

Sexually Transmitted Infections – Patient Testing at the Point of Care

White_paper – As at 04/2023 – Art. No. MDQ-01.733-01-LoC-126



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Sexually transmitted infections (STIs) transmitted through sexual contact can be caused by more than 30 pathogens, which, according to World Health Organization (WHO) estimates, cause one million infections worldwide every day, and the rate is increasing.¹ Countries with STI surveillance programs such as the United States and Canada have also recently reported to WHO an increase in at least 3 STIs: syphilis, gonorrhea, and chlamydia. Since not all infections display immediate symptoms, they often go undetected. However, both symptomatic and asymptomatic infections can lead to serious health problems with a negative impact on sexual health. Women are disproportionately affected by STIs and often experience complications including infertility and chronic pelvic pain that can have lifelong impacts. STIs can lead to fatal consequences in pregnancy e.g., ectopic pregnancy, peripartum morbidity and mortality.²

In case symptoms occur, they may be very similar or overlap for several pathogens, making clinical diagnosis and appropriate therapy difficult. Therefore, sexually transmitted infections (STIs) are considered a serious public health issue worldwide. The 2022–2030 global health sector strategies on sexually transmitted infections of the WHO show a global awareness for the existing problem paired with recommendations for several measures with the aim of ending the health care issue of STIs by 2030. One of the recommended measures is to establish integrated testing as a key element for people-centered health services with multiplex testing and point of care testing playing a crucial role in the concept.⁴ Unfortunately, the WHO call for action is not yet sufficiently implemented on the regional or national level. Initiatives for better access to STI testing such as the bi-annual European testing week³ are a step in the right direction, but such events are still rare.

Due to the high risk of transmission of STIs, a PCR test result at the point of care (POC) would be of enormous benefit both in diagnosing and improving the containment of STIs. Since infections are often asymptomatic and co-infections with multiple STI pathogens can occur, the possibility of testing multiple pathogens simultaneously would be advantageous, allowing the immediate detection of several pathogens with just a single patient sample e.g., swab or urine.

Such a rapid POC PCR test detecting several sexually transmitted pathogens with one patient sample has further advantages both for the patient and the clinician: Usually, PCR tests are performed by specialized laboratories with the need to transport the patient sample to the laboratory. Hence, it takes several days before the results are available and the clinician can start appropriate treatment. Depending on the POC test used, clear and easy-to-interpret PCR results can be obtained within one hour. Rapid PCR tests capable of detecting several pathogens simultaneously have the enormous advantage that an immediate test result for several pathogens allows the physician to start with the appropriate treatment straight away. Besides the positive effect of immediate treatment this approach also helps to break the chain of infection.

