

In the US, individuals can purchase kits for syphilis testing with at-home sample collection. The tests do not provide the user with rapid results, but facilitate the user to collect their own fingerprint blood sample that is then sent by mail to a lab for processing. The results are usually returned within 7 business days. Some, but not all, of these at-home test kits include follow-up advice from a medical professional upon receipt of the results. The use of these sorts of tests may increase access for some, but their use requires the ability to pay out of pocket for the point-of-care kits, and internet access to be able to order them. Despite the availability of these tests to the individual, none of these tests have FDA authorization for at-home use. These tests cost between US\$29 and US\$78.

Clinical trials are ongoing in China evaluating the use of a rapid saliva-based molecular detection test for syphilis.<sup>23</sup> Researchers have identified high levels of *T. pallidum* DNA in



saliva samples of people diagnosed with laboratory-confirmed syphilis.  $^{24}$  Saliva samples are collected in convenient and non-invasive ways and their use in testing could help to increase acceptability and ease of use.  $^{24}$ 

## **Looking Ahead**

The service restrictions related to the COVID-19 pandemic resulted in a decrease in routine screening procedures and uptake of voluntary STI testing and screening.<sup>25</sup> This decreased uptake has highlighted the potential for increasing testing and screening outside of traditional clinical settings and using alternative testing and sample collection methods.<sup>25</sup> The use of point-of-care testing, at-home self-testing, at-home sample collection methods, and telemedicine and virtual care options may be interventions to consider as health care systems move forward and work to catch up on the screening backlog and missed tests, and also find ways to connect with people who have previously been harder to reach.<sup>25</sup>



#### References

- 1. Naidu P, Tsang RSW. Canadian Public Health Laboratory Network guidelines for the use of point-of-care tests for Treponema pallidum in Canada. *Jammi.* 2022;7(2):85-96.
- 2. Medmira. MultiPlo rapid TP/HIV test. 2020; https://medmira.com/multiplex/. Accessed 2022 Sep 19.
- 3. INSTI Multiplex HIV-1 / HIV-2 / syphilis antibody test. [2022]; https://www.insti.com/multiplex-test/. Accessed 2022 Sep 19.
- 4. Wong J. New rapid test for syphilis can give patients immediate access to treatment, Alberta doctors say. 2022; <a href="https://www.cbc.ca/news/canada/edmonton/rapid-syphilis-testing-1.6461167">https://www.cbc.ca/news/canada/edmonton/rapid-syphilis-testing-1.6461167</a>. Accessed 2022 Sep 19.
- 5. Aho J, Lybeck C, Tetteh A, et al. Rising syphilis rates in Canada, 2011-2020. Can Commun Dis Rep. 2022;48(23):52-60. https://www.ncbi.nlm.nih.gov/pubmed/35341093. Accessed 2022 Sep 20. PubMed
- 6. Epidemiological review of syphilis in the Americas. Washington, D.C.: Pan American Health Organization; 2021: <a href="https://iris.paho.org/bitstream/handle/10665.2/56085/PAHOCDEHT220009\_eng.pdf?sequence=1&isAllowed=v">https://iris.paho.org/bitstream/handle/10665.2/56085/PAHOCDEHT220009\_eng.pdf?sequence=1&isAllowed=v</a>. Accessed 2022 Sep 20.
- 7. Ritchie S. Personal communication. Richmond (BC): bioLytical Laboratories Inc.; 2022 Sep 28.
- Adamson PC, Loeffelholz MJ, Klausner JD. Point-of-care testing for sexually transmitted infections: a review of recent developments. Arch Pathol Lab Med. 2020;144(11):1344-1351. <u>PubMed</u>
- 9. Gliddon HD, Peeling RW, Kamb ML, Toskin I, Wi TE, Taylor MM. A systematic review and meta-analysis of studies evaluating the performance and operational characteristics of dual point-of-care tests for HIV and syphilis. Sex Transm Infect. 2017;93(S4):S3-S15. PubMed
- 10. Public Health Agency of Canada. Syphilis guide: screening and diagnostic testing. 2022; <a href="https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis/screening-diagnostic-testing.html">https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/syphilis/screening-diagnostic-testing.html</a>. Accessed 2022 Sep 20.
- 11. Levett PN, Fonseca K, Tsang RS, et al. Canadian Public Health Laboratory Network laboratory guidelines for the use of serological tests (excluding point-of-care tests) for the diagnosis of syphilis in Canada. Can J Infect Dis Med Microbiol. 2015;26 Suppl A:6A-12A.
- 12. Tsang RS, Shuel M, Hayden K, Van Caeseele P, Stein D. Laboratory evaluation of two point-of-care test kits for the identification of infectious syphilis. *Can Commun Dis Rep.* 2022;48(2-3):82-88. PubMed
- 13. Van Den Heuvel A, Smet H, Prat I, et al. Laboratory evaluation of four HIV/syphilis rapid diagnostic tests. BMC Infect Dis. 2019;19(1):1. PubMed
- 14. Pereira LE, McCormick J, Dorji T, et al. Laboratory evaluation of a commercially available rapid syphilis test. J Clin Microbiol. 2018;56(10):10. PubMed
- 15. Stafylis C, Bristow CC, Natoli LJ, et al. Field evaluation of a dual rapid human immunodeficiency virus and treponemal syphilis rapid test in community-based clinics in Los Angeles and New York. Diagn Microbiol Infect Dis. 2019;93(4):325-328. PubMed
- 16. Obafemi OA, Wendel KA, Anderson TS, et al. Rapid syphilis testing for men who have sex with men in outreach settings: evaluation of test performance and impact on time to treatment. Sex Transm Dis. 2019;46(3):191-195. PubMed
- 17. Angel-Muller E, Grillo-Ardila CF, Amaya-Guio J, Torres-Montanez N. Diagnostic accuracy of rapid point-of-care tests for detecting active syphilis: a systematic review and meta-analysis. Sex Transm Dis. 2021;48(12):e202-e208. PubMed
- 18. Bristow CC, Klausner JD, Tran A. Clinical test performance of a rapid point-of-care syphilis treponemal antibody test: a systematic review and meta-analysis. Clin Infect Dis. 2020;71(Suppl 1):S52-S57. PubMed
- 19. Angel-Muller E, Grillo-Ardila CF, Amaya-Guio J, Torres-Montanez NA, Vasquez-Velez LF. Point of care rapid test for diagnosis of syphilis infection in men and nonpregnant women. *Cochrane Database Syst Rev.* 2018;2018(5) (no pagination).
- 20. Mullens AB, Duyker J, Brownlow C, Lemoire J, Daken K, Gow J. Point-of-care testing (POCT) for HIV/STI targeting MSM in regional Australia at community 'beat' locations. BMC Health Serv Res. 2019;19(1):93. PubMed
- 21. Caya C, Maheu-Giroux M, Xia Y, et al. Stopping syphilis transmission in Arctic communities through rapid diagnostic testing: the STAR study protocol. *PLoS ONE* [Electronic Resource]. 2022;17(9):e0273713. PubMed
- 22. Medical News Today. 5 of the best at-home syphilis tests of 2022. 2022; <a href="https://www.medicalnewstoday.com/articles/home-syphilis-tests">https://www.medicalnewstoday.com/articles/home-syphilis-tests</a>. Accessed 2022 Sep 19.
- 23. Shanghai Skin Disease Hospital. ChiCTR2100046329: Establishment and evaluation of a new rapid saliva-based molecular detection method used for screening of syphilis. Chinese Clinical Trial Registry; 2021: <a href="http://www.chictr.org.cn/showproj.aspx?proj=126580">http://www.chictr.org.cn/showproj.aspx?proj=126580</a>. Accessed 2022 Sep 21.
- Wang C, Hu Z, Zheng X, et al. A new specimen for syphilis diagnosis: evidence by high loads of treponema pallidum DNA in saliva. Clin Infect Dis. 2021;73(9):e3250-e3258. <a href="https://www.ncbi.nlm.nih.gov/pubmed/33099614">https://www.ncbi.nlm.nih.gov/pubmed/33099614</a>. Accessed 2022 Sep 21. <a href="https://www.ncbi.nlm.nih.gov/pubmed/33099614">PubMed</a>
- 25. Kersh EN, Shukla M, Raphael BH, Habel M, Park I. At-home specimen self-collection and self-testing for sexually transmitted infection screening demand accelerated by the COVID-19 pandemic: a review of laboratory implementation issues. *J Clin Microbiol.* 2021;59(11):e0264620. PubMed