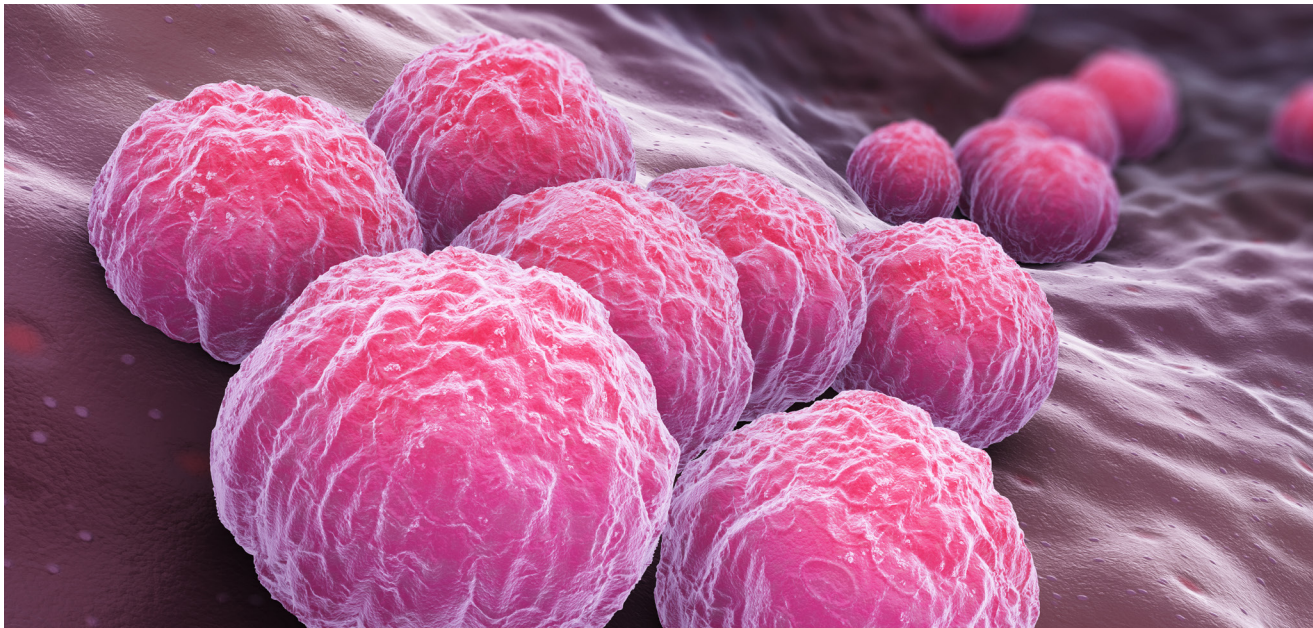
With the Vivalytic test portfolio for detecting STIs, Bosch currently offers two STI test systems: Vivalytic STI and Vivalytic MG, MH, UP/UU. Vivalytic STI is one of the few rapid PCR tests for use at the POC which can detect up to ten different sexually transmitted pathogens in a single test run with no further need to use a stepwise diagnostic approach, with results available after 2.5 hours. If targeted testing for mycoplasmas and/or ureaplasmas is indicated, with Vivalytic MG, MH, UP/UU, a PCR result is already available after about one hour. Bosch is dedicated to adding more tests to its Vivalytic STI test portfolio in the future.

The epidemiology of STIs

The WHO currently estimates about 374 million new infections with 1 of 4 most common curable STIs chlamydia, gonorrhea, syphilis, and trichomoniasis each year.⁴ Compared to other regions worldwide, the prevalence and incidence of the four most common curable STIs in the European Region are among the lowest. Nevertheless, surveillance data of the EU from 2018 reflect WHO estimates and show that, despite a significant variation in testing and notification of cases between countries, chlamydia is the most frequently reported STI in Europe (406,406 cases) followed by gonorrhea (100,673 cases) and syphilis (33,927 cases).⁵

However, in some EU countries no regulated reporting to authorities exists, hence the data basis can be considered weak. In countries with comprehensive STI screening programs for chlamydia, such as Denmark, the prevalence is up to four times higher than the European average: The EU average is 146 cases per 100,000 inhabitants compared to Denmark with 578 cases per 100,000 inhabitants.

This can be seen even more clearly regarding chlamydia cases detected in the United Kingdom. Here, a comprehensive screening program targeting 15–24-year-olds has been in place since 2008, so that chlamydia cases reported from the UK in 2019 accounted for 60% of the total cases reported in the European Region.⁶ The actual infection rate in countries without systematic screening are likely to be much higher than reflected by the official figures.



In contrast to the presumably underestimated incidences of STIs in the European Region, an increase of officially confirmed STIs is well documented. Among the 27 European countries which reported data between 2010 and 2019, reported cases of gonorrhea more than doubled for both sexes since 2010.⁷ A similar trend can also be seen for syphilis cases reported between 2010 and 2019 in the European Region. In this case, the number of cases almost doubled among those aged 35-44 years and 25-34 years, with the numbers for men were nine times higher than for women.⁸

Gaps in the current strategy: Elaborate campaigns but inadequate testing services

The growing concern regarding STIs has been recognized throughout Europe. As part of its response, the European Centre for Disease Prevention (ECDC) regularly publishes updates on the current status of STIs at the European level and places a special focus on the importance of testing for STIs with its recent report from 2021 titled “Technologies, strategies and approaches for testing populations at risk of sexually transmitted infections in the EU/EEA”.⁵

Whereas in various European countries different screening programs for chlamydia are in place, easily accessible testing or screening options for other STI pathogens are usually not available.

The lack of easily accessible testing options in combination with the fact that infections are often asymptomatic further enhances the risk of the spread of STIs and prevents effective containment of STIs. For example, about 70 percent of women and about 50 percent of men experience no symptoms when infected with chlamydia.⁹

Therefore, it is important to counter the spread of STIs with prevention campaigns and, if possible, to accompany prevention campaigns with low-threshold testing opportunities. Hence, knowledge can be followed by action in the form of testing. The screening program for chlamydia testing in UK initiated in 2008 highlights the benefits of such efforts. The program offering community-based testing services outside of clinics for sexually transmitted infections resulted in a large increase in chlamydia diagnoses from 2008 onwards, dramatically reducing the estimated number of unreported cases.⁶



Infection and co-infections of STIs: Differential diagnosis required

Co-infections, defined as a simultaneous infection with more than one sexually transmitted pathogen, may occur and most likely be missed since testing very often does not include several sexually transmitted pathogens at once. In addition, if the patient has symptoms they cannot always be distinguished easily by the physician since different pathogens can cause similar or overlapping symptoms. Nevertheless, the majority of STIs, even in high-risk groups, is caused by one sexually transmitted pathogen.¹⁰

Where co-infections need to be detected, a rapid, accurate and comprehensive differential diagnosis of sexually transmitted pathogens can be considered crucial to be able to immediately start an appropriate therapy.

Not to be underestimated: rapid results at the point of care

Due to the high transmission rate, rapid detection and treatment of STIs is important to minimize the further spread of STIs. Performing STI diagnostics in a specialized laboratory usually involves a delay of up to several days until the test results are available to the physician. The delay is due to several reasons: Transport of a patient sample to the laboratory takes time, analysis in the laboratory depends on the workflow, test result must be transferred to the clinician. After that, another appointment must take place to discuss both test result and treatment options with the patient. Hence, the delay will take days or up to 1-2 weeks until appropriate treatment of the patient, and if necessary, of their sexual partner can be started. Patient compliance often decreases in such a setting, and the second appointment may not be kept.

With the Vivalytic STI test, results are available directly at the POC in less than two and a half hours from sample collection to result. Transport of samples to a central laboratory is eliminated. The patient can receive the test result on the day of the visit and appropriate treatment can be initiated.

PCR diagnostics at the point of care: direct path to accurate results

Tests for sexually transmitted pathogens are normally performed in a specialized laboratory, nowadays mostly using PCR technology (NAAT*). POC testing was often considered minor to laboratory-based testing due to its lower sensitivity. Rapid PCR tests for the POC combine the high sensitivity of laboratory-based tests with the speed and ease of use of rapid tests, allowing for simultaneous testing of multiple pathogens.

POC tests using rapid PCR technologies are becoming increasingly popular due to their various advantages and are now also perceived as new innovative testing technologies in the European Region.⁵ In Germany, experts from different associations (RKI, DSTIG, PEI and reference laboratories) also published a statement in 2020 with a special focus on rapid diagnosis of STIs, recommending rapid PCR testing if available in most settings.¹¹ Decentralized testing opportunities, rapid and precise diagnosis followed by an immediate start of targeted treatment are amongst the most important advantages of POC PCR testing.

* Nucleic Acid Amplification Technology

Multiplex STI tests: advantages

Multiplex STI tests can detect co-infections with a single test, identifying sexually transmitted pathogens that would otherwise have been missed. Depending on the number of pathogens detected with the test system, up to ten sexually transmitted pathogens can be detected with only one sample. If detection of co-infections is combined with the option to use a test at the POC, for example with the Vivalytic STI test from Bosch, several steps of a traditional stepwise approach are combined in one test. Hence the Vivalytic test result supports an early diagnosis and fast initiation of the appropriate treatment.

This significantly increases the efficiency of the diagnosis both for the patient and the clinician: Follow-up appointments for further diagnosis can be greatly reduced, saving time, health care costs, and most importantly enhancing the containment of the spread of STIs.

Decentralized testing for co-infections with only one sample of populations at high-risk of STIs but with no or limited access to the healthcare system further emphasizes the huge advantage of POC testing with a multiplex STI test.

Gynecology (hospitals and practitioners)

Women are disproportionately affected by STIs throughout life. Although STIs mostly remain asymptomatic and therefore are usually not detected, women often experience complications from STIs, including infertility and chronic pelvic pain, that can have a lifelong impact. Since STIs can increase peripartum morbidity and mortality both in industrialized areas and in rural and underserved areas of developed countries, women are directly affected if serious consequences for their unborn child occur.²

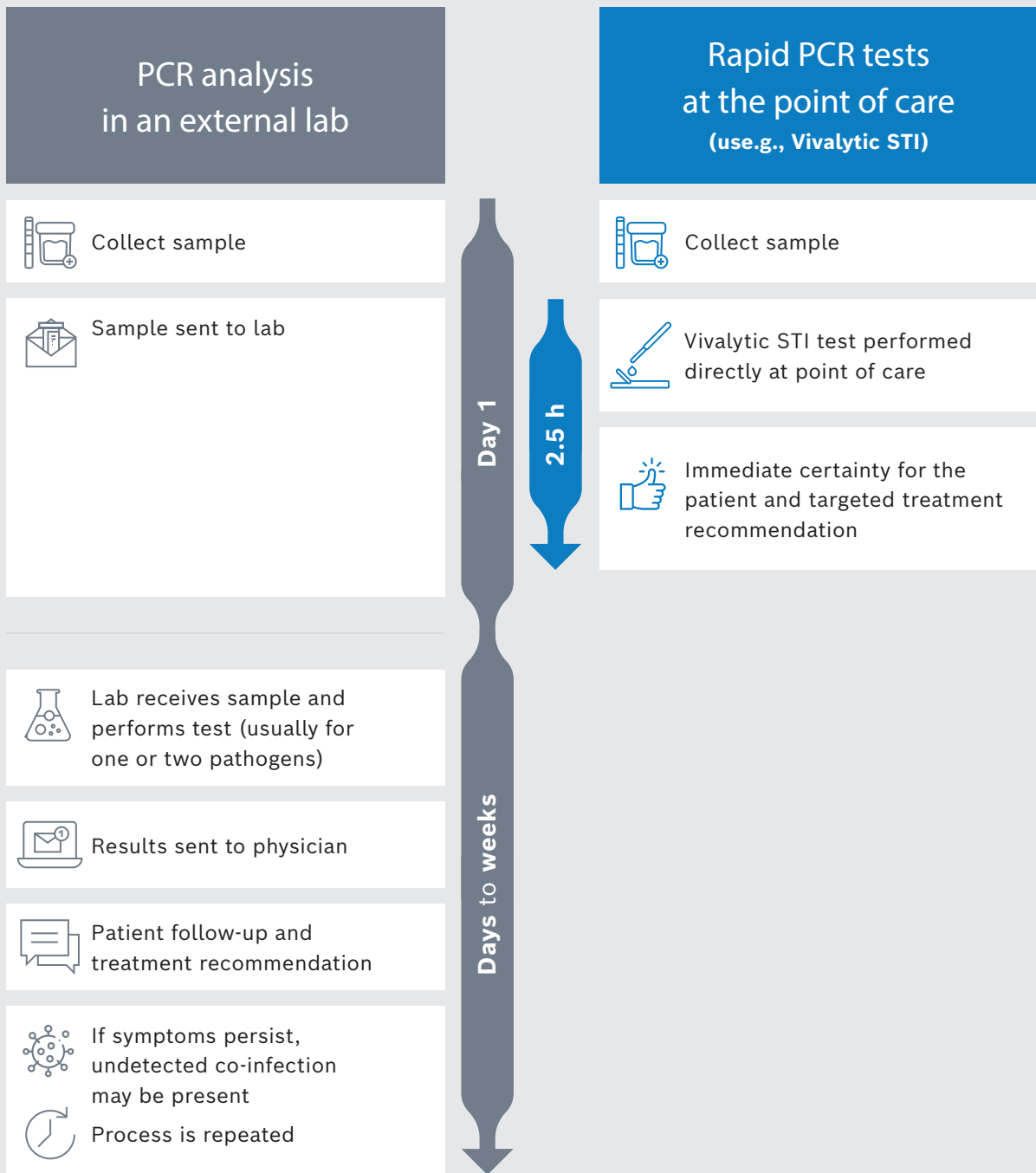
Congenital syphilis poses the biggest threat and can only be eliminated if mother-to-child transmission of syphilis during pregnancy is prevented. The WHO aims at eliminating congenital syphilis by 2030. Unfortunately, the WHO currently estimates that nearly one million pregnant women worldwide were infected with syphilis in 2016, resulting in over 350,000 adverse birth outcomes³ including 143,000 early fetal deaths and stillbirths, 61,000 neonatal deaths and 41,000 preterm or low-birth-weight births in 2016.¹²

Infertility and adverse birth outcomes can only be prevented if screening programs are in place and if pregnant women are routinely screened for the presence of sexually transmitted pathogens that could be dangerous for the unborn child or neonate. In most countries, currently only screening programs for chlamydia of women <25 years do exist.

Fertility clinics

An unfulfilled desire to have children may be due to male or female infertility. In the United States, among married women aged 15 to 49 years with no prior births, about 1 in 5 (19%) are unable to get pregnant after one year of trying.¹³ Since STIs are often asymptomatic but nonetheless are the leading cause of tubal factor infertility in women¹⁴, screening programs for women <25 years to test, for example, for chlamydia are in place in many countries worldwide.

Testing for STI pathogens can be helpful in finding the cause of an unfilled wish to have children. Narrowing down the diverse causes of an unfulfilled desire to have children can provide clarity for couples and help them to find the right decision for their family planning.



Advantages: Rapid PCR tests at the point of care

Rapid results

- + Rapid certainty for the patient
- + Immediate start of treatment
- + Rapid interruption of infection chains

Rapid results of co-infections with Vivalytic STI

- + Certainty for the patient regarding co-infections
- + Targeted treatment tailored to detected pathogens

Urology (hospitals and practitioners)

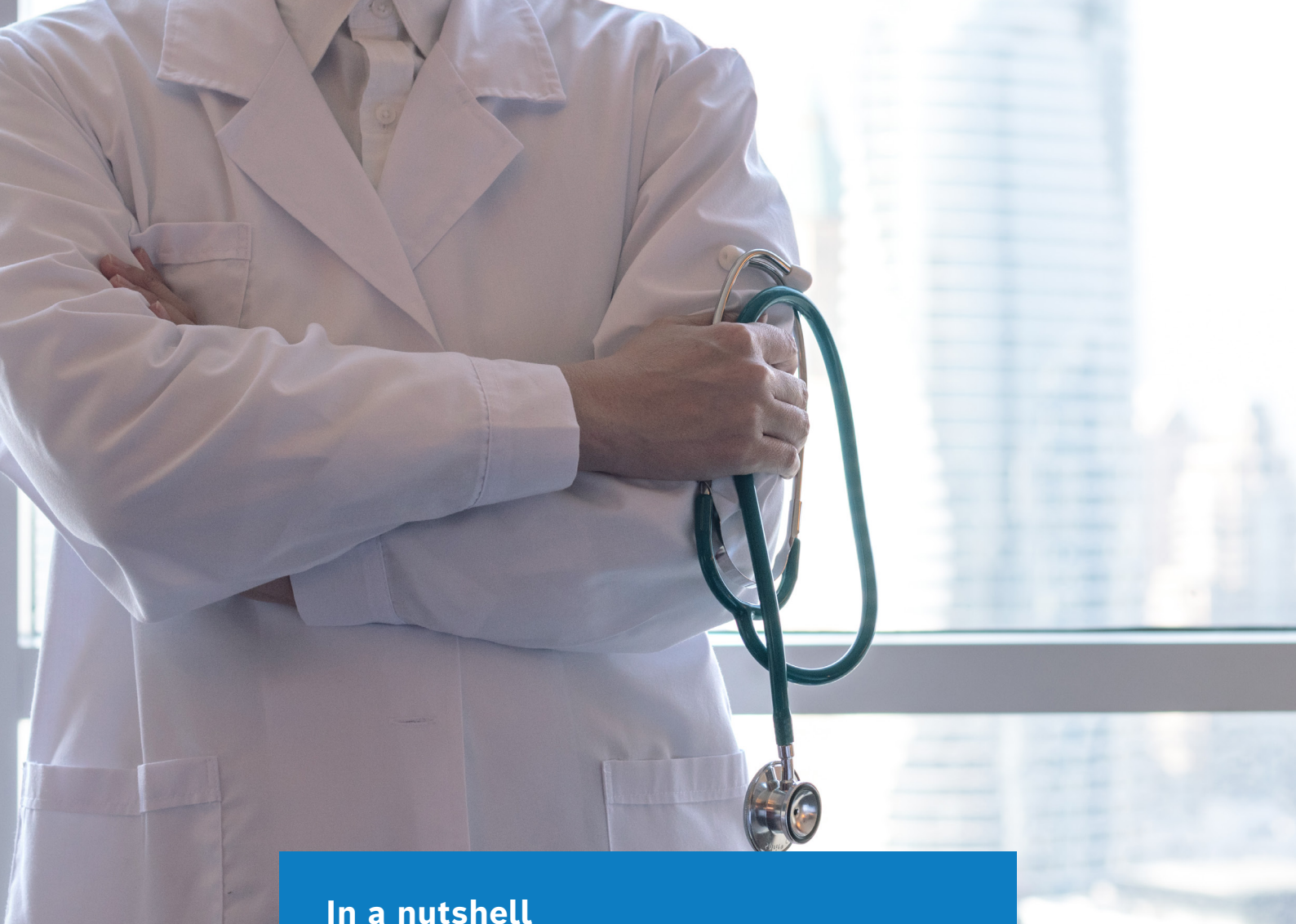
Infections of the urogenital tract may be caused by sexually transmitted pathogens. Urethritis for example can be either of infectious or non-infectious origin. Inflammation of the urethra presents usually with lower urinary tract symptoms and must be distinguished from other infections of the lower urinary tract. From a therapeutic and clinical point of view, gonorrheal urethritis (GU) caused by *N. gonorrhoeae* must be differentiated from non-gonococcal urethritis (NGU) whereas non-gonococcal urethritis must be considered a non-specific diagnosis. Causative pathogens include *C. trachomatis*, *M. genitalium*, *U. urealyticum*, and *T. vaginalis*. Other diseases potentially involving STIs are epididymitis and bacterial prostatitis.¹⁵

The above-mentioned sometimes painful diseases easily explain why testing for sexually transmitted pathogens is performed in urology in addition to the diagnosis of obvious skin symptoms where visible.

Dermatology (hospitals and practitioners)

If symptomatic, patients suffering from a sexually transmitted infection, often show symptoms involving the skin. Hence, it is not surprising that some patients visit a dermatologist if symptoms are visible on the skin. Therefore, incorporating rapid PCR testing options might be beneficial both for the patient and the dermatologist.

Historically, dermatologists have played a key role in the diagnosis and treatment of STIs, which can be traced back to the 1930s when for example the present American Board of Dermatology was originally founded as the “American Board of Dermatology and Syphilology”.¹⁶



In a nutshell

There are many reasons why sexually transmitted infections spread. Most STIs are asymptomatic, leading to a high number of unrecorded and untreated cases with a potentially fatal outcome depending on the sexually transmitted pathogen. In addition to widespread awareness, a decentralized low-threshold testing strategy can make an important contribution to reducing the number of infections, especially for high-risk groups. If testing is performed speed as well as comprehensive testing of the relevant pathogens are important factors to improve the targeted therapy as well as the containment of the respective STI. Rapid PCR tests for use at the POC are new technologies and are gaining importance due to various advantages: On the one hand the patient receives the result on the same day and gets the appropriate treatment immediately. Hence, the patient gets clarity with just one visit. On the other hand, the clinician can give their patient the best up to date diagnosis and treatment and this can also happen in a decentralized setting for patients at high-risk with no or limited access to the healthcare system as well as in a hospital setting.

- ¹ [https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-\(stis\);](https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis);) retrieved on March 30, 2023
- ² Van Gerwen OT, Muzny CA, Marrazzo JM. Sexually transmitted infections and female reproductive health. *Nat Microbiol.* 2022 Aug;7(8):1116-1126. Doi: 10.1038/s41564-022-01177-x. Epub 2022 Aug 2. PMID: 35918418; PMCID: PMC9362696.
- ³ <https://www.testingweek.eu/about-european-testing-week/;> retrieved on March 30, 2023
- ⁴ Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030. Geneva: World Health Organization; 2022. Licence: CC BY-NC-SA 3.0 IGO
- ⁵ European Centre for Disease Prevention and Control. Technical Report: Technologies, strategies and approaches for testing populations at risk of sexually transmitted infections in the EU/EEA. Stockholm: ECDC March 2021
- ⁶ ECDC Surveillance Report Chlamydia Infection, Annual Epidemiological Report for 2019
- ⁷ ECDC Surveillance Report Gonorrhoea; Annual Epidemiological Report for 2019
- ⁸ ECDC Surveillance Report Syphilis; Annual Epidemiological Report for 2019
- ⁹ ECDC Factsheet Chlamydia, <https://www.ecdc.europa.eu/en/chlamydia/facts;> retrieved on March 30 2023xx
- ¹⁰ Jansen K, Steffen G, Potthoff A, Schuppe AK, Beer D, Jessen H, Scholten S, Spornraft-Ragaller P, Bremer V, Tiemann C; MSM Screening Study group. STI in times of PrEP: high prevalence of chlamydia, gonorrhea, and mycoplasma at different anatomic sites in men who have sex with men in Germany. *BMC Infect Dis.* 2020 Feb 7;20(1):110. doi: 10.1186/s12879-020-4831-4. PMID: 32033533; PMCID: PMC7007644.
- ¹¹ Meyer T, Eberle J, Roß RS, Schüttler CG, Baier M, Buder S, Kohl PK, Münstermann D, Hagedorn HJ, Nick S, Jansen K, Bremer V, Mau M, Brockmeyer NH. Schnelltestdiagnostik sexuell übertragbarer Infektionen: Gemeinsame Stellungnahme von DSTIG, RKI, PEI sowie den Referenzzentren für HIV, HBV und HCV und Konsiliarlaboren für Chlamydien, Gonokokken und Treponema pallidum [Rapid diagnosis of sexually transmitted infections: Joint statement of DSTIG, RKI, and PEI, as well as the reference centers for HIV, HBV, and HCV and consulting laboratories for Chlamydia, gonococci, and Treponema pallidum]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz.* 2020 Oct;63(10):1271-1286. German. doi: 10.1007/s00103-020-03218-4. PMID: 32930821.
- ¹² Korenromp EL, Rowley J, Alonso M, Mello MB, Wijesooriya NS, Mahiané SG, Ishikawa N, Le LV, Newman-Owiredu M, Nagelkerke N, Newman L, Kamb M, Broutet N, Taylor MM. Global burden of maternal and congenital syphilis and associated adverse birth outcomes-Estimates for 2016 and progress since 2012. *PLoS One.* 2019 Feb 27;14(2):e0211720. doi: 10.1371/journal.pone.0211720. Erratum in: *PLoS One.* 2019 Jul 5;14(7):e0219613. PMID: 30811406; PMCID: PMC6392238.
- ¹³ <https://www.cdc.gov/reproductivehealth/index.html;> retrieved on March 30, 2023
- ¹⁴ Tuddenham S, Hamill MM, Ghanem KG. Diagnosis and Treatment of Sexually Transmitted Infections: A Review. *JAMA.* 2022 Jan 11;327(2):161-172. doi: 10.1001/jama.2021.23487. PMID: 35015033.
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- ¹⁶ <https://www.aad.org/dw/monthly/2023/january/feature-talking-to-patients-about-stis;> retrieved on March 30, 2023



Rapid and reliable results at the point of care

What is Vivalytic?

Vivalytic is a powerful, fully automated universal platform for molecular diagnostics utilizing PCR (NAAT) to test for pathogens with applications available for different medical disciplines with only few steps from sample to result. After collection of the patient sample, the sample is processed automatically within the Vivalytic *one* Analyser and thereafter the test result is shown on the display of the Vivalytic *one* Analyser. Time to result varies depending on the Vivalytic application: The Vivalytic STI test is a qualitative PCR-based assay for simultaneous detection of 10 common sexually transmitted pathogens with a time to result of 2.5 hours. The Vivalytic MG, MH, UP/UU test to test for mycoplasmas and/or ureaplasmas has a time to result of about one hour.

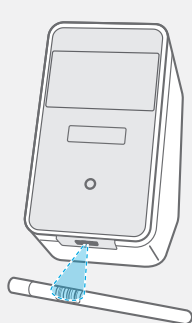
Fully automated analysis with Vivalytic at the point of care can save hospitals, labs and doctor's offices valuable time in their routine processes.

Vivalytic at a glance

- ▶ The Vivalytic system enables fully automated sample analysis with only a few manual steps.
- ▶ It requires no costly and complex laboratory equipment.
- ▶ With Vivalytic, single, low, and multiplex tests are possible.
- ▶ No peripheral equipment, such as laptop, keyboard, barcode scanner, or charging station is required for the Vivalytic *one* Analyser.
- ▶ The cartridge can be used hygienically and safely as a closed system.
- ▶ The cartridges can be used and stored at room temperature.
- ▶ The Vivasuite cloud-based solution ensures convenient device management.
- ▶ The Vivalytic *one* Analyser can be easily integrated into existing IT structures (via HL7, Ethernet, USB, WLAN).

Vivalytic STI	Vivalytic MG, MH, UP, UU
<ul style="list-style-type: none"> ▶ <i>Chlamydia trachomatis</i> ▶ <i>Neisseria gonorrhoeae</i> ▶ <i>Trichomonas vaginalis</i> ▶ <i>Mycoplasma genitalium</i> ▶ <i>Treponema pallidum</i> ▶ <i>Mycoplasma hominis</i> ▶ <i>Ureaplasma urealyticum</i> ▶ <i>Haemophilus ducreyi</i> ▶ Herpes simplex virus I ▶ Herpes simplex virus II 	<ul style="list-style-type: none"> ▶ <i>Mycoplasma genitalium</i> ▶ <i>Mycoplasma hominis</i> ▶ <i>Ureaplasma parvum/Ureaplasma urealyticum</i>

Only a few steps from sample to result



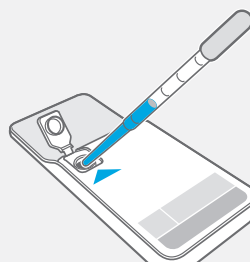
01

Scan sample code.



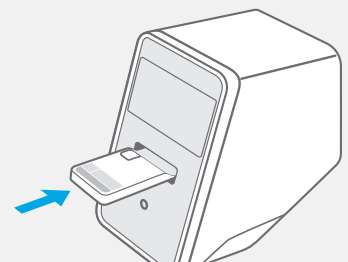
02

Scan cartridge code.



03

Insert the sample and close cartridge lid.



04

Insert cartridge. The test starts automatically

Click here to learn more about the current
Vivalytic test portfolio



